



Clinical trial results:

A phase III, open, controlled study to evaluate the immunogenicity, safety and reactogenicity of GSK Biologicals' 10- valent pneumococcal conjugate vaccine administered to children with sickle cell disease between 8 weeks and 2 years of age, as compared to healthy children.

Summary

EudraCT number	2012-000254-64
Trial protocol	Outside EU/EEA
Global end of trial date	23 May 2013

Results information

Result version number	v2
This version publication date	28 April 2016
First version publication date	25 July 2015
Version creation reason	• New data added to full data set Data for secondary endpoints have been added.

Trial information

Trial identification

Sponsor protocol code	114056
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01175083
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMA-000673-PIP01-09
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	04 August 2015
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	23 May 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the immunogenicity of GSK Biologicals' 10-valent pneumococcal conjugate vaccine when co-administered with DTPw-HBV/Hib and OPV vaccines in children with sickle cell disease, one month after completion of the 3-dose primary vaccination course before 6 months of age

Protection of trial subjects:

All subjects were supervised after vaccination/product administration with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 June 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Burkina Faso: 300
Worldwide total number of subjects	300
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	300
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:

During the screening the following steps occurred: check for inclusion/exclusion criteria, contraindications/precautions, medical history of the subjects and signing informed consent forms.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	<6S Group

Arm description:

Children below 6 months of age with sickle cell disease, receiving a 3-dose primary vaccination with 10Pn-PD-DiT vaccine at approximately 8-12-16 weeks of age and booster vaccination at 9-10 months of age. Subjects received DTPw-HBV/Hib + OPV as co-administered vaccines. The allowable intervals between the primary vaccination doses were 28-42 days.

Arm type	Experimental
Investigational medicinal product name	GSK1024850A (Synflorix™)
Investigational medicinal product code	
Other name	GSK Biologicals' 10-valent pneumococcal polysaccharide and non-typeable Haemophilus influenzae (H. influenzae) protein D conjugate vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 intramuscular vaccine doses were administered intramuscularly into the right thigh.

Investigational medicinal product name	Tritanrix-HB
Investigational medicinal product code	
Other name	DTPw-HBV
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection, 4 doses in the left thigh.

Investigational medicinal product name	Polio Sabin
Investigational medicinal product code	
Other name	OPV
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

4 doses administered orally.

Investigational medicinal product name	Hiberix™
Investigational medicinal product code	
Other name	Hib
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

White frozen dried pellet in monodose vial to be reconstituted with DTPw-HBV vaccine, intramuscular injection 4 doses in the left thigh.

Arm title	<6NS Group
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Arm description:

Healthy children below 6 months of age, receiving a 3-dose primary vaccination with 10Pn-PD-DiT vaccine at approximately 8-12-16 weeks of age and booster vaccination at 9-10 months of age. Subjects received DTPw-HBV/Hib + OPV as co-administered vaccines. The allowable intervals between the primary vaccination doses were 28-42 days.

Arm type	Active comparator
Investigational medicinal product name	GSK1024850A (Synflorix™)
Investigational medicinal product code	
Other name	GSK Biologicals' 10-valent pneumococcal polysaccharide and non-typeable Haemophilus influenzae (H. influenzae) protein D conjugate vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 intramuscular vaccine doses were administered intramuscularly into the right thigh.

Investigational medicinal product name	Tritanrix-HB
Investigational medicinal product code	
Other name	DTPw-HB
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection, 4 doses in the left thigh.

Investigational medicinal product name	Polio Sabin
Investigational medicinal product code	
Other name	OPV
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

4 doses administered orally.

Investigational medicinal product name	Hiberix™
Investigational medicinal product code	
Other name	Hib
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

White frozen dried pellet in monodose vial to be reconstituted with DTPw-HBV vaccine, intramuscular injection 4 doses in the left thigh.

Arm title	7-11S Group
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Arm description:

Children between 7-11 months of age with sickle cell disease, receiving a 2-dose primary vaccination with 10Pn-PD-DiT vaccine starting at 7-11 months of age with an interval of at least 4 weeks (28-42 days) between primary doses. Subjects received a booster after an interval of 2 to 4 months since the previous dose.

Arm type	Experimental
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Investigational medicinal product name	GSK1024850A (Synflorix™)
Investigational medicinal product code	
Other name	GSK Biologicals' 10-valent pneumococcal polysaccharide and non-typeable Haemophilus influenzae (H. influenzae) protein D conjugate vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
2 intramuscular vaccine doses were administered intramuscularly into the right thigh.	
Arm title	7-11NS Group
Arm description:	
Healthy children between 7-11 months of age, receiving a 2-dose primary vaccination with 10Pn-PD-DiT vaccine starting at 7-11 months of age with an interval of at least 4 weeks (28-42 days) between primary doses. Subjects received a booster after an interval of 2 to 4 months since the previous dose.	
Arm type	Active comparator
Investigational medicinal product name	GSK1024850A (Synflorix™)
Investigational medicinal product code	
Other name	GSK Biologicals' 10-valent pneumococcal polysaccharide and non-typeable Haemophilus influenzae (H. influenzae) protein D conjugate vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
2 intramuscular vaccine doses were administered intramuscularly into the right thigh.	
Arm title	12-23S Group
Arm description:	
Children between 12-23 months of age with sickle cell disease, receiving a 2-dose vaccination with 10Pn-PD-DiT vaccine starting at 12-23 months of age with an interval of 2 to 4 months between doses.	
Arm type	Experimental
Investigational medicinal product name	GSK1024850A (Synflorix™)
Investigational medicinal product code	
Other name	GSK Biologicals' 10-valent pneumococcal polysaccharide and non-typeable Haemophilus influenzae (H. influenzae) protein D conjugate vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
2 intramuscular vaccine doses were administered intramuscularly into the right thigh.	
Arm title	12-23NS Group
Arm description:	
Healthy children between 12-23 months of age, receiving a 2-dose vaccination with 10Pn-PD-DiT vaccine starting at 12-23 months of age with an interval of 2 to 4 months between doses.	
Arm type	Active comparator
Investigational medicinal product name	GSK1024850A (Synflorix™)
Investigational medicinal product code	
Other name	GSK Biologicals' 10-valent pneumococcal polysaccharide and non-typeable Haemophilus influenzae (H. influenzae) protein D conjugate vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
2 intramuscular vaccine doses were administered intramuscularly into the right thigh.	

Number of subjects in period 1	<6S Group	<6NS Group	7-11S Group
Started	50	50	50
Completed	49	49	49
Not completed	1	1	1
Adverse event, serious fatal	-	-	1
Consent withdrawn by subject	-	-	-
Not coming back for booster vaccination	1	1	-
Lost to follow-up	-	-	-

Number of subjects in period 1	7-11NS Group	12-23S Group	12-23NS Group
Started	50	50	50
Completed	49	50	47
Not completed	1	0	3
Adverse event, serious fatal	-	-	-
Consent withdrawn by subject	1	-	2
Not coming back for booster vaccination	-	-	-
Lost to follow-up	-	-	1

Baseline characteristics

Reporting groups

Reporting group title	<6S Group
Reporting group description: Children below 6 months of age with sickle cell disease, receiving a 3-dose primary vaccination with 10Pn-PD-DiT vaccine at approximately 8-12-16 weeks of age and booster vaccination at 9-10 months of age. Subjects received DTPw-HBV/Hib + OPV as co-administered vaccines. The allowable intervals between the primary vaccination doses were 28-42 days.	
Reporting group title	<6NS Group
Reporting group description: Healthy children below 6 months of age, receiving a 3-dose primary vaccination with 10Pn-PD-DiT vaccine at approximately 8-12-16 weeks of age and booster vaccination at 9-10 months of age. Subjects received DTPw-HBV/Hib + OPV as co-administered vaccines. The allowable intervals between the primary vaccination doses were 28-42 days.	
Reporting group title	7-11S Group
Reporting group description: Children between 7-11 months of age with sickle cell disease, receiving a 2-dose primary vaccination with 10Pn-PD-DiT vaccine starting at 7-11 months of age with an interval of at least 4 weeks (28-42 days) between primary doses. Subjects received a booster after an interval of 2 to 4 months since the previous dose.	
Reporting group title	7-11NS Group
Reporting group description: Healthy children between 7-11 months of age, receiving a 2-dose primary vaccination with 10Pn-PD-DiT vaccine starting at 7-11 months of age with an interval of at least 4 weeks (28-42 days) between primary doses. Subjects received a booster after an interval of 2 to 4 months since the previous dose.	
Reporting group title	12-23S Group
Reporting group description: Children between 12-23 months of age with sickle cell disease, receiving a 2-dose vaccination with 10Pn-PD-DiT vaccine starting at 12-23 months of age with an interval of 2 to 4 months between doses.	
Reporting group title	12-23NS Group
Reporting group description: Healthy children between 12-23 months of age, receiving a 2-dose vaccination with 10Pn-PD-DiT vaccine starting at 12-23 months of age with an interval of 2 to 4 months between doses.	

Reporting group values	<6S Group	<6NS Group	7-11S Group
Number of subjects	50	50	50
Age categorical Units: Subjects			
Infants and toddlers (28 days-23 months)	50	50	50
Gender categorical Units: Subjects			
Female	21	29	26
Male	29	21	24

Reporting group values	7-11NS Group	12-23S Group	12-23NS Group
Number of subjects	50	50	50
Age categorical Units: Subjects			
Infants and toddlers (28 days-23 months)	50	50	50

Gender categorical Units: Subjects			
Female	32	15	24
Male	18	35	26

Reporting group values	Total		
Number of subjects	300		
Age categorical Units: Subjects			
Infants and toddlers (28 days-23 months)	300		
Gender categorical Units: Subjects			
Female	147		
Male	153		

End points

End points reporting groups

Reporting group title	<6S Group
Reporting group description: Children below 6 months of age with sickle cell disease, receiving a 3-dose primary vaccination with 10Pn-PD-DiT vaccine at approximately 8-12-16 weeks of age and booster vaccination at 9-10 months of age. Subjects received DTPw-HBV/Hib + OPV as co-administered vaccines. The allowable intervals between the primary vaccination doses were 28-42 days.	
Reporting group title	<6NS Group
Reporting group description: Healthy children below 6 months of age, receiving a 3-dose primary vaccination with 10Pn-PD-DiT vaccine at approximately 8-12-16 weeks of age and booster vaccination at 9-10 months of age. Subjects received DTPw-HBV/Hib + OPV as co-administered vaccines. The allowable intervals between the primary vaccination doses were 28-42 days.	
Reporting group title	7-11S Group
Reporting group description: Children between 7-11 months of age with sickle cell disease, receiving a 2-dose primary vaccination with 10Pn-PD-DiT vaccine starting at 7-11 months of age with an interval of at least 4 weeks (28-42 days) between primary doses. Subjects received a booster after an interval of 2 to 4 months since the previous dose.	
Reporting group title	7-11NS Group
Reporting group description: Healthy children between 7-11 months of age, receiving a 2-dose primary vaccination with 10Pn-PD-DiT vaccine starting at 7-11 months of age with an interval of at least 4 weeks (28-42 days) between primary doses. Subjects received a booster after an interval of 2 to 4 months since the previous dose.	
Reporting group title	12-23S Group
Reporting group description: Children between 12-23 months of age with sickle cell disease, receiving a 2-dose vaccination with 10Pn-PD-DiT vaccine starting at 12-23 months of age with an interval of 2 to 4 months between doses.	
Reporting group title	12-23NS Group
Reporting group description: Healthy children between 12-23 months of age, receiving a 2-dose vaccination with 10Pn-PD-DiT vaccine starting at 12-23 months of age with an interval of 2 to 4 months between doses.	

Primary: Concentrations of antibodies against Vaccine Pneumococcal Serotypes - <6S and <6NS groups.

End point title	Concentrations of antibodies against Vaccine Pneumococcal Serotypes - <6S and <6NS groups. ^{[1][2]}
End point description: Antibodies assessed for this outcome measure were those against the vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (ANTI-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F). Antibody concentrations were measured by 22F enzyme-linked immunosorbent assay (ELISA), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 µg/mL. Antibody concentrations < 0.05 µg/mL were given an arbitrary value of half the cut-off for the purpose of GMC calculation. Primary outcome variables correspond to Results at Month 3.	
End point type	Primary
End point timeframe: Prior to (Month 0) and one month after primary vaccination (Month 3), prior to (Month 8) and one month after booster vaccination (Month 9)	
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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was	

performed.

[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: Results are provided only for 2 groups as timeframe has been defined specifically for those 2 groups.

End point values	<6S Group	<6NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	46		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-1 [Month 0] (N=46,42)	0.09 (0.06 to 0.12)	0.09 (0.06 to 0.12)		
Anti-1 [Month 3] (N=48,46)	3.51 (2.77 to 4.44)	3.63 (2.91 to 4.53)		
Anti-1 [Month 8] (N=44,38)	0.67 (0.54 to 0.84)	0.69 (0.52 to 0.9)		
Anti-1 [Month 9] (N=44,38)	5.34 (4.07 to 7.02)	5.14 (3.52 to 7.5)		
Anti-4 [Month 0] (N=48,45)	0.04 (0.03 to 0.06)	0.06 (0.04 to 0.08)		
Anti-4 [Month 3] (N=47,46)	4.25 (3.18 to 5.67)	3.51 (2.73 to 4.51)		
Anti-4 [Month 8] (N=44,38)	1.2 (0.91 to 1.59)	1.08 (0.77 to 1.52)		
Anti-4 [Month 9] (N=44,38)	7.04 (5.53 to 8.97)	6.02 (4.4 to 8.24)		
Anti-5 [Month 0] (N=48,46)	0.06 (0.05 to 0.09)	0.07 (0.06 to 0.1)		
Anti-5 [Month 3] (N=47,46)	5.15 (4.07 to 6.51)	5.94 (4.91 to 7.18)		
Anti-5 [Month 8] (N=44,38)	1.13 (0.87 to 1.47)	1.23 (0.93 to 1.63)		
Anti-5 [Month 9] (N=43,37)	6.3 (4.94 to 8.04)	6.91 (4.92 to 9.73)		
Anti-6B [Month 0] (N=47,40)	0.07 (0.05 to 0.09)	0.11 (0.07 to 0.18)		
Anti-6B [Month 3] (N=48,46)	1.29 (0.83 to 1.99)	1.13 (0.74 to 1.72)		
Anti-6B [Month 8] (N=44,38)	1.94 (1.55 to 2.44)	1.62 (1.25 to 2.09)		
Anti-6B [Month 9] (N=44,37)	5.07 (4.16 to 6.18)	5 (3.71 to 6.74)		
Anti-7F [Month 0] (N=47,44)	0.08 (0.06 to 0.11)	0.13 (0.09 to 0.19)		
Anti-7F [Month 3] (N=48,46)	4.91 (3.84 to 6.28)	4.28 (3.49 to 5.26)		
Anti-7F [Month 8] (N=44,38)	1.83 (1.41 to 2.37)	1.57 (1.21 to 2.05)		
Anti-7F [Month 9] (N=44,38)	9.03 (7.18 to 11.37)	8.19 (6.18 to 10.86)		
Anti-9V [Month 0] (N=47,44)	0.12 (0.08 to 0.16)	0.12 (0.09 to 0.16)		
Anti-9V [Month 3] (N=47,46)	4.56 (3.51 to 5.92)	4.59 (3.7 to 5.7)		
Anti-9V [Month 8] (N=44,38)	1.61 (1.17 to 2.21)	1.44 (1.13 to 1.82)		
Anti-9V [Month 9] (N=44,38)	8.19 (6.61 to 10.14)	7.95 (5.94 to 10.63)		

Anti-14 [Month 0] (N=48,44)	0.77 (0.53 to 1.12)	0.65 (0.42 to 0.99)		
Anti-14 [Month 3] (N=46,46)	4.3 (3.08 to 6)	5.95 (4.27 to 8.29)		
Anti-14 [Month 8] (N=44,38)	2.58 (1.9 to 3.51)	2.1 (1.32 to 3.34)		
Anti-14 [Month 9] (N=44,38)	8.66 (6.91 to 10.85)	7.43 (4.72 to 11.7)		
Anti-18C [Month 0] (N=48,45)	0.13 (0.1 to 0.18)	0.13 (0.09 to 0.18)		
Anti-18C [Month 3] (N=47,45)	14.6 (11.01 to 19.36)	11.33 (8.47 to 15.17)		
Anti-18C [Month 8] (N=44,38)	3.82 (2.97 to 4.92)	3.16 (2.32 to 4.31)		
Anti-18C [Month 9] (N=44,38)	16.52 (12.81 to 21.32)	16.74 (12.98 to 21.58)		
Anti-19F [Month 0] (N=48,45)	0.34 (0.23 to 0.51)	0.3 (0.21 to 0.44)		
Anti-19F [Month 3] (N=47,46)	11.87 (9.05 to 15.57)	9.78 (7.01 to 13.64)		
Anti-19F [Month 8] (N=44,38)	3.31 (2.51 to 4.38)	3.27 (2.21 to 4.84)		
Anti-19F [Month 9] (N=44,38)	10.96 (8.37 to 14.34)	11.27 (8.18 to 15.54)		
Anti-23F [Month 0] (N=48,43)	0.13 (0.09 to 0.2)	0.1 (0.07 to 0.14)		
Anti-23F [Month 3] (N=48,46)	1.32 (0.9 to 1.93)	1.41 (0.95 to 2.11)		
Anti-23F [Month 8] (N=44,38)	0.67 (0.48 to 0.94)	0.77 (0.51 to 1.17)		
Anti-23F [Month 9] (N=44,38)	4.86 (3.34 to 7.07)	4.54 (2.7 to 7.62)		

Statistical analyses

No statistical analyses for this end point

Primary: Concentrations of Antibodies against Protein D (PD) - <6S and <6NS groups.

End point title	Concentrations of Antibodies against Protein D (PD) - <6S and <6NS groups. ^{[3][4]}
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End point description:

Anti-protein D (Anti-PD) antibody concentrations by Enzyme-Linked Immunosorbent Assay (ELISA) were calculated, expressed as geometric mean concentrations (GMCs) in ELISA unit per milli-liter (EL.U/mL) and tabulated. The seropositivity cut-off for the assay was ≥ 100 EL.U/mL. Antibody concentrations < 100 EL.U/mL were given an arbitrary value of half the cut-off for the purpose of GMC calculation. Primary outcome variables correspond to Results at Month 3.

End point type	Primary
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End point timeframe:

Prior to (Month 0) and one month after primary vaccination (Month 3), prior to (Month 8) and one month after booster vaccination (Month 9)

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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

[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: Results are provided only for 2 groups as timeframe has been defined specifically for those 2 groups.

End point values	<6S Group	<6NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	46		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD [Month 0] (N=47,46)	64.75 (50.56 to 82.92)	70.97 (53.71 to 93.78)		
Anti-PD [Month 3] (N=47,46)	2789.09 (2313.89 to 3361.87)	3065.4 (2530.54 to 3713.31)		
Anti-PD [Month 8] (N=44,38)	859.87 (681.75 to 1084.52)	840.88 (641.5 to 1102.23)		
Anti-PD [Month 9] (N=44,38)	2871.72 (2338.21 to 3526.96)	3137.87 (2459.92 to 4002.68)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and Grade 3 solicited local symptoms (Primary vaccination -<6S and <6NS Groups)

End point title	Number of subjects with any and Grade 3 solicited local symptoms (Primary vaccination -<6S and <6NS Groups) ^[5]
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End point description:

Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = pain that prevented normal activity. Grade 3 redness/swelling = redness/swelling spreading beyond 30 millimeters (mm) of injection site.

End point type	Secondary
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End point timeframe:

During the 4-day (Days 0-3) post-vaccination period following each dose and across doses.

Notes:

[5] - 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: Results are provided only for 2 groups as timeframe has been defined specifically for those 2 groups.

End point values	<6S Group	<6NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: Subjects				
Any Pain, Dose 1	8	12		
Grade 3 Pain, Dose 1	0	0		
Any Redness, Dose 1	0	0		
Grade 3 Redness, Dose 1	0	0		
Any Swelling, Dose 1	0	0		
Grade 3 Swelling, Dose 1	0	0		

Any Pain, Dose 2	7	7		
Grade 3 Pain, Dose 2	0	0		
Any Redness, Dose 2	0	0		
Grade 3 Redness, Dose 2	0	0		
Any Swelling, Dose 2	0	1		
Grade 3 Swelling, Dose 2	0	0		
Any Pain, Dose 3	4	6		
Grade 3 Pain, Dose 3	0	0		
Any Redness, Dose 3	0	0		
Grade 3 Redness, Dose 3	0	0		
Any Swelling, Dose 3	0	0		
Grade 3 Swelling, Dose 3	0	0		
Any Pain, Across	17	23		
Grade 3 Pain, Across	0	0		
Any Redness, Across	0	0		
Grade 3 Redness, Across	0	0		
Any Swelling, Across	0	1		
Grade 3 Swelling, Across	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any, Grade 3 and related solicited general symptoms (Primary vaccination -<6S and <6NS Groups)

End point title	Number of subjects with any, Grade 3 and related solicited general symptoms (Primary vaccination -<6S and <6NS Groups) ^[6]
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End point description:

Assessed solicited general symptoms were drowsiness, irritability, loss of appetite and fever [defined as rectal temperature equal to or above 38 degrees Celsius (°C)]. Any = occurrence of the symptom regardless of intensity grade. Grade 3 symptom = symptom that prevented normal activity. Grade 3 fever = fever > 40.0 °C. Related = symptom assessed by the investigator as related to the vaccination.

End point type	Secondary
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End point timeframe:

During the 4-day (Days 0-3) post-vaccination period following each dose and across doses.

Notes:

[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: Results are provided only for 2 groups as timeframe has been defined specifically for those 2 groups.

End point values	<6S Group	<6NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: Subjects				
Any Drowsiness, Dose 1	0	0		
Grade 3 Drowsiness, Dose 1	0	0		
Related Drowsiness, Dose 1	0	0		
Any Irritability, Dose 1	0	2		
Grade 3 Irritability, Dose 1	0	0		

Related Irritability, Dose 1	0	0		
Any Loss of appetite, Dose 1	0	0		
Grade 3 Loss of appetite, Dose 1	0	0		
Related Loss of appetite, Dose 1	0	0		
Any Fever, Dose 1	34	31		
Grade 3 Fever, Dose 1	0	0		
Related Fever, Dose 1	31	29		
Any Drowsiness, Dose 2	0	0		
Grade 2 Drowsiness, Dose 2	0	0		
Related Drowsiness, Dose 2	0	0		
Any Irritability, Dose 2	0	0		
Grade 3 Irritability, Dose 2	0	0		
Related Irritability, Dose 2	0	0		
Any Loss of appetite, Dose 2	0	0		
Grade 3 Loss of appetite, Dose 2	0	0		
Related Loss of appetite, Dose 2	0	0		
Any Fever, Dose 2	40	30		
Grade 3 Fever, Dose 2	0	0		
Related Fever, Dose 2	38	28		
Any Drowsiness, Dose 3	0	0		
Grade 3 Drowsiness, Dose 3	0	0		
Related Drowsiness, Dose 3	0	0		
Any Irritability, Dose 3	3	4		
Grade 3 Irritability, Dose 3	0	0		
Related Irritability, Dose 3	3	3		
Any Loss of appetite, Dose 3	0	1		
Grade 3 Loss of appetite, Dose 3	0	0		
Related Loss of appetite, Dose 3	0	0		
Any Fever, Dose 3	30	30		
Grade 3 Fever, Dose 3	0	0		
Related Fever, Dose 3	26	28		
Any Drowsiness, Across Doses	0	0		
Grade 3 Drowsiness, Across Doses	0	0		
Related Drowsiness, Across Doses	0	0		
Any Irritability, Across Doses	3	6		
Grade 3 Irritability, Across Doses	0	0		
Related Irritability, Across Doses	3	3		
Any Loss of appetite, Across Doses	0	1		
Grade 3 Loss of appetite, Across Doses	0	0		
Related Loss of appetite, Across Doses	0	0		
Any Fever, Across Doses	48	43		
Grade 3 Fever, Across Doses	0	0		
Related Fever, Across Doses	46	43		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any unsolicited adverse events (AEs) (<6S,

<6NS, 7-11S, 7-11NS Groups)

End point title	Number of subjects with any unsolicited adverse events (AEs) (<6S, <6NS, 7-11S, 7-11NS Groups) ^[7]
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End point description:

An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product and reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any was defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination.

End point type	Secondary
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End point timeframe:

Within 31 days (Days 0-30) post primary and booster vaccination.

Notes:

[7] - 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: Results are provided only for 4 groups as timeframe has been defined specifically for those 4 groups.

End point values	<6S Group	<6NS Group	7-11S Group	7-11NS Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	50	50	50
Units: Subjects				
Any AEs post primary vaccination [N=50,50,50,50]	37	34	32	37
Any AEs post-booster vaccination [N=49,49,50,50]	8	17	18	12

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs) (all groups).

End point title	Number of subjects with serious adverse events (SAEs) (all groups).
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End point description:

Serious adverse events (SAEs) assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity.

End point type	Secondary
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End point timeframe:

During the entire study period.

End point values	<6S Group	<6NS Group	7-11S Group	7-11NS Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	50	50	50
Units: Subjects				
Any SAEs	3	9	3	4

End point values	12-23S Group	12-23NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: Subjects				
Any SAEs	2	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any unsolicited adverse events (AEs) (12-23S and 12-23NS Groups)

End point title	Number of subjects with any unsolicited adverse events (AEs) (12-23S and 12-23NS Groups) ^[8]
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End point description:

An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product and reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any was defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination.

End point type	Secondary
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End point timeframe:

Within the 31-day (Days 0-30) post vaccination period.

Notes:

[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: Results are provided only for 2 groups as timeframe has been defined specifically for those 2 groups.

End point values	12-23S Group	12-23NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: Subjects				
Any AE(s)	23	25		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and Grade 3 solicited local symptoms (Booster vaccination - <6S, <6NS, 7-11S, 7-11NS Groups).

End point title	Number of subjects with any and Grade 3 solicited local symptoms (Booster vaccination - <6S, <6NS, 7-11S, 7-11NS Groups). ^[9]
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End point description:

Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom

regardless of intensity grade. Grade 3 pain = pain that prevented normal activity. Grade 3 redness/swelling = redness/swelling spreading beyond 30 millimeters (mm) of injection site.

End point type	Secondary
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End point timeframe:

During the 4-day (Days 0-3) post-booster vaccination period.

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Results are provided only for 4 groups as timeframe has been defined specifically for those 4 groups.

End point values	<6S Group	<6NS Group	7-11S Group	7-11NS Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	49	50	50
Units: Subjects				
Any Pain	11	6	3	0
Grade 3 Pain	0	0	0	0
Any Redness	0	0	0	0
Grade 3 Redness	0	0	0	0
Any Swelling	1	0	1	0
Grade 3 Swelling	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and Grade 3 solicited local symptoms.(12-23S and 12-23NS Groups)

End point title	Number of subjects with any and Grade 3 solicited local symptoms.(12-23S and 12-23NS Groups) ^[10]
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End point description:

Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = pain that prevented normal activity. Grade 3 redness/swelling = redness/swelling spreading beyond 30 millimeters (mm) of injection site.

End point type	Secondary
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End point timeframe:

During the 4-day (Days 0-3) post-vaccination period following each dose and across doses.

Notes:

[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: Results are provided only for 2 groups as timeframe has been defined specifically for those 2 groups.

End point values	12-23S Group	12-23NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: Subjects				
Any Pain, Dose 1 [N=50,50]	9	6		
Grade 3 Pain, Dose 1 [N=50,50]	0	0		
Any Redness, Dose 1 [N=50,50]	0	0		
Grade 3 Redness, Dose 1 [N=50,50]	0	0		

Any Swelling, Dose 1 [N=50,50]	1	1		
Grade 3 Swelling, Dose 1 [N=50,50]	0	0		
Any Pain, Dose 2 [N=50,48]	5	3		
Grade 3 Pain, Dose 2 [N=50,48]	0	0		
Any Redness, Dose 2 [N=50,48]	0	0		
Grade 3 Redness, Dose 2 [N=50,48]	0	0		
Any Swelling, Dose 2 [N=50,48]	0	0		
Grade 3 Swelling, Dose 2 [N=50,48]	0	0		
Any Pain, Across Doses [N=50,50]	13	9		
Grade 3 Pain, Across Doses [N=50,50]	0	0		
Any Redness, Across Doses [N=50,50]	0	0		
Grade 3 Redness, Across Doses [N=50,50]	0	0		
Any Swelling, Across Doses [N=50,50]	1	1		
Grade 3 Swelling, Across Doses [N=50,50]	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any, Grade 3 and related solicited general symptoms (Primary vaccination - 7-11S and 7-11NS Groups)

End point title	Number of subjects with any, Grade 3 and related solicited general symptoms (Primary vaccination - 7-11S and 7-11NS Groups) ^[11]
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End point description:

Assessed solicited general symptoms were drowsiness, irritability, loss of appetite and fever [defined as rectal temperature equal to or above 38 degrees Celsius (°C)]. Any = occurrence of the symptom regardless of intensity grade. Grade 3 symptom = symptom that prevented normal activity. Grade 3 fever = fever > 40.0 °C. Related = symptom assessed by the investigator as related to the vaccination.

End point type	Secondary
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End point timeframe:

During the 4-day (Days 0-3) post-vaccination period following each dose and across doses.

Notes:

[11] - 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: Results are provided only for 2 groups as timeframe has been defined specifically for those 2 groups.

End point values	7-11S Group	7-11NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: Subjects				
Any Drowsiness, Dose 1	0	1		
Grade 3 Drowsiness, Dose 1	0	0		
Related Drowsiness, Dose 1	0	1		
Any Irritability, Dose 1	0	0		
Grade 3 Irritability, Dose 1	0	0		
Related Irritability, Dose 1	0	0		
Any Loss of appetite, Dose 1	0	0		

Grade 3 Loss of appetite, Dose 1	0	0		
Related Loss of appetite, Dose 1	0	0		
Any Fever, Dose 1	22	26		
Grade 3 Fever, Dose 1	0	0		
Related Fever, Dose 1	19	22		
Any Drowsiness, Dose 2	0	0		
Grade 3 Drowsiness, Dose 2	0	0		
Related Drowsiness, Dose 2	0	0		
Any Irritability, Dose 2	0	0		
Grade 3 Irritability, Dose 2	0	0		
Related Irritability, Dose 2	0	0		
Any Loss of appetite, Dose 2	0	0		
Grade 3 Loss of appetite, Dose 2	0	0		
Related Loss of appetite, Dose 2	0	0		
Any Fever, Dose 2	22	11		
Grade 3 Fever, Dose 2	0	0		
Related Fever, Dose 2	20	9		
Any Drowsiness, Across Doses	0	1		
Grade 3 Drowsiness, Across Doses	0	0		
Related Drowsiness, Across Doses	0	1		
Any Irritability, Across Doses	0	0		
Grade 3 Irritability, Across Doses	0	0		
Related Irritability, Across Doses	0	0		
Any Loss of appetite, Across Doses	0	0		
Grade 3 Loss of appetite, Across Doses	0	0		
Related Loss of appetite, Across Doses	0	0		
Any Fever, Across Doses	31	29		
Grade 3 Fever, Across Doses	0	0		
Related Fever, Across Doses	29	25		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any, Grade 3 and related solicited general symptoms. (Booster vaccination – <6S, <6NS, 7-11S, 7-11NS groups)

End point title	Number of subjects with any, Grade 3 and related solicited general symptoms. (Booster vaccination – <6S, <6NS, 7-11S, 7-11NS groups) ^[12]
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End point description:

Assessed solicited general symptoms were drowsiness, irritability, loss of appetite and fever [defined as rectal temperature equal to or above 38 degrees Celsius (°C)]. Any = occurrence of the symptom regardless of intensity grade. Grade 3 symptom = symptom that prevented normal activity. Grade 3 fever = fever > 40.0 °C. Related = symptom assessed by the investigator as related to the vaccination.

End point type	Secondary
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End point timeframe:

During the 4-day (Days 0-3) post-booster vaccination period.

Notes:

[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: Results are provided only for 4 groups as timeframe has been defined specifically for those 4 groups.

End point values	<6S Group	<6NS Group	7-11S Group	7-11NS Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	49	50	50
Units: Subjects				
Any Drowsiness	0	0	0	0
Grade 3 Drowsiness	0	0	0	0
Related Drowsiness	0	0	0	0
Any Irritability	6	0	0	0
Grade 3 Irritability	0	0	0	0
Related Irritability	5	0	0	0
Any Loss of appetite	0	0	0	0
Grade 3 Loss of appetite	0	0	0	0
Related Loss of appetite	0	0	0	0
Any Fever	38	31	14	13
Grade 3 Fever	0	0	0	0
Related Fever	35	28	13	13

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and Grade 3 solicited local symptoms (Primary vaccination – 7-11S and 7-11NS Groups)

End point title	Number of subjects with any and Grade 3 solicited local symptoms (Primary vaccination – 7-11S and 7-11NS Groups) ^[13]
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End point description:

Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = pain that prevented normal activity. Grade 3 redness/swelling = redness/swelling spreading beyond 30 millimeters (mm) of injection site.

End point type	Secondary
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End point timeframe:

During the 4-day (Days 0-3) post-vaccination period following each dose and across doses.

Notes:

[13] - 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: Results are provided only for 2 groups as timeframe has been defined specifically for those 2 groups.

End point values	7-11S Group	7-11NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: Subjects				
Any Pain, Dose 1	7	10		
Grade 3 Pain, Dose 1	0	0		
Any Redness, Dose 1	0	0		

Grade 3 Redness, Dose 1	0	0		
Any Swelling, Dose 1	0	0		
Grade 3 Swelling, Dose 1	0	0		
Any Pain, Dose 2	5	7		
Grade 3 Pain, Dose 2	0	0		
Any Redness, Dose 2	0	0		
Grade 3 Redness, Dose 2	0	0		
Any Swelling, Dose 2	0	1		
Grade 3 Swelling, Dose 2	0	0		
Any Pain, Across Doses	12	15		
Grade 3 Pain, Across Doses	0	0		
Any Redness, Across Doses	0	0		
Grade 3 Redness, Across Doses	0	0		
Any Swelling, Across Doses	0	1		
Grade 3 Swelling, Across Doses	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any, Grade 3 and related solicited general symptoms (12-23S and 12-23NS Groups)

End point title	Number of subjects with any, Grade 3 and related solicited general symptoms (12-23S and 12-23NS Groups) ^[14]
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End point description:

Assessed solicited general symptoms were drowsiness, irritability, loss of appetite and fever [defined as rectal temperature equal to or above 38 degrees Celsius (°C)]. Any = occurrence of the symptom regardless of intensity grade. Grade 3 symptom = symptom that prevented normal activity. Grade 3 fever = fever > 40.0 °C. Related = symptom assessed by the investigator as related to the vaccination.

End point type	Secondary
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End point timeframe:

During the 4-day (Days 0-3) post-vaccination period following each dose and across doses.

Notes:

[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: Results are provided only for 2 groups as timeframe has been defined specifically for those 2 groups.

End point values	12-23S Group	12-23NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: Subjects				
Any Drowsiness, Dose 1 [N=50,50]	0	0		
Grade 3 Drowsiness, Dose 1 [N=50,50]	0	0		
Related Drowsiness, Dose 1 [N=50,50]	0	0		
Any Irritability, Dose 1 [N=50,50]	1	0		
Grade 3 Irritability, Dose 1 [N=50,50]	0	0		
Related Irritability, Dose 1 [N=50,50]	1	0		
Any Loss of appetite, Dose 1 [N=50,50]	0	1		
Grade 3 Loss of appetite, Dose 1 [N=50,50]	0	0		

Related Loss of appetite, Dose 1 [N=50,50]	0	1		
Any Fever, Dose 1 [N=50,50]	21	15		
Grade 3 Fever, Dose 1 [N=50,50]	0	0		
Related Fever, Dose 1 [N=50,50]	21	13		
Any Drowsiness, Dose 2 [N=50,48]	0	0		
Grade 3 Drowsiness, Dose 2 [N=50,48]	0	0		
Related Drowsiness, Dose 2 [N=50,48]	0	0		
Any Irritability, Dose 2 [N=50,48]	1	0		
Grade 3 Irritability, Dose 2 [N=50,48]	0	0		
Related Irritability, Dose 2 [N=50,48]	1	0		
Any Loss of appetite, Dose 2 [N=50,48]	0	0		
Grade 3 Loss of appetite, Dose 2 [N=50,48]	0	0		
Related Loss of appetite, Dose 2 [N=50,48]	0	0		
Any Fever, Dose 2 [N=50,48]	12	12		
Grade 3 Fever, Dose 2 [N=50,48]	0	0		
Related Fever, Dose 2 [N=50,48]	10	9		
Any Drowsiness, Across Doses [N=50,50]	0	0		
Grade 3 Drowsiness, Across Doses [N=50,50]	0	0		
Related Drowsiness, Across Doses [N=50,50]	0	0		
Any Irritability, Across Doses [N=50,50]	2	0		
Grade 3 Irritability, Across Doses [N=50,50]	0	0		
Related Irritability, Across Doses [N=50,50]	2	0		
Any Loss of appetite, Across Doses [N=50,50]	0	1		
Grade 3 Loss of appetite, Across Doses [N=50,50]	0	0		
Related Loss of appetite, Across Doses [N=50,50]	0	1		
Any Fever, Across Doses [N=50,50]	29	20		
Grade 3 Fever, Across Doses [N=50,50]	0	0		
Related Fever, Across Doses [N=50,50]	28	17		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against Cross-reactive Pneumococcal Serotype 6A and 19A - <6S and <6NS groups.

End point title	Concentrations of antibodies against Cross-reactive Pneumococcal Serotype 6A and 19A - <6S and <6NS groups. ^[15]
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End point description:

Antibodies assessed for this outcome measure were those against the cross-reactive pneumococcal serotype 6A (ANTI-6A) and 19A (ANTI-19A). Antibody concentrations were measured by 22F enzyme-linked immunosorbent assay (ELISA), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 µg/mL. Antibody concentrations < 0.05 µg/mL were given an arbitrary value of half the cut-off

for the purpose of GMC calculation.

End point type	Secondary
End point timeframe:	
Prior to (Month 0) and one month after primary vaccination (Month 3), prior to (Month 8) and one month after booster vaccination (Month 9)	

Notes:

[15] - 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: Results are provided only for 2 groups as timeframe has been defined specifically for those 2 groups.

End point values	<6S Group	<6NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	45		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-6A [Month 0] (N=47,41)	0.1 (0.07 to 0.14)	0.15 (0.1 to 0.23)		
Anti-6A [Month 3] (N=46,43)	0.12 (0.08 to 0.17)	0.1 (0.07 to 0.13)		
Anti-6A [Month 8] (N=37,30)	0.4 (0.27 to 0.61)	0.18 (0.1 to 0.3)		
Anti-6A [Month 9] (N=36,29)	0.48 (0.31 to 0.74)	0.36 (0.23 to 0.55)		
Anti-19A [Month 0] (N=47,44)	0.24 (0.17 to 0.36)	0.23 (0.16 to 0.33)		
Anti-19A [Month 3] (N=48,45)	0.26 (0.17 to 0.39)	0.25 (0.17 to 0.37)		
Anti-19A [Month 8] (N=44,38)	0.23 (0.15 to 0.37)	0.21 (0.13 to 0.35)		
Anti-19A [Month 9] (N=44,37)	1.09 (0.65 to 1.83)	0.85 (0.5 to 1.43)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against Vaccine Pneumococcal Serotypes - 7-11S and 7-11NS group.

End point title	Concentrations of antibodies against Vaccine Pneumococcal Serotypes - 7-11S and 7-11NS group. ^[16]
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End point description:

Antibodies assessed for this outcome measure were those against the vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (ANTI-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F). Antibody concentrations were measured by 22F enzyme-linked immunosorbent assay (ELISA), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 µg/mL. Antibody concentrations < 0.05 µg/mL were given an arbitrary value of half the cut-off for the purpose of GMC calculation.

End point type	Secondary
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End point timeframe:

Prior to (Month 0) and one month after primary vaccination (Month 2), prior to (Month 3) and one month after booster vaccination (Month 4)

Notes:

[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: Results are provided only for 2 groups as timeframe has been defined specifically for those 2 groups.

End point values	7-11S Group	7-11NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-1 [Month 0] (N=48,46)	0.03 (0.03 to 0.03)	0.04 (0.03 to 0.05)		
Anti-1 [Month 2] (N=50,48)	5.48 (4.34 to 6.93)	3.99 (3.24 to 4.91)		
Anti-1 [Month 3] (N=50,49)	2.68 (2.12 to 3.39)	2.44 (1.99 to 2.98)		
Anti-1 [Month 4] (N=49,48)	5.51 (4.27 to 7.1)	4.92 (3.74 to 6.48)		
Anti-4 [Month 0] (N=49,50)	0.03 (0.03 to 0.04)	0.03 (0.02 to 0.04)		
Anti-4 [Month 2] (N=49,47)	10.88 (8.94 to 13.24)	7.55 (6 to 9.5)		
Anti-4 [Month 3] (N=50,48)	5.72 (4.66 to 7.03)	4.32 (3.51 to 5.32)		
Anti-4 [Month 4] (N=49,48)	9.75 (7.67 to 12.39)	7.88 (6.28 to 9.89)		
Anti-5 [Month 0] (N=48,50)	0.04 (0.03 to 0.06)	0.06 (0.05 to 0.08)		
Anti-5 [Month 2] (N=50,47)	6.76 (5.14 to 8.89)	4.59 (3.58 to 5.88)		
Anti-5 [Month 3] (N=50,49)	3.68 (2.87 to 4.73)	3.4 (2.66 to 4.33)		
Anti-5 [Month 4] (N=49,48)	7.75 (6.05 to 9.92)	7.87 (6.02 to 10.29)		
Anti-6B [Month 0] (N=49,46)	0.03 (0.02 to 0.03)	0.03 (0.02 to 0.03)		
Anti-6B [Month 2] (N=49,49)	1.61 (1.03 to 2.52)	1.48 (1.02 to 2.13)		
Anti-6B [Month 3] (N=50,49)	1.51 (1.06 to 2.15)	1.35 (0.98 to 1.87)		
Anti-6B [Month 4] (N=49,48)	3.12 (2.1 to 4.64)	2.93 (2.17 to 3.95)		
Anti-7F [Month 0] (N=50,50)	0.04 (0.03 to 0.05)	0.04 (0.03 to 0.05)		
Anti-7F [Month 2] (N=49,49)	8.51 (6.94 to 10.42)	6.67 (5.44 to 8.19)		
Anti-7F [Month 3] (N=50,49)	5.46 (4.37 to 6.83)	4.68 (3.76 to 5.81)		
Anti-7F [Month 4] (N=48,48)	11.08 (8.9 to 13.81)	10.29 (7.92 to 13.37)		
Anti-9V [Month 0] (N=49,48)	0.04 (0.03 to 0.05)	0.04 (0.03 to 0.05)		
Anti-9V [Month 2] (N=49,49)	2.55 (1.86 to 3.49)	1.67 (1.21 to 2.29)		
Anti-9V [Month 3] (N=50,49)	1.9 (1.42 to 2.56)	1.52 (1.16 to 2)		
Anti-9V [Month 4] (N=49,48)	4.73 (3.4 to 6.58)	3.76 (2.67 to 5.3)		

Anti-14 [Month 0] (N=47,48)	0.08 (0.06 to 0.12)	0.07 (0.05 to 0.1)		
Anti-14 [Month 2] (N=50,46)	4.91 (3.48 to 6.95)	4.81 (3.67 to 6.29)		
Anti-14 [Month 3] (N=50,49)	4.71 (3.45 to 6.43)	4.98 (4.01 to 6.2)		
Anti-14 [Month 4] (N=49,48)	10.24 (7.96 to 13.18)	10.69 (8.34 to 13.71)		
Anti-18C [Month 0] (N=50,49)	0.03 (0.03 to 0.03)	0.03 (0.03 to 0.04)		
Anti-18C [Month 2] (N=49,47)	12.92 (9.93 to 16.82)	14.62 (11.61 to 18.4)		
Anti-18C [Month 3] (N=50,49)	8.43 (6.53 to 10.88)	11.49 (9.24 to 14.29)		
Anti-18C [Month 4] (N=49,48)	23.57 (18.38 to 30.22)	31.88 (25.34 to 40.11)		
Anti-19F [Month 0] (N=49,48)	0.05 (0.04 to 0.06)	0.04 (0.04 to 0.06)		
Anti-19F [Month 2] (N=50,49)	11.13 (7.97 to 15.54)	9.77 (6.16 to 15.48)		
Anti-19F [Month 3] (N=50,49)	6.54 (4.79 to 8.92)	7.39 (5.04 to 10.81)		
Anti-19F [Month 4] (N=49,48)	15.59 (11.24 to 21.62)	15.85 (10.52 to 23.89)		
Anti-23F [Month 0] (N=48,48)	0.03 (0.03 to 0.04)	0.04 (0.03 to 0.05)		
Anti-23F [Month 2] (N=50,48)	1.29 (0.79 to 2.1)	0.93 (0.6 to 1.45)		
Anti-23F [Month 3] (N=50,48)	1 (0.65 to 1.56)	1.08 (0.74 to 1.56)		
Anti-23F [Month 4] (N=49,48)	3.11 (1.85 to 5.24)	3.17 (2.04 to 4.91)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against Cross-reactive Pneumococcal Serotype 6A and 19A – 7-11S and 7-11NS groups.

End point title	Concentrations of antibodies against Cross-reactive Pneumococcal Serotype 6A and 19A – 7-11S and 7-11NS groups. ^[17]
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End point description:

Antibodies assessed for this outcome measure were those against the cross-reactive pneumococcal serotype 6A (ANTI-6A) and 19A (ANTI-19A). Antibody concentrations were measured by 22F enzyme-linked immunosorbent assay (ELISA), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 µg/mL. Antibody concentrations < 0.05 µg/mL were given an arbitrary value of half the cut-off for the purpose of GMC calculation.

End point type	Secondary
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End point timeframe:

Prior to (Month 0) and one month after primary vaccination (Month 2), prior to (Month 3) and one month after booster vaccination (Month 4)

Notes:

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

Justification: Results are provided only for 2 groups as timeframe has been defined specifically for those

2 groups.

End point values	7-11S Group	7-11NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	49		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-6A [Month 0] (N=47,44)	0.03 (0.03 to 0.04)	0.03 (0.03 to 0.04)		
Anti-6A [Month 2] (N=48,46)	0.18 (0.11 to 0.3)	0.16 (0.11 to 0.24)		
Anti-6A [Month3] (N=50,47)	0.23 (0.14 to 0.37)	0.22 (0.16 to 0.32)		
Anti-6A [Month 4] (N=48,48)	0.44 (0.28 to 0.7)	0.43 (0.3 to 0.62)		
Anti-19A [Month 0] (N=48,49)	0.04 (0.03 to 0.06)	0.06 (0.04 to 0.1)		
Anti-19A [Month 2] (N=50,49)	0.46 (0.28 to 0.76)	0.77 (0.5 to 1.18)		
Anti-19A [Month3] (N=50,48)	0.44 (0.27 to 0.7)	0.77 (0.51 to 1.17)		
Anti-19A [Month 4] (N=49,48)	1.49 (0.93 to 2.38)	2.35 (1.5 to 3.67)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against Vaccine Pneumococcal Serotypes - 12-23S and 12-23NS group.

End point title	Concentrations of antibodies against Vaccine Pneumococcal Serotypes - 12-23S and 12-23NS group. ^[18]
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End point description:

Antibodies assessed for this outcome measure were those against the vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (ANTI-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F). Antibody concentrations were measured by 22F enzyme-linked immunosorbent assay (ELISA), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 µg/mL. Antibody concentrations < 0.05 µg/mL were given an arbitrary value of half the cut-off for the purpose of GMC calculation.

End point type	Secondary
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End point timeframe:

Prior to (Month 0), one month after first dose vaccination (Month 2) and one month after second dose vaccination (Month 3)

Notes:

[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: Results are provided only for 2 groups as timeframe has been defined specifically for those 2 groups.

End point values	12-23S Group	12-23NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	47		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-1 [Month 0] (N=47,45)	0.04 (0.03 to 0.05)	0.04 (0.03 to 0.05)		
Anti-1 [Month 2] (N=48,47)	1.39 (1.07 to 1.8)	1.49 (1.18 to 1.89)		
Anti-1 [Month 3] (N=48,46)	4.67 (3.75 to 5.81)	4.26 (3.38 to 5.37)		
Anti-4 [Month 0] (N=48,47)	0.04 (0.03 to 0.05)	0.04 (0.03 to 0.05)		
Anti-4 [Month 2] (N=47,47)	4.22 (3.23 to 5.51)	3.74 (2.96 to 4.72)		
Anti-4 [Month 3] (N=47,46)	8.87 (7.03 to 11.19)	7.02 (5.85 to 8.43)		
Anti-5 [Month 0] (N=48,47)	0.06 (0.04 to 0.08)	0.08 (0.06 to 0.11)		
Anti-5 [Month 2] (N=48,47)	1.06 (0.77 to 1.47)	1.1 (0.83 to 1.44)		
Anti-5 [Month 3] (N=48,46)	5.52 (4.23 to 7.2)	4.07 (3.06 to 5.42)		
Anti-6B [Month 0] (N=48,47)	0.03 (0.03 to 0.04)	0.04 (0.03 to 0.05)		
Anti-6B [Month 2] (N=48,47)	0.41 (0.28 to 0.62)	0.34 (0.24 to 0.48)		
Anti-6B [Month 3] (N=48,46)	1.37 (0.91 to 2.07)	1.25 (0.87 to 1.79)		
Anti-7F [Month 0] (N=48,47)	0.07 (0.05 to 0.11)	0.05 (0.04 to 0.07)		
Anti-7F [Month 2] (N=48,47)	2.74 (2.13 to 3.52)	3.17 (2.56 to 3.93)		
Anti-7F [Month 3] (N=48,46)	6.81 (5.32 to 8.7)	6.36 (5.25 to 7.69)		
Anti-9V [Month 0] (N=48,47)	0.08 (0.05 to 0.12)	0.05 (0.04 to 0.07)		
Anti-9V [Month 2] (N=48,47)	0.99 (0.72 to 1.34)	0.83 (0.62 to 1.11)		
Anti-9V [Month 3] (N=48,46)	2.35 (1.85 to 3)	1.72 (1.31 to 2.25)		
Anti-14 [Month 0] (N=47,46)	0.11 (0.07 to 0.16)	0.09 (0.06 to 0.12)		
Anti-14 [Month 2] (N=48,47)	1.87 (1.46 to 2.4)	1.24 (0.92 to 1.66)		
Anti-14 [Month 3] (N=47,45)	7.59 (5.84 to 9.87)	5.75 (4.33 to 7.62)		
Anti-18C [Month 0] (N=48,47)	0.04 (0.03 to 0.06)	0.05 (0.04 to 0.07)		
Anti-18C [Month 2] (N=48,47)	6.21 (4.77 to 8.1)	6.12 (4.56 to 8.21)		
Anti-18C [Month 3] (N=47,45)	25.52 (20.66 to 31.53)	22.64 (18.14 to 28.26)		
Anti-19F [Month 0] (N=48,47)	0.06 (0.04 to 0.09)	0.08 (0.05 to 0.12)		
Anti-19F [Month 2] (N=48,47)	5.88 (4.44 to 7.8)	5.12 (3.79 to 6.94)		
Anti-19F [Month 3] (N=48,46)	18 (13.97 to 23.2)	14.46 (10.81 to 19.34)		

Anti-23F [Month 0] (N=48,47)	0.03 (0.03 to 0.04)	0.05 (0.03 to 0.07)		
Anti-23F [Month 2] (N=48,47)	0.5 (0.32 to 0.77)	0.35 (0.25 to 0.49)		
Anti-23F [Month 3] (N=47,46)	1.95 (1.32 to 2.87)	1.4 (1.05 to 1.87)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against Cross-reactive Pneumococcal Serotype 6A and 19A – 12-23S and 12-23NS groups.

End point title	Concentrations of antibodies against Cross-reactive Pneumococcal Serotype 6A and 19A – 12-23S and 12-23NS groups. ^[19]
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End point description:

Antibodies assessed for this outcome measure were those against the cross-reactive pneumococcal serotype 6A (ANTI-6A) and 19A (ANTI-19A). Antibody concentrations were measured by 22F enzyme-linked immunosorbent assay (ELISA), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 µg/mL. Antibody concentrations < 0.05 µg/mL were given an arbitrary value of half the cut-off for the purpose of GMC calculation.

End point type	Secondary
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End point timeframe:

Prior to (Month 0), one month after first dose vaccination (Month 2) and one month after second dose vaccination (Month 3)

Notes:

[19] - 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: Results are provided only for 2 groups as timeframe has been defined specifically for those 2 groups.

End point values	12-23S Group	12-23NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	47		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-6A [Month 0] (N=45,44)	0.03 (0.03 to 0.03)	0.04 (0.03 to 0.05)		
Anti-6A [Month 2] (N=47,47)	0.15 (0.1 to 0.23)	0.12 (0.08 to 0.18)		
Anti-6A [Month 3] (N=47,46)	0.39 (0.23 to 0.66)	0.31 (0.2 to 0.48)		
Anti-19A [Month 0] (N=47,45)	0.06 (0.04 to 0.09)	0.07 (0.04 to 0.11)		
Anti-19A [Month 2] (N=48,47)	0.77 (0.5 to 1.17)	0.75 (0.47 to 1.19)		
Anti-19A [Month 3] (N=48,46)	3.15 (2.13 to 4.65)	2.79 (1.93 to 4.05)		

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic Titers Against Vaccine Pneumococcal Serotypes - <6S and <6NS groups.

End point title	Opsonophagocytic Titers Against Vaccine Pneumococcal Serotypes - <6S and <6NS groups. ^[20]
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End point description:

Pneumococcal vaccine serotypes assessed were 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F and were calculated, expressed as geometric mean titers (GMTs). The seropositivity cut-off for the assay was ≥ 8 . Antibody titers < 8 were given an arbitrary value of half the cut-off for the purpose of GMT calculation.

End point type	Secondary
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End point timeframe:

One month after primary vaccination (Month 3), prior to (Month 8) and one month after booster vaccination (Month 9)

Notes:

[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: Results are provided only for 2 groups as timeframe has been defined specifically for those 2 groups.

End point values	<6S Group	<6NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	41		
Units: Titer				
geometric mean (confidence interval 95%)				
Opsono-1 Month 3 (N=45,41)	106.4 (56 to 202.2)	94.6 (49.9 to 179.5)		
Opsono-1 Month 8 (N=41,33)	11.7 (6.8 to 20.1)	10.9 (6 to 20.1)		
Opsono-1 Month 9 (N=41,35)	930.5 (606.3 to 1427.9)	750.4 (401.4 to 1403)		
Opsono-4 Month 3 (N=44,38)	1316.6 (1014 to 1709.7)	992.5 (680 to 1448.4)		
Opsono-4 Month 8 (N=40,31)	222.1 (130.6 to 377.8)	108.3 (51.6 to 227.6)		
Opsono-4 Month 9 (N=41,33)	2064.2 (1625.3 to 2621.8)	2079.3 (1425.7 to 3032.7)		
Opsono-5 Month 3 (N=44,41)	106.9 (66.8 to 171.2)	119.4 (81.4 to 175.2)		
Opsono-5 Month 8 (N=40,33)	14.9 (8.9 to 24.9)	15.8 (9.6 to 26.1)		
Opsono-5 Month 9 (N=41,33)	273.2 (200.6 to 372)	277.5 (168.8 to 456.1)		
Opsono-6B Month 3 (N=41,37)	1043.3 (605.3 to 1798.3)	446.2 (207.4 to 960)		
Opsono-6B Month 8 (N=39,32)	285.3 (150.1 to 542.1)	245.6 (115 to 524.3)		
Opsono-6B Month 9 (N=40,33)	952.2 (638.8 to 1419.3)	989.2 (530.6 to 1843.9)		
Opsono-7F Month 3 (N=42,37)	4644.1 (3519.3 to 6128.4)	4924.2 (3430.2 to 7068.8)		
Opsono-7F Month 8 (N=40,32)	1747.2 (1225.4 to 2491.3)	1585.7 (1133.8 to 2217.8)		

Opsono-7F Month 9 (N=39,32)	7262.9 (5257.6 to 10033.1)	8120.3 (5802.1 to 11364.8)		
Opsono-9V Month 3 (N=46,39)	1438.6 (1084 to 1909.3)	1116.8 (679.6 to 1835.2)		
Opsono-9V Month 8 (N=38,32)	215.5 (97.5 to 476.1)	244.5 (123.9 to 482.2)		
Opsono-9V Month 9 (N=40,32)	2062.3 (1569 to 2710.8)	2987.2 (2149.4 to 4151.6)		
Opsono-14 Month 3 (N=44,41)	1689.9 (1090.7 to 2618.2)	1062.3 (562.8 to 2005.2)		
Opsono-14 Month 8 (N=39,26)	215.9 (113.6 to 410.1)	132.5 (60.3 to 291.5)		
Opsono-14 Month 9 (N=40,33)	1571.5 (1114.2 to 2216.4)	1454.1 (741.8 to 2850.5)		
Opsono-18C Month 3 (N=40,37)	873.8 (591.7 to 1290.4)	524.7 (319.6 to 861.6)		
Opsono-18C Month 8 (N=39,30)	46.5 (28.5 to 75.7)	28.7 (17.5 to 47.3)		
Opsono-18C Month 9 (N=39,31)	1246 (776.7 to 1999)	1011.8 (686.4 to 1491.4)		
Opsono-19F Month 3 (N=43,39)	558.9 (376.3 to 830.2)	266.1 (148.2 to 477.8)		
Opsono-19F Month 8 (N=41,32)	60.7 (37.1 to 99.3)	43.4 (22.6 to 83.2)		
Opsono-19F Month 9 (N=40,33)	652.9 (413.3 to 1031.5)	486.7 (278.9 to 849.4)		
Opsono-23F Month 3 (N=44,37)	705.1 (309.2 to 1607.8)	759.7 (326.7 to 1766.6)		
Opsono-23F Month 8 (N=36,31)	85.2 (27.5 to 264.4)	41.6 (14.6 to 118.9)		
Opsono-23F Month 9 (N=39,33)	4231.2 (2793.7 to 6408.3)	1454 (736.1 to 2872.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic Titers against Cross-reactive Pneumococcal Serotypes 6A and 19A.- <6S and <6NS groups

End point title	Opsonophagocytic Titers against Cross-reactive Pneumococcal Serotypes 6A and 19A.- <6S and <6NS groups ^[21]
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End point description:

Cross-reactive Pneumococcal vaccine serotypes assessed were 6A and 19A and were calculated, expressed as geometric mean titers (GMTs). The seropositivity cut-off for the assay was ≥ 8 . Antibody titers < 8 were given an arbitrary value of half the cut-off for the purpose of GMT calculation

End point type	Secondary
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End point timeframe:

One month after primary vaccination (Month 3), prior to (Month 8) and one month after booster vaccination (Month 9)

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: Results are provided only for 2 groups as timeframe has been defined specifically for those 2 groups.

End point values	<6S Group	<6NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	41		
Units: Titers				
geometric mean (confidence interval 95%)				
Opsono-6A [Month 3] (N=42,41)	24.73 (11.46 to 53.37)	9.45 (5.32 to 16.75)		
Opsono-6A [Month 8] (N=40,33)	18.23 (8.97 to 37.09)	17.59 (8.08 to 38.3)		
Opsono-6A [Month 9] (N=38,32)	35.35 (15.6 to 80.12)	30.7 (12.14 to 77.64)		
Opsono-19A [Month 3] (N=38,34)	9.42 (5.65 to 15.7)	5.04 (3.83 to 6.63)		
Opsono-19A [Month 8] (N=34,23)	6.31 (4.28 to 9.32)	5.83 (3.95 to 8.61)		
Opsono-19A [Month 9] (N=26,28)	22.06 (9.49 to 51.3)	19.44 (10.25 to 36.86)		

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic Titers Against Vaccine Pneumococcal Serotypes – 7-11S and 7-11NS groups.

End point title	Opsonophagocytic Titers Against Vaccine Pneumococcal Serotypes – 7-11S and 7-11NS groups. ^[22]
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End point description:

Pneumococcal vaccine serotypes assessed were 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F and were calculated, expressed as geometric mean titers (GMTs). The seropositivity cut-off for the assay was ≥ 8 . Antibody titers < 8 were given an arbitrary value of half the cut-off for the purpose of GMT calculation.

End point type	Secondary
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End point timeframe:

One month after primary vaccination (Month 2), prior to (Month 3) and one month after booster vaccination (Month 4)

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: Results are provided only for 2 groups as timeframe has been defined specifically for those 2 groups.

End point values	7-11S Group	7-11NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	46		
Units: Titer				
geometric mean (confidence interval 95%)				
Opsono-1 Month 2 (N=48,45)	134.7 (83.6 to 216.9)	88.1 (53.7 to 144.6)		
Opsono-1 Month 3 (N=48,46)	74.2 (42.6 to 129.3)	48 (26.6 to 86.7)		
Opsono-1 Month 4 (N=48,44)	516 (307.6 to 865.7)	511.3 (293.2 to 891.8)		
Opsono-4 Month 2 (N=49,44)	1636.3 (1217.5 to 2199.2)	1771.1 (1359 to 2308.2)		
Opsono-4 Month 3 (N=45,45)	812.7 (584.5 to 1130.1)	1048.3 (790.4 to 1390.3)		
Opsono-4 Month 4 (N=48,43)	2130.5 (1639.1 to 2769.2)	2415.5 (1686.5 to 3459.8)		
Opsono-5 Month 2 (N=49,46)	105.7 (67.7 to 165.1)	85.8 (59.4 to 124)		
Opsono-5 Month 3 (N=47,47)	54.1 (34.9 to 83.6)	49.2 (31.7 to 76.3)		
Opsono-5 Month 4 (N=48,43)	277.4 (180.7 to 425.7)	289.6 (190.9 to 439.3)		
Opsono-6B Month 2 (N=48,43)	702.5 (413.2 to 1194.2)	696.6 (388.5 to 1249.2)		
Opsono-6B Month 3 (N=44,45)	708.3 (422.9 to 1186.1)	615.5 (337.3 to 1123.1)		
Opsono-6B Month 4 (N=46,43)	1360 (860.2 to 2150.3)	1305.4 (731.9 to 2328.4)		
Opsono-7F Month 2 (N=47,40)	6694.3 (5055.1 to 8864.9)	10452 (7782.7 to 14036.6)		
Opsono-7F Month 3 (N=46,46)	7776.9 (6000.8 to 10078.7)	9336.3 (6752.4 to 12908.9)		
Opsono-7F Month 4 (N=47,39)	10854.8 (9051.6 to 13017.2)	9362.8 (6882.3 to 12737.3)		
Opsono-9V Month 2 (N=48,42)	2858.2 (1875.3 to 4356.2)	2667.9 (1677.9 to 4242)		
Opsono-9V Month 3 (N=44,46)	1982.9 (1192.1 to 3298.2)	1986.2 (1167.8 to 3378.2)		
Opsono-9V Month 4 (N=48,41)	3047.9 (2389.7 to 3887.3)	2719.2 (1681 to 4398.9)		
Opsono-14 Month 2 (N=44,43)	2109.5 (1299 to 3425.9)	4009.9 (2501.9 to 6426.7)		
Opsono-14 Month 3 (N=46,46)	1431.6 (865.2 to 2368.6)	2128.3 (1477.5 to 3065.9)		
Opsono-14 Month 4 (N=46,40)	3414.9 (2237.4 to 5211.9)	3717.3 (2403.9 to 5748.5)		
Opsono-18C Month 2 (N=39,37)	744.4 (393.3 to 1409.2)	1605.6 (937.1 to 2751.1)		

Opsono-18C Month 3 (N=40,42)	411.4 (214.4 to 789.7)	746.4 (430.5 to 1294.1)		
Opsono-18C Month 4 (N=44,40)	2218.9 (1577.5 to 3121.2)	3238.7 (1874.7 to 5595)		
Opsono-19F Month 2 (N=47,43)	393.4 (214.4 to 722)	491.5 (256.8 to 940.6)		
Opsono-19F Month 3 (N=45,46)	160.2 (86.8 to 295.6)	279.5 (161.1 to 484.9)		
Opsono-19F Month 4 (N=47,41)	1347.7 (813.6 to 2232.3)	1174.4 (605.6 to 2277.3)		
Opsono-23F Month 2 (N=46,44)	1545.1 (788.3 to 3028.2)	2107.5 (1155 to 3845.5)		
Opsono-23F Month 3 (N=40,46)	1168.8 (560.8 to 2435.8)	1026.2 (458.3 to 2298)		
Opsono-23F Month 4 (N=47,43)	2038.8 (977.1 to 4254.4)	3525.1 (1974.2 to 6294.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic Titers against Cross-reactive Pneumococcal Serotypes 6A and 19A.- 7-11S and 7-11NS groups

End point title	Opsonophagocytic Titers against Cross-reactive Pneumococcal Serotypes 6A and 19A.- 7-11S and 7-11NS groups ^[23]
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End point description:

Cross-reactive Pneumococcal vaccine serotypes assessed were 6A and 19A and were calculated, expressed as geometric mean titers (GMTs). The seropositivity cut-off for the assay was ≥ 8 . Antibody titers < 8 were given an arbitrary value of half the cut-off for the purpose of GMT calculation.

End point type	Secondary
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End point timeframe:

One month after primary vaccination (Month 2), prior to (Month 3) and one month after booster vaccination (Month 4)

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: Results are provided only for 2 groups as timeframe has been defined specifically for those 2 groups.

End point values	7-11S Group	7-11NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	45		
Units: Titers				
geometric mean (confidence interval 95%)				
Opsono-6A [Month 2] (N=49,39)	40.59 (19.11 to 86.23)	51.23 (22.85 to 114.88)		
Opsono-6A [Month 3] (N=44,45)	38.11 (17.04 to 85.21)	36.27 (16.89 to 77.89)		
Opsono-6A [Month 4] (N=45,43)	77.09 (35.58 to 167.04)	98.18 (43.05 to 223.96)		
Opsono-19A [Month 2] (N=40,31)	15.21 (7.95 to 29.08)	108.31 (49.55 to 236.78)		

Opsono-19A [Month 3] (N=37,26)	14.65 (7.71 to 27.81)	19.4 (8.04 to 46.82)		
Opsono-19A [Month 4] (N=31,29)	76.09 (30.5 to 189.83)	449.06 (170.05 to 1185.87)		

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic Titers Against Vaccine Pneumococcal Serotypes – 12-23S and 12-23NS groups.

End point title	Opsonophagocytic Titers Against Vaccine Pneumococcal Serotypes – 12-23S and 12-23NS groups. ^[24]
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End point description:

Pneumococcal vaccine serotypes assessed were 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F and were calculated, expressed as geometric mean titers (GMTs). The seropositivity cut-off for the assay was ≥ 8 . Antibody titers < 8 were given an arbitrary value of half the cut-off for the purpose of GMT calculation.

End point type	Secondary
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End point timeframe:

One month after first dose vaccination (Month 2) and one month after second dose vaccination (Month 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: Results are provided only for 2 groups as timeframe has been defined specifically for those 2 groups.

End point values	12-23S Group	12-23NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	45		
Units: Titer				
geometric mean (confidence interval 95%)				
Opsono-1 Month 2 (N=46,45)	9.3 (6.1 to 14.3)	10.9 (6.8 to 17.4)		
Opsono-1 Month 3 (N=45,43)	195.7 (119.9 to 319.3)	115.1 (64 to 206.8)		
Opsono-4 Month 2 (N=44,43)	1086.3 (758.4 to 1555.9)	1539.4 (1128.4 to 2100.1)		
Opsono-4 Month 3 (N=44,43)	2089.7 (1635 to 2670.8)	3193.9 (2241.3 to 4551.4)		
Opsono-5 Month 2 (N=45,45)	9.8 (7.1 to 13.7)	9.6 (6.6 to 13.7)		
Opsono-5 Month 3 (N=44,44)	151.3 (99.8 to 229.2)	84 (53.5 to 131.8)		
Opsono-6B Month 2 (N=41,42)	345.1 (172.4 to 690.7)	278.4 (131.8 to 588.4)		
Opsono-6B Month 3 (N=43,43)	748.4 (425.9 to 1315)	866.4 (511.8 to 1466.7)		
Opsono-7F Month 2 (N=44,45)	5462.3 (4108.9 to 7261.4)	5802.2 (4678.6 to 7195.6)		

Opsono-7F Month 3 (N=44,42)	10279.4 (7836.7 to 13483.6)	10131.4 (8303.7 to 12361.6)		
Opsono-9V Month 2 (N=43,44)	1976.2 (1392.6 to 2804.4)	2359 (1514.3 to 3674.9)		
Opsono-9V Month 3 (N=44,43)	3778.2 (2880 to 4956.4)	4276.8 (3122.3 to 5858.3)		
Opsono-14 Month 2 (N=42,40)	711.2 (400.7 to 1262.4)	865.6 (583.2 to 1284.9)		
Opsono-14 Month 3 (N=45,40)	2704.5 (1856.4 to 3940)	2737.5 (1890 to 3965.1)		
Opsono-18C Month 2 (N=32,34)	1035.5 (507.6 to 2112.5)	449.2 (222.8 to 905.9)		
Opsono-18C Month 3 (N=40,40)	2873.1 (2070 to 3987.6)	2126.8 (1509.7 to 2996.3)		
Opsono-19F Month 2 (N=44,43)	229.1 (132.9 to 395)	248 (143 to 430.1)		
Opsono-19F Month 3 (N=45,43)	1845.3 (1169.3 to 2912.1)	1271.4 (825.4 to 1958.3)		
Opsono-23F Month 2 (N=44,44)	2572.2 (1264.1 to 5233.9)	2433.6 (1309.7 to 4522)		
Opsono-23F Month 3 (N=42,41)	5016.6 (3176.6 to 7922.4)	5325.4 (2857.8 to 9923.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic Titers against Cross-reactive Pneumococcal Serotypes 6A and 19A.- 12-23S and 12-23NS groups

End point title	Opsonophagocytic Titers against Cross-reactive Pneumococcal Serotypes 6A and 19A.- 12-23S and 12-23NS groups ^[25]
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End point description:

Cross-reactive Pneumococcal vaccine serotypes assessed were 6A and 19A and were calculated, expressed as geometric mean titers (GMTs). The seropositivity cut-off for the assay was ≥ 8 . Antibody titers < 8 were given an arbitrary value of half the cut-off for the purpose of GMT calculation.

End point type	Secondary
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End point timeframe:

One month after first dose vaccination (Month 2) and one month after second dose vaccination (Month 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: Results are provided only for 2 groups as timeframe has been defined specifically for those 2 groups.

End point values	12-23S Group	12-23NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	42		
Units: Titers				
geometric mean (confidence interval 95%)				
Opsono-6A [Month 2] (N=44,42)	82.82 (40.27 to 170.33)	77.25 (31.81 to 187.64)		
Opsono-6A [Month 3] (N=40,39)	147.91 (63.11 to 346.68)	157.37 (59.23 to 418.11)		
Opsono-19A [Month 2] (N=23,27)	28.37 (11.84 to 67.98)	25.68 (11.6 to 56.84)		
Opsono-19A [Month 3] (N=19,23)	214.17 (75.58 to 606.93)	321.14 (144.75 to 712.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of Antibodies against Protein D (PD) – 7-11S and 7-11NS groups.

End point title	Concentrations of Antibodies against Protein D (PD) – 7-11S and 7-11NS groups. ^[26]
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End point description:

Anti-protein D (Anti-PD) antibody concentrations by Enzyme-Linked Immunosorbent Assay (ELISA) were calculated, expressed as geometric mean concentrations (GMCs) in ELISA unit per milli-liter (EL.U/mL) and tabulated. The seropositivity cut-off for the assay was ≥ 100 EL.U/mL. Antibody concentrations < 100 EL.U/mL were given an arbitrary value of half the cut-off for the purpose of GMC calculation.

End point type	Secondary
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End point timeframe:

Prior to (Month 0) and one month after primary vaccination (Month 2), prior to (Month 3) and one month after booster vaccination (Month 4)

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: Results are provided only for 2 groups as timeframe has been defined specifically for those 2 groups.

End point values	7-11S Group	7-11NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD [Month 0] (N=47,48)	72.73 (57.23 to 92.42)	88.74 (70.85 to 111.13)		
Anti-PD [Month 2] (N=50,50)	1313.39 (1014.3 to 1700.67)	1489.78 (1171.98 to 1893.76)		
Anti-PD [Month 3] (N=50,49)	932.52 (732.63 to 1186.96)	1063.54 (844.52 to 1339.37)		

Anti-PD [Month 4] (N=49,48)	2695.5 (2150.74 to 3378.24)	2638.27 (2049.91 to 3395.49)		
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Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of Antibodies against Protein D (PD) – 12-23S and 12-23NS groups.

End point title	Concentrations of Antibodies against Protein D (PD) – 12-23S and 12-23NS groups. ^[27]
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End point description:

Anti-protein D (Anti-PD) antibody concentrations by Enzyme-Linked Immunosorbent Assay (ELISA) were calculated, expressed as geometric mean concentrations (GMCs) in ELISA unit per milli-liter (EL.U/mL) and tabulated. The seropositivity cut-off for the assay was ≥ 100 EL.U/mL. Antibody concentrations < 100 EL.U/mL were given an arbitrary value of half the cut-off for the purpose of GMC calculation.

End point type	Secondary
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End point timeframe:

Prior to (Month 0) and one month after first dose vaccination (Month 2) and one month after second dose vaccination (Month 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: Results are provided only for 2 groups as timeframe has been defined specifically for those 2 groups.

End point values	12-23S Group	12-23NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	47		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD [Month 0] (N=47,46)	79.59 (62.08 to 102.04)	76.22 (61.39 to 94.63)		
Anti-PD [Month 2] (N=48,47)	199.23 (150.51 to 263.72)	184.34 (140.21 to 242.35)		
Anti-PD [Month 3] (N=48,46)	1376.56 (1020.71 to 1856.46)	760.99 (553.23 to 1046.77)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of Antibodies Against Diphtheria Toxoid (DT) and Tetanus Toxoid (TT) - <6S and <6NS groups

End point title	Concentrations of Antibodies Against Diphtheria Toxoid (DT) and Tetanus Toxoid (TT) - <6S and <6NS groups ^[28]
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End point description:

Concentrations of antibodies are presented as geometric mean concentrations expressed as International units per millilitre (IU/mL). Seroprotection status, defined as Anti-DT or Anti-TT antibody concentration equal to or greater than 0.1 IU/mL.

End point type	Secondary
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End point timeframe:

Prior to (Month 0) and one month after primary vaccination (Month 3), prior to (Month 8) and one month after booster vaccination (Month 9)

Notes:

[28] - 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: Results are provided only for 2 groups as timeframe has been defined specifically for those 2 groups.

End point values	<6S Group	<6NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	46		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-DT Month 0 (N=48,45)	0.07 (0.05 to 0.08)	0.06 (0.05 to 0.07)		
Anti-DT Month 3 (N=48,46)	3.22 (2.59 to 4)	3.5 (2.82 to 4.34)		
Anti-DT Month 8 (N=44,37)	0.62 (0.5 to 0.77)	0.9 (0.72 to 1.12)		
Anti-DT Month 9 (N=44,38)	6.58 (5.44 to 7.97)	7.55 (6.11 to 9.32)		
Anti-TT Month 0 (N=48,46)	1.54 (1.13 to 2.09)	1.22 (0.85 to 1.76)		
Anti-TT Month 3 (N=48,46)	4.04 (3.26 to 5.01)	4.13 (3.27 to 5.22)		
Anti-TT Month 8 (N=44,38)	1.19 (0.96 to 1.48)	1.33 (1.08 to 1.63)		
Anti-TT Month 9 (N=44,38)	10.88 (9.24 to 12.81)	11.11 (9.62 to 12.83)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of Antibodies against Bordetella Pertussis (BPT) - <6S and <6NS groups

End point title	Concentrations of Antibodies against Bordetella Pertussis (BPT) - <6S and <6NS groups ^[29]
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End point description:

Concentrations of antibodies are presented as geometric mean concentrations expressed as Enzyme-Linked Immuno-Sorbent Assay (ELISA) units per millilitre (EL.U/mL). Seropositivity was defined as an antibody concentration equal to or greater than 15 EL.U/mL

End point type	Secondary
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End point timeframe:

Prior to (Month 0) and one month after primary vaccination (Month 3), prior to (Month 8) and one month after booster vaccination (Month 9)

Notes:

[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: Results are provided only for 2 groups as timeframe has been defined specifically for those 2 groups.

End point values	<6S Group	<6NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	46		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-BPT Month 0 (N=48,46)	7.71 (7.29 to 8.16)	7.77 (7.39 to 8.17)		
Anti-BPT Month 3 (N=48,46)	105.61 (86.93 to 128.3)	101.74 (84.56 to 122.42)		
Anti-BPT Month 8 (N=44,38)	22.67 (17.45 to 29.45)	22.69 (17.88 to 28.8)		
Anti-BPT Month 9 (N=44,38)	177.87 (152.1 to 207.99)	190.58 (167.67 to 216.63)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms: within 4 days after each vaccination dose.

Unsolicited symptoms: within 31 days after each vaccination.

SAEs: during the whole study period.

Adverse event reporting additional description:

The occurrence of reported AEs (all/related) was not available and is encoded as equal to the number of subjects affected.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	14.0
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Reporting groups

Reporting group title	<6S Group
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Reporting group description:

Children below 6 months of age with sickle cell disease, receiving a 3-dose primary vaccination with 10Pn-PD-DiT vaccine at approximately 8-12-16 weeks of age and booster vaccination at 9-10 months of age. Subjects received DTPw-HBV/Hib + OPV as co-administered vaccines. The allowable intervals between the primary vaccination doses were 28-42 days.

Reporting group title	<6NS Group
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Reporting group description:

Healthy children below 6 months of age, receiving a 3-dose primary vaccination with 10Pn-PD-DiT vaccine at approximately 8-12-16 weeks of age and booster vaccination at 9-10 months of age. Subjects received DTPw-HBV/Hib + OPV as co-administered vaccines. The allowable intervals between the primary vaccination doses were 28-42 days.

Reporting group title	7-11S Group
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Reporting group description:

Children between 7-11 months of age with sickle cell disease, receiving a 2-dose primary vaccination with 10Pn-PD-DiT vaccine starting at 7-11 months of age with an interval of at least 4 weeks (28-42 days) between primary doses. Subjects received a booster after an interval of 2 to 4 months since the previous dose.

Reporting group title	7-11NS Group
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Reporting group description:

Healthy children between 7-11 months of age, receiving a 2-dose primary vaccination with 10Pn-PD-DiT vaccine starting at 7-11 months of age with an interval of at least 4 weeks (28-42 days) between primary doses. Subjects received a booster after an interval of 2 to 4 months since the previous dose.

Reporting group title	12-23S Group
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Reporting group description:

Children between 12-23 months of age with sickle cell disease, receiving a 2-dose vaccination with 10Pn-PD-DiT vaccine starting at 12-23 months of age with an interval of 2 to 4 months between doses.

Reporting group title	12-23NS Group
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Reporting group description:

Healthy children between 12-23 months of age, receiving a 2-dose vaccination with 10Pn-PD-DiT vaccine starting at 12-23 months of age with an interval of 2 to 4 months between doses.

Serious adverse events	<6S Group	<6NS Group	7-11S Group
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 50 (6.00%)	9 / 50 (18.00%)	3 / 50 (6.00%)
number of deaths (all causes)	1	1	1

number of deaths resulting from adverse events			
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Gastrointestinal disorders			
Enteritis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 50 (2.00%)	6 / 50 (12.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 1	0 / 6	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaria			
subjects affected / exposed	3 / 50 (6.00%)	3 / 50 (6.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 50 (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 rotavirus			

subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis Salmonella			
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Osteomyelitis acute			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 50 (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
Urinary tract infection			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Malnutrition			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0

Serious adverse events	7-11NS Group	12-23S Group	12-23NS Group
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 50 (8.00%)	2 / 50 (4.00%)	2 / 50 (4.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 50 (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			
Enteritis			

subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	0 / 50 (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			
Gastroenteritis			
subjects affected / exposed	2 / 50 (4.00%)	0 / 50 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaria			
subjects affected / exposed	1 / 50 (2.00%)	1 / 50 (2.00%)	2 / 50 (4.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	0 / 50 (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 rotavirus			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 50 (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 Salmonella			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 50 (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
Osteomyelitis acute			

subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Malnutrition			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	<6S Group	<6NS Group	7-11S Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	48 / 50 (96.00%)	43 / 50 (86.00%)	31 / 50 (62.00%)
General disorders and administration site conditions			
Pain (Primary vaccination)			
alternative assessment type: Systematic			
subjects affected / exposed	17 / 50 (34.00%)	23 / 50 (46.00%)	12 / 50 (24.00%)
occurrences (all)	17	23	12
Pain (Booster vaccination)	Additional description: Groups 12-23S and 12-23NS were not included in the analysis since they received no booster dose, so the numbers presented for them are placeholder values.		
alternative assessment type: Systematic			
subjects affected / exposed ^[1]	11 / 49 (22.45%)	6 / 49 (12.24%)	3 / 50 (6.00%)
occurrences (all)	11	6	3
Irritability (Primary vaccination)			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 50 (6.00%)	6 / 50 (12.00%)	0 / 50 (0.00%)
occurrences (all)	3	6	0
Irritability (Booster vaccination)	Additional description: Groups 12-23S and 12-23NS were not included in the analysis since they received no booster dose, so the numbers presented for them are placeholder values.		
alternative assessment type: Systematic			

subjects affected / exposed ^[2] occurrences (all)	6 / 49 (12.24%) 6	0 / 49 (0.00%) 0	0 / 50 (0.00%) 0
Fever (Primary vaccination) alternative assessment type: Systematic subjects affected / exposed occurrences (all)	Additional description: Fever was assessed rectally.		
	48 / 50 (96.00%) 48	43 / 50 (86.00%) 43	31 / 50 (62.00%) 31
Fever (Booster vaccination) alternative assessment type: Systematic subjects affected / exposed ^[3] occurrences (all)	Additional description: Fever was assessed rectally. Groups 12-23S and 12-23NS were not included in the analysis since they received no booster dose, so the numbers presented for them are placeholder values.		
	38 / 49 (77.55%) 38	31 / 49 (63.27%) 31	14 / 50 (28.00%) 14
Pyrexia subjects affected / exposed occurrences (all)	1 / 50 (2.00%) 1	1 / 50 (2.00%) 1	3 / 50 (6.00%) 3
Blood and lymphatic system disorders Sickle cell anaemia with crisis subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 50 (0.00%) 0	3 / 50 (6.00%) 3
Gastrointestinal disorders Diarrhoea (Primary) subjects affected / exposed occurrences (all)	7 / 50 (14.00%) 7	4 / 50 (8.00%) 4	1 / 50 (2.00%) 1
Enteritis (Primary) subjects affected / exposed occurrences (all)	2 / 50 (4.00%) 2	3 / 50 (6.00%) 3	6 / 50 (12.00%) 6
Enteritis (Booster) subjects affected / exposed ^[4] occurrences (all)	Additional description: Groups 12-23S and 12-23NS were not included in the analysis since they received no booster dose, so the numbers presented for them are placeholder values.		
	0 / 49 (0.00%) 0	2 / 49 (4.08%) 2	0 / 50 (0.00%) 0
Diarrhoea (Booster) subjects affected / exposed ^[5] occurrences (all)	1 / 49 (2.04%) 1	2 / 49 (4.08%) 2	3 / 50 (6.00%) 3
Abdominal pain subjects affected / exposed occurrences (all)	3 / 50 (6.00%) 3	1 / 50 (2.00%) 1	2 / 50 (4.00%) 2
Respiratory, thoracic and mediastinal disorders			

Cough subjects affected / exposed occurrences (all)	4 / 50 (8.00%) 4	5 / 50 (10.00%) 5	1 / 50 (2.00%) 1
Infections and infestations			
Malaria (Primary) subjects affected / exposed occurrences (all)	10 / 50 (20.00%) 10	7 / 50 (14.00%) 7	9 / 50 (18.00%) 9
Malaria (Booster)	Additional description: Groups 12-23S and 12-23NS were not included in the analysis since they received no booster dose, so the numbers presented for them are placeholder values.		
subjects affected / exposed ^[6] occurrences (all)	0 / 49 (0.00%) 0	8 / 49 (16.33%) 8	8 / 50 (16.00%) 8
Bronchitis subjects affected / exposed occurrences (all)	9 / 50 (18.00%) 9	10 / 50 (20.00%) 10	3 / 50 (6.00%) 3
Gastroenteritis subjects affected / exposed occurrences (all)	6 / 50 (12.00%) 6	5 / 50 (10.00%) 5	3 / 50 (6.00%) 3
Rhinitis subjects affected / exposed occurrences (all)	4 / 50 (8.00%) 4	7 / 50 (14.00%) 7	4 / 50 (8.00%) 4
Nasopharyngitis subjects affected / exposed occurrences (all)	6 / 50 (12.00%) 6	4 / 50 (8.00%) 4	2 / 50 (4.00%) 2
Gastrointestinal fungal infection subjects affected / exposed occurrences (all)	4 / 50 (8.00%) 4	5 / 50 (10.00%) 5	3 / 50 (6.00%) 3
Conjunctivitis subjects affected / exposed occurrences (all)	2 / 50 (4.00%) 2	3 / 50 (6.00%) 3	0 / 50 (0.00%) 0
Ear infection subjects affected / exposed occurrences (all)	3 / 50 (6.00%) 3	1 / 50 (2.00%) 1	0 / 50 (0.00%) 0

Non-serious adverse events	7-11NS Group	12-23S Group	12-23NS Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 50 (58.00%)	29 / 50 (58.00%)	20 / 50 (40.00%)

General disorders and administration site conditions			
Pain (Primary vaccination) alternative assessment type: Systematic subjects affected / exposed occurrences (all)	15 / 50 (30.00%) 15	13 / 50 (26.00%) 13	9 / 50 (18.00%) 9
Pain (Booster vaccination) alternative assessment type: Systematic subjects affected / exposed ^[1] occurrences (all)	Additional description: Groups 12-23S and 12-23NS were not included in the analysis since they received no booster dose, so the numbers presented for them are placeholder values.		
	0 / 50 (0.00%) 0	0 / 1 (0.00%) 0	0 / 1 (0.00%) 0
Irritability (Primary vaccination) alternative assessment type: Systematic subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	2 / 50 (4.00%) 2	0 / 50 (0.00%) 0
Irritability (Booster vaccination) alternative assessment type: Systematic subjects affected / exposed ^[2] occurrences (all)	Additional description: Groups 12-23S and 12-23NS were not included in the analysis since they received no booster dose, so the numbers presented for them are placeholder values.		
	0 / 50 (0.00%) 0	0 / 1 (0.00%) 0	0 / 1 (0.00%) 0
Fever (Primary vaccination) alternative assessment type: Systematic subjects affected / exposed occurrences (all)	Additional description: Fever was assessed rectally.		
	29 / 50 (58.00%) 39	29 / 50 (58.00%) 29	20 / 50 (40.00%) 20
Fever (Booster vaccination) alternative assessment type: Systematic subjects affected / exposed ^[3] occurrences (all)	Additional description: Fever was assessed rectally. Groups 12-23S and 12-23NS were not included in the analysis since they received no booster dose, so the numbers presented for them are placeholder values.		
	13 / 50 (26.00%) 13	0 / 1 (0.00%) 0	0 / 1 (0.00%) 0
Pyrexia subjects affected / exposed occurrences (all)	1 / 50 (2.00%) 1	0 / 50 (0.00%) 0	1 / 50 (2.00%) 1
Blood and lymphatic system disorders Sickle cell anaemia with crisis subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	10 / 50 (20.00%) 10	0 / 50 (0.00%) 0
Gastrointestinal disorders			

Diarrhoea (Primary) subjects affected / exposed occurrences (all)	3 / 50 (6.00%) 3	1 / 50 (2.00%) 1	1 / 50 (2.00%) 1
Enteritis (Primary) subjects affected / exposed occurrences (all)	2 / 50 (4.00%) 2	0 / 50 (0.00%) 0	1 / 50 (2.00%) 1
Enteritis (Booster)	Additional description: Groups 12-23S and 12-23NS were not included in the analysis since they received no booster dose, so the numbers presented for them are placeholder values.		
subjects affected / exposed ^[4] occurrences (all)	3 / 50 (6.00%) 3	0 / 1 (0.00%) 0	0 / 1 (0.00%) 0
Diarrhoea (Booster) subjects affected / exposed ^[5] occurrences (all)	1 / 50 (2.00%) 1	0 / 1 (0.00%) 0	0 / 1 (0.00%) 0
Abdominal pain subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	0 / 50 (0.00%) 0	0 / 50 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	1 / 50 (2.00%) 1	1 / 50 (2.00%) 1	0 / 50 (0.00%) 0
Infections and infestations Malaria (Primary) subjects affected / exposed occurrences (all)	13 / 50 (26.00%) 13	10 / 50 (20.00%) 10	10 / 50 (20.00%) 10
Malaria (Booster)	Additional description: Groups 12-23S and 12-23NS were not included in the analysis since they received no booster dose, so the numbers presented for them are placeholder values.		
subjects affected / exposed ^[6] occurrences (all)	4 / 50 (8.00%) 4	0 / 1 (0.00%) 0	0 / 1 (0.00%) 0
Bronchitis subjects affected / exposed occurrences (all)	8 / 50 (16.00%) 8	1 / 50 (2.00%) 1	4 / 50 (8.00%) 4
Gastroenteritis subjects affected / exposed occurrences (all)	9 / 50 (18.00%) 9	1 / 50 (2.00%) 1	6 / 50 (12.00%) 6
Rhinitis			

subjects affected / exposed	3 / 50 (6.00%)	3 / 50 (6.00%)	4 / 50 (8.00%)
occurrences (all)	3	3	4
Nasopharyngitis			
subjects affected / exposed	7 / 50 (14.00%)	3 / 50 (6.00%)	5 / 50 (10.00%)
occurrences (all)	7	3	5
Gastrointestinal fungal infection			
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	0 / 50 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis			
subjects affected / exposed	1 / 50 (2.00%)	2 / 50 (4.00%)	0 / 50 (0.00%)
occurrences (all)	1	2	0
Ear infection			
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	1 / 50 (2.00%)
occurrences (all)	1	0	1

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis of the non-serious adverse event included only subjects with documented data.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis of the non-serious adverse event included only subjects with documented data.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis of the non-serious adverse event included only subjects with documented data.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis of the non-serious adverse event included only subjects with documented data.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis of the non-serious adverse event included only subjects with documented data.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: The analysis of the non-serious adverse event included only subjects with documented data.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 April 2010	The oral polio vaccine was to be provided in multidose vials Changes in the randomization of treatment Inconsistencies regarding the age for booster vaccination in the 7-11 month groups Changes in the priority ranking of immunological assays Changes in the definition of the Epochs Update of Rationale of the study
03 September 2010	•For clarification, the inclusion criteria for children with sickle cell disease have been further detailed. •An additional blood sample for SCD testing was planned to be taken at the pre-vaccination timepoint from subjects aged 7-11 and 12-23 months without hemoglobin status confirmed by electrophoresis available. •Presentation of oral polio vaccine that was to be used has changed: 10- or 20-dose vials were used. In addition, the use of one 10- or 20-dose vial to vaccinate up to 10 or 20 subjects, respectively, on the same day was allowed. •The immunogenicity objectives related to the co-administered OPV have been removed since there are no plans to test poliovirus immune response. •The contact details for the emergency code break have been clarified.
08 May 2012	The main changes and their rationale are the following: •Additional information was given about administration of vaccines through the local EPI program. •Extension of the recruitment period due to a lower enrolment rate than expected. •Additional exclusion criterion for children of the <6S and <6NS groups to clarify differences between groups with regard to administration of vaccines included in the EPI program either as study vaccines or outside the study. •Additional exclusion criterion for all groups, i.e. exclusion of subjects being heterozygous or carriers of abnormal haemoglobin (e.g. haemoglobin S, haemoglobin C) who are not considered to have SCD, to avoid potential bias and to keep homogeneity of the examined groups.
09 April 2013	In the past few months, GSK Biologicals has been investigating the quality of some serology assays used in clinical studies, including the Streptococcus pneumonia opsonophagocytic activity (OPA) assay used in the present trial. This protocol amendment reflected the fact that delays in the availability of the assay results would lead to changes in the analysis plan. Therefore, the sequence of analysis has been modified to perform study analysis in one final step on all immunogenicity and safety data obtained up to one month after administration of the last dose of study vaccine for all study groups. The results of this final analysis were presented in a final clinical study report.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported