Clinical trial results:
A phase II, open-label, randomized, multicentre study to evaluate the feasibility of GSK Biologicals' DTPa-IPV/Hib-MenC-TT vaccine co-administered with Prevenar compared with Pediacel co-administered with Menjugate and Prevenar, when given in healthy infants as a three-dose primary vaccination course at 2, 3 and 4 months of age and to evaluate Menitorix given to these children as a booster dose at 12 months of age

Summary

EudraCT number	2008-003741-87
Trial protocol	GB
Global end of trial date	09 December 2010

Results information

Result version number	v1
This version publication date	02 May 2016
First version publication date	30 October 2014

Trial information

Trial identification

Sponsor protocol code	111709

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00871338
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, 044 2089-904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	09 December 2010
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 December 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

•To demonstrate that GSK Biologicals' DTPa IPV/Hib-MenC-TT vaccine co-administered with Prevenar (MenC-Combo group) is non-inferior to Pediacel co-administered with Prevenar and Menjugate (Control group), in terms of immune response to Hib and MenC, one month after the third dose of primary vaccination.
Criteria for non-inferiority:
Non-inferiority in terms of response to PRP will be demonstrated if the upper limit of the 95% confidence interval (CI) on the group difference (Control minus MenC-Combo group) in percentage of subjects with anti-PRP concentrations >= 0.15 micrograms/ml is <=10%.
Non-inferiority in terms of response to MenC will be demonstrated if the upper limit of the 95% CI on the group difference (Control minus MenC-Combo group) in percentage of subjects with SBA-MenC titres >= 8 is <=10%.

Protection of trial subjects:

The vaccinees were observed closely for at least 30 minutes following the administration of vaccines, with appropriate medical treatment readily available in case of a rare anaphylactic reaction.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 June 2009
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	United Kingdom: 284
Worldwide total number of subjects	284
EEA total number of subjects	284

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)	0

Children (2-11 years)	284
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:

A total of 284 subjects were enrolled in the study.

Pre-assignment

Screening details:

Out of the 284 subjects who enrolled in the study, 5 didn't complete the first period. Furthermore not all of the subjects who completed period 1 (Prior to Booster) started period 2 (After Booster).

Period 1

Period 1 title	Prior to booster
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	GSK2197870A Group

Arm description: -

Arm type	Experimental
Investigational medicinal product name	GSK2197870A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses given at 2, 3 and 4 months of age

Investigational medicinal product name	Prevenar™
Investigational medicinal product code	
Other name	Pfizer’s 13-valent pneumococcal polysaccharide conjugate vaccine
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 co-administered doses, intramuscular into right thigh

Investigational medicinal product name	Menitorix™
Investigational medicinal product code	
Other name	GSK Biologicals’ combined Haemophilus influenzae type b and Neisseria meningitidis serogroup C tetanus toxoid conjugate vaccine.
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 booster dose at 12 months of age was administered in the right upper anterolateral thigh

Arm title	Pediacel Group

Arm description: -

Arm type	Active comparator

Investigational medicinal product name	Prevenar™
Investigational medicinal product code	
Other name	Pfizer's 13-valent pneumococcal polysaccharide conjugate vaccine
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 co-administered doses, intramuscular into right thigh

Investigational medicinal product name	Menitorix™
Investigational medicinal product code	
Other name	GSK Biologicals' combined Haemophilus influenzae type b and Neisseria meningitidis serogroup C tetanus toxoid conjugate vaccine.
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 booster dose at 12 months of age was administered in the right upper anterolateral thigh

Investigational medicinal product name	Pediacel™
Investigational medicinal product code	
Other name	Sanofi-Pasteur-MSD's combined DTPa-inactivated polio-Haemophilus influenzae type b vaccine.
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses given at 2, 3 and 4 months of age

Investigational medicinal product name	Menjugate™
Investigational medicinal product code	
Other name	Novartis' meningococcal serogroup C CRM197 protein conjugated vaccine.
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 doses given at 3 and 4 months of age

Number of subjects in period 1	GSK2197870A Group	Pediacel Group
Started	142	142
Completed	140	139
Not completed	2	3
Consent withdrawn by subject	1	3
Lost to follow-up	1	-

Period 2

Period 2 title	After Booster
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	GSK2197870A Group

Arm description: -

Arm type	Experimental
Investigational medicinal product name	GSK2197870A
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses given at 2, 3 and 4 months of age

Investigational medicinal product name	Prevenar™
Investigational medicinal product code	
Other name	Pfizer’s 13-valent pneumococcal polysaccharide conjugate vaccine
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 co-administered doses, intramuscular into right thigh

Investigational medicinal product name	Menitorix™
Investigational medicinal product code	
Other name	GSK Biologicals’ combined Haemophilus influenzae type b and Neisseria meningitidis serogroup C tetanus toxoid conjugate vaccine.
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 booster dose at 12 months of age was administered in the right upper anterolateral thigh

Arm title	Pediacel Group

Arm description: -

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

Dosage and administration details:

3 co-administered doses, intramuscular into right thigh

Investigational medicinal product name	Menitorix™
Investigational medicinal product code	
Other name	GSK Biologicals’ combined Haemophilus influenzae type b and Neisseria meningitidis serogroup C tetanus toxoid conjugate vaccine.
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:	
1 booster dose at 12 months of age was administered in the right upper anterolateral thigh	
Investigational medicinal product name	Pediacel™
Investigational medicinal product code	
Other name	Sanofi-Pasteur-MSD's combined DTPa-inactivated polio-Haemophilus influenzae type b vaccine.
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use
Dosage and administration details:	
3 doses given at 2, 3 and 4 months of age	
Investigational medicinal product name	Menjugate™
Investigational medicinal product code	
Other name	Novartis' meningococcal serogroup C CRM197 protein conjugated vaccine.
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use
Dosage and administration details:	
2 doses given at 3 and 4 months of age	

Number of subjects in period 2[1]	GSK2197870A Group	Pediacel Group
Started	139	135
Completed	139	135

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Not all subjects returned for the booster phase of the study.

Baseline characteristics

Reporting groups	
Reporting group title	GSK2197870A Group
Reporting group description: -	
Reporting group title	Pediacel Group
Reporting group description: -	

Reporting group values	GSK2197870A Group	Pediacel Group	Total
Number of subjects	142	142	284
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: weeks			
arithmetic mean	8.2	8.1	
standard deviation	± 0.69	± 0.74	-
Gender categorical Units: Subjects			
Female	59	78	137
Male	83	64	147

End points

End points reporting groups

Reporting group title	GSK2197870A Group
Reporting group description: -	
Reporting group title	Pediacel Group
Reporting group description: -	
Reporting group title	GSK2197870A Group
Reporting group description: -	
Reporting group title	Pediacel Group
Reporting group description: -	

Primary: Number of seroprotected subjects for anti-polyribosylribitol phosphate (anti-PRP).

End point title	Number of seroprotected subjects for anti-polyribosylribitol phosphate (anti-PRP).[1]

End point description:

A seroprotected subject was defined as a vaccinated subject who had anti-PRP antibody concentrations ≥ 0.15 micrograms per milliliter (µg/mL).

End point type	Primary

End point timeframe:

At Month 3

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

End point values	GSK2197870A Group	Pediacel Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	108	119		
Units: Subjects				
Anti-PRP	108	111		

Statistical analyses

No statistical analyses for this end point

Primary: Number of seropositive subjects against Neisseria meningitidis using baby rabbit complement (rSBA-MenC)

End point title	Number of seropositive subjects against Neisseria meningitidis using baby rabbit complement (rSBA-MenC)[2]

End point description:

A seropositive subject was defined as a vaccinated subject who had rSBA-MenC ≥ 1:8.

End point type	Primary

End point timeframe:

At Month 2 and Month 3.

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed

End point values	GSK2197870A Group	Pediacel Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	109	113		
Units: Subjects				
rSBA-MenC at Month 2 [N=109;111]	104	109		
rSBA-MenC at Month 3 [N=105;113]	101	113		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-PRP concentrations antibody above the cut-off.

End point title	Number of subjects with anti-PRP concentrations antibody above the cut-off.

End point description:

The reference cut-off was ≥ 1.0 micrograms per milliliter (µg/mL).

End point type	Secondary

End point timeframe:

At Month 3

End point values	GSK2197870A Group	Pediacel Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	108	119		
Units: Subjects				
Anti-PRP	96	98		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-polysaccharide C (anti-PSC) antibody concentrations above the cut-offs.

End point title	Number of subjects with anti-polysaccharide C (anti-PSC) antibody concentrations above the cut-offs.

End point description:

The reference cut-offs were ≥ 0.3 µg/mL and ≥ 2 µg/mL.

End point type	Secondary

End point timeframe:

At Month 2 and Month 3.

End point values	GSK2197870A Group	Pediacel Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	113	115		
Units: Subjects				
Anti-PSC ≥ 0.3 µg/mL at Month 2 [N=113;115]	113	115		
Anti-PSC ≥ 0.3 µg/mL at Month 3 [N=108;114]	108	114		
Anti-PSC ≥ 2.0 µg/mL at Month 2 [N=113;115]	113	113		
Anti-PSC ≥ 2.0 µg/mL at Month 3 [N=108;114]	107	144		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects for anti-diphtheria (anti-D) and anti-tetanus (anti-T) antibodies.

End point title	Number of seroprotected subjects for anti-diphtheria (anti-D) and anti-tetanus (anti-T) antibodies.

End point description:

A seroprotected subject was defined as a vaccinated subject who had anti-D and anti-T antibody concentrations ≥ 0.1 international units per milliliter (IU/mL).

End point type	Secondary

End point timeframe:

At Month 3.

End point values	GSK2197870A Group	Pediacel Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	108	119		
Units: Subjects				
Anti-T	108	119		
Anti-D	108	119		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects against anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN).

End point title	Number of seropositive subjects against anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN).

End point description:

A seropositive subject was defined as a vaccinated subject who had anti-PT, anti-FHA and anti-PRN antibody concentrations ≥ 5 enzyme-linked immunosorbent assay (ELISA) units per milliliters (EL.U/mL).

End point type	Secondary

End point timeframe:

At Month 3.

End point values	GSK2197870A Group	Pediacel Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	108	120		
Units: Subjects				
Anti-PT [N=107;117]	107	117		
Anti-FHA [N=106;119]	106	119		
Anti-PRN [N=108;120]	108	119		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects for anti-poliovirus (anti-polio) types 1, 2 and 3.

End point title	Number of seroprotected subjects for anti-poliovirus (anti-polio) types 1, 2 and 3.

End point description:

A seroprotected subject was defined as a vaccinated subject who had anti-polio 1, 2 and 3 antibody concentrations ≥ 1:8.

End point type	Secondary

End point timeframe:

At Month 3.

End point values	GSK2197870A Group	Pediacel Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	94		
Units: Subjects				
Anti-polio 1	89	93		
Anti-polio 2	88	92		
Anti-polio 3	89	94		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for anti-pneumococcal (anti-PNE) serotypes.

End point title	Number of seropositive subjects for anti-pneumococcal (anti-PNE) serotypes.

End point description:

A seropositive subject was defined as a vaccinated subject who had anti- pneumococcal antibody concentrations ≥ 0.2 micrograms per milliliter (µg/mL). The anti-PNE serotypes assessed were 4, 6B, 9V, 14, 18C, 19F and 23F.

End point type	Secondary

End point timeframe:

At Month 3

End point values	GSK2197870A Group	Pediacel Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	108	112		
Units: Subjects				
Anti- PNE 4 [N=47;52]	47	52		
Anti- PNE 6B [N=46;52]	14	13		
Anti- PNE 9V [N=47;51]	46	49		
Anti- PNE 14 [N=47;52]	47	50		
Anti- PNE 18C [N=46;52]	45	51		
Anti- PNE 19F [N=47;52]	46	52		
Anti- PNE 23F [N=47;52]	37	49		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations for anti-PRP.

End point title	Concentrations for anti-PRP.

End point description:

Concentrations were expressed as geometric mean concentrations (GMCs). The seroprotection reference cut-off value was ≥ 0.15 µg/mL.

End point type	Secondary

End point timeframe:

At Month 3.

End point values	GSK2197870A Group	Pediacel Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	108	119		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PRP	4.347 (3.507 to 5.389)	4.347 (3.507 to 5.389)		

Statistical analyses

No statistical analyses for this end point

Secondary: Titers for rSBA-MenC.

End point title	Titers for rSBA-MenC.

End point description:

Titers were expressed as geometric mean titers (GMCs). The seropositivity reference cut-off value was ≥ 1:8.

End point type	Secondary

End point timeframe:

At Month 2 and Month 3.

End point values	GSK2197870A Group	Pediacel Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	109	113		
Units: Titers				
geometric mean (confidence interval 95%)				
rSBA-MenC at Month 2 [N=109;111]	339.4 (254.4 to 452.7)	257 (204.5 to 323)		
rSBA-MenC at Month 3 [N=105;113]	393.2 (292.5 to 528.7)	3110.5 (2612 to 3704.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations for anti-PSC.

End point title	Concentrations for anti-PSC.

End point description:

Concentrations were expressed as geometric mean concentrations (GMCs). The seroprotection reference

cut-off value was ≥ 0.3 µg/mL.

End point type	Secondary

End point timeframe:

At Month 2 and Month 3.

End point values	GSK2197870A Group	Pediacel Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	113	115		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PSC at Month 2 [N=113;115]	18.2 (15.91 to 20.82)	10.77 (9.61 to 12.08)		
Anti-PSC at Month 3 [N=108;114]	15.1 (13 to 17.55)	17.29 (15.53 to 19.25)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations for anti-T and anti-D.

End point title	Concentrations for anti-T and anti-D.

End point description:

Concentrations were expressed as geometric mean concentrations (GMCs). The seroprotection reference cut-off value was ≥ 0.1 IU/mL.

End point type	Secondary

End point timeframe:

At Month 3.

End point values	GSK2197870A Group	Pediacel Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	108	119		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-T	2.694 (2.394 to 3.032)	1.034 (0.895 to 1.195)		
Anti-D	1.767 (1.548 to 2.019)	1.817 (1.589 to 2.078)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations for anti-PT, anti-FHA and anti-PRN.

End point title	Concentrations for anti-PT, anti-FHA and anti-PRN.

End point description:

Concentrations were expressed as geometric mean concentrations (GMCs). The seropositivity reference cut-off value was ≥ 5 EL.U/mL.

End point type	Secondary

End point timeframe:

At Month 3.

End point values	GSK2197870A Group	Pediacel Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	108	120		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PT [N=107;117]	45.4 (40 to 51.4)	45.1 (39.8 to 51.2)		
Anti-FHA [N=106;119]	234.4 (203.7 to 269.6)	204.9 (178.2 to 235.6)		
Anti-PRN [N=108;120]	121.6 (103.6 to 142.7)	49.9 (41.4 to 60.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Titers for anti-polio 1, 2 and 3.

End point title	Titers for anti-polio 1, 2 and 3.

End point description:

Titers were expressed as geometric mean titers (GMTs). The seropositivity reference cut-off value was ≥ 1:8.

End point type	Secondary

End point timeframe:

At Month 3.

End point values	GSK2197870A Group	Pediacel Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	94		
Units: Titers				
geometric mean (confidence interval 95%)				

Anti-polio 1	169.4 (127 to 226)	89.3 (71.1 to 112.2)		
Anti-polio 2	90.2 (68.5 to 118.7)	77.7 (59.7 to 101.1)		
Anti-polio 3	367.9 (288.1 to 469.9)	250.5 (195.9 to 320.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations for anti-PNE serotypes.

End point title	Concentrations for anti-PNE serotypes.

End point description:

Concentrations were expressed as geometric mean concentreations (GMCs). The seropositivity reference cut-off value was ≥ 0.2 µg/mL.

End point type	Secondary

End point timeframe:

At Month 3.

End point values	GSK2197870A Group	Pediacel Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	94		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti- PNE 4 [N=47;52]	2.56 (2.13 to 3.07)	2.18 (1.87 to 2.53)		
Anti- PNE 6B [N=46;52]	0.12 (0.08 to 0.17)	0.12 (0.08 to 0.16)		
Anti- PNE 9V [N=47;51]	2.56 (1.92 to 3.43)	1.85 (1.43 to 2.39)		
Anti- PNE 14 [N=47;52]	3.78 (2.7 to 5.28)	2.71 (2 to 3.67)		
Anti- PNE 18C [N=46;52]	2.26 (1.59 to 3.2)	2.74 (2.12 to 3.56)		
Anti- PNE 19F [N=47;52]	3 (2.21 to 4.06)	3.15 (2.51 to 3.95)		
Anti- PNE 23F [N=47;52]	0.58 (0.4 to 0.82)	0.89 (0.69 to 1.14)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects for anti-PRP.

End point title	Number of seroprotected subjects for anti-PRP.

End point description:

A seroprotected subject was defined as a vaccinated subject who had anti-PRP antibody concentrations ≥ 0.15 micrograms per milliliter (µg/mL).

End point type	Secondary

End point timeframe:

At Month 10 and Month 11.

End point values	GSK2197870A Group	Pediacel Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	112		
Units: Subjects				
Anti-PRP at Month 10 [N=89;98]	76	81		
Anti-PRP at Month 11 [N=98;112]	98	112		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects against rSBA-MenC.

End point title	Number of seropositive subjects against rSBA-MenC.

End point description:

A seropositive subject was defined as a vaccinated subject who had rSBA-MenC ≥ 1:8.

End point type	Secondary

End point timeframe:

At Month 10 and Month 11.

End point values	GSK2197870A Group	Pediacel Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94	109		
Units: Subjects				
rSBA-MenC at Month 10 [N=87;93]	70	78		
rSBA-MenC at Month 11 [N=94;109]	93	109		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-PSC antibody concentrations above the cut-offs.

End point title	Number of subjects with anti-PSC antibody concentrations

	above the cut-offs.

End point description:

The reference cut-offs were ≥ 0.3 µg/mL and ≥ 2 µg/mL.

End point type	Secondary

End point timeframe:

At Month 10 and Month 11.

End point values	GSK2197870A Group	Pediacel Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	111		
Units: Subjects				
Anti-PSC ≥ 0.3 µg/mL at Month 10 [N=86;97]	81	89		
Anti-PSC ≥ 0.3 µg/mL at Month 11 [N=100;111]	100	111		
Anti-PSC ≥ 2.0 µg/mL at Month 10 [N=86;97]	22	14		
Anti-PSC ≥ 2.0 µg/mL at Month 11 [N=100;111]	92	80		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotive subjects for anti-D and anti-T antibodies.

End point title	Number of seroprotive subjects for anti-D and anti-T antibodies.

End point description:

A seropositive subject was defined as a vaccinated subject who had anti-D (ELISA) and anti-T antibody concentrations ≥ 0.1 IU/mL. Seropositivity for anti-D was also defined with the ≥ 0.016 IU/mL cut-off (Neutralisation assay).

End point type	Secondary

End point timeframe:

At Month 10.

End point values	GSK2197870A Group	Pediacel Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	98		
Units: Subjects				
Anti-T ≥ 0.1 IU/mL [N=89;98]	86	87		
Anti-D ≥ 0.1 IU/mL [N=89;98]	72	94		
Anti-D ≥ 0.016 IU/mL [N=16;3]	11	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for anti-PT, anti-FHA and anti-PRN.

End point title	Number of seropositive subjects for anti-PT, anti-FHA and anti-PRN.

End point description:

A seropositive subject was defined as a vaccinated subject who had anti-PT, anti-FHA and anti-PRN antibody concentrations ≥ 5 enzyme-linked immunosorbent assay (ELISA) units per milliliters (EL.U/mL).

End point type	Secondary

End point timeframe:

At Month 10.

End point values	GSK2197870A Group	Pediacel Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	100		
Units: Subjects				
Anti-PT [N=89;100]	60	88		
Anti-FHA [N=89;99]	89	98		
Anti-PRN [N=89;100]	75	72		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects for anti-anti-polio types 1, 2 and 3.

End point title	Number of seroprotected subjects for anti-anti-polio types 1, 2 and 3.

End point description:

A seroprotected subject was defined as a vaccinated subject who had anti-polio 1, 2 and 3 antibody concentrations ≥ 1:8.

End point type	Secondary

End point timeframe:

At Month 10.

End point values	GSK2197870A Group	Pediacel Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	86		
Units: Subjects				
Anti-polio 1 [N=78;86]	68	62		
Anti-polio 2 [N=78;85]	63	69		
Anti-polio 3 [N=78;86]	74	76		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations for anti-PRP.

End point title	Concentrations for anti-PRP.

End point description:

Concentrations were expressed as geometric mean concentrations (GMCs). The seroprotection reference cut-off value was ≥ 0.15 µg/mL.

End point type	Secondary

End point timeframe:

At Month 10 and Month 11.

End point values	GSK2197870A Group	Pediacel Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	98	112		
Units: µg /mL				
geometric mean (confidence interval 95%)				
Anti-PRP at Month 10 [N=89;98]	0.423 (0.339 to 0.528)	0.574 (0.436 to 0.756)		
Anti-PRP at Month 11 [N=98;112]	66.697 (53.271 to 83.507)	26.899 (20.931 to 34.569)		

Statistical analyses

No statistical analyses for this end point

Secondary: Titers for rSBA-MenC.

End point title	Titers for rSBA-MenC.

End point description:

Titers were expressed as geometric mean titers (GMCs). The seropositivity reference cut-off value was ≥ 1:8.

End point type	Secondary

End point timeframe:

At Month 10 and Month 11.

End point values	GSK2197870A Group	Pediacel Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	93	109		
Units: Titers				
geometric mean (confidence interval 95%)				
rSBA-MenC at Month 10 [N=87;94]	62.1 (43.3 to 89.1)	67.1 (48.5 to 92.7)		
rSBA-MenC at Month 11 [N=93;109]	3062.9 (2421.2 to 3874.6)	954 (761.3 to 1195.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations for anti-PSC.

End point title	Concentrations for anti-PSC.

End point description:

Concentrations were expressed as geometric mean concentrations (GMCs). The seroprotection reference cut-off value was ≥ 0.3 µg/mL.

End point type	Secondary

End point timeframe:

At Month 10 and Month 11.

End point values	GSK2197870A Group	Pediacel Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	100	111		
Units: µg /mL				
geometric mean (confidence interval 95%)				
Anti-PSC at Month 10 [N=86;97]	0.94 (0.76 to 1.15)	0.87 (0.74 to 1.04)		
Anti-PSC at Month 11 [N=100;111]	6.15 (5.24 to 7.22)	2.88 (2.49 to 3.32)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations for anti-T and anti-D.

End point title	Concentrations for anti-T and anti-D.

End point description:

Concentrations were expressed as geometric mean concentrations (GMCs). The seroprotection reference cut-off value was ≥ 0.1 IU/mL. Seropositivity for anti-D was also defined with the ≥ 0.016 IU/mL cut-off (Neutralisation assay).

End point type	Secondary

End point timeframe:

At Month 10.

End point values	GSK2197870A Group	Pediacel Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	98		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-T ≥ 0.1 IU/mL [N=89;98]	0.428 (0.361 to 0.508)	0.26 (0.217 to 0.311)		
Anti-D ≥ 0.1 IU/mL [N=89;98]	0.249 (0.202 to 0.307)	0.385 (0.33 to 0.448)		
Anti-D ≥ 0.016 IU/mL [N=16;3]	0.015 (0.012 to 0.02)	0.02 (0.008 to 0.052)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations for anti-PT, anti-FHA and anti-PRN.

End point title	Concentrations for anti-PT, anti-FHA and anti-PRN.

End point description:

Concentrations were expressed as geometric mean concentrations (GMCs). The seropositivity reference cut-off value was ≥ 5 EL.U/mL.

End point type	Secondary

End point timeframe:

At Month 10.

End point values	GSK2197870A Group	Pediacel Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	100		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PT [N=89;100]	7.3 (6.1 to 8.8)	9.8 (8.5 to 11.4)		

Anti-FHA [N=89;99]	35.3 (28.3 to 44)	48.8 (40.4 to 58.9)		
Anti-PRN [N=89;100]	15 (11.8 to 19)	9.6 (7.7 to 11.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Titers for anti-polio 1, 2 and 3.

End point title	Titers for anti-polio 1, 2 and 3.

End point description:

Titers were expressed as geometric mean titers (GMTs). The seroprotection reference cut-off value was ≥ 1:8.

End point type	Secondary

End point timeframe:

At Month 10.

End point values	GSK2197870A Group	Pediacel Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	89		
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-polio 1 [N=78;86]	36.3 (26.5 to 49.8)	18.8 (14.4 to 24.7)		
Anti-polio 2 [N=78;85]	28.5 (20.9 to 39)	24.5 (18.8 to 32)		
Anti-polio 3 [N=78;86]	70.1 (51 to 96.3)	50.7 (37 to 69.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with a booster response to rSBA-MenC antibodies.

End point title	Number of subjects with a booster response to rSBA-MenC antibodies.

End point description:

Booster response defined as: for initially seronegative subjects, antibody titre ≥ 1:32 at post-booster (Month 11); for initially seropositive subjects, antibody titres at post-booster ≥ 4 fold the pre-booster.

End point type	Secondary

End point timeframe:

At Month 11

End point values	GSK2197870A Group	Pediacel Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	79		
Units: Subjects				
rSBA-MenC	68	61		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with a booster response to anti-PRP antibodies.

End point title	Number of subjects with a booster response to anti-PRP antibodies.

End point description:

Booster response defined as: for initially seronegative subjects, antibody concentration ≥ 0.6 µg/mL at post-booster (Month 11); for initially seropositive subjects, antibody concentrations at post-booster ≥ 4 fold the pre-booster.

End point type	Secondary

End point timeframe:

At Month 11

End point values	GSK2197870A Group	Pediacel Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	75	87		
Units: Subjects				
Anti-PRP	75	85		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with a booster response to anti-PSC antibodies.

End point title	Number of subjects with a booster response to anti-PSC antibodies.

End point description:

Booster response defined as: for initially seronegative subjects, antibody concentration ≥ 1.2 µg/mL at post-booster (Month 11); for initially seropositive subjects, antibody concentrations at post-booster ≥ 4 fold the pre-booster.

End point type	Secondary

End point timeframe:

At Month 11

End point values	GSK2197870A Group	Pediacel Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	75	83		
Units: Subjects				
Anti-PSC	48	27		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any solicited local symptoms.

End point title	Number of subjects reporting any solicited local symptoms.

End point description:

Solicited local symptoms assessed were pain, redness and swelling. Any = occurrence of any local symptom regardless of intensity grade.

End point type	Secondary

End point timeframe:

During the 8-day (Days 0-7)

End point values	GSK2197870A Group	Pediacel Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	142	141		
Units: Subjects				
Any pain	57	57		
Any redness	86	77		
Any swelling	60	48		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any solicited local symptoms.

End point title	Number of subjects reporting any solicited local symptoms.

End point description:

Solicited local symptoms assessed were pain, redness and swelling. Any = occurrence of any local symptom regardless of intensity grade.

End point type	Secondary

End point timeframe:

During the 8-day (Days 0-7)

End point values	GSK2197870A Group	Pediacel Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	134		
Units: Subjects				
Any pain	24	11		
Any redness	74	56		
Any swelling	35	20		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any solicited general symptoms.

End point title	Number of subjects reporting any solicited general symptoms.

End point description:

Solicited general symptoms assessed were drowsiness, irritability, loss of appetite and fever [axillary temperature above (≥) 37.5 degrees Celsius (°C)]. Any = occurrence of any local symptom regardless of intensity grade.

End point type	Secondary

End point timeframe:

During the 8-day (Days 0-7)

End point values	GSK2197870A Group	Pediacel Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	142	141		
Units: Subjects				
Any drowsiness	103	103		
Any irritability	122	117		
Any loss of appetite	79	77		
Any fever	59	49		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any solicited general symptoms.

End point title	Number of subjects reporting any solicited general symptoms.

End point description:

Solicited general symptoms assessed were drowsiness, irritability, loss of appetite and fever [axillary temperature above (≥) 37.5 degrees Celsius (°C)]. Any = occurrence of any local symptom regardless of intensity grade.

End point type	Secondary

End point timeframe:

During the 8-day (Days 0-7)

End point values	GSK2197870A Group	Pediacel Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	134		
Units: Subjects				
Any drowsiness	43	40		
Any irritability	75	66		
Any loss of appetite	41	40		
Any fever	18	20		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited adverse events (AEs).

End point title	Number of subjects reporting any unsolicited adverse events (AEs).

End point description:

An unsolicited AE is any AE (i.e. any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with use of a medicinal product, whether or not considered related to the medicinal product) 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 = occurrence of an AE regardless of intensity grade or relationship to study vaccination.

End point type	Secondary

End point timeframe:

Within the 31-day (Days 0-30) follow up period after vaccination.

End point values	GSK2197870A Group	Pediacel Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	142	142		
Units: Subjects				
Any AEs	114	112		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited adverse events (AEs).

End point title	Number of subjects reporting any unsolicited adverse events (AEs).

End point description:

An unsolicited AE is any AE (i.e. any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with use of a medicinal product, whether or not considered related to the medicinal product) 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 = occurrence of an AE regardless of intensity grade or relationship to study vaccination.

End point type	Secondary

End point timeframe:

Within the 31-day (Days 0-30) follow up period after vaccination.

End point values	GSK2197870A Group	Pediacel Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	139	135		
Units: Subjects				
Any AEs	75	66		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any serious adverse events (SAEs).

End point title	Number of subjects reporting any serious adverse events (SAEs).

End point description:

SAEs assessed include medical occurrences that results in death, are life threatening, require hospitalization or prolongation of hospitalization or results in disability/incapacity of a study subjects. Any SAE = any SAE regardless of assessment of relationship to study vaccination.

End point type	Secondary

End point timeframe:

During the entire study period (Month 0 to Month 11)

End point values	GSK2197870A Group	Pediacel Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	142	142		
Units: Subjects				
Any SAEs	9	6		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms: 8-day follow-up period after vaccination; unsolicited AEs: 31-day follow-up period after vaccination; SAEs: during the entire study period (Months 0-11).

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

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.1

Reporting groups

Reporting group title	GSK2197870A Group

Reporting group description:

Subjects aged between and including 6 and 12 weeks of age at the time of first vaccination received 3 doses of GSK2197870A vaccine at Months 0, 1 and 2, 2 doses of Prevenar™ vaccine at Months 0 and 2 and a booster dose of Menitorix™ vaccine at Month 10. All vaccines were administered intramuscularly. GSK2197870A and Menitorix™ vaccines were administered in the right upper anterolateral thigh and Prevenar™ vaccine in the left upper anterolateral thigh.

Reporting group title	Pediacel Group

Reporting group description:

Subjects aged between and including 6 and 12 weeks of age at the time of first vaccination received 3 doses of Pediacel™ vaccine at Months 0, 1 and 2, 2 doses of Prevenar™ vaccine at Months 0 and 2, 2 doses of Menjugate™ vaccine at Months 1 and 2 and a booster dose of Menitorix™ at Month 10. All vaccines were administered intramuscularly. Pediacel™ and Menitorix™ vaccines were administered in the right upper anterolateral thigh and Prevenar™ vaccine in the left upper anterolateral thigh and Menjugate™ vaccine in the left lower anterolateral thigh.

Serious adverse events	GSK2197870A Group	Pediacel Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 142 (6.34%)	6 / 142 (4.23%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 142 (0.70%)	0 / 142 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral atrophy			

subjects affected / exposed	0 / 142 (0.00%)	1 / 142 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	0 / 142 (0.00%)	1 / 142 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Lymph node abscess			
subjects affected / exposed	0 / 142 (0.00%)	1 / 142 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Developmental delay			
subjects affected / exposed	1 / 142 (0.70%)	0 / 142 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Intussusception			
subjects affected / exposed	1 / 142 (0.70%)	0 / 142 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	1 / 142 (0.70%)	0 / 142 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 142 (0.00%)	1 / 142 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			

Arthropathy			
subjects affected / exposed	1 / 142 (0.70%)	0 / 142 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	1 / 142 (0.70%)	2 / 142 (1.41%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 142 (0.00%)	1 / 142 (0.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	2 / 142 (1.41%)	0 / 142 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 142 (0.70%)	0 / 142 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 142 (0.70%)	0 / 142 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	GSK2197870A Group	Pediacel Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	122 / 142 (85.92%)	117 / 142 (82.39%)	
General disorders and administration site conditions			
Rash (Symptom reported during the booster phase.)			

subjects affected / exposed	7 / 142 (4.93%)	9 / 142 (6.34%)	
occurrences (all)	7	9	
Pain (Symptom reported during the primary phase.)			
alternative assessment type: Systematic			
subjects affected / exposed[1]	57 / 142 (40.14%)	57 / 141 (40.43%)	
occurrences (all)	57	57	
Redness (Symptom reported during the primary phase.)			
alternative assessment type: Systematic			
subjects affected / exposed[2]	86 / 142 (60.56%)	77 / 141 (54.61%)	
occurrences (all)	86	77	
Swelling (Symptom reported during the primary phase.)			
alternative assessment type: Systematic			
subjects affected / exposed[3]	60 / 142 (42.25%)	48 / 141 (34.04%)	
occurrences (all)	60	48	
Pain (Symptom reported during the booster phase.)			
alternative assessment type: Systematic			
subjects affected / exposed[4]	24 / 136 (17.65%)	11 / 134 (8.21%)	
occurrences (all)	24	11	
Redness (Symptom reported during the booster phase.)			
alternative assessment type: Systematic			
subjects affected / exposed[5]	76 / 136 (55.88%)	56 / 134 (41.79%)	
occurrences (all)	76	56	
Swelling (Symptom reported during the booster phase.)			
alternative assessment type: Systematic			
subjects affected / exposed[6]	35 / 136 (25.74%)	20 / 134 (14.93%)	
occurrences (all)	35	20	
Drowsiness (Symptom reported during the primary phase.)			
alternative assessment type: Systematic			
subjects affected / exposed[7]	103 / 142 (72.54%)	103 / 141 (73.05%)	
occurrences (all)	103	103	
Irritability (Symptom reported during the primary phase.)			

alternative assessment type: Systematic			
subjects affected / exposed[8]	122 / 142 (85.92%)	117 / 141 (82.98%)	
occurrences (all)	122	117	
Loss of appetite (Symptom reported during the primary phase.)			
alternative assessment type: Systematic			
subjects affected / exposed[9]	79 / 142 (55.63%)	77 / 141 (54.61%)	
occurrences (all)	79	77	
Fever (Symptom reported during the primary phase.)			
alternative assessment type: Systematic			
subjects affected / exposed[10]	59 / 142 (41.55%)	49 / 141 (34.75%)	
occurrences (all)	59	49	
Drowsiness (Symptom reported during the booster phase.)			
alternative assessment type: Systematic			
subjects affected / exposed[11]	43 / 136 (31.62%)	40 / 134 (29.85%)	
occurrences (all)	43	40	
Irritability (Symptom reported during the booster phase.)			
alternative assessment type: Systematic			
subjects affected / exposed[12]	75 / 136 (55.15%)	66 / 134 (49.25%)	
occurrences (all)	75	66	
Loss of appetite (Symptom reported during the booster phase.)			
alternative assessment type: Systematic			
subjects affected / exposed[13]	41 / 136 (30.15%)	40 / 134 (29.85%)	
occurrences (all)	41	40	
Fever (Symptom reported during the booster phase.)			
alternative assessment type: Systematic			
subjects affected / exposed[14]	18 / 136 (13.24%)	20 / 134 (14.93%)	
occurrences (all)	18	20	
Gastrointestinal disorders			
Teething (Symptom reported during the primary phase.)			
subjects affected / exposed	31 / 142 (21.83%)	29 / 142 (20.42%)	
occurrences (all)	31	29	
Diarrhoea (Symptom reported during			

the primary phase.)			
subjects affected / exposed	19 / 142 (13.38%)	18 / 142 (12.68%)	
occurrences (all)	19	18	
Vomiting (Symptom reported during the primary phase.)			
subjects affected / exposed	21 / 142 (14.79%)	14 / 142 (9.86%)	
occurrences (all)	21	14	
Teething (Symptom reported during the booster phase.)			
subjects affected / exposed	28 / 142 (19.72%)	23 / 142 (16.20%)	
occurrences (all)	28	23	
Diarrhoea (Symptom reported during the booster phase.)			
subjects affected / exposed	5 / 142 (3.52%)	7 / 142 (4.93%)	
occurrences (all)	5	7	
Respiratory, thoracic and mediastinal disorders			
Cough	Additional description: Symptom reported during the primary phase.		
subjects affected / exposed	7 / 142 (4.93%)	15 / 142 (10.56%)	
occurrences (all)	7	15	
Skin and subcutaneous tissue disorders			
Eczema	Additional description: Symptom reported during the primary phase.		
subjects affected / exposed	7 / 142 (4.93%)	14 / 142 (9.86%)	
occurrences (all)	7	14	
Infections and infestations			
Rhinitis (Symptom reported during the primary phase.)			
subjects affected / exposed	42 / 142 (29.58%)	35 / 142 (24.65%)	
occurrences (all)	42	35	
Nasopharyngitis (Symptom reported during the primary phase.)			
subjects affected / exposed	13 / 142 (9.15%)	18 / 142 (12.68%)	
occurrences (all)	13	18	
Upper respiratory tract infection (Symptom reported during the primary phase.)			
subjects affected / exposed	5 / 142 (3.52%)	7 / 142 (4.93%)	
occurrences (all)	5	7	
Nasopharyngitis	Additional description: Symptom reported during the booster phase.		
subjects affected / exposed	11 / 142 (7.75%)	2 / 142 (1.41%)	
occurrences (all)	11	2	

Upper respiratory tract infection	Additional description: Symptom reported during the booster phase.		
subjects affected / exposed	5 / 142 (3.52%)	7 / 142 (4.93%)	
occurrences (all)	5	7	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The number of subjects exposed is different depending on the phase of the study (primary vaccination or booster) in which the symptom was reported. For solicited local and general symptoms, the number may further differ as not all subjects had their symptom sheets completed.

[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 number of subjects exposed is different depending on the phase of the study (primary vaccination or booster) in which the symptom was reported. For solicited local and general symptoms, the number may further differ as not all subjects had their symptom sheets completed.

[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 number of subjects exposed is different depending on the phase of the study (primary vaccination or booster) in which the symptom was reported. For solicited local and general symptoms, the number may further differ as not all subjects had their symptom sheets completed.

[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 number of subjects exposed is different depending on the phase of the study (primary vaccination or booster) in which the symptom was reported. For solicited local and general symptoms, the number may further differ as not all subjects had their symptom sheets completed.

[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 number of subjects exposed is different depending on the phase of the study (primary vaccination or booster) in which the symptom was reported. For solicited local and general symptoms, the number may further differ as not all subjects had their symptom sheets completed.

[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 number of subjects exposed is different depending on the phase of the study (primary vaccination or booster) in which the symptom was reported. For solicited local and general symptoms, the number may further differ as not all subjects had their symptom sheets completed.

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The number of subjects exposed is different depending on the phase of the study (primary vaccination or booster) in which the symptom was reported. For solicited local and general symptoms, the number may further differ as not all subjects had their symptom sheets completed.

[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The number of subjects exposed is different depending on the phase of the study (primary vaccination or booster) in which the symptom was reported. For solicited local and general symptoms, the number may further differ as not all subjects had their symptom sheets completed.

[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The number of subjects exposed is different depending on the phase of the study (primary vaccination or booster) in which the symptom was reported. For solicited local and general symptoms, the number may further differ as not all subjects had their symptom sheets completed.

[10] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The number of subjects exposed is different depending on the phase of the study (primary vaccination or booster) in which the symptom was reported. For solicited local and general symptoms, the number may further differ as not all subjects had their symptom sheets completed.

[11] - 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 number of subjects exposed is different depending on the phase of the study (primary vaccination or booster) in which the symptom was reported. For solicited local and general symptoms, the number may further differ as not all subjects had their symptom sheets completed.

[12] - 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 number of subjects exposed is different depending on the phase of the study (primary vaccination or booster) in which the symptom was reported. For solicited local and general symptoms, the number may further differ as not all subjects had their symptom sheets completed.

[13] - 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 number of subjects exposed is different depending on the phase of the study (primary vaccination or booster) in which the symptom was reported. For solicited local and general symptoms, the number may further differ as not all subjects had their symptom sheets completed.
[14] - 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 number of subjects exposed is different depending on the phase of the study (primary vaccination or booster) in which the symptom was reported. For solicited local and general symptoms, the number may further differ as not all subjects had their symptom sheets completed.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 February 2010	• This amendment reflects the recommendation of the Department of Health issued on 19 January 2010 to immunise babies with a 13-valent pneumococcal vaccine, rather than the 7-valent pneumococcal vaccine as foreseen in the original protocol. Since this recommendation was made during the course of the trial and since the 13-valent vaccine is not yet in routine use at the time of the amendment, the amended protocol will allow for the use of the 13-valent pneumococcal vaccine at the last visit of the study after finishing all study related procedures and will therefore not have an effect on the study endpoints. • An interim analysis on immunogenicity data in terms of rSBA MenC and anti-PRP response after the primary series was added. • Additionally, updated information on back-up contact for reporting of SAEs has been provided.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported