Clinical trial results:
A PHASE 3, RANDOMIZED, DOUBLE-BLIND TRIAL TO EVALUATE THE SAFETY AND IMMUNOGENICITY OF A 20-VALENT PNEUMOCOCCAL CONJUGATE VACCINE GIVEN AS A SERIES OF 2 INFANT DOSES AND 1 TODDLER DOSE IN HEALTHY INFANTS

Summary

EudraCT number	2019-003306-27
Trial protocol	NO CZ EE FI PL SK DK BE NL IT
Global end of trial date	18 February 2023

Results information

Result version number	v1 (current)
This version publication date	01 September 2023
First version publication date	01 September 2023

Trial information

Trial identification

Sponsor protocol code	B7471012

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04546425
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer Inc., Pfizer ClinicalTrials.gov Call Center, 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 18007181021, ClinicalTrials.gov_Inquiries@pfizer.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002330-PIP01-18
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	20 March 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 February 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Safety: To describe the safety profile of 20vPnC. Safety assessments included local reactions, systemic events and adverse events. Primary immunogenicity objectives for primary study population: Noninferiority (NI) of 20vPnC to 13vPnC based on IgG GMCs at 1 month after Dose 2 and 1 month after Dose 3; Percentage of subjects with predefined IgG concentrations 1 month after Dose 2; NI of percentage of subjects with prespecified antibody levels to specific concomitant vaccine antigens 1 month after Dose 3. Primary immunogenicity objectives for Russian Cohort: to describe IgG responses induced by 20vPnC (Percentages of participants with predefined IgG concentrations at 1 month after Dose 2; IgG GMCs at 1 month after Dose 2 and 1 month after Dose 3)

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 Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 September 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 2
Country: Number of subjects enrolled	Belgium: 15
Country: Number of subjects enrolled	Czechia: 72
Country: Number of subjects enrolled	Denmark: 3
Country: Number of subjects enrolled	Estonia: 78
Country: Number of subjects enrolled	Finland: 354
Country: Number of subjects enrolled	Italy: 72
Country: Number of subjects enrolled	Netherlands: 14
Country: Number of subjects enrolled	Norway: 14
Country: Number of subjects enrolled	Poland: 546
Country: Number of subjects enrolled	Slovakia: 34
Country: Number of subjects enrolled	Russian Federation: 51
Worldwide total number of subjects	1255
EEA total number of subjects	1202

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)	1255
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: -

Pre-assignment

Screening details:

For primary study population,1207 participants were enrolled & assigned to receive 3 doses of 20-valent pneumococcal conjugate vaccine (20vPnC) or 13vPnC of which 3 participants were not vaccinated, 1204 were vaccinated with 20vPnC or 13vPnC.Additional 51 Russian subjects were enrolled, all of which were vaccinated with 20vPnC or 13vPnC.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	20vPnC: Primary Study Population

Arm description:

Infants 42 to 112 days of age were enrolled to receive 3 doses of 0.5 mL 20vPnC intramuscularly. Dose 1 was given at enrollment and Dose 2 was given 42 to 63 days later. Dose 3 was administered at 335 to 386 days of age.

Arm type	Experimental
Investigational medicinal product name	20-Valent Pneumococcal Conjugate Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 0.5 mL dose of 20vPnC intramuscularly on Visits 1, 2, and 4 with Dose 1, 2, 3 respectively.

Arm title	13vPnC: Primary Study Population

Arm description:

Infants 42 to 112 days of age were enrolled to receive 3 doses of 0.5 mL 13vPnC intramuscularly. Dose 1 was given at enrollment and Dose 2 was given 42 to 63 days later. Dose 3 was administered at 335 to 386 days of age.

Arm type	Active comparator
Investigational medicinal product name	13-Valent Pneumococcal Conjugate Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 0.5 mL dose of 13vPnC intramuscularly on Visits 1, 2, and 4 with Dose 1, 2, 3 respectively.

Arm title	20vPnC: Russian Cohort

Arm description:

Infants 42 to 70 days of age were enrolled to receive 3 doses of 0.5 mL 20vPnC intramuscularly. Dose 1 was given at enrollment and Dose 2 was given 60 to 90 days later. Dose 3 was administered at 335 to 455 days of age.

Arm type	Experimental
Investigational medicinal product name	20-Valent Pneumococcal Conjugate Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 0.5 mL dose of 20vPnC intramuscularly on Visits 1, 2, and 4 with Dose 1, 2, 3 respectively.

Arm title	13vPnC: Russian Cohort

Arm description:

Infants 42 to 70 days of age were enrolled to receive 3 doses of 0.5 mL 13vPnC intramuscularly. Dose 1 was given at enrollment and Dose 2 was given 60 to 90 days later. Dose 3 was administered at 335 to 455 days of age.

Arm type	Active comparator
Investigational medicinal product name	13-Valent Pneumococcal Conjugate Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 0.5 mL dose of 13vPnC intramuscularly on Visits 1, 2, and 4 with Dose 1, 2, 3 respectively.

Number of subjects in period 1	20vPnC: Primary Study Population	13vPnC: Primary Study Population	20vPnC: Russian Cohort
Started	601	603	24
Dose 1	601	603	24
Dose 2	593	598	24
Dose 3	588	594	22
Completed	583	590	22
Not completed	18	13	2
Adverse event, non-fatal	3	-	-
Lost to follow-up	5	4	-
Withdrawal by parent/guardian	6	5	1
Protocol deviation	1	1	-
No Longer met eligibility criteria	3	3	1

Number of subjects in period 1	13vPnC: Russian Cohort
Started	27
Dose 1	27
Dose 2	27
Dose 3	25
Completed	25
Not completed	2

Adverse event, non-fatal	-
Lost to follow-up	-
Withdrawal by parent/guardian	1
Protocol deviation	-
No Longer met eligibility criteria	1

Baseline characteristics

Reporting groups	
Reporting group title	20vPnC: Primary Study Population
Reporting group description:	
Infants 42 to 112 days of age were enrolled to receive 3 doses of 0.5 mL 20vPnC intramuscularly. Dose 1 was given at enrollment and Dose 2 was given 42 to 63 days later. Dose 3 was administered at 335 to 386 days of age.	
Reporting group title	13vPnC: Primary Study Population
Reporting group description:	
Infants 42 to 112 days of age were enrolled to receive 3 doses of 0.5 mL 13vPnC intramuscularly. Dose 1 was given at enrollment and Dose 2 was given 42 to 63 days later. Dose 3 was administered at 335 to 386 days of age.	
Reporting group title	20vPnC: Russian Cohort
Reporting group description:	
Infants 42 to 70 days of age were enrolled to receive 3 doses of 0.5 mL 20vPnC intramuscularly. Dose 1 was given at enrollment and Dose 2 was given 60 to 90 days later. Dose 3 was administered at 335 to 455 days of age.	
Reporting group title	13vPnC: Russian Cohort
Reporting group description:	
Infants 42 to 70 days of age were enrolled to receive 3 doses of 0.5 mL 13vPnC intramuscularly. Dose 1 was given at enrollment and Dose 2 was given 60 to 90 days later. Dose 3 was administered at 335 to 455 days of age.	

Reporting group values	20vPnC: Primary Study Population	13vPnC: Primary Study Population	20vPnC: Russian Cohort
Number of subjects	601	603	24
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	601	603	24
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: Days			
arithmetic mean	69.2	69.7	64.2
standard deviation	± 17.76	± 18.32	± 6.98
Sex: Female, Male Units: Subjects			
Female	302	292	16
Male	299	311	8
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	8	5	0

Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	1	0
White	585	592	24
More than one race	1	0	0
Unknown or Not Reported	7	5	0
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	4	1	0
Not Hispanic or Latino	577	586	22
Unknown or Not Reported	20	16	2

Reporting group values	13vPnC: Russian Cohort	Total	
Number of subjects	27	1255	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	27	1255	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous			
Units: Days			
arithmetic mean	63.3		
standard deviation	± 6.21	-	
Sex: Female, Male			
Units: Subjects			
Female	12	622	
Male	15	633	
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	1	14	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	1	
White	26	1227	
More than one race	0	1	
Unknown or Not Reported	0	12	
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	0	5	
Not Hispanic or Latino	25	1210	
Unknown or Not Reported	2	40	

End points

End points reporting groups

Reporting group title	20vPnC: Primary Study Population
Reporting group description:	
Infants 42 to 112 days of age were enrolled to receive 3 doses of 0.5 mL 20vPnC intramuscularly. Dose 1 was given at enrollment and Dose 2 was given 42 to 63 days later. Dose 3 was administered at 335 to 386 days of age.	
Reporting group title	13vPnC: Primary Study Population
Reporting group description:	
Infants 42 to 112 days of age were enrolled to receive 3 doses of 0.5 mL 13vPnC intramuscularly. Dose 1 was given at enrollment and Dose 2 was given 42 to 63 days later. Dose 3 was administered at 335 to 386 days of age.	
Reporting group title	20vPnC: Russian Cohort
Reporting group description:	
Infants 42 to 70 days of age were enrolled to receive 3 doses of 0.5 mL 20vPnC intramuscularly. Dose 1 was given at enrollment and Dose 2 was given 60 to 90 days later. Dose 3 was administered at 335 to 455 days of age.	
Reporting group title	13vPnC: Russian Cohort
Reporting group description:	
Infants 42 to 70 days of age were enrolled to receive 3 doses of 0.5 mL 13vPnC intramuscularly. Dose 1 was given at enrollment and Dose 2 was given 60 to 90 days later. Dose 3 was administered at 335 to 455 days of age.	

Primary: Percentage of Subjects With Local Reactions Within 7 Days After Dose 1: Primary Study Population

End point title	Percentage of Subjects With Local Reactions Within 7 Days After Dose 1: Primary Study Population[1][2]
End point description:	
Local reactions included redness, swelling and, pain at the injection site, recorded by parent's/legal guardians of subjects in an electronic diary (e-diary). Redness and swelling were measured and recorded in measuring device units. 1 measuring device unit =0.5 centimeter (cm). Redness and swelling were graded as mild (greater than [>] 0 to 2.0 cm), moderate (> 2.0 to 7.0 cm) and severe (>7.0 cm). Pain at injection site was graded as mild (hurt if gently touched example, whimpered, winced, protested, or withdrew), moderate (hurt if gently touched, with crying), and severe (caused limitation of limb movement). 95 percent (%) confidence interval (CI) was based on Clopper and Pearson method.Safety analysis set included all subjects who received at least 1 dose of 20vPnC or 13vPnC and had safety data assessed after any dose. Here, "Number of subjects Analyzed" signifies the number of subjects with any e-diary data after Dose 1.	
End point type	Primary
End point timeframe:	
Within 7 days after Dose 1	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This endpoint was planned to be analysed only for the specified reporting arms

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only descriptive analysis was planned for this endpoint

End point values	20vPnC: Primary Study Population	13vPnC: Primary Study Population		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	598	603		
Units: Percentage of subjects				
number (confidence interval 95%)				
Redness: Mild	20.7 (17.6 to 24.2)	22.7 (19.4 to 26.3)		
Redness: Moderate	4.5 (3.0 to 6.5)	4.8 (3.2 to 6.8)		
Redness: Severe	0 (0.0 to 0.6)	0 (0.0 to 0.6)		
Swelling: Mild	12.7 (10.1 to 15.6)	12.9 (10.4 to 15.9)		
Swelling: Moderate	8.7 (6.6 to 11.2)	7.3 (5.4 to 9.7)		
Swelling: Severe	0 (0.0 to 0.6)	0 (0.0 to 0.6)		
Pain at Injection Site: Mild	16.7 (13.8 to 20.0)	17.9 (14.9 to 21.2)		
Pain at Injection Site: Moderate	12.0 (9.5 to 14.9)	11.4 (9.0 to 14.3)		
Pain at Injection Site: Severe	0.3 (0.0 to 1.2)	0 (0.0 to 0.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Local Reactions Within 7 Days After Dose 2: Primary Study Population

End point title	Percentage of Subjects With Local Reactions Within 7 Days After Dose 2: Primary Study Population[3][4]

End point description:

Local reactions included redness, swelling and, pain at the injection site, recorded by parent's/legal guardians of subjects in an e-diary. Redness and swelling were measured and recorded in measuring device units. 1 measuring device unit =0.5 cm. Redness and swelling were graded as mild (>0 to 2.0 cm), moderate (> 2.0 to 7.0 cm) and severe (>7.0 cm). Pain at injection site was graded as mild (hurt if gently touched example, whimpered, winced, protested, or withdrew), moderate (hurt if gently touched, with crying), and severe (caused limitation of limb movement). 95% CI was based on Clopper and Pearson method. Safety analysis set included all subjects who received at least 1 dose of 20vPnC or 13vPnC and had safety data assessed after any dose. Here, "Number of Subjects Analyzed" signifies the number of subjects with any e-diary data after Dose 2.

End point type	Primary

End point timeframe:

Within 7 days after Dose 2

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This endpoint was planned to be analysed only for the specified reporting arms

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only descriptive analysis was planned for this endpoint

End point values	20vPnC: Primary Study Population	13vPnC: Primary Study Population		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	592	594		
Units: Percentage of subjects				
number (confidence interval 95%)				
Redness: Mild	24.8 (21.4 to 28.5)	22.9 (19.6 to 26.5)		
Redness: Moderate	3.7 (2.3 to 5.6)	5.1 (3.4 to 7.1)		
Redness: Severe	0 (0.0 to 0.6)	0.2 (0.0 to 0.9)		
Swelling: Mild	13.7 (11.0 to 16.7)	14.1 (11.4 to 17.2)		
Swelling: Moderate	8.3 (6.2 to 10.8)	6.2 (4.4 to 8.5)		
Swelling: Severe	0 (0.0 to 0.6)	0.2 (0.0 to 0.9)		
Pain at Injection Site: Mild	13.3 (10.7 to 16.4)	16.5 (13.6 to 19.7)		
Pain at Injection Site: Moderate	9.3 (7.1 to 11.9)	7.9 (5.9 to 10.4)		
Pain at Injection Site: Severe	0.2 (0.0 to 0.9)	0.2 (0.0 to 0.9)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Local Reactions Within 7 Days After Dose 3: Primary Study Population

End point title	Percentage of Subjects With Local Reactions Within 7 Days After Dose 3: Primary Study Population[5][6]

End point description:

Local reactions included redness, swelling and, pain at the injection site, recorded by parent's/legal guardians of subjects in an e-diary. Redness and swelling were measured and recorded in measuring device units. 1 measuring device unit =0.5 cm. Redness and swelling were graded as mild (>0 to 2.0 cm), moderate (> 2.0 to 7.0 cm) and severe (>7.0 cm). Pain at injection site was graded as mild (hurt if gently touched example, whimpered, winced, protested, or withdrew), moderate (hurt if gently touched, with crying), and severe (caused limitation of limb movement). 95% CI was based on Clopper and Pearson method.Safety analysis set included all subjects who received at least 1 dose of 20vPnC or 13vPnC and had safety data assessed after any dose. Here, "Number of Subjects Analyzed" signifies the number of subjects with any e-diary data after Dose 3.

End point type	Primary

End point timeframe:

Within 7 days after Dose 3

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This endpoint was planned to be analysed only for the specified reporting arms

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only descriptive analysis was planned for this endpoint

End point values	20vPnC: Primary Study Population	13vPnC: Primary Study Population		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	580	586		
Units: Percentage of subjects				
number (confidence interval 95%)				
Redness: Mild	23.3 (19.9 to 26.9)	25.1 (21.6 to 28.8)		
Redness: Moderate	13.4 (10.8 to 16.5)	8.5 (6.4 to 11.1)		
Redness: Severe	0.2 (0.0 to 1.0)	0.2 (0.0 to 0.9)		
Swelling: Mild	17.8 (14.7 to 21.1)	14.5 (11.8 to 17.6)		
Swelling: Moderate	11.9 (9.4 to 14.8)	9.7 (7.5 to 12.4)		
Swelling: Severe	0.2 (0.0 to 1.0)	0.3 (0.0 to 1.2)		
Pain at Injection Site: Mild	24.7 (21.2 to 28.4)	22.4 (19.0 to 25.9)		
Pain at Injection Site: Moderate	17.4 (14.4 to 20.8)	17.2 (14.3 to 20.5)		
Pain at Injection Site: Severe	0.3 (0.0 to 1.2)	0.3 (0.0 to 1.2)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Systemic Events Within 7 Days After Dose 1: Primary Study Population

End point title	Percentage of Subjects With Systemic Events Within 7 Days After Dose 1: Primary Study Population[7][8]

End point description:

Systemic events:fever,decreased appetite,drowsiness/increased sleep & irritability, recorded by parents/legal guardians of subjects using e-diary. Fever: temperature >=38.0 degree C & categorized as >=38.0 to 38.4 degree C,>38.4 to 38.9 degree C,>38.9 to 40.0 degree C & >40.0-degree C.Decreased appetite: mild (decreased interest in eating), moderate (decreased oral intake) & severe (refusal to feed).Drowsiness was graded as mild (increased/prolonged sleeping bouts), moderate (slightly subdued, interfered with daily activity) & severe (disabling, not interested in usual daily activity).Irritability: mild (easily consolable), moderate (required increased attention) & severe (inconsolable, crying could not be comforted). 95% CI was based on Clopper & Pearson method. Safety analysis set: all subjects who received at least 1 dose of 20vPnC or 13vPnC & had safety data assessed after any dose. Here,"Number of Subjects Analyzed":number of subjects with any e-diary data after Dose1

End point type	Primary

End point timeframe:

Within 7 Days after Dose 1

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This endpoint was planned to be analysed only for the specified reporting arms.

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only descriptive analysis was planned for this endpoint

End point values	20vPnC: Primary Study Population	13vPnC: Primary Study Population		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	598	603		
Units: Percentage of subjects				
number (confidence interval 95%)				
Fever: >=38.0 degrees C to 38.4 degrees C	7.5 (5.5 to 9.9)	6.8 (4.9 to 9.1)		
Fever: >38.4 degrees C to 38.9 degrees C	1.3 (0.6 to 2.6)	1.3 (0.6 to 2.6)		
Fever: >38.9 degrees C to 40.0 degrees C	0 (0.0 to 0.6)	0.3 (0.0 to 1.2)		
Fever: >40.0 degrees C	0 (0.0 to 0.6)	0 (0.0 to 0.6)		
Decreased appetite: Mild	16.2 (13.4 to 19.4)	13.3 (10.7 to 16.2)		
Decreased appetite: Moderate	7.5 (5.5 to 9.9)	8.8 (6.7 to 11.3)		
Decreased appetite: Severe	1.0 (0.4 to 2.2)	0.5 (0.1 to 1.4)		
Drowsiness: Mild	46.0 (41.9 to 50.1)	48.6 (44.5 to 52.7)		
Drowsiness: Moderate	14.4 (11.7 to 17.5)	14.3 (11.6 to 17.3)		
Drowsiness: Severe	0.8 (0.3 to 1.9)	0.8 (0.3 to 1.9)		
Irritability: Mild	17.6 (14.6 to 20.8)	17.4 (14.5 to 20.7)		
Irritability: Moderate	46.2 (42.1 to 50.2)	46.4 (42.4 to 50.5)		
Irritability: Severe	8.2 (6.1 to 10.7)	8.6 (6.5 to 11.2)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Systemic Events Within 7 Days After Dose 2: Primary Study Population

End point title	Percentage of Subjects With Systemic Events Within 7 Days After Dose 2: Primary Study Population[9][10]

End point description:

Systemic events:fever,decreased appetite,drowsiness/increased sleep & irritability, recorded by parents/legal guardians of subject's using e-diary. Fever: temperature >=38.0 degree C & categorized as >=38.0 to 38.4 degree C,>38.4 to 38.9 degree C,>38.9 to 40.0 degree C & >40.0-degree C. Decreased appetite: mild (decreased interest in eating), moderate (decreased oral intake) & severe (refusal to feed).Drowsiness was graded as mild (increased/prolonged sleeping bouts), moderate (slightly subdued, interfered with daily activity) & severe (disabling, not interested in usual daily activity).Irritability: mild (easily consolable), moderate (required increased attention) & severe (inconsolable, crying could not be comforted). 95% CI was based on Clopper & Pearson method. Safety analysis set: all subjects who received at least 1 dose of 20vPnC or 13vPnC & had safety data assessed after any dose. Here,"Number of Subjects Analyzed": number of subjects with any e-diary data after Dose2

End point type	Primary

End point timeframe:

Within 7 Days after Dose 2

Notes:

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

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms

End point values	20vPnC: Primary Study Population	13vPnC: Primary Study Population		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	592	594		
Units: Percentage of subjects				
number (confidence interval 95%)				
Fever: >=38.0 degrees C to 38.4 degrees C	11.7 (9.2 to 14.5)	11.6 (9.2 to 14.5)		
Fever: >38.4 degrees C to 38.9 degrees C	2.5 (1.4 to 4.1)	2.0 (1.0 to 3.5)		
Fever: >38.9 degrees C to 40.0 degrees C	0.7 (0.2 to 1.7)	0.3 (0.0 to 1.2)		
Fever: >40.0 degrees C	0 (0.0 to 0.6)	0 (0.0 to 0.6)		
Decreased appetite: Mild	13.5 (10.9 to 16.5)	12.1 (9.6 to 15.0)		
Decreased appetite: Moderate	10.1 (7.8 to 12.9)	6.4 (4.6 to 8.7)		
Decreased appetite: Severe	1.0 (0.4 to 2.2)	0.8 (0.3 to 2.0)		
Drowsiness: Mild	37.8 (33.9 to 41.9)	37.0 (33.1 to 41.1)		
Drowsiness: Moderate	13.2 (10.6 to 16.2)	13.5 (10.8 to 16.5)		
Drowsiness: Severe	0.3 (0.0 to 1.2)	0.2 (0.0 to 0.9)		
Irritability: Mild	22.8 (19.5 to 26.4)	21.2 (18.0 to 24.7)		
Irritability: Moderate	43.1 (39.0 to 47.2)	40.6 (36.6 to 44.6)		
Irritability: Severe	5.7 (4.0 to 7.9)	6.6 (4.7 to 8.9)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Systemic Events Within 7 Days After Dose 3: Primary Study Population

End point title	Percentage of Subjects With Systemic Events Within 7 Days After Dose 3: Primary Study Population[11][12]

End point description:

Systemic events:fever,decreased appetite,drowsiness/increased sleep & irritability, recorded by parents/legal guardians of subject's using e-diary. Fever: temperature >=38.0 degree C & categorized as >=38.0 to 38.4 degree C,>38.4 to 38.9 degree C,>38.9 to 40.0 degree C & >40.0-degree C. Decreased appetite: mild (decreased interest in eating), moderate (decreased oral intake) & severe (refusal to feed).Drowsiness was graded as mild (increased/prolonged sleeping bouts), moderate (slightly subdued, interfered with daily activity) & severe (disabling, not interested in usual daily activity).Irritability: mild (easily consolable), moderate (required increased attention) & severe (inconsolable, crying could not be comforted). 95% CI was based on Clopper & Pearson method. Safety analysis set: all subjects who received at least 1 dose of 20vPnC or 13vPnC & had safety data assessed

after any dose. Here,"Number of Subjects Analyzed": number of subjects with any e-diary data after Dose 3.

End point type	Primary

End point timeframe:

Within 7 Days after Dose 3

Notes:

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

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms

End point values	20vPnC: Primary Study Population	13vPnC: Primary Study Population		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	580	586		
Units: Percentage of subjects				
number (confidence interval 95%)				
Fever: >=38.0 degrees C to 38.4 degrees C	13.4 (10.8 to 16.5)	13.5 (10.8 to 16.5)		
Fever: >38.4 degrees C to 38.9 degrees C	6.9 (5.0 to 9.3)	7.0 (5.1 to 9.4)		
Fever: >38.9 degrees C to 40.0 degrees C	3.6 (2.3 to 5.5)	3.2 (2.0 to 5.0)		
Fever: >40.0 degrees C	0.3 (0.0 to 1.2)	0 (0.0 to 0.6)		
Decreased appetite: Mild	20.0 (16.8 to 23.5)	15.5 (12.7 to 18.7)		
Decreased appetite: Moderate	17.1 (14.1 to 20.4)	18.9 (15.8 to 22.4)		
Decreased appetite: Severe	2.2 (1.2 to 3.8)	2.0 (1.1 to 3.5)		
Drowsiness: Mild	34.8 (30.9 to 38.9)	32.8 (29.0 to 36.7)		
Drowsiness: Moderate	15.3 (12.5 to 18.5)	14.7 (11.9 to 17.8)		
Drowsiness: Severe	0.7 (0.2 to 1.8)	1.2 (0.5 to 2.4)		
Irritability: Mild	23.4 (20.1 to 27.1)	21.3 (18.1 to 24.9)		
Irritability: Moderate	43.4 (39.4 to 47.6)	45.4 (41.3 to 49.5)		
Irritability: Severe	4.1 (2.7 to 6.1)	4.1 (2.6 to 6.0)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Serious Adverse Events (SAEs) From Dose 1 to 1 Month After Dose 3: Primary Study Population

End point title	Percentage of Subjects With Serious Adverse Events (SAEs) From Dose 1 to 1 Month After Dose 3: Primary Study Population[13][14]

End point description:

An SAE was any untoward medical occurrence that occurred, at any dose: resulted in death; required

inpatient hospitalization or prolongation of existing hospitalization; was life-threatening; resulted in persistent or significant disability/ incapacity; was a congenital anomaly/birth defect and other important medical events. 95% CI was based on the Clopper and Pearson method. Safety analysis set included all subjects who received at least 1 dose of 20vPnC or 13vPnC and had safety data assessed after any dose.

End point type	Primary

End point timeframe:

From Dose 1 to 1 month after Dose 3

Notes:

[13] - 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 analysis was planned for this endpoint

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms

End point values	20vPnC: Primary Study Population	13vPnC: Primary Study Population		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	601	603		
Units: Percentage of subjects				
number (confidence interval 95%)	5.7 (3.9 to 7.8)	6.6 (4.8 to 8.9)		

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Subjects With Adverse Events (AEs) From Dose 3 to 1 Month After Dose 3: Primary Study Population[15][16]

End point description:

An AE was any untoward medical occurrence in a subject, temporally associated with the use of study treatment, whether or not considered related to the study treatment. 95% CI was based on the Clopper and Pearson method. AEs reported in this outcome measure excluded local reactions and systemic events collected from e-diary. Safety analysis set included all subjects who received at least 1 dose of 20vPnC or 13vPnC and had safety data assessed after any dose. Here, "Number of Subjects Analyzed" signifies the number of subjects who received Dose 3.

End point type	Primary

End point timeframe:

From Dose 3 to 1 month after Dose 3

Notes:

[15] - 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 analysis was planned for this endpoint

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms

End point values	20vPnC: Primary Study Population	13vPnC: Primary Study Population		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	588	594		
Units: Percentage of subjects				
number (confidence interval 95%)	15.5 (12.6 to 18.7)	16.5 (13.6 to 19.7)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Adverse Events (AEs) From Dose 1 to 1 Month After Dose 2: Primary Study Population

End point title	Percentage of Subjects With Adverse Events (AEs) From Dose 1 to 1 Month After Dose 2: Primary Study Population[17][18]

End point description:

An AE was any untoward medical occurrence in a subject, temporally associated with the use of study treatment, whether or not considered related to the study treatment. 95% CI was based on the Clopper and Pearson method. AEs reported in this outcome measure excluded local reactions and systemic events collected from e-diary. Safety analysis set included all subjects who received at least 1 dose of 20vPnC or 13vPnC and had safety data assessed after any dose.

End point type	Primary

End point timeframe:

From Dose 1 to 1 month after Dose 2

Notes:

[17] - 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 analysis was planned for this endpoint

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms

End point values	20vPnC: Primary Study Population	13vPnC: Primary Study Population		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	601	603		
Units: Percentage of subjects				
number (confidence interval 95%)	13.8 (11.2 to 16.8)	14.4 (11.7 to 17.5)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Newly Diagnosed Chronic Medical Condition (NDCMC) From Dose 1 to 1 Month After Dose 3: Primary Study Population

End point title	Percentage of Subjects With Newly Diagnosed Chronic Medical Condition (NDCMC) From Dose 1 to 1 Month After Dose 3:

	Primary Study Population[19][20]

End point description:

An NDCMC was defined as a disease or medical condition, not previously identified, that was expected to be persistent or was otherwise long-lasting in its effects. 95% CI was based on the Clopper and Pearson method. Safety analysis set included all subjects who received at least 1 dose of 20vPnC or 13vPnC and had safety data assessed after any dose.

End point type	Primary

End point timeframe:

From Dose 1 to 1 month after Dose 3

Notes:

[19] - 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: This endpoint was planned to be analysed only for the specified reporting arms

[20] - 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: Only descriptive analysis was planned for this endpoint

End point values	20vPnC: Primary Study Population	13vPnC: Primary Study Population		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	601	603		
Units: Percentage of subjects				
number (confidence interval 95%)	1.0 (0.4 to 2.2)	1.0 (0.4 to 2.2)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Predefined Pneumococcal Immunoglobulin G (IgG) Antibody 1 Month After Dose 2: Primary Study Population

End point title	Percentage of Subjects With Predefined Pneumococcal Immunoglobulin G (IgG) Antibody 1 Month After Dose 2: Primary Study Population[21]

End point description:

Predefined IgG concentrations were as follows: for serotype 1, 3, 4, 6A, 7F, 9V, 14, 18C, 19F, 23F, 8, 10A, 11A, 12F, 15B, 22F, 33F: >=0.35 microgram per mL (mcg/mL), for serotype 5: >=0.23 mcg/mL, for serotype 6B. >=0.10 mcg/mL and for serotype 19A: >=0.12 mcg/mL. 95% CI was based on the Clopper and Pearson method. Dose 2 evaluable immunogenicity population: eligible subjects 42-112 days of age at first vaccination, received first 2 doses as randomized, at least 1 valid immunogenicity results from blood collection (27 to 56 days after Dose 2),no other major protocol deviations. "Number of Subjects Analyzed"= subjects in Dose 2 evaluable immunogenicity population, "n"= subjects with valid IgG assay results for specified serotype.

End point type	Primary

End point timeframe:

1 month after Dose 2

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms

End point values	20vPnC: Primary Study Population	13vPnC: Primary Study Population		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	567	562		
Units: Percentage of subjects				
number (confidence interval 95%)				
Serotype 1, n=566, 562	70.7 (66.7 to 74.4)	84.2 (80.9 to 87.1)		
Serotype 3, n=566, 562	58.0 (53.8 to 62.1)	75.8 (72.0 to 79.3)		
Serotype 4, n=566, 562	68.6 (64.5 to 72.4)	79.5 (76.0 to 82.8)		
Serotype 5, n=566, 562	63.4 (59.3 to 67.4)	76.0 (72.2 to 79.5)		
Serotype 6A, n=566, 562	59.5 (55.4 to 63.6)	73.7 (69.8 to 77.3)		
Serotype 6B, n=564, 561	20.7 (17.5 to 24.3)	36.5 (32.5 to 40.7)		
Serotype 7F, n=566, 562	87.6 (84.6 to 90.2)	90.2 (87.5 to 92.5)		
Serotype 9V, n=566, 562	60.2 (56.1 to 64.3)	74.6 (70.7 to 78.1)		
Serotype 14, n=565, 562	78.6 (75.0 to 81.9)	81.9 (78.4 to 85.0)		
Serotype 18C, n=566, 562	71.0 (67.1 to 74.7)	76.5 (72.8 to 80.0)		
Serotype 19A, n=566, 562	92.2 (89.7 to 94.3)	94.0 (91.6 to 95.8)		
Serotype 19F, n=566, 562	94.3 (92.1 to 96.1)	95.7 (93.7 to 97.2)		
Serotype 23F, n=566, 562	23.5 (20.1 to 27.2)	41.8 (37.7 to 46.0)		
Serotype 8, n=567, 561	96.5 (94.6 to 97.8)	2.9 (1.6 to 4.6)		
Serotype 10A, n=567, 562	28.9 (25.2 to 32.8)	2.7 (1.5 to 4.4)		
Serotype 11A, n=567, 562	94.2 (91.9 to 96.0)	2.0 (1.0 to 3.5)		
Serotype 12F, n=567, 562	30.3 (26.6 to 34.3)	0.2 (0.0 to 1.0)		
Serotype 15B, n=566, 562	94.3 (92.1 to 96.1)	8.5 (6.4 to 11.2)		
Serotype 22F, n=567, 562	94.4 (92.1 to 96.1)	2.0 (1.0 to 3.5)		
Serotype 33F, n=566, 562	46.8 (42.6 to 51.0)	2.7 (1.5 to 4.4)		

Statistical analyses

Statistical analysis title	20vPnC Versus 13vPnC

Statistical analysis description:

Serotype 4: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.

Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population

Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent Difference
Point estimate	-11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16
upper limit	-5.9

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 3: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent Difference
Point estimate	-17.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.2
upper limit	-12.4

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 5: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent Difference
Point estimate	-12.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.8
upper limit	-7.2

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 1: 2-Sided 95% CIs are calculated using the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage.	
Comparison groups	13vPnC: Primary Study Population v 20vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent Difference
Point estimate	-13.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.3
upper limit	-8.7

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 7F: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent Difference
Point estimate	-2.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.3
upper limit	1.1

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 6A: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent Difference
Point estimate	-14.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.5
upper limit	-8.6

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 9V: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent Difference
Point estimate	-14.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.7
upper limit	-8.9

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 6B: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent Difference
Point estimate	-15.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21
upper limit	-10.6

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 19A: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population

Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent Difference
Point estimate	-1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8
upper limit	1.3

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 19F: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent Difference
Point estimate	-1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	1.2

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 23F: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent Difference
Point estimate	-18.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.6
upper limit	-12.9

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 8: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	59.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	55.6
upper limit	64.1

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 10A: 2-Sided 95% CI based on the Percent difference for the difference in proportions expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	-7.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.1
upper limit	-2.1

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 14: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent Difference
Point estimate	-3.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.9
upper limit	1.4

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 18C: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent Difference
Point estimate	-5.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.6
upper limit	-0.4

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 11A: 2-Sided 95% CI based on the Percent difference for the difference in proportions expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	57.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	53.1
upper limit	61.9

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 22F: 2-Sided 95% CI based on the Percent difference for the difference in proportions expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population

Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	57.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	53.3
upper limit	62.1

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 33F: 2-Sided 95% CI based on the Percent difference for the difference in proportions expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	10.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.5
upper limit	16

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 12F: 2-Sided 95% CI based on the Percent difference for the difference in proportions expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	-6.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.7
upper limit	-0.7

Statistical analysis title	20vPnC Versus 13vPnC

Statistical analysis description:

Serotype 15B: 2-Sided 95% CI based on the Percent difference for the difference in proportions expressed as a percentage.

Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	57.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	53.3
upper limit	62.1

Primary: Geometric Mean Concentration (GMC) of Serotype-specific Pneumococcal IgG Antibody 1 Month After Dose 2: Primary Study Population

End point title	Geometric Mean Concentration (GMC) of Serotype-specific Pneumococcal IgG Antibody 1 Month After Dose 2: Primary Study Population[22]

End point description:

Pneumococcal serotype-specific IgG concentration was measured for serum sample for 13vPnC serotype:1, 3, 4,5,6A,6B,7F,9V,14,18C,19A,19F,23F, 7 additional serotype:8, 10A, 11A, 12F, 15B, 22F, 33F.GMC & corresponding 2-sided 95% CIs were calculated by exponentiating mean logarithm of concentration, corresponding 2-sided 95% CIs (based on Student's t distribution).Assay result below LLOQ was set to 0.5×LLOQ.GMRs were reported in statistical analysis section & were calculated by exponentiating mean difference of logarithm of concentration & corresponding 2-sided 95% CIs (based on Student's t distribution).Dose 2 evaluable immunogenicity population:eligible subject 42-112 days of age at first vaccination,received 1st 2 doses as randomized,at least 1 valid immunogenicity result from blood collection (27-56 days after Dose2). "Number of Subject Analyzed"=subject in Dose 2 evaluable immunogenicity population, "n"= subject with valid IgG assay result for specified serotype.

End point type	Primary

End point timeframe:

1 month after Dose 2

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms

End point values	20vPnC: Primary Study Population	13vPnC: Primary Study Population		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	567	562		
Units: mcg/mL				
geometric mean (confidence interval 95%)				
Serotype 1, n=566, 562	0.57 (0.52 to 0.62)	0.93 (0.86 to 1.01)		
Serotype 3, n=566, 562	0.41 (0.38 to 0.45)	0.58 (0.54 to 0.63)		

Serotype 4, n=566, 562	0.55 (0.50 to 0.61)	0.92 (0.83 to 1.02)		
Serotype 5, n=566, 562	0.34 (0.30 to 0.38)	0.56 (0.50 to 0.62)		
Serotype 6A, n=566, 562	0.45 (0.40 to 0.52)	0.84 (0.73 to 0.95)		
Serotype 6B, n=564, 561	0.03 (0.03 to 0.04)	0.06 (0.05 to 0.07)		
Serotype 7F, n=566, 562	1.02 (0.94 to 1.10)	1.41 (1.30 to 1.53)		
Serotype 9V, n=566, 562	0.45 (0.40 to 0.51)	0.77 (0.68 to 0.87)		
Serotype 14, n=565, 562	1.05 (0.94 to 1.18)	1.28 (1.14 to 1.43)		
Serotype 18C, n=566, 562	0.69 (0.62 to 0.77)	0.87 (0.78 to 0.98)		
Serotype 19A, n=566, 562	0.67 (0.61 to 0.74)	1.13 (1.01 to 1.26)		
Serotype 19F, n=566, 562	2.21 (2.04 to 2.40)	3.06 (2.80 to 3.34)		
Serotype 23F, n=566, 562	0.13 (0.12 to 0.15)	0.25 (0.22 to 0.28)		
Serotype 8, n=567, 561	1.62 (1.51 to 1.74)	0.02 (0.02 to 0.02)		
Serotype 10A, n=567, 562	0.16 (0.14 to 0.18)	0.02 (0.02 to 0.02)		
Serotype 11A, n=567, 562	1.62 (1.50 to 1.75)	0.02 (0.02 to 0.02)		
Serotype 12F, n=567, 562	0.15 (0.13 to 0.17)	0.01 (0.01 to 0.01)		
Serotype 15B, n=566, 562	3.33 (3.00 to 3.70)	0.04 (0.04 to 0.04)		
Serotype 22F, n=567, 562	2.25 (2.06 to 2.45)	0.01 (0.01 to 0.01)		
Serotype 33F, n=566, 562	0.31 (0.28 to 0.34)	0.03 (0.02 to 0.03)		

Statistical analyses

Statistical analysis title	20vPnC Versus 13vPnC

Statistical analysis description:

Serotype 4: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student’s t distribution) for the mean difference of the logarithm of the concentrations.

Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.52
upper limit	0.69

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description: Serotype 3: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	0.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	0.79

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description: Serotype 1: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	0.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	0.69

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description: Serotype 9V: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population

Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	0.69

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 7F: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	0.8

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 6B: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	0.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	0.61

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 6A: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.45
upper limit	0.65

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 5: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.52
upper limit	0.7

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 12F: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	2.48

Confidence interval	
level	95 %
sides	2-sided
lower limit	2.08
upper limit	2.97

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 15B: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	54.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	46.35
upper limit	64.3

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 22F: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	36.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	31.57
upper limit	42.89

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 11A: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population

Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	26.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	22.95
upper limit	30.82

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 10A: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	2.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.25
upper limit	3.17

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 8: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	26.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	22.98
upper limit	30.67

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 23F: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.44
upper limit	0.62

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 19F: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	0.82

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 19A: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	0.59

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.51
upper limit	0.69

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 33F: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	5.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.27
upper limit	5.92

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 14: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	0.96

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 18C: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population

Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	0.92

Primary: GMC of Serotype-specific Pneumococcal IgG Antibody 1 Month After Dose 3: Primary Study Population

End point title	GMC of Serotype-specific Pneumococcal IgG Antibody 1 Month After Dose 3: Primary Study Population[23]

End point description:

Pneumococcal serotype-specific IgG concentrations were measured for serum samples for 13vPnC serotypes:1,3,4, 5,6A,6B,7F,9V,14,18C,19A,19F, 23F, 7additional serotype: 8, 10A, 11A, 12F, 15B, 22F,33F. GMC & corresponding 2-sided 95% CI were calculated by exponentiating mean logarithm of concentrations & corresponding 2-sided 95% CI (based on Student's t distribution).Assay result below LLOQ were set to 0.5×LLOQ.GMRs were reported in statistical analysis section & were calculated by exponentiating mean difference of logarithm of concentration & corresponding 2-sided 95% CI(based on Student's t distribution).Dose 3 evaluable immunogenicity population(EIP)=eligible subject 42-112 days of age at first vaccination,received all 3 dose as randomized with 335-386 day of age at Dose 3 atleast 1 valid immunogenicity results within 27-56 days after Dose 3,no major protocol deviation "Number of Subjects Analyzed"=subjects in Dose 3 EIP;"n"=subjects with valid IgG results for specified serotype.

End point type	Primary

End point timeframe:

1 month after Dose 3

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms

End point values	20vPnC: Primary Study Population	13vPnC: Primary Study Population		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	497	504		
Units: mcg/mL				
geometric mean (confidence interval 95%)				
Serotype 1, n=494, 502	1.71 (1.58 to 1.84)	2.53 (2.33 to 2.75)		
Serotype 3, n=494, 502	0.72 (0.67 to 0.78)	1.09 (1.01 to 1.17)		
Serotype 4, n=494, 502	4.11 (3.77 to 4.48)	5.36 (4.91 to 5.85)		
Serotype 5, n=494, 502	1.74 (1.60 to 1.89)	2.41 (2.21 to 2.64)		
Serotype 6A, n=494, 501	7.75 (7.04 to 8.53)	11.82 (10.66 to 13.11)		
Serotype 6B, n=494, 501	2.64 (2.36 to 2.95)	4.63 (4.09 to 5.25)		

Serotype 7F, n=494, 502	3.61 (3.40 to 3.84)	4.93 (4.63 to 5.24)		
Serotype 9V, n=494, 502	3.68 (3.42 to 3.97)	5.04 (4.67 to 5.43)		
Serotype 14, n=493, 501	4.52 (4.08 to 5.00)	5.66 (5.12 to 6.26)		
Serotype 18C, n=494, 502	2.71 (2.52 to 2.93)	3.61 (3.33 to 3.91)		
Serotype 19A, n=494, 502	4.51 (4.11 to 4.94)	5.49 (5.02 to 6.01)		
Serotype 19F, n=494, 502	6.19 (5.68 to 6.75)	8.08 (7.40 to 8.83)		
Serotype 23F, n=494, 502	2.64 (2.40 to 2.91)	4.40 (3.95 to 4.90)		
Serotype 8, n=495, 501	3.57 (3.32 to 3.83)	0.03 (0.03 to 0.03)		
Serotype 10A, n=495, 502	4.86 (4.41 to 5.36)	0.01 (0.01 to 0.01)		
Serotype 11A, n=495, 502	3.74 (3.44 to 4.07)	0.02 (0.01 to 0.02)		
Serotype 12F, n=495, 502	1.86 (1.71 to 2.01)	0.01 (0.01 to 0.01)		
Serotype 15B, n=495, 502	13.09 (12.10 to 14.15)	0.02 (0.02 to 0.03)		
Serotype 22F, n=495, 502	9.27 (8.52 to 10.08)	0.00 (0.00 to 0.00)		
Serotype 33F, n=495, 501	6.37 (5.83 to 6.95)	0.01 (0.01 to 0.01)		

Statistical analyses

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 3: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	0.73

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 1: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.	

Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	0.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	0.75

Statistical analysis title	20vPnC Versus 13vPnC

Statistical analysis description:

Serotype 4: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student’s t distribution) for the mean difference of the logarithm of the concentrations.

Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	0.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	0.87

Statistical analysis title	20vPnC Versus 13vPnC

Statistical analysis description:

Serotype 5: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student’s t distribution) for the mean difference of the logarithm of the concentrations.

Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	0.81

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 6A: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student’s t distribution) for the mean difference of the logarithm of the concentrations.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	0.75

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 6B: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student’s t distribution) for the mean difference of the logarithm of the concentrations.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	0.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.48
upper limit	0.67

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 7F: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student’s t distribution) for the mean difference of the logarithm of the concentrations.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population

Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	0.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	0.8

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 14: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	0.92

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 9V: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	0.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	0.81

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 18C: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	0.84

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 12F: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	0.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	0.87

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 11A: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	1.55

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.37
upper limit	1.75

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 19A: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	0.93

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 19F: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	0.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	0.87

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 23F: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population

Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.52
upper limit	0.69

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 8: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	1.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.32
upper limit	1.66

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 10A: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	2.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.77
upper limit	2.3

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 15B: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	5.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.82
upper limit	6.1

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 22F: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	3.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.4
upper limit	4.34

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 33F: 2-sided 95% CI was calculated by exponentiating the CI (based on the Student's t distribution) for the mean difference of the logarithm of the concentrations.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	2.64

Confidence interval	
level	95 %
sides	2-sided
lower limit	2.33
upper limit	2.99

Primary: Percentage of Subjects With Predefined Antibody Levels for Concomitant Vaccine Antigens 1 Month After Dose 3: Primary Study Population

End point title	Percentage of Subjects With Predefined Antibody Levels for Concomitant Vaccine Antigens 1 Month After Dose 3: Primary Study Population[24]

End point description:

Diphtheria & tetanus toxoids:concentration(conc) of antibody(AB)(in international units[IU]) to diphtheria & tetanus toxoid(prespecified level>=0.1 IU/mL); Pertussis antigens-pertussis toxin (PT),filamentous hemagglutinin (FHA),pertactin (PRN):prespecified level>=observed antipertussis AB concentration achieved by 95% of 13vPnC recipient; HBsAg prespecified level >=10 milli-IU per mL (mIU/mL); Poliovirus strains (types 1, 2, and 3): prespecified level: >=1:8; Haemophilus influenzae type b(Hib): prespecified level>=0.15 mcg/mL polyribosylribitol phosphate (anti-PRP) in mcg/mL.Dose3 EIP=eligible subject 42-112 day(D) of age at 1st vaccine,received 3 dose as randomized with 335-386 D of age at Dose3,1 valid immunogenicity result within 27-56 D after Dose3.n=subjects in Dose3 EIP.Concomitant vaccine response was assessed from subset of randomly selected study subjects.

End point type	Primary

End point timeframe:

1 month after Dose 3

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms

End point values	20vPnC: Primary Study Population	13vPnC: Primary Study Population		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	497	504		
Units: Percentage of subjects				
number (confidence interval 95%)				
Diphtheria toxoid, n=494, 498	99.6 (98.5 to 100.0)	99.8 (98.9 to 100.0)		
Tetanus toxoid, n=494, 498	99.4 (98.2 to 99.9)	100.0 (99.3 to 100.0)		
Pertussis: PT, n=494, 498	92.9 (90.3 to 95.0)	95.2 (92.9 to 96.9)		
Pertussis: FHA, n=494, 498	95.3 (93.1 to 97.0)	95.2 (92.9 to 96.9)		
Pertussis: PRN, n=494, 498	96.8 (94.8 to 98.1)	95.2 (92.9 to 96.9)		
Hepatitis B, n=173, 178	100.0 (97.9 to 100.0)	98.9 (96.0 to 99.9)		
Poliovirus: Type 1, n=81, 89	100.0 (95.5 to 100.0)	100.0 (95.9 to 100.0)		
Poliovirus: Type 2, n=81, 89	100.0 (95.5 to 100.0)	100.0 (95.9 to 100.0)		
Poliovirus: Type 3, n=81, 89	100.0 (95.5 to 100.0)	100.0 (95.9 to 100.0)		

Haemophilus influenzae type b, n=185, 169	100.0 (98.0 to 100.0)	100.0 (97.8 to 100.0)		

Statistical analyses

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
PT: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	-2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.3
upper limit	0.7

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Tetanus: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions (20vPnc - 13vPnC) expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	0.2

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Diphtheria: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions (20vPnc - 13vPnC) expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population

Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	0.8

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Poliovirus Type 1: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions (20vPnc - 13vPnC) expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.6
upper limit	4.2

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Poliovirus Type 2: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions (20vPnc - 13vPnC) expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.6
upper limit	4.2

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Poliovirus Type 3: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions (20vPnc - 13vPnC) expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.6
upper limit	4.2

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Hepatitis B: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions (20vPnc - 13vPnC) expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	4

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Hib: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions (20vPnc - 13vPnC) expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	0

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	2.2

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
FHA: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.6
upper limit	2.9

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
PRN: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	4.2

Primary: GMC of Measles Virus Antibody 1 Month After Dose 3: Primary Study Population

End point title	GMC of Measles Virus Antibody 1 Month After Dose 3: Primary Study Population[25]

End point description:

Pre-specified vaccine antigen (measles) was administered concomitantly with 20vPnC or 13vPnC at Dose 3 and responses measured 1 month after Dose 3. Assay results below the lower limit of quantitation (LLOQ) were set to 0.5*LLOQ in the analysis. GMCs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the concentrations and the corresponding CIs (based on the Student’s t distribution). The immune responses were only measured on random subset of subjects. Dose 3 evaluable immunogenicity population = eligible subjects 42-112 days of age at first vaccination, received all 3 doses as randomized with 335-386 days of age at Dose 3, at least 1 valid immunogenicity results from blood collection within 27 to 56 days after Dose 3, no major protocol deviations. Here, "Number of Subjects Analyzed"= subjects in Dose 3 evaluable immunogenicity population, received measles vaccine and had valid assay results measle vaccine antigen.

End point type	Primary

End point timeframe:

1 month after Dose 3

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: This endpoint was planned to be analysed only for the specified reporting arms

End point values	20vPnC: Primary Study Population	13vPnC: Primary Study Population		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	132		
Units: Arbitrary units per milliliter				
geometric mean (confidence interval 95%)	228.63 (186.34 to 280.52)	216.72 (174.92 to 268.52)		

Statistical analyses

Statistical analysis title	20vPnC Versus 13vPnC

Statistical analysis description:

Measles: GMR and 2-sided 95% CIs were calculated by exponentiating the mean differences of the logarithms of the concentrations (20vPnC − 13vPnC) and the corresponding CIs (based on the Student's t distribution).

Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	260
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	1.42

Primary: GMC of Rubella Virus Antibody 1 Month After Dose 3: Primary Study Population

End point title	GMC of Rubella Virus Antibody 1 Month After Dose 3: Primary Study Population[26]

End point description:

Pre-specified vaccine antigen (rubella) was administered concomitantly with 20vPnC or 13vPnC at Dose 3 and responses measured 1 month after Dose 3. Assay results below LLOQ were set to 0.5*LLOQ in the analysis. GMCs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the concentrations and the corresponding CIs (based on the Student's t distribution). The immune responses were only measured on random subset of subjects. Dose 3 evaluable immunogenicity population = eligible subjects 42-112 days of age at first vaccination, received all 3 doses as randomized with 335-386 days of age at Dose 3, at least 1 valid immunogenicity results from blood collection within 27 to 56 days after Dose 3, no major protocol deviations. Here, "Number of Subjects Analyzed"= subjects in Dose 3 evaluable immunogenicity population, received rubella vaccine and had valid assay results rubella vaccine antigen.

End point type	Primary

End point timeframe:

1 month after Dose 3

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms

End point values	20vPnC: Primary Study Population	13vPnC: Primary Study Population		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	132		
Units: International units per milliliter				
geometric mean (confidence interval 95%)	31.81 (25.54 to 39.62)	38.20 (32.10 to 45.45)		

Statistical analyses

Statistical analysis title	20vPnC Versus 13vPnC

Statistical analysis description:

Rubella: GMR and 2-sided 95% CIs were calculated by exponentiating the mean differences of the logarithms of the concentrations (20vPnC − 13vPnC) and the corresponding CIs (based on the Student's t distribution).

Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	260
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	1.1

Primary: GMC of Mumps Virus Antibody 1 Month After Dose 3: Primary Study

Population	
End point title	GMC of Mumps Virus Antibody 1 Month After Dose 3: Primary Study Population[27]

End point description:

Pre-specified vaccine antigen (mumps) was administered concomitantly with 20vPnC or 13vPnC at Dose 3 and responses measured 1 month after Dose 3. Assay results below the LLOQ were set to 0.5*LLOQ in the analysis. GMCs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the concentrations and the corresponding CIs (based on the Student's t distribution). The immune responses were only measured on random subset of subjects.Dose 3 evaluable immunogenicity population = eligible subjects 42-112 days of age at first vaccination, received all 3 doses as randomized with 335-386 days of age at Dose 3, at least 1 valid immunogenicity results from blood collection within 27 to 56 days after Dose 3, no major protocol deviations. Here, "Number of Subjects Analyzed"= subjects in Dose 3 evaluable immunogenicity population, received mumps vaccine and had valid assay results mumps vaccine antigen.

End point type	Primary

End point timeframe:

1 month after Dose 3

Notes:

[27] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms

End point values	20vPnC: Primary Study Population	13vPnC: Primary Study Population		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	133		
Units: Arbitrary units per milliliter				
geometric mean (confidence interval 95%)	36.81 (29.12 to 46.54)	35.25 (28.14 to 44.17)		

Statistical analyses

Statistical analysis title	20vPnC Versus 13vPnC

Statistical analysis description:

Mumps: GMR and 2-sided 95% CIs were calculated by exponentiating the mean differences of the logarithms of the concentrations (20vPnC − 13vPnC) and the corresponding CIs (based on the Student's t distribution).

Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	261
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	1.44

Primary: Percentage of Subjects With Local Reactions Within 7 Days After Dose 1: Russian Cohort

End point title	Percentage of Subjects With Local Reactions Within 7 Days After Dose 1: Russian Cohort[28][29]

End point description:

Local reactions included redness, swelling and, pain at the injection site, recorded by parent's/legal guardians of subjects in an e-diary. Redness and swelling were measured and recorded in measuring device units. 1 measuring device unit =0.5 cm. Redness and swelling were graded as mild (>0 to 2.0 cm), moderate (> 2.0 to 7.0 cm) and severe (>7.0 cm). Pain at injection site was graded as mild (hurt if gently touched example, whimpered, winced, protested, or withdrew), moderate (hurt if gently touched, with crying), and severe (caused limitation of limb movement). 95% CI was based on Clopper and Pearson method. Safety analysis set included all subjects who received at least 1 dose of 20vPnC or 13vPnC and had safety data assessed after any dose.Here, "Number of subjects Analyzed" signifies number of subjects with any e-diary data after Dose 1

End point type	Primary

End point timeframe:

Within 7 days after Dose 1

Notes:

[28] - 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: This endpoint was planned to be analysed only for the specified reporting arms

[29] - 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: Only descriptive analysis was planned for this endpoint

End point values	20vPnC: Russian Cohort	13vPnC: Russian Cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	27		
Units: Percentage of subjects				
number (confidence interval 95%)				
Redness: Mild	4.2 (0.1 to 21.1)	7.4 (0.9 to 24.3)		
Redness: Moderate	4.2 (0.1 to 21.1)	3.7 (0.1 to 19.0)		
Redness: Severe	0 (0.0 to 14.2)	0 (0.0 to 12.8)		
Swelling: Mild	0 (0.0 to 14.2)	0 (0.0 to 12.8)		
Swelling: Moderate	4.2 (0.1 to 21.1)	0 (0.0 to 12.8)		
Swelling: Severe	0 (0.0 to 14.2)	0 (0.0 to 12.8)		
Pain at Injection Site: Mild	8.3 (1.0 to 27.0)	7.4 (0.9 to 24.3)		
Pain at Injection Site: Moderate	0 (0.0 to 14.2)	3.7 (0.1 to 19.0)		
Pain at Injection Site: Severe	0 (0.0 to 14.2)	0 (0.0 to 12.8)		

Statistical analyses

No statistical analyses for this end point

Primary: GMC of Varicella Virus Antibody 1 Month After Dose 3: Primary Study Population

End point title	GMC of Varicella Virus Antibody 1 Month After Dose 3: Primary Study Population[30]

End point description:

Pre-specified vaccine antigen (varicella) was administered concomitantly with 20vPnC or 13vPnC at Dose 3 and responses measured 1 month after Dose 3. Assay results below the lower limit of quantitation (LLOQ) were set to 0.5*LLOQ in the analysis. GMCs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the concentrations and the corresponding CIs (based on the Student’s t distribution). The immune responses were only measured on random subset of subjects. Dose 3 evaluable immunogenicity population = eligible subjects 42-112 days of age at first vaccination, received all 3 doses as randomized with 335-386 days of age at Dose 3, at least 1 valid immunogenicity results from blood collection within 27 to 56 days after Dose 3, no major protocol deviations. Here, "Number of Subjects Analyzed"= subjects in Dose 3 evaluable immunogenicity population, received varicella vaccine and had valid assay results varicella vaccine antigen.

End point type	Primary

End point timeframe:

1 month after Dose 3

Notes:

[30] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms

End point values	20vPnC: Primary Study Population	13vPnC: Primary Study Population		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	132		
Units: Milli-international units per milliliter				
geometric mean (confidence interval 95%)	195.58 (165.14 to 231.62)	157.60 (133.57 to 185.95)		

Statistical analyses

Statistical analysis title	20vPnC Versus 13vPnC

Statistical analysis description:

Varicella: GMR and 2-sided 95% CIs were calculated by exponentiating the mean differences of the logarithms of the concentrations (20vPnC − 13vPnC) and the corresponding CIs (based on the Student's t distribution).

Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	260
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Geometric Mean Ratio
Point estimate	1.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.98
upper limit	1.57

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

Russian Cohort

End point title	Percentage of Subjects With Local Reactions Within 7 Days After Dose 2: Russian Cohort[31][32]

End point description:

Local reactions included redness, swelling and, pain at the injection site, recorded by parent's/legal guardians of subjects in an e-diary. Redness and swelling were measured and recorded in measuring device units. 1 measuring device unit =0.5 cm. Redness and swelling were graded as mild (>0 to 2.0 cm), moderate (> 2.0 to 7.0 cm) and severe (>7.0 cm). Pain at injection site was graded as mild (hurt if gently touched example, whimpered, winced, protested, or withdrew), moderate (hurt if gently touched, with crying), and severe (caused limitation of limb movement). 95% CI was based on Clopper and Pearson method. Safety analysis set included all subjects who received at least 1 dose of 20vPnC or 13vPnC and had safety data assessed after any dose. Here, "Number of Subjects Analyzed" signifies the number of subjects with any e-diary data after Dose 2.

End point type	Primary

End point timeframe:

Within 7 days after Dose 2

Notes:

[31] - 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: This endpoint was planned to be analysed only for the specified reporting arms

[32] - 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: Only descriptive analysis was planned for this endpoint

End point values	20vPnC: Russian Cohort	13vPnC: Russian Cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	27		
Units: Percentage of subjects				
number (confidence interval 95%)				
Redness: Mild	0 (0.0 to 14.8)	3.7 (0.1 to 19.0)		
Redness: Moderate	4.3 (0.1 to 21.9)	0 (0.0 to 12.8)		
Redness: Severe	0 (0.0 to 14.8)	0 (0.0 to 12.8)		
Swelling: Mild	0 (0.0 to 14.8)	7.4 (0.9 to 24.3)		
Swelling: Moderate	8.7 (1.1 to 28.0)	0 (0.0 to 12.8)		
Swelling: Severe	0 (0.0 to 14.8)	0 (0.0 to 12.8)		
Pain at Injection Site: Mild	8.7 (1.1 to 28.0)	7.4 (0.9 to 24.3)		
Pain at Injection Site: Moderate	4.3 (0.1 to 21.9)	0 (0.0 to 12.8)		
Pain at Injection Site: Severe	0 (0.0 to 14.8)	0 (0.0 to 12.8)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Local Reactions Within 7 Days After Dose 3: Russian Cohort

End point title	Percentage of Subjects With Local Reactions Within 7 Days After Dose 3: Russian Cohort[33][34]

End point description:

Local reactions included redness, swelling and, pain at the injection site, recorded by parent's/legal guardians of subjects in an e-diary. Redness and swelling were measured and recorded in measuring device units. 1 measuring device unit =0.5 cm. Redness and swelling were graded as mild (>0 to 2.0 cm), moderate (> 2.0 to 7.0 cm) and severe (>7.0 cm). Pain at injection site was graded as mild (hurt if gently touched example, whimpered, winced, protested, or withdrew), moderate (hurt if gently touched, with crying), and severe (caused limitation of limb movement). 95% CI was based on Clopper and Pearson method. Safety analysis set included all subjects who received at least 1 dose of 20vPnC or 13vPnC and had safety data assessed after any dose. Here, "Number of Subjects Analyzed" signifies the number of subjects with any e-diary data after Dose 3.

End point type	Primary

End point timeframe:

Within 7 days after Dose 3

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: This endpoint was planned to be analysed only for the specified reporting arms

[34] - 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: Only descriptive analysis was planned for this endpoint

End point values	20vPnC: Russian Cohort	13vPnC: Russian Cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	25		
Units: Percentage of subjects				
number (confidence interval 95%)				
Redness: Mild	0 (0.0 to 15.4)	4.0 (0.1 to 20.4)		
Redness: Moderate	4.5 (0.1 to 22.8)	0 (0.0 to 13.7)		
Redness: Severe	0 (0.0 to 15.4)	4.0 (0.1 to 4.0)		
Swelling: Mild	0 (0.0 to 15.4)	0 (0.0 to 13.7)		
Swelling: Moderate	9.1 (1.1 to 29.2)	0 (0.0 to 13.7)		
Swelling: Severe	0 (0.0 to 15.4)	4.0 (0.1 to 20.4)		
Pain at Injection Site: Mild	13.6 (2.9 to 34.9)	8.0 (1.0 to 26.0)		
Pain at Injection Site: Moderate	0 (0.0 to 15.4)	0 (0.0 to 13.7)		
Pain at Injection Site: Severe	0 (0.0 to 15.4)	0 (0.0 to 13.7)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Systemic Events Within 7 Days After Dose 1: Russian cohort

End point title	Percentage of Subjects With Systemic Events Within 7 Days After Dose 1: Russian cohort[35][36]

End point description:

Systemic events:fever,decreased appetite,drowsiness/increased sleep & irritability, recorded by parents/legal guardians of subject's using e-diary.Fever: temperature >=38.0 degree C & categorized as >=38.0 to 38.4 degree C,>38.4 to 38.9 degree C,>38.9 to 40.0 degree C & >40.0-degree C. Decreased appetite:mild (decreased interest in eating), moderate (decreased oral intake) & severe (refusal to

feed).Drowsiness was graded as mild (increased/prolonged sleeping bouts), moderate (slightly subdued, interfered with daily activity) & severe (disabling, not interested in usual daily activity).Irritability: mild (easily consolable), moderate (required increased attention) & severe (inconsolable, crying could not be comforted).95% CI was based on Clopper & Pearson method. Safety analysis set:all subjects who received at least 1 dose of 20vPnC or 13vPnC & had safety data assessed after any dose.Here, "Number of subjects Analyzed" signifies number of subjects with any e-diary data after Dose 1.

End point type	Primary

End point timeframe:

Within 7 Days after Dose 1

Notes:

[35] - 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: This endpoint was planned to be analysed only for the specified reporting arms

[36] - 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: Only descriptive analysis was planned for this endpoint

End point values	20vPnC: Russian Cohort	13vPnC: Russian Cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	27		
Units: Percentage of subjects				
number (confidence interval 95%)				
Fever: >=38.0 degrees C to 38.4 degrees C	4.2 (0.1 to 21.1)	0 (0.0 to 12.8)		
Fever: >38.4 degrees C to 38.9 degrees C	0 (0.0 to 14.2)	0 (0.0 to 12.8)		
Fever: >38.9 degrees C to 40.0 degrees C	0 (0.0 to 14.2)	0 (0.0 to 12.8)		
Fever: >40.0 degrees C	0 (0.0 to 14.2)	0 (0.0 to 12.8)		
Decreased appetite: Mild	16.7 (4.7 to 37.4)	14.8 (4.2 to 33.7)		
Decreased appetite: Moderate	0 (0.0 to 14.2)	3.7 (0.1 to 19.0)		
Decreased appetite: Severe	0 (0.0 to 14.2)	0 (0.0 to 12.8)		
Drowsiness: Mild	20.8 (7.1 to 42.2)	18.5 (6.3 to 38.1)		
Drowsiness: Moderate	8.3 (1.0 to 27.0)	11.1 (2.4 to 29.2)		
Drowsiness: Severe	0 (0.0 to 14.2)	0 (0.0 to 12.8)		
Irritability: Mild	12.5 (2.7 to 32.4)	7.4 (0.9 to 24.3)		
Irritability: Moderate	8.3 (1.0 to 27.0)	14.8 (4.2 to 33.7)		
Irritability: Severe	4.2 (0.1 to 21.1)	0 (0.0 to 12.8)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Systemic Events Within 7 Days After Dose 2: Russian cohort

End point title	Percentage of Subjects With Systemic Events Within 7 Days After Dose 2: Russian cohort[37][38]

End point description:

Systemic events: fever, decreased appetite, drowsiness/increased sleep & irritability, recorded by parents/legal guardians of participant's using e-diary. Fever: temperature >=38.0 degree C & categorized as >=38.0 to 38.4 degree C,>38.4 to 38.9 degree C,>38.9 to 40.0 degree C & >40.0-degree C. Decreased appetite: mild (decreased interest in eating), moderate (decreased oral intake) & severe (refusal to feed).Drowsiness was graded as mild (increased/prolonged sleeping bouts), moderate (slightly subdued, interfered with daily activity) & severe (disabling, not interested in usual daily activity).Irritability: mild (easily consolable), moderate (required increased attention) & severe (inconsolable, crying could not be comforted). 95% CI was based on Clopper & Pearson method. Safety analysis set: all subjects who received at least 1 dose of 20vPnC or 13vPnC & had safety data assessed after any dose.Here,"Number of Subjects Analyzed": number of subjects with any e-diary data after Dose 2

End point type	Primary

End point timeframe:

Within 7 Days after Dose 2

Notes:

[37] - 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: This endpoint was planned to be analysed only for the specified reporting arms

[38] - 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: Only descriptive analysis was planned for this endpoint

End point values	20vPnC: Russian Cohort	13vPnC: Russian Cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	27		
Units: Percentage of subjects				
number (confidence interval 95%)				
Fever: >=38.0 degrees C to 38.4 degrees C	0 (0.0 to 14.8)	11.1 (2.4 to 29.2)		
Fever: >38.4 degrees C to 38.9 degrees C	4.3 (0.1 to 21.9)	0 (0.0 to 12.8)		
Fever: >38.9 degrees C to 40.0 degrees C	0 (0.0 to 14.8)	0 (0.0 to 12.8)		
Fever: >40.0 degrees C	0 (0.0 to 14.8)	0 (0.0 to 12.8)		
Decreased appetite: Mild	4.3 (0.1 to 21.9)	7.4 (0.9 to 24.3)		
Decreased appetite: Moderate	4.3 (0.1 to 21.9)	3.7 (0.1 to 19.0)		
Decreased appetite: Severe	0 (0.0 to 14.8)	0 (0.0 to 12.8)		
Drowsiness: Mild	4.3 (0.1 to 21.9)	3.7 (0.1 to 19.0)		
Drowsiness: Moderate	0 (0.0 to 14.8)	3.7 (0.1 to 19.0)		
Drowsiness: Severe	0 (0.0 to 14.8)	0 (0.0 to 12.8)		
Irritability: Mild	13.0 (2.8 to 33.6)	22.2 (8.6 to 42.3)		
Irritability: Moderate	4.3 (0.1 to 21.9)	18.5 (6.3 to 38.1)		
Irritability: Severe	0 (0.0 to 14.8)	3.7 (0.1 to 19.0)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Systemic Events Within 7 Days After Dose 3: Russian cohort

End point title	Percentage of Subjects With Systemic Events Within 7 Days After Dose 3: Russian cohort[39][40]

End point description:

Systemic events: fever, decreased appetite, drowsiness/increased sleep & irritability, recorded by parents/legal guardians of subjects using e-diary. Fever: temperature >=38.0 degree C & categorized as >=38.0 to 38.4 degree C,>38.4 to 38.9 degree C,>38.9 to 40.0 degree C & >40.0-degree C. Decreased appetite: mild (decreased interest in eating), moderate (decreased oral intake) & severe (refusal to feed).Drowsiness was graded as mild (increased/prolonged sleeping bouts), moderate (slightly subdued, interfered with daily activity) & severe (disabling, not interested in usual daily activity).Irritability: mild (easily consolable), moderate (required increased attention) & severe (inconsolable, crying could not be comforted). 95% CI was based on Clopper & Pearson method. Safety analysis set:all subjects who received at least 1 dose of 20vPnC or 13vPnC & had safety data assessed after any dose.Here,"Number of Subjects Analyzed": number of subjects with any e-diary data after Dose 3

End point type	Primary

End point timeframe:

Within 7 Days after Dose 3

Notes:

[39] - 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: This endpoint was planned to be analysed only for the specified reporting arms

[40] - 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: Only descriptive analysis was planned for this endpoint

End point values	20vPnC: Russian Cohort	13vPnC: Russian Cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	25		
Units: Percentage of subjects				
number (confidence interval 95%)				
Fever: >=38.0 degrees C to 38.4 degrees C	0 (0.0 to 15.4)	0 (0.0 to 13.7)		
Fever: >38.4 degrees C to 38.9 degrees C	0 (0.0 to 15.4)	4.0 (0.1 to 20.4)		
Fever: >38.9 degrees C to 40.0 degrees C	4.5 (0.1 to 22.8)	0 (0.0 to 13.7)		
Fever: >40.0 degrees C	0 (0.0 to 15.4)	0 (0.0 to 13.7)		
Decreased appetite: Mild	9.1 (1.1 to 29.2)	8.0 (1.0 to 26.0)		
Decreased appetite: Moderate	9.1 (1.1 to 29.2)	0 (0.0 to 13.7)		
Decreased appetite: Severe	0 (0.0 to 15.4)	0 (0.0 to 13.7)		
Drowsiness: Mild	13.6 (2.9 to 34.9)	20.0 (6.8 to 40.7)		
Drowsiness: Moderate	0 (0.0 to 15.4)	4.0 (0.1 to 20.4)		
Drowsiness: Severe	0 (0.0 to 15.4)	0 (0.0 to 13.7)		
Irritability: Mild	27.3 (10.7 to 50.2)	16.0 (4.5 to 36.1)		
Irritability: Moderate	9.1 (1.1 to 29.2)	8.0 (1.0 to 26.0)		
Irritability: Severe	0 (0.0 to 15.4)	0 (0.0 to 13.7)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With SAEs From Dose 1 to 1 month after Dose 3: Russian cohort

End point title	Percentage of Subjects With SAEs From Dose 1 to 1 month after Dose 3: Russian cohort[41][42]

End point description:

An SAE was any untoward medical occurrence that occurred, at any dose: resulted in death; required inpatient hospitalization or prolongation of existing hospitalization; was life-threatening; resulted in persistent or significant disability/ incapacity; was a congenital anomaly/birth defect and other important medical events. 95% CI was based on the Clopper and Pearson method. Safety analysis set included all subjects who received at least 1 dose of 20vPnC or 13vPnC and had safety data assessed after any dose.

End point type	Primary

End point timeframe:

From Dose 1 to 1 month after Dose 3

Notes:

[41] - 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 analysis was planned for this endpoint

[42] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms

End point values	20vPnC: Russian Cohort	13vPnC: Russian Cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	27		
Units: Percentage of subjects				
number (confidence interval 95%)	0 (0 to 0)	0 (0 to 0)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With AEs From Dose 1 to 1 Month After Dose 2: Russian Cohort

End point title	Percentage of Subjects With AEs From Dose 1 to 1 Month After Dose 2: Russian Cohort[43][44]

End point description:

An AE was any untoward medical occurrence in a participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. 95% CI was based on the Clopper and Pearson method. Safety analysis set included all subjects who received at least 1 dose of 20vPnC or 13vPnC and had safety data assessed after any dose.

End point type	Primary

End point timeframe:

From Dose 1 to 1 month after Dose 2

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: This endpoint was planned to be analysed only for the specified reporting arms

[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: Only descriptive analysis was planned for this endpoint

End point values	20vPnC: Russian Cohort	13vPnC: Russian Cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	27		
Units: Percentage of subjects				
number (confidence interval 95%)	8.3 (1.0 to 27.0)	3.7 (0.1 to 19.0)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With AEs From Dose 3 to 1 Month After Dose 3: Russian Cohort

End point title	Percentage of Subjects With AEs From Dose 3 to 1 Month After Dose 3: Russian Cohort[45][46]

End point description:

An AE was any untoward medical occurrence in a subject, temporally associated with the use of study treatment, whether or not considered related to the study treatment. 95% CI was based on the Clopper and Pearson method. AEs reported in this outcome measure excluded local reactions and systemic events. Safety analysis set included all subjects who received at least 1 dose of 20vPnC or 13vPnC and had safety data assessed after any dose. Here, "Number of Subjects Analyzed" signifies the number of subjects who received Dose 3.

End point type	Primary

End point timeframe:

From Dose 3 to 1 month after Dose 3

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 analysis was planned for this endpoint.

[46] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms

End point values	20vPnC: Russian Cohort	13vPnC: Russian Cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	25		
Units: Percentage of subjects				
number (confidence interval 95%)	4.5 (0.1 to 22.8)	0 (0.0 to 13.7)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Predefined Pneumococcal IgG Antibody 1 Month After Dose 2: Russian Cohort

End point title	Percentage of Subjects With Predefined Pneumococcal IgG Antibody 1 Month After Dose 2: Russian Cohort[47][48]

End point description:

Predefined IgG concentrations were as follows: for serotype 1, 3, 4, 6A, 7F, 9V, 14, 18C, 19F, 23F, 8, 10A, 11A, 12F, 15B, 22F, 33F: >=0.35 microgram per mL (mcg/mL), for serotype 5: >=0.23 mcg/mL, for serotype 6B. >=0.10 mcg/mL and for serotype 19A: >=0.12 mcg/mL. 95% CI was based on the Clopper and Pearson method. Dose 2 evaluable immunogenicity population: eligible subjects 42-70 days of age at first vaccination, received first 2 doses as randomized, at least 1 valid immunogenicity results within 27 to 56 days after Dose 2, no other major protocol deviations. "Number of Subjects Analyzed"= subjects with valid IgG assay results for specified serotype.

End point type	Primary

End point timeframe:

1 month after Dose 2

Notes:

[47] - 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 analysis was planned for this endpoint

[48] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms

End point values	20vPnC: Russian Cohort	13vPnC: Russian Cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	27		
Units: Percentage of subjects				
number (confidence interval 95%)				
Serotype 1	70.8 (48.9 to 87.4)	77.8 (57.7 to 91.4)		
Serotype 3	37.5 (18.8 to 59.4)	59.3 (38.8 to 77.6)		
Serotype 4	75.0 (53.3 to 90.2)	74.1 (53.7 to 88.9)		
Serotype 5	66.7 (44.7 to 84.4)	81.5 (61.9 to 93.7)		
Serotype 6A	54.2 (32.8 to 74.4)	81.5 (61.9 to 93.7)		
Serotype 6B	20.8 (7.1 to 42.2)	59.3 (38.8 to 77.6)		
Serotype 7F	95.8 (78.9 to 99.9)	92.6 (75.7 to 99.1)		
Serotype 9V	41.7 (22.1 to 63.4)	81.5 (61.9 to 93.7)		
Serotype 14	83.3 (62.6 to 95.3)	85.2 (66.3 to 95.8)		

Serotype 18C	66.7 (44.7 to 84.4)	81.5 (61.9 to 93.7)		
Serotype 19A	87.5 (67.6 to 97.3)	92.6 (75.7 to 99.1)		
Serotype 19F	79.2 (57.8 to 92.9)	96.3 (81.0 to 99.9)		
Serotype 23F	37.5 (18.8 to 59.4)	70.4 (49.8 to 86.2)		
Serotype 8	75.0 (53.3 to 90.2)	33.3 (16.5 to 54.0)		
Serotype 10A	41.7 (22.1 to 63.4)	18.5 (6.3 to 38.1)		
Serotype 11A	83.3 (62.6 to 95.3)	18.5 (6.3 to 38.1)		
Serotype 12F	12.5 (2.7 to 32.4)	14.8 (4.2 to 33.7)		
Serotype 15B	66.7 (44.7 to 84.4)	33.3 (16.5 to 54.0)		
Serotype 22F	66.7 (44.7 to 84.4)	14.8 (4.2 to 33.7)		
Serotype 33F	45.8 (25.6 to 67.2)	25.9 (11.1 to 46.3)		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With NDCMC From Dose 1 to 1 Month After Dose 3: Russian Cohort

End point title	Percentage of Subjects With NDCMC From Dose 1 to 1 Month After Dose 3: Russian Cohort[49][50]

End point description:

An NDCMC was defined as a disease or medical condition, not previously identified, that was expected to be persistent or was otherwise long-lasting in its effects. 95% CI was based on the Clopper and Pearson method. Safety analysis set included all subjects who received at least 1 dose of 20vPnC or 13vPnC and had safety data assessed after any dose.

End point type	Primary

End point timeframe:

From Dose 1 to 1 month after Dose 3

Notes:

[49] - 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 analysis was planned for this endpoint

[50] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms

End point values	20vPnC: Russian Cohort	13vPnC: Russian Cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	27		
Units: Percentage of subjects				
number (confidence interval 95%)	0 (0 to 0)	0 (0 to 0)		

Statistical analyses

No statistical analyses for this end point

Primary: GMC of Serotype-specific Pneumococcal IgG Antibody 1 Month After Dose 2: Russian Cohort

End point title	GMC of Serotype-specific Pneumococcal IgG Antibody 1 Month After Dose 2: Russian Cohort[51][52]

End point description:

Pneumococcal serotype-specific IgG concentrations were measured for serum samples for 13vPnC serotypes: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F and 7 additional serotypes: 8, 10A, 11A, 12F, 15B, 22F, 33F. Assay results below the LLOQ were set to 0.5 × LLOQ. GMC & corresponding 2-sided 95% CIs were calculated by exponentiating mean logarithm of concentration, corresponding 2-sided 95% CIs (based on Student's t distribution). Dose 2 evaluable immunogenicity population: eligible subjects 42-70days of age at first vaccination, received first 2 doses as randomized, at least 1 valid immunogenicity results within 27 to 56 days after Dose 2, no other major protocol deviations. "Number of Subjects Analyzed"= subjects with valid IgG assay results for specified serotype.

End point type	Primary

End point timeframe:

1 month after Dose 2

Notes:

[51] - 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 analysis was planned for this endpoint

[52] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms

End point values	20vPnC: Russian Cohort	13vPnC: Russian Cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	27		
Units: mcg/mL				
geometric mean (confidence interval 95%)				
Serotype 1	0.76 (0.49 to 1.19)	1.04 (0.64 to 1.69)		
Serotype 3	0.28 (0.19 to 0.42)	0.47 (0.31 to 0.72)		
Serotype 4	0.67 (0.45 to 1.00)	1.00 (0.58 to 1.71)		
Serotype 5	0.53 (0.31 to 0.92)	0.75 (0.40 to 1.40)		
Serotype 6A	0.45 (0.20 to 1.03)	1.57 (0.80 to 3.10)		
Serotype 6B	0.07 (0.03 to 0.16)	0.27 (0.12 to 0.63)		
Serotype 7F	1.06 (0.68 to 1.65)	1.89 (1.32 to 2.71)		
Serotype 9V	0.44 (0.23 to 0.84)	1.22 (0.73 to 2.06)		

Serotype 14	1.56 (0.88 to 2.75)	2.66 (1.46 to 4.86)		
Serotype 18C	0.94 (0.46 to 1.91)	0.94 (0.50 to 1.78)		
Serotype 19A	1.15 (0.47 to 2.82)	1.21 (0.59 to 2.49)		
Serotype 19F	1.51 (0.84 to 2.72)	3.32 (2.03 to 5.44)		
Serotype 23F	0.25 (0.11 to 0.55)	0.73 (0.37 to 1.42)		
Serotype 8	0.79 (0.37 to 1.69)	0.07 (0.03 to 0.18)		
Serotype 10A	0.31 (0.10 to 0.94)	0.04 (0.01 to 0.10)		
Serotype 11A	0.83 (0.43 to 1.60)	0.04 (0.02 to 0.09)		
Serotype 12F	0.06 (0.03 to 0.11)	0.02 (0.01 to 0.04)		
Serotype 15B	1.19 (0.46 to 3.05)	0.16 (0.05 to 0.50)		
Serotype 22F	0.48 (0.16 to 1.47)	0.02 (0.01 to 0.06)		
Serotype 33F	0.40 (0.18 to 0.88)	0.07 (0.03 to 0.16)		

Statistical analyses

No statistical analyses for this end point

Primary: GMC of Serotype-specific Pneumococcal IgG Antibody 1 Month After Dose 3: Russian Cohort

End point title	GMC of Serotype-specific Pneumococcal IgG Antibody 1 Month After Dose 3: Russian Cohort[53][54]

End point description:

Pneumococcal serotype-specific IgG concentrations were measured for serum samples for 13vPnC serotypes: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F and additional serotypes: 8, 10A, 11A, 12F, 15B, 22F and 33F. Assay results below the LLOQ were set to 0.5 × LLOQ. GMC & corresponding 2-sided 95% CIs were calculated by exponentiating mean logarithm of concentration, corresponding 2-sided 95% CIs (based on Student's t distribution). Dose 3 evaluable immunogenicity population = eligible subjects 42-70 days of age at first vaccination, received all 3 doses as randomized with 335-455 days of age at Dose 3, at least 1 valid immunogenicity results from blood collection within 27 to 56 days after Dose 3, no major protocol deviations.Here, "Number of Subjects Analyzed" signifies the subjects with valid IgG assay result for specified serotype.

End point type	Primary

End point timeframe:

1 month after Dose 3

Notes:

[53] - 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 analysis was planned for this endpoint

[54] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms

End point values	20vPnC: Russian Cohort	13vPnC: Russian Cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	24		
Units: mcg/mL				
geometric mean (confidence interval 95%)				
Serotype 1	1.61 (0.93 to 2.78)	1.65 (0.94 to 2.90)		
Serotype 3	0.84 (0.44 to 1.60)	0.57 (0.32 to 1.01)		
Serotype 4	3.05 (1.50 to 6.20)	3.04 (1.72 to 5.36)		
Serotype 5	1.50 (0.80 to 2.82)	1.72 (0.90 to 3.29)		
Serotype 6A	6.63 (2.96 to 14.86)	5.63 (2.96 to 10.72)		
Serotype 6B	1.94 (0.82 to 4.56)	1.49 (0.67 to 3.32)		
Serotype 7F	3.53 (1.97 to 6.33)	4.14 (2.73 to 6.26)		
Serotype 9V	2.32 (1.28 to 4.19)	2.27 (1.19 to 4.35)		
Serotype 14	4.01 (1.64 to 9.77)	5.06 (3.04 to 8.40)		
Serotype 18C	2.60 (1.24 to 5.44)	2.64 (1.49 to 4.69)		
Serotype 19A	4.81 (2.07 to 11.16)	2.69 (1.12 to 6.45)		
Serotype 19F	4.97 (2.30 to 10.76)	4.58 (2.36 to 8.90)		
Serotype 23F	3.52 (1.68 to 7.38)	2.96 (1.33 to 6.56)		
Serotype 8	1.33 (0.50 to 3.56)	0.09 (0.04 to 0.24)		
Serotype 10A	1.99 (0.63 to 6.29)	0.03 (0.01 to 0.09)		
Serotype 11A	1.50 (0.58 to 3.87)	0.06 (0.02 to 0.16)		
Serotype 12F	0.17 (0.05 to 0.56)	0.02 (0.01 to 0.03)		
Serotype 15B	4.90 (1.67 to 14.37)	0.07 (0.03 to 0.20)		
Serotype 22F	1.52 (0.38 to 6.03)	0.02 (0.01 to 0.08)		
Serotype 33F	1.38 (0.53 to 3.59)	0.04 (0.02 to 0.10)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Predefined Pneumococcal IgG Antibody 1 Month After Dose 3: Primary Study Population

End point title	Percentage of Subjects With Predefined Pneumococcal IgG Antibody 1 Month After Dose 3: Primary Study Population[55]

End point description:

Predefined IgG concentrations were as follows: for serotype 1, 3, 4, 6A, 7F, 9V, 14, 18C, 19F, 23F, 8, 10A, 11A, 12F, 15B, 22F, 33F: >=0.35 microgram per mL (mcg/mL), for serotype 5: >=0.23 mcg/mL, for serotype 6B. >=0.10 mcg/mL and for serotype 19A: >=0.12 mcg/mL. 95% CI was based on the Clopper and Pearson method.Dose 3 evaluable immunogenicity population = eligible subjects 42-112 days of age at first vaccination, received all 3 doses as randomized with 335-386 days of age at Dose 3, at least 1 valid immunogenicity results from blood collection within 27 to 56 days after Dose 3, no major protocol deviations. "Number of Subjects Analyzed"= subjects in Dose 3 evaluable immunogenicity population; "n"= subjects with valid IgG results for specified serotype.

End point type	Secondary

End point timeframe:

1 Month after Dose 3

Notes:

[55] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms

End point values	20vPnC: Primary Study Population	13vPnC: Primary Study Population		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	497	504		
Units: Percentage of subjects				
number (confidence interval 95%)				
Serotype 1, n=494, 502	97.2 (95.3 to 98.4)	98.2 (96.6 to 99.2)		
Serotype 3, n=494, 502	82.6 (79.0 to 85.8)	93.2 (90.7 to 95.3)		
Serotype 4, n=494, 502	99.2 (97.9 to 99.8)	99.2 (98.0 to 99.8)		
Serotype 5, n=494, 502	98.4 (96.8 to 99.3)	98.0 (96.4 to 99.0)		
Serotype 6A, n=494, 501	98.8 (97.4 to 99.6)	98.8 (97.4 to 99.6)		
Serotype 6B, n=494, 501	98.4 (96.8 to 99.3)	97.6 (95.9 to 98.8)		
Serotype 7F, n=494, 502	99.6 (98.5 to 100.0)	100.0 (99.3 to 100.0)		
Serotype 9V, n=494, 502	99.2 (97.9 to 99.8)	98.8 (97.4 to 99.6)		
Serotype 14, n=493, 501	96.6 (94.5 to 98.0)	98.0 (96.4 to 99.0)		
Serotype 18C, n=494, 502	99.2 (97.9 to 99.8)	98.2 (96.6 to 99.2)		
Serotype 19A, n=494, 502	99.6 (98.5 to 100.0)	99.6 (98.6 to 100.0)		
Serotype 19F, n=494, 502	99.6 (98.5 to 100.0)	99.4 (98.3 to 99.9)		
Serotype 23F, n=494, 502	96.4 (94.3 to 97.8)	97.2 (95.4 to 98.5)		
Serotype 8, n=495, 501	99.2 (97.9 to 99.8)	3.6 (2.1 to 5.6)		
Serotype 10A, n=495, 502	97.8 (96.1 to 98.9)	1.6 (0.7 to 3.1)		
Serotype 11A, n=495, 502	98.4 (96.8 to 99.3)	4.6 (2.9 to 6.8)		
Serotype 12F, n=495, 502	96.6 (94.6 to 98.0)	0.2 (0.0 to 1.1)		
Serotype 15B, n=495, 502	99.4 (98.2 to 99.9)	4.8 (3.1 to 7.0)		

Serotype 22F, n=495, 502	99.2 (97.9 to 99.8)	1.4 (0.6 to 2.9)		
Serotype 33F, n=495, 501	98.6 (97.1 to 99.4)	1.8 (0.8 to 3.4)		

Statistical analyses

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 4: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	1.3

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 3: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	-10.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.7
upper limit	-6.7

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 1: 2-Sided 95% CIs are calculated using the Miettinen and Nurminen method for the difference in proportions, expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population

Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.1
upper limit	0.9

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 5: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	2.2

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 6A: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	1.5

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description: Serotype 6B: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	2.7

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description: Serotype 14: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	-1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.7
upper limit	0.6

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description: Serotype 9V: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	0.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	1.9

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 7F: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	0.4

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 18C: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	2.7

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 19A: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population

Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	1.1

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 19F: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	1.4

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 23F: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.2
upper limit	1.4

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 8: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	3.9

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 10A: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	2.7

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 11A: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	1.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	3.2

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 12F: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.9
upper limit	1.6

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 15B: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	4.1

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Serotype 22F: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population

Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	3.9

Statistical analysis title	20vPnC Versus 13vPnC

Statistical analysis description:

Serotype 33F: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions expressed as a percentage.

Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1001
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	3.4

Secondary: Geometric Mean Titers (GMTs) of Serotype-specific Opsonophagocytic Activity (OPA) 1 Month After Dose 2: Primary Study Population

End point title	Geometric Mean Titers (GMTs) of Serotype-specific Opsonophagocytic Activity (OPA) 1 Month After Dose 2: Primary Study Population[56]

End point description:

OPA titers for the 20 pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F, 8, 10A, 11A, 12F, 15B, 22F, and 33F) were determined in randomly selected subsets of subjects at 1 month after Dose 2. Results were expressed as OPA titers. GMTs and 2-sided CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs based on the Student's t distribution. Dose 2 evaluable immunogenicity population: eligible subjects 42-112 days of age at first vaccination, received first 2 doses as randomized, at least 1 valid immunogenicity results within 27 to 56 days after Dose 2, no other major protocol deviations. "Number of Subjects Analyzed"= subjects in Dose 2 evaluable immunogenicity population, "n"= subjects with valid OPA assay results for specified serotype.

End point type	Secondary

End point timeframe:

1 month after Dose 2

Notes:

[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: This endpoint was planned to be analysed only for the specified reporting arms

End point values	20vPnC: Primary Study Population	13vPnC: Primary Study Population		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	567	562		
Units: Titers				
geometric mean (confidence interval 95%)				
Serotype 1, n=113, 107	14 (12 to 16)	23 (19 to 28)		
Serotype 3, n=114, 102	31 (26 to 36)	40 (34 to 47)		
Serotype 4, n=113, 112	333 (270 to 413)	391 (314 to 486)		
Serotype 5, n=112, 102	21 (18 to 23)	27 (23 to 31)		
Serotype 6A, n=112, 100	347 (273 to 441)	409 (318 to 527)		
Serotype 6B, n=106, 97	54 (42 to 71)	105 (76 to 144)		
Serotype 7F, n=114, 111	858 (736 to 1000)	895 (781 to 1027)		
Serotype 9V, n=567, 112	233 (182 to 298)	285 (228 to 358)		
Serotype 14, n=111, 101	287 (215 to 383)	360 (264 to 489)		
Serotype 18C, n=114, 112	588 (467 to 741)	719 (590 to 876)		
Serotype 19A, n=115, 111	57 (43 to 75)	91 (69 to 121)		
Serotype 19F, n=114, 103	97 (81 to 116)	117 (94 to 146)		
Serotype 23F, n=105, 108	59 (42 to 84)	68 (48 to 96)		
Serotype 8, n=103, 115	164 (133 to 203)	17 (15 to 18)		
Serotype 10A, n=109, 115	855 (610 to 1199)	39 (34 to 44)		
Serotype 11A, n=105, 116	327 (253 to 423)	49 (47 to 51)		
Serotype 12F, n=96, 116	4788 (3779 to 6067)	26 (23 to 28)		
Serotype 15B, n=104, 117	846 (605 to 1183)	17 (15 to 19)		
Serotype 22F, n=104, 117	4444 (3666 to 5386)	10 (9 to 11)		
Serotype 33F, n=102, 115	2373 (1759 to 3202)	178 (163 to 195)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titers (GMTs) of Serotype-specific Opsonophagocytic Activity (OPA) 1 Month After Dose 3: Primary Study Population

End point title	Geometric Mean Titers (GMTs) of Serotype-specific Opsonophagocytic Activity (OPA) 1 Month After Dose 3: Primary Study Population[57]

End point description:

OPA titers for the 20 pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F, 8, 10A, 11A, 12F, 15B, 22F, and 33F) were determined in randomly selected subsets of subjects at 1

month after Dose 3. Results were expressed as OPA titers. GMTs and 2-sided CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs based on the Student's t distribution. Dose 3 evaluable immunogenicity population = eligible subjects 42-112 days of age at first vaccination, received all 3 doses as randomized with 335-386 days of age at Dose 3, at least 1 valid immunogenicity results from blood collection within 27 to 56 days after Dose 3, no major protocol deviations. "Number of Subjects Analyzed"= subjects in Dose 3 evaluable immunogenicity population; "n"= subjects with valid assay results for specified OPA serotype.

End point type	Secondary

End point timeframe:

1 Month after Dose 3

Notes:

[57] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms

End point values	20vPnC: Primary Study Population	13vPnC: Primary Study Population		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	497	504		
Units: Titers				
geometric mean (confidence interval 95%)				
Serotype 1, n=104, 97	54 (43 to 69)	101 (79 to 129)		
Serotype 3, n=105, 98	99 (84 to 117)	129 (111 to 150)		
Serotype 4, n=99, 100	904 (752 to 1086)	992 (777 to 1266)		
Serotype 5, n=106, 98	60 (50 to 72)	82 (66 to 101)		
Serotype 6A, n=105, 96	1101 (897 to 1350)	1304 (1018 to 1671)		
Serotype 6B, n=102, 96	537 (408 to 706)	864 (664 to 1125)		
Serotype 7F, n=100, 103	1811 (1553 to 2112)	2197 (1905 to 2533)		
Serotype 9V, n=97, 99	3254 (2596 to 4079)	4544 (3681 to 5610)		
Serotype 14, n=105, 95	738 (606 to 899)	926 (751 to 1142)		
Serotype 18C, n=98, 102	1296 (1048 to 1602)	1870 (1489 to 2348)		
Serotype 19A, n=99, 100	754 (627 to 907)	707 (558 to 896)		
Serotype 19F, n=105, 97	183 (140 to 237)	258 (192 to 347)		
Serotype 23F, n=100, 101	697 (530 to 917)	975 (734 to 1296)		
Serotype 8, n=92, 105	1398 (1088 to 1796)	31 (25 to 39)		
Serotype 10A, n=91, 107	3403 (2600 to 4455)	69 (52 to 91)		
Serotype 11A, n=87, 92	2966 (2212 to 3978)	66 (51 to 85)		
Serotype 12F, n=88, 108	5501 (4499 to 6725)	29 (25 to 35)		
Serotype 15B, n=91, 504	2676 (1948 to 3677)	23 (18 to 30)		
Serotype 22F, n=83, 103	6523 (4848 to 8777)	17 (13 to 24)		

Serotype 33F, n=72, 99	11315 (8107 to 15794)	708 (545 to 920)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Fold Rise (GMFRs) of IgG Concentrations From Before Dose 3 to 1 Month After Dose 3: Primary Study Population

End point title	Geometric Mean Fold Rise (GMFRs) of IgG Concentrations From Before Dose 3 to 1 Month After Dose 3: Primary Study Population[58]

End point description:

20vPnC serotypes included: 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F, and 33F. Assay results below the LLOQ were set to 0.5*LLOQ in the analysis. GMFRs and the corresponding 2-sided CIs were calculated by exponentiating the mean logarithm of the fold rises and the corresponding CIs (based on the Student's t distribution). Dose 3 evaluable immunogenicity population = eligible subjects 42-112 days of age at first vaccination, received all 3 doses as randomized with 335-386 days of age at Dose 3, at least 1 valid immunogenicity results from blood collection within 27 to 56 days after Dose 3, no major protocol deviations. "Number of Subjects Analyzed"= subjects in Dose 3 evaluable immunogenicity population; "n"= subjects with valid IgG assay results for specified serotype at both timepoints

End point type	Secondary

End point timeframe:

1 month after Dose 3

Notes:

[58] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms

End point values	20vPnC: Primary Study Population	13vPnC: Primary Study Population		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	497	504		
Units: Fold rise				
geometric mean (confidence interval 95%)				
Serotype 1, n=482, 495	13.9 (12.7 to 15.3)	13.9 (12.8 to 15.1)		
Serotype 3, n=482, 495	13.7 (12.4 to 15.1)	15.2 (13.9 to 16.7)		
Serotype 4, n=482, 495	29.8 (27.0 to 32.9)	27.7 (25.0 to 30.6)		
Serotype 5, n=482, 495	14.0 (12.9 to 15.2)	13.6 (12.6 to 14.7)		
Serotype 6A, n=482, 493	26.9 (24.2 to 30.0)	28.7 (25.9 to 31.7)		
Serotype 6B, n=481, 493	36.8 (33.3 to 40.6)	40.2 (36.8 to 44.0)		
Serotype 7F, n=482, 495	8.5 (7.9 to 9.2)	9.3 (8.6 to 10.0)		
Serotype 9V, n=482, 495	22.5 (20.4 to 24.7)	19.9 (18.3 to 21.6)		

Serotype 14, n=480, 494	9.7 (8.7 to 10.8)	8.4 (7.6 to 9.4)		
Serotype 18C, n=482, 495	15.8 (14.5 to 17.1)	17.0 (15.7 to 18.4)		
Serotype 19A, n=481, 495	39.3 (34.6 to 44.7)	40.7 (36.4 to 45.5)		
Serotype 19F, n=482, 495	20.5 (18.4 to 22.9)	21.4 (19.4 to 23.7)		
Serotype 23F, n=482, 495	32.3 (29.2 to 35.7)	38.3 (34.7 to 42.4)		
Serotype 8, n=483, 493	12.7 (11.6 to 13.9)	1.4 (1.3 to 1.5)		
Serotype 10A, n=484, 495	14.8 (13.3 to 16.4)	1.1 (1.0 to 1.2)		
Serotype 11A, n=484, 495	13.8 (12.4 to 15.3)	1.1 (1.0 to 1.2)		
Serotype 12F, n=484, 495	16.5 (15.0 to 18.0)	1.0 (1.0 to 1.1)		
Serotype 15B, n=484, 495	13.4 (11.9 to 15.1)	1.3 (1.2 to 1.4)		
Serotype 22F, n=484, 495	12.8 (11.5 to 14.3)	1.3 (1.1 to 1.4)		
Serotype 33F, n=484, 494	12.9 (11.6 to 14.3)	1.1 (1.0 to 1.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Predefined Antibody Levels for Concomitant Vaccine Antigens 1 Month After Dose 2: Primary Study Population

End point title	Percentage of Subjects With Predefined Antibody Levels for Concomitant Vaccine Antigens 1 Month After Dose 2: Primary Study Population[59]

End point description:

Diphtheria & tetanus toxoids:concentration(conc) of antibody(AB)(in international units[IU]) to diphtheria & tetanus toxoid(prespecified level>=0.1 IU/mL); Pertussis antigens-pertussis toxin (PT),filamentous hemagglutinin (FHA),pertactin (PRN):prespecified level>=observed antipertussis AB concentration achieved by 95% of 13vPnC recipient; HBsAg prespecified level >=10 milli-IU per mL (mIU/mL); Poliovirus strains (types 1, 2, and 3): prespecified level: >=1:8; Haemophilus influenzae type b(Hib): prespecified level>=0.15 mcg/mL polyribosylribitol phosphate (anti-PRP) in mcg/mL.Dose3 EIP=eligible subject 42-112 day(D) of age at 1st vaccine,received 2 dose as randomized,1 valid immunogenicity result within 27-56 D after Dose2."Number of Subjects Analyzed"=subjects in Dose 3 evaluable immunogenicity population; Concomitant vaccine response was assessed from subset of randomly selected study subjects.

End point type	Secondary

End point timeframe:

1 month after Dose 2

Notes:

[59] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms

End point values	20vPnC: Primary Study Population	13vPnC: Primary Study Population		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	567	562		
Units: Percentage of subjects				
number (confidence interval 95%)				
Diphtheria toxoid, n=170, 179	85.0 (79.3 to 89.6)	89.5 (84.4 to 93.4)		
Tetanus toxoid, n=191, 197	95.5 (91.6 to 97.9)	98.5 (95.7 to 99.7)		
Pertussis: PT, n=189, 190	94.5 (90.4 to 97.2)	95.0 (91.0 to 97.6)		
Pertussis: FHA, n=187, 190	93.5 (89.1 to 96.5)	95.0 (91.0 to 97.6)		
Pertussis: PRN, n=187, 190	93.5 (89.1 to 96.5)	95.0 (91.0 to 97.6)		
Poliovirus: Type 1, n=91, 102	94.8 (88.3 to 98.3)	98.1 (93.2 to 99.8)		
Poliovirus: Type 2, n=85, 95	88.5 (80.4 to 94.1)	91.3 (84.2 to 96.0)		
Poliovirus: Type 3, n=92, 104	95.8 (89.7 to 98.9)	100.0 (96.5 to 100.0)		
Haemophilus influenzae type b, n=207, 193	100.0 (98.2 to 100.0)	100.0 (98.1 to 100.0)		

Statistical analyses

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Diphtheria: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions (20vPnC - 13vPnC) expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	-4.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.2
upper limit	2.1

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Tetanus: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions (20vPnC - 13vPnC) expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population

Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	-3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7
upper limit	0.4

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
PT: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions (20vPnC - 13vPnC) expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.2
upper limit	4.1

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
FHA: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions (20vPnC - 13vPnC) expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	-1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.4
upper limit	3.3

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
PRN: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions (20vPnC - 13vPnC) expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	-1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.4
upper limit	3.3

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Poliovirus Type 1: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions (20vPnC - 13vPnC) expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	-3.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10
upper limit	2.2

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Poliovirus Type 2: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions (20vPnC - 13vPnC) expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	-2.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.8
upper limit	5.8

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Poliovirus Type 3: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions (20vPnC - 13vPnC) expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	-4.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.2
upper limit	-0.5

Statistical analysis title	20vPnC Versus 13vPnC
Statistical analysis description:	
Hib: 2-Sided 95% CI based on the Miettinen and Nurminen method for the difference in proportions (20vPnC - 13vPnC) expressed as a percentage.	
Comparison groups	20vPnC: Primary Study Population v 13vPnC: Primary Study Population
Number of subjects included in analysis	1129
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Percent difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	2

Secondary: Percentage of Subjects With Predefined Pneumococcal IgG Antibody 1 Month After Dose 3: Russian Cohort

End point title	Percentage of Subjects With Predefined Pneumococcal IgG Antibody 1 Month After Dose 3: Russian Cohort[60]

End point description:

Predefined IgG concentrations were as follows: for serotype 1, 3, 4, 6A, 7F, 9V, 14, 18C, 19F, 23F, 8, 10A, 11A, 12F, 15B, 22F, 33F: >=0.35 microgram per mL (mcg/mL), for serotype 5: >=0.23 mcg/mL, for serotype 6B. >=0.10 mcg/mL and for serotype 19A: >=0.12 mcg/mL. 95% CI was based on the Clopper and Pearson method. Dose 3 evaluable immunogenicity population = eligible subjects 42-70 days of age at first vaccination, received all 3 doses as randomized with 335-455 days of age at Dose 3, at least 1 valid immunogenicity results from blood collection within 27 to 56 days after Dose 3, no major protocol deviations. "Number of Subjects Analyzed"= subjects in Dose 3 evaluable immunogenicity population.

End point type	Secondary

End point timeframe:

1 Month after Dose 3

Notes:

[60] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms

End point values	20vPnC: Russian Cohort	13vPnC: Russian Cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	24		
Units: Percentage of subjects				
number (confidence interval 95%)				
Serotype 1	90.9 (70.8 to 98.9)	83.3 (62.6 to 95.3)		
Serotype 3	68.2 (45.1 to 86.1)	50.0 (29.1 to 70.9)		
Serotype 4	95.5 (77.2 to 99.9)	100.0 (85.8 to 100.0)		
Serotype 5	90.9 (70.8 to 98.9)	91.7 (73.0 to 99.0)		
Serotype 6A	95.5 (77.2 to 99.9)	100.0 (85.8 to 100.0)		
Serotype 6B	90.9 (70.8 to 98.9)	91.7 (73.0 to 99.0)		
Serotype 7F	95.5 (77.2 to 99.0)	100.0 (85.8 to 100.0)		
Serotype 9V	100.0 (84.6 to 100.0)	83.3 (62.6 to 95.3)		
Serotype 14	90.9 (70.8 to 98.9)	100.0 (85.8 to 100.0)		
Serotype 18C	90.9 (70.8 to 98.9)	95.8 (78.9 to 99.9)		
Serotype 19A	100.0 (84.6 to 100.0)	95.8 (78.9 to 99.9)		
Serotype 19F	100.0 (84.6 to 100.0)	91.7 (73.0 to 99.0)		
Serotype 23F	90.9 (70.8 to 98.9)	79.2 (57.8 to 92.9)		
Serotype 8	68.2 (45.1 to 86.1)	25.0 (9.8 to 46.7)		
Serotype 10A	68.2 (45.1 to 86.1)	16.7 (4.7 to 37.4)		
Serotype 11A	77.3 (54.6 to 92.2)	20.8 (7.1 to 42.2)		
Serotype 12F	36.4 (17.2 to 59.3)	4.2 (0.1 to 21.1)		
Serotype 15B	90.9 (70.8 to 98.9)	20.8 (7.1 to 42.2)		

Serotype 22F	63.6 (40.7 to 82.8)	12.5 (2.7 to 32.4)		
Serotype 33F	72.7 (49.8 to 89.3)	20.8 (7.1 to 42.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: GMTs of Serotype-specific OPA 1 Month After Dose 2: Russian Cohort

End point title	GMTs of Serotype-specific OPA 1 Month After Dose 2: Russian Cohort[61]

End point description:

OPA titers for the 20 pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F, 8, 10A, 11A, 12F, 15B, 22F, and 33F) were determined in randomly selected subsets of subjects at 1 month after Dose 2. Results were expressed as OPA titers. GMTs and 2-sided CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs based on the Student's t distribution. Dose 2 evaluable immunogenicity population: eligible subjects 42-70 days of age at first vaccination, received first 2 doses as randomized, at least 1 valid immunogenicity results from blood collection (27 to 56 days after Dose 2), no other major protocol deviations. "Number of Subjects Analyzed"= subjects in Dose 2 evaluable immunogenicity population, "n"= subjects with valid OPA assay results for specified serotype.

End point type	Secondary

End point timeframe:

1 month after Dose 2

Notes:

[61] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms

End point values	20vPnC: Russian Cohort	13vPnC: Russian Cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	27		
Units: Titers				
geometric mean (confidence interval 95%)				
Serotype 1, n=8, 9	17 (7 to 40)	33 (10 to 105)		
Serotype 3, n=8, 9	79 (42 to 149)	31 (13 to 73)		
Serotype 4, n=8, 9	166 (38 to 736)	163 (32 to 840)		
Serotype 5, n=8, 9	28 (11 to 76)	31 (14 to 71)		
Serotype 6A, n=8, 9	222 (32 to 1553)	247 (60 to 1011)		
Serotype 6B, n=7, 8	314 (27 to 3584)	216 (39 to 1186)		
Serotype 7F, n=8, 9	809 (481 to 1361)	717 (246 to 2084)		
Serotype 9V, n=8, 9	218 (70 to 676)	293 (85 to 1008)		
Serotype 14, n=7, 9	984 (492 to 1970)	247 (69 to 886)		
Serotype 18C, n=8, 9	968 (403 to 2326)	268 (43 to 1655)		

Serotype 19A, n=7, 9	314 (68 to 1443)	31 (8 to 118)		
Serotype 19F, n=8, 9	120 (27 to 529)	230 (48 to 1097)		
Serotype 23F, n=8, 9	35 (6 to 196)	56 (9 to 346)		
Serotype 8, n=7, 9	203 (19 to 2155)	38 (9 to 161)		
Serotype 10A, n=6, 5	559 (50 to 6233)	232 (8 to 6478)		
Serotype 11A, n=6, 7	3537 (863 to 14497)	2717 (470 to 15716)		
Serotype 12F, n=7, 9	698 (77 to 6301)	198 (41 to 960)		
Serotype 15B, n=7, 8	142 (9 to 2269)	242 (18 to 3267)		
Serotype 22F, n=7, 8	413 (32 to 5406)	499 (28 to 8837)		
Serotype 33F, n=7, 9	3508 (349 to 35250)	3961 (706 to 22238)		

Statistical analyses

No statistical analyses for this end point

Secondary: GMTs of Serotype-specific OPA 1 Month After Dose 3: Russian Cohort

End point title	GMTs of Serotype-specific OPA 1 Month After Dose 3: Russian Cohort[62]

End point description:

OPA titers for the 20 pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F, 8, 10A, 11A, 12F, 15B, 22F, and 33F) were determined in randomly selected subsets of subjects at 1 month after Dose 3. Results were expressed as OPA titers. GMTs and 2-sided CIs were calculated by exponentiating the mean logarithm of the titers and the corresponding CIs based on the Student's t distribution. Dose 3 evaluable immunogenicity population = eligible subjects 42-70 days of age at first vaccination, received all 3 doses as randomized with 335-455 days of age at Dose 3, at least 1 valid immunogenicity results from blood collection within 27 to 56 days after Dose 3, no major protocol deviations. "Number of Subjects Analyzed"= subjects in Dose 3 evaluable immunogenicity population; "n"= subjects with valid OPA assay results for specified serotype.

End point type	Secondary

End point timeframe:

1 Month after Dose 3

Notes:

[62] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was planned to be analysed only for the specified reporting arms

End point values	20vPnC: Russian Cohort	13vPnC: Russian Cohort		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	24		
Units: Titers				
geometric mean (confidence interval 95%)				
Serotype 1, n=8, 9	85 (17 to 421)	93 (22 to 394)		
Serotype 3, n=8, 9	126 (41 to 383)	107 (37 to 309)		

Serotype 4, n=8, 8	310 (86 to 1123)	429 (38 to 4863)		
Serotype 5, n=8, 9	116 (28 to 476)	108 (26 to 456)		
Serotype 6A, n=7, 9	2922 (311 to 27459)	1580 (393 to 6351)		
Serotype 6B, n=7, 7	4417 (998 to 19951)	1397 (150 to 12967)		
Serotype 7F, n=8, 8	1039 (509 to 2122)	1411 (373 to 5340)		
Serotype 9V, n=8, 7	1574 (369 to 6711)	1067 (150 to 7583)		
Serotype 14, n=7, 9	1151 (321 to 4132)	628 (137 to 2890)		
Serotype 18C, n=8, 8	583 (149 to 2284)	973 (89 to 10606)		
Serotype 19A, n=8, 7	652 (131 to 3234)	435 (14 to 13833)		
Serotype 19F, n=7, 9	1570 (239 to 10337)	701 (124 to 3958)		
Serotype 23F, n=8, 8	152 (24 to 966)	410 (22 to 7594)		
Serotype 8, n=4, 6	368 (11 to 12078)	149 (9 to 2337)		
Serotype 10A, n=4, 6	2851 (1309 to 6210)	117 (15 to 916)		
Serotype 11A, n=4, 4	7137 (1036 to 49164)	1789 (36 to 89068)		
Serotype 12F, n=4, 7	757 (15 to 37522)	241 (16 to 3734)		
Serotype 15B, n=5, 7	822 (42 to 16070)	147 (10 to 2214)		
Serotype 22F, n=4, 7	1983 (390 to 10085)	1635 (165 to 16157)		
Serotype 33F, n=3, 7	5903 (53 to 657862)	3619 (948 to 13817)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Local reactions & Systemic events [systematic assessment (SA)]: Within 7 days after Dose 1,2, or 3; SAEs(non-SA): From Dose 1 up to 1 month after Dose 3 & other AEs (non-SAE): From Dose 1 up to 1 month after Dose 2 & from Dose 3 up to 1 month after Dose 3

Adverse event reporting additional description:

Same event may appear as both SAE & non-SAE.However, what is presented are distinct events.Event may be classified as serious in 1 subject & non-serious in another, or 1 subject may have experienced both during study.Safety analysis set evaluated. MedDRA 25.0 was used for primary cohorts and 26.0 was used for Russian cohort.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	20vPnC: Primary Study Population

Reporting group description:

Infants 42 to 112 days of age were enrolled to receive 3 doses of 0.5 mL 20vPnC intramuscularly. Dose 1 was given at enrollment and Dose 2 was given 42 to 63 days later. Dose 3 was administered at 11 to 12 months of age.

Reporting group title	13vPnC: Russian Cohort

Reporting group description:

Infants 42 to 70 days of age were enrolled to receive 3 doses of 0.5 mL 13vPnC intramuscularly. Dose 1 was given at enrollment and Dose 2 was given 60 to 90 days later. Dose 3 was administered at 28 to 42 days after Dose 2.

Reporting group title	20vPnC: Russian Cohort

Reporting group description:

Infants 42 to 70 days of age were enrolled to receive 3 doses of 0.5 mL 20vPnC intramuscularly. Dose 1 was given at enrollment and Dose 2 was given 60 to 90 days later. Dose 3 was administered at 28 to 42 days after Dose 2

Reporting group title	13vPnC: Primary Study Population

Reporting group description:

Infants 42 to 112 days of age were enrolled to receive 3 doses of 0.5 mL 13vPnC intramuscularly. Dose 1 was given at enrollment and Dose 2 was given 42 to 63 days later. Dose 3 was administered at 11 to 12 months of age.

Serious adverse events	20vPnC: Primary Study Population	13vPnC: Russian Cohort	20vPnC: Russian Cohort
Total subjects affected by serious adverse events			
subjects affected / exposed	34 / 601 (5.66%)	0 / 27 (0.00%)	0 / 24 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign salivary gland neoplasm	Additional description: MedDRA 26.0 was used for Russian Cohorts.		

subjects affected / exposed	1 / 601 (0.17%)	0 / 27 (0.00%)	0 / 24 (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
General disorders and administration site conditions			
Inflammation	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 601 (0.17%)	0 / 27 (0.00%)	0 / 24 (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
Immune system disorders			
Anaphylactic reaction	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	0 / 601 (0.00%)	0 / 27 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Bronchial hyperreactivity	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 601 (0.17%)	0 / 27 (0.00%)	0 / 24 (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
Injury, poisoning and procedural complications			
Foreign body aspiration	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	0 / 601 (0.00%)	0 / 27 (0.00%)	0 / 24 (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
Thermal burn	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 601 (0.17%)	0 / 27 (0.00%)	0 / 24 (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
Skull fracture	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 601 (0.17%)	0 / 27 (0.00%)	0 / 24 (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			
Aorticopulmonary septal defect	Additional description: MedDRA 26.0 was used for Russian Cohorts.		

subjects affected / exposed	1 / 601 (0.17%)	0 / 27 (0.00%)	0 / 24 (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
Bronchogenic cyst	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 601 (0.17%)	0 / 27 (0.00%)	0 / 24 (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			
Febrile convulsion	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 601 (0.17%)	0 / 27 (0.00%)	0 / 24 (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
Cerebral haemorrhage	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 601 (0.17%)	0 / 27 (0.00%)	0 / 24 (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
Intracranial pressure increased	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 601 (0.17%)	0 / 27 (0.00%)	0 / 24 (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
Hypotonia	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	0 / 601 (0.00%)	0 / 27 (0.00%)	0 / 24 (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
Seizure	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	0 / 601 (0.00%)	0 / 27 (0.00%)	0 / 24 (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
Blood and lymphatic system disorders			
Thymus enlargement	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	0 / 601 (0.00%)	0 / 27 (0.00%)	0 / 24 (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
Lymphadenitis	Additional description: MedDRA 26.0 was used for Russian Cohorts.		

subjects affected / exposed	1 / 601 (0.17%)	0 / 27 (0.00%)	0 / 24 (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
Neutropenia	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	0 / 601 (0.00%)	0 / 27 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	0 / 601 (0.00%)	0 / 27 (0.00%)	0 / 24 (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
Skin and subcutaneous tissue disorders			
Urticaria	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	0 / 601 (0.00%)	0 / 27 (0.00%)	0 / 24 (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
Dermatitis atopic	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	0 / 601 (0.00%)	0 / 27 (0.00%)	0 / 24 (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
Renal and urinary disorders			
Nephritis	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	0 / 601 (0.00%)	0 / 27 (0.00%)	0 / 24 (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
Tubulointerstitial nephritis	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 601 (0.17%)	0 / 27 (0.00%)	0 / 24 (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
Vesicoureteric reflux	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 601 (0.17%)	0 / 27 (0.00%)	0 / 24 (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

Infections and infestations			
Bacterial infection	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 601 (0.17%)	0 / 27 (0.00%)	0 / 24 (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
Bronchiolitis	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	2 / 601 (0.33%)	0 / 27 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 601 (0.17%)	0 / 27 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	0 / 601 (0.00%)	0 / 27 (0.00%)	0 / 24 (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
Erythema infectiosum	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	0 / 601 (0.00%)	0 / 27 (0.00%)	0 / 24 (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
Escherichia urinary tract infection	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	0 / 601 (0.00%)	0 / 27 (0.00%)	0 / 24 (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
Gastroenteritis	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	4 / 601 (0.67%)	0 / 27 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis rotavirus	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	0 / 601 (0.00%)	0 / 27 (0.00%)	0 / 24 (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
Lower respiratory tract infection viral	Additional description: MedDRA 26.0 was used for Russian Cohorts.		

subjects affected / exposed	0 / 601 (0.00%)	0 / 27 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal infection	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	2 / 601 (0.33%)	0 / 27 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal viral infection	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	0 / 601 (0.00%)	0 / 27 (0.00%)	0 / 24 (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
Herpangina	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 601 (0.17%)	0 / 27 (0.00%)	0 / 24 (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
Laryngitis	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 601 (0.17%)	0 / 27 (0.00%)	0 / 24 (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
Gastroenteritis viral	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	0 / 601 (0.00%)	0 / 27 (0.00%)	0 / 24 (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
Otitis media	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	0 / 601 (0.00%)	0 / 27 (0.00%)	0 / 24 (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
Oral candidiasis	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	0 / 601 (0.00%)	0 / 27 (0.00%)	0 / 24 (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
Meningitis enteroviral	Additional description: MedDRA 26.0 was used for Russian Cohorts.		

subjects affected / exposed	0 / 601 (0.00%)	0 / 27 (0.00%)	0 / 24 (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
Meningitis	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 601 (0.17%)	0 / 27 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 601 (0.17%)	0 / 27 (0.00%)	0 / 24 (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
Urinary tract infection	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	4 / 601 (0.67%)	0 / 27 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 601 (0.17%)	0 / 27 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchiolitis	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	2 / 601 (0.33%)	0 / 27 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 601 (0.17%)	0 / 27 (0.00%)	0 / 24 (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
Pyelonephritis	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 601 (0.17%)	0 / 27 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia respiratory syncytial viral	Additional description: MedDRA 26.0 was used for Russian Cohorts.		

subjects affected / exposed	1 / 601 (0.17%)	0 / 27 (0.00%)	0 / 24 (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
Viral infection	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	3 / 601 (0.50%)	0 / 27 (0.00%)	0 / 24 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Underweight	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 601 (0.17%)	0 / 27 (0.00%)	0 / 24 (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
Type 1 diabetes mellitus	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 601 (0.17%)	0 / 27 (0.00%)	0 / 24 (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
Poor feeding infant	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	0 / 601 (0.00%)	0 / 27 (0.00%)	0 / 24 (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
Feeding disorder	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	0 / 601 (0.00%)	0 / 27 (0.00%)	0 / 24 (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

Serious adverse events	13vPnC: Primary Study Population		
Total subjects affected by serious adverse events			
subjects affected / exposed	40 / 603 (6.63%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign salivary gland neoplasm	Additional description: MedDRA 26.0 was used for Russian Cohorts.		

subjects affected / exposed	0 / 603 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Inflammation	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	0 / 603 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Anaphylactic reaction	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 603 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Bronchial hyperreactivity	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	0 / 603 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Foreign body aspiration	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 603 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thermal burn	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	0 / 603 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skull fracture	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	0 / 603 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Congenital, familial and genetic disorders			
Aorticopulmonary septal defect	Additional description: MedDRA 26.0 was used for Russian Cohorts.		

subjects affected / exposed	0 / 603 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchogenic cyst	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	0 / 603 (0.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Febrile convulsion	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 603 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cerebral haemorrhage	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	0 / 603 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intracranial pressure increased	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	0 / 603 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypotonia	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 603 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Seizure	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 603 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Thymus enlargement	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 603 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lymphadenitis	Additional description: MedDRA 26.0 was used for Russian Cohorts.		

subjects affected / exposed	1 / 603 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neutropenia	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 603 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Colitis	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 603 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Urticaria	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 603 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dermatitis atopic	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 603 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Nephritis	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 603 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tubulointerstitial nephritis	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	0 / 603 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vesicoureteric reflux	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	0 / 603 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Infections and infestations			
Bacterial infection	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	0 / 603 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchiolitis	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	2 / 603 (0.33%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Bronchitis	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	0 / 603 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
COVID-19	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 603 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Erythema infectiosum	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 603 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Escherichia urinary tract infection	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	2 / 603 (0.33%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	5 / 603 (0.83%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis rotavirus	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 603 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lower respiratory tract infection viral	Additional description: MedDRA 26.0 was used for Russian Cohorts.		

subjects affected / exposed	1 / 603 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal infection	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	2 / 603 (0.33%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal viral infection	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 603 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Herpangina	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	0 / 603 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Laryngitis	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	2 / 603 (0.33%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis viral	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 603 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Otitis media	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 603 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Oral candidiasis	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 603 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Meningitis enteroviral	Additional description: MedDRA 26.0 was used for Russian Cohorts.		

subjects affected / exposed	1 / 603 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Meningitis	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	0 / 603 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	3 / 603 (0.50%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	4 / 603 (0.66%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Skin infection	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	0 / 603 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory syncytial virus bronchiolitis	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 603 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis acute	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 603 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	0 / 603 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia respiratory syncytial viral	Additional description: MedDRA 26.0 was used for Russian Cohorts.		

subjects affected / exposed	0 / 603 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Viral infection	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 603 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Underweight	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	0 / 603 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Type 1 diabetes mellitus	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	0 / 603 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Poor feeding infant	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	1 / 603 (0.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Feeding disorder	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	3 / 603 (0.50%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	20vPnC: Primary Study Population	13vPnC: Russian Cohort	20vPnC: Russian Cohort
Total subjects affected by non-serious adverse events			
subjects affected / exposed	589 / 601 (98.00%)	20 / 27 (74.07%)	17 / 24 (70.83%)
Nervous system disorders			
Hypersomnia (INCREASED SLEEP)	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
alternative assessment type: Systematic			

subjects affected / exposed	495 / 601 (82.36%)	11 / 27 (40.74%)	8 / 24 (33.33%)
occurrences (all)	965	16	11
General disorders and administration site conditions			
Injection site erythema (REDNESS)	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
alternative assessment type: Systematic			
subjects affected / exposed	331 / 601 (55.07%)	4 / 27 (14.81%)	3 / 24 (12.50%)
occurrences (all)	534	6	4
Injection site pain (PAIN)	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
alternative assessment type: Systematic			
subjects affected / exposed	343 / 601 (57.07%)	6 / 27 (22.22%)	7 / 24 (29.17%)
occurrences (all)	555	7	8
Injection site swelling (SWELLING)	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
alternative assessment type: Systematic			
subjects affected / exposed	260 / 601 (43.26%)	3 / 27 (11.11%)	4 / 24 (16.67%)
occurrences (all)	431	3	5
Pyrexia (FEVER)	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
alternative assessment type: Systematic			
subjects affected / exposed	212 / 601 (35.27%)	4 / 27 (14.81%)	2 / 24 (8.33%)
occurrences (all)	282	4	3
Psychiatric disorders			
Irritability (IRRITABILITY)	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
alternative assessment type: Systematic			
subjects affected / exposed	553 / 601 (92.01%)	15 / 27 (55.56%)	13 / 24 (54.17%)
occurrences (all)	1266	24	18
Infections and infestations			
Upper respiratory tract infection	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	21 / 601 (3.49%)	0 / 27 (0.00%)	1 / 24 (4.17%)
occurrences (all)	21	0	1
Metabolism and nutrition disorders			
Decreased appetite (DECREASED APPETITE)	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
alternative assessment type: Systematic			
subjects affected / exposed	345 / 601 (57.40%)	8 / 27 (29.63%)	9 / 24 (37.50%)
occurrences (all)	522	10	10

Non-serious adverse events	13vPnC: Primary Study Population		

Total subjects affected by non-serious adverse events			
subjects affected / exposed	593 / 603 (98.34%)		
Nervous system disorders			
Hypersomnia (INCREASED SLEEP)	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
alternative assessment type: Systematic			
subjects affected / exposed	512 / 603 (84.91%)		
occurrences (all)	970		
General disorders and administration site conditions			
Injection site erythema (REDNESS)	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
alternative assessment type: Systematic			
subjects affected / exposed	333 / 603 (55.22%)		
occurrences (all)	531		
Injection site pain (PAIN)	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
alternative assessment type: Systematic			
subjects affected / exposed	347 / 603 (57.55%)		
occurrences (all)	557		
Injection site swelling (SWELLING)	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
alternative assessment type: Systematic			
subjects affected / exposed	251 / 603 (41.63%)		
occurrences (all)	388		
Pyrexia (FEVER)	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
alternative assessment type: Systematic			
subjects affected / exposed	214 / 603 (35.49%)		
occurrences (all)	273		
Psychiatric disorders			
Irritability (IRRITABILITY)	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
alternative assessment type: Systematic			
subjects affected / exposed	556 / 603 (92.21%)		
occurrences (all)	1258		
Infections and infestations			
Upper respiratory tract infection	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
subjects affected / exposed	35 / 603 (5.80%)		
occurrences (all)	40		
Metabolism and nutrition disorders			
Decreased appetite (DECREASED APPETITE)	Additional description: MedDRA 26.0 was used for Russian Cohorts.		
alternative assessment type: Systematic			

subjects affected / exposed occurrences (all)	323 / 603 (53.57%) 465		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 June 2021	amendment 2:Added noninferiority of IgG GMCs and the percentage of participants with predefined thresholds after 2 infant doses as primary immunogenicity objectives and moved objective for IgG percentage of participants with predefined thresholds after toddler dose to secondary objective, based on Scientific Advice from CHMP. The statistical sections for these objectives were updated accordingly. Added country-specific appendix for Russian cohort to add approximately 60 participants and address comments from a national agency on schedule, concomitant vaccines and other study aspects, including management of Russian cohort data. Made updates throughout the protocol on managing the Russian cohort.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported