Clinical trial results:
A phase III randomized, single-blind, controlled study to demonstrate the non-inferiority of co-administration of GSK Biologicals' 10-valent pneumococcal conjugate vaccine with Pediacel versus co-administration with Infanrix hexa, when administered to infants as a three-dose primary vaccination course during the first six months of life and as a booster dose at 11-13 months of age.

Summary

EudraCT number	2007-004002-26
Trial protocol	NL
Global end of trial date	01 December 2010

Results information

Result version number	v3 (current)
This version publication date	14 May 2023
First version publication date	19 June 2015
Version creation reason	• Correction of full data set Correction of full data set and alignment between registries.

Trial information

Trial identification

Sponsor protocol code	110142, 111053

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00652951
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	12 December 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 May 2009
Global end of trial reached?	Yes
Global end of trial date	01 December 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that GSK Biologicals' 10 valent pneumococcal conjugate vaccine (Synflorix) when co-administered with Pediacel is non-inferior to co-administration with Infanrix hexa, in terms of immune response to the 10 pneumococcal vaccine serotypes and to protein D, when administered as a three-dose primary vaccination course.
Criteria for non-inferiority: For each of the 10 pneumococcal vaccine serotypes and protein D, non-inferiority will be demonstrated if the upper limit of the 2-sided 95% CI of the geometric mean concentrations (GMCs) ratio between groups (Synflorix + Infanrix hexa Group over Synflorix + Pediacel Group), is lower than 2.

Protection of trial subjects:

All subjects were supervised for 30 min after vaccination/product administration with appropriate medical treatment readily available in case of a rare anaphylactic reaction. Vaccines/products were administered by qualified and trained personnel. Vaccines/products were administered only to eligible subjects that had no contraindications to any components of the vaccines/products. Also, all Intramuscular injections were administered into the anterolateral region of the thigh or into the deltoid. The buttock was not used for administration of vaccines because of the potential risk of injury to the sciatic nerve and the risk of decreased immunogenicity because of inadvertent subcutaneous injection or injection into deep fat tissue.
For all intramuscular injections, the needle was selected long enough to reach the muscle mass and prevent vaccine from seeping into subcutaneous tissue, but not so long as to involve underling nerves and blood vessels or bone. Vaccinators were familiar with the anatomy of the area into which they are injecting vaccine. When appropriate, an individual decision on needle size and site of injection was made for each person on the basis of age, and the size of the muscle. Subjects were followed-up for 31 days after the last vaccination/product administration for adverse events following vaccination. Subjects were also followed during the entire study period for serious adverse events (SAEs).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 April 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	Netherlands: 780
Worldwide total number of subjects	780
EEA total number of subjects	780

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)	780
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:

The study included a Primary (PRI) Phase, up to Month 3, followed by a Booster (BST) Phase, up to Month 9.

Pre-assignment

Screening details:

At screening the following was performed: informed consent was obtained and signed from subjects' parents/guardians, check for inclusion/exclusion criteria and contraindications/precautions was performed as regards to vaccination, and medical history of subjects was collected. Subjects' pre-vaccination body temperature was evaluated.

Period 1

Period 1 title	Primary Phase
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Synflorix + Infanrix hexa Group

Arm description:

Subjects received 3 doses of Synflorix vaccine co-administered with Infanrix hexa at 2, 3 and 4 months of age (Study Months 0, 1, 2) and received a booster dose of each vaccine between 11 and 13 months of age (Study Month 9). All vaccines were administered intramuscularly in the right (Synflorix) or left (Infanrix hexa) thigh or deltoid.

Arm type	Experimental
Investigational medicinal product name	Synflorix
Investigational medicinal product code	10Pn-PD-DiT
Other name	10Pn-PD-DiT, 10Pn, GSK1024850A
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses at 2, 3 and 4 months of age (Study Months 0, 1, 2) followed by a booster dose between 11 and 13 months of age (Study Month 9). Vaccine was administered in the right thigh or deltoid.

Investigational medicinal product name	Infanrix hexa
Investigational medicinal product code	DTPa-HBV-IPV/Hib
Other name	DTPa-HBV-IPV/Hib
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses at 2, 3 and 4 months of age (Study Months 0, 1, 2) followed by a booster dose between 11 and 13 months of age (Study Month 9). Vaccine was administered in the left thigh or deltoid.

Arm title	Synflorix + Pediacel Group

Arm description:

Subjects received 3 doses of Synflorix vaccine co-administered with Pediacel at 2, 3 and 4 months of age (Study Months 0, 1, 2) and received a booster dose of each vaccine between 11 and 13 months of age (Study Month 9). All vaccines were administered intramuscularly in the right (Synflorix) or left (Pediacel) thigh or deltoid.

Arm type	Experimental

Investigational medicinal product name	Synflorix
Investigational medicinal product code	10Pn-PD-DiT
Other name	10Pn-PD-DiT, 10Pn, GSK1024850A
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses at 2, 3 and 4 months of age (Study Months 0, 1, 2) followed by a booster dose between 11 and 13 months of age (Study Month 9). Vaccine was administered in the right thigh or deltoid.

Investigational medicinal product name	Pediacel
Investigational medicinal product code	DTPa-IPV-Hib
Other name	DTPa-IPV-Hib
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses at 2, 3 and 4 months of age (Study Months 0, 1, 2) followed by a booster dose between 11 and 13 months of age (Study Month 9). Vaccine was administered in the left thigh or deltoid.

Arm title	Prevenar + Pediacel Group

Arm description:

Subjects received 3 doses of Prevenar co-administered with Pediacel vaccine at 2, 3 and 4 months of age (Study Months 0, 1, 2) and received a booster dose of each vaccine between 11 and 13 months of age (Study Month 9). All vaccines were administered intramuscularly in the right (Prevenar) or left (Pediacel) thigh or deltoid.

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

Dosage and administration details:

3 doses at 2, 3 and 4 months of age (Study Months 0, 1, 2) followed by a booster dose between 11 and 13 months of age (Study Month 9). Vaccine was administered in the right thigh or deltoid.

Investigational medicinal product name	Pediacel
Investigational medicinal product code	DTPa-IPV-Hib
Other name	DTPa-IPV-Hib
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses at 2, 3 and 4 months of age (Study Months 0, 1, 2) followed by a booster dose between 11 and 13 months of age (Study Month 9). Vaccine was administered in the left thigh or deltoid.

Number of subjects in period 1	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group
Started	260	260	260
Completed	260	260	260

Period 2

Period 2 title	Booster Phase
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Synflorix + Infanrix hexa Group

Arm description:

Subjects received 3 doses of Synflorix vaccine co-administered with Infanrix hexa at 2, 3 and 4 months of age (Study Months 0, 1, 2) and received a booster dose of each vaccine between 11 and 13 months of age (Study Month 9). All vaccines were administered intramuscularly in the right (Synflorix) or left (Infanrix hexa) thigh or deltoid.

Arm type	Experimental
Investigational medicinal product name	Synflorix
Investigational medicinal product code	10Pn-PD-DiT
Other name	10Pn-PD-DiT, 10Pn, GSK1024850A
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses at 2, 3 and 4 months of age (Study Months 0, 1, 2) followed by a booster dose between 11 and 13 months of age (Study Month 9). Vaccine was administered in the right thigh or deltoid.

Investigational medicinal product name	Infanrix hexa
Investigational medicinal product code	DTPa-HBV-IPV/Hib
Other name	DTPa-HBV-IPV/Hib
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses at 2, 3 and 4 months of age (Study Months 0, 1, 2) followed by a booster dose between 11 and 13 months of age (Study Month 9). Vaccine was administered in the left thigh or deltoid.

Arm title	Synflorix + Pediacel Group

Arm description:

Subjects received 3 doses of Synflorix vaccine co-administered with Pediacel at 2, 3 and 4 months of age (Study Months 0, 1, 2) and received a booster dose of each vaccine between 11 and 13 months of age (Study Month 9). All vaccines were administered intramuscularly in the right (Synflorix) or left (Pediacel) thigh or deltoid.

Arm type	Experimental
Investigational medicinal product name	Synflorix
Investigational medicinal product code	10Pn-PD-DiT
Other name	10Pn-PD-DiT, 10Pn, GSK1024850A
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses at 2, 3 and 4 months of age (Study Months 0, 1, 2) followed by a booster dose between 11 and 13 months of age (Study Month 9). Vaccine was administered in the right thigh or deltoid.

Investigational medicinal product name	Pediacel
Investigational medicinal product code	DTPa-IPV-Hib
Other name	DTPa-IPV-Hib
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses at 2, 3 and 4 months of age (Study Months 0, 1, 2) followed by a booster dose between 11 and

13 months of age (Study Month 9). Vaccine was administered in the left thigh or deltoid.

Arm title	Prevenar + Pediacel Group

Arm description:

Subjects received 3 doses of Prevenar co-administered with Pediacel vaccine at 2, 3 and 4 months of age (Study Months 0, 1, 2) and received a booster dose of each vaccine between 11 and 13 months of age (Study Month 9). All vaccines were administered intramuscularly in the right (Prevenar) or left (Pediacel) thigh or deltoid.

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

Dosage and administration details:

3 doses at 2, 3 and 4 months of age (Study Months 0, 1, 2) followed by a booster dose between 11 and 13 months of age (Study Month 9). Vaccine was administered in the right thigh or deltoid.

Investigational medicinal product name	Pediacel
Investigational medicinal product code	DTPa-IPV-Hib
Other name	DTPa-IPV-Hib
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses at 2, 3 and 4 months of age (Study Months 0, 1, 2) followed by a booster dose between 11 and 13 months of age (Study Month 9). Vaccine was administered in the left thigh or deltoid.

Number of subjects in period 2[1]	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group
Started	257	259	258
Completed	256	258	258
Not completed	1	1	0
Adverse event, non-fatal	-	1	-
Not specified	1	-	-

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 study participants returned in time for every study visit, but they were allowed to continue the study nonetheless. The number of participants who started each study period depends on the actual rate of return of the subjects.

Baseline characteristics

Reporting groups	
Reporting group title	Synflorix + Infanrix hexa Group
Reporting group description:	
Subjects received 3 doses of Synflorix vaccine co-administered with Infanrix hexa at 2, 3 and 4 months of age (Study Months 0, 1, 2) and received a booster dose of each vaccine between 11 and 13 months of age (Study Month 9). All vaccines were administered intramuscularly in the right (Synflorix) or left (Infanrix hexa) thigh or deltoid.	
Reporting group title	Synflorix + Pediacel Group
Reporting group description:	
Subjects received 3 doses of Synflorix vaccine co-administered with Pediacel at 2, 3 and 4 months of age (Study Months 0, 1, 2) and received a booster dose of each vaccine between 11 and 13 months of age (Study Month 9). All vaccines were administered intramuscularly in the right (Synflorix) or left (Pediacel) thigh or deltoid.	
Reporting group title	Prevenar + Pediacel Group
Reporting group description:	
Subjects received 3 doses of Prevenar co-administered with Pediacel vaccine at 2, 3 and 4 months of age (Study Months 0, 1, 2) and received a booster dose of each vaccine between 11 and 13 months of age (Study Month 9). All vaccines were administered intramuscularly in the right (Prevenar) or left (Pediacel) thigh or deltoid.	

Reporting group values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group
Number of subjects	260	260	260
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	260	260	260
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: weeks			
arithmetic mean	7.4	7.6	7.6
standard deviation	± 1.2	± 1.29	± 1.26
Gender categorical Units: Subjects			
Female	118	130	136
Male	142	130	124

Reporting group values	Total		
Number of subjects	780		
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)	780		
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			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	384		
Male	396		

End points reporting groups

Reporting group title	Synflorix + Infanrix hexa Group

Reporting group description:

Subjects received 3 doses of Synflorix vaccine co-administered with Infanrix hexa at 2, 3 and 4 months of age (Study Months 0, 1, 2) and received a booster dose of each vaccine between 11 and 13 months of age (Study Month 9). All vaccines were administered intramuscularly in the right (Synflorix) or left (Infanrix hexa) thigh or deltoid.

Reporting group title	Synflorix + Pediacel Group

Reporting group description:

Subjects received 3 doses of Synflorix vaccine co-administered with Pediacel at 2, 3 and 4 months of age (Study Months 0, 1, 2) and received a booster dose of each vaccine between 11 and 13 months of age (Study Month 9). All vaccines were administered intramuscularly in the right (Synflorix) or left (Pediacel) thigh or deltoid.

Reporting group title	Prevenar + Pediacel Group

Reporting group description:

Subjects received 3 doses of Prevenar co-administered with Pediacel vaccine at 2, 3 and 4 months of age (Study Months 0, 1, 2) and received a booster dose of each vaccine between 11 and 13 months of age (Study Month 9). All vaccines were administered intramuscularly in the right (Prevenar) or left (Pediacel) thigh or deltoid.

Reporting group title	Synflorix + Infanrix hexa Group

Reporting group description:

Subjects received 3 doses of Synflorix vaccine co-administered with Infanrix hexa at 2, 3 and 4 months of age (Study Months 0, 1, 2) and received a booster dose of each vaccine between 11 and 13 months of age (Study Month 9). All vaccines were administered intramuscularly in the right (Synflorix) or left (Infanrix hexa) thigh or deltoid.

Reporting group title	Synflorix + Pediacel Group

Reporting group description:

Subjects received 3 doses of Synflorix vaccine co-administered with Pediacel at 2, 3 and 4 months of age (Study Months 0, 1, 2) and received a booster dose of each vaccine between 11 and 13 months of age (Study Month 9). All vaccines were administered intramuscularly in the right (Synflorix) or left (Pediacel) thigh or deltoid.

Reporting group title	Prevenar + Pediacel Group

Reporting group description:

Subjects received 3 doses of Prevenar co-administered with Pediacel vaccine at 2, 3 and 4 months of age (Study Months 0, 1, 2) and received a booster dose of each vaccine between 11 and 13 months of age (Study Month 9). All vaccines were administered intramuscularly in the right (Prevenar) or left (Pediacel) thigh or deltoid.

Primary: Antibody concentrations against 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) - Primary vaccination

End point title	Antibody concentrations against 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) - Primary vaccination

End point description:

Anti-pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antibody concentrations (Anti-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F) were measured by 22F-inhibition Enzyme-Linked ImmunSorbent Assay (ELISA); presented as geometric mean concentrations (GMCs) and expressed in micrograms per milliliter (µg/mL). The seropositivity cut-off for the assay was greater than or equal to (≥) 0.05 µg/mL.
The Primary ATP cohort for immunogenicity included all evaluable subjects for whom data concerning immunogenicity outcome measures were available. This included subjects for whom assay results were available for antibodies against at least one study vaccine antigen component post-dose III.

End point type	Primary

End point timeframe:

At Month 3, one month after the administration of the third dose of pneumococcal conjugate vaccine

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	194	189	192	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-1 (N=181;178;178)	1.17 (1.02 to 1.33)	1.31 (1.16 to 1.48)	0.03 (0.03 to 0.03)	
Anti-4 (N=192;185;191)	1.61 (1.41 to 1.84)	1.59 (1.38 to 1.83)	2.44 (2.19 to 2.73)	
Anti-5 (N=187;181;178)	2.11 (1.88 to 2.37)	2.16 (1.92 to 2.43)	0.03 (0.03 to 0.03)	
Anti-6B (N=177;174;180)	0.33 (0.26 to 0.4)	0.35 (0.28 to 0.43)	0.41 (0.34 to 0.51)	
Anti-7F (N=192;187;183)	1.7 (1.52 to 1.9)	1.77 (1.57 to 1.99)	0.04 (0.03 to 0.04)	
Anti-9V (N=185;186;187)	1.4 (1.2 to 1.63)	1.47 (1.29 to 1.68)	2.14 (1.91 to 2.4)	
Anti-14 (N=192;187;192)	3.38 (2.99 to 3.81)	3.33 (2.93 to 3.78)	3.64 (3.24 to 4.1)	
Anti-18C (N=194;189;191)	1.73 (1.45 to 2.05)	1.07 (0.92 to 1.25)	2.1 (1.83 to 2.4)	
Anti-19F (N=189;183;189)	2.07 (1.73 to 2.48)	1.96 (1.64 to 2.34)	3.04 (2.71 to 3.42)	
Anti-23F (N=179;175;184)	0.5 (0.41 to 0.6)	0.54 (0.44 to 0.66)	1.24 (1.04 to 1.47)	

Statistical analyses

Statistical analysis title	Immune response non-inferiority - serotype 1

Statistical analysis description:

The 2-sided 95% confidence interval (CI) of the geometric mean concentration (GMC) ratio between the Synflorix + Infanrix hexa and Synflorix + Pediacel groups (Synflorix + Infanrix hexa Group over Synflorix + Pediacel Group), at one month after Dose 3 of pneumococcal vaccine, was computed for each of the 10 pneumococcal vaccine serotypes and protein D. This statistical method concerns pneumococcal vaccine serotype 1.

Comparison groups	Synflorix + Infanrix hexa Group v Synflorix + Pediacel Group
Number of subjects included in analysis	383
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	GMC ratio
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	1.07

Notes:

[1] - Non-inferiority criteria: The upper limit (UL) of the 2-sided 95% confidence interval (CI) of the GMC ratio for between groups (Synflorix + Infanrix hexa Group over Synflorix + Pediacel Group), was lower than 2 for the pneumococcal vaccine serotype 1.

Statistical analysis title	Immune response non-inferiority - serotype 4

Statistical analysis description:

The 2-sided 95% CI of the geometric mean concentration (GMC) ratio between the Synflorix + Infanrix hexa and Synflorix + Pediacel groups (Synflorix + Infanrix hexa Group over Synflorix + Pediacel Group), at one month after Dose 3 of pneumococcal vaccine, was computed for each of the 10 pneumococcal vaccine serotypes and protein D. This statistical method concerns pneumococcal vaccine serotype 4.

Comparison groups	Synflorix + Infanrix hexa Group v Synflorix + Pediacel Group
Number of subjects included in analysis	383
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	GMC ratio
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.23

Notes:

[2] - Non-inferiority criteria: The upper limit (UL) of the 2-sided 95% CI of the GMC ratio for between groups (Synflorix + Infanrix hexa Group over Synflorix + Pediacel Group), was lower than 2 for the pneumococcal vaccine serotype 4.

Statistical analysis title	Immune response non-inferiority - serotype 5

Statistical analysis description:

The 2-sided 95% CI of the geometric mean concentration (GMC) ratio between the Synflorix + Infanrix hexa and Synflorix + Pediacel groups (Synflorix + Infanrix hexa Group over Synflorix + Pediacel Group), at one month after Dose 3 of pneumococcal vaccine, was computed for each of the 10 pneumococcal vaccine serotypes and protein D. This statistical method concerns pneumococcal vaccine serotype 5.

Comparison groups	Synflorix + Infanrix hexa Group v Synflorix + Pediacel Group
Number of subjects included in analysis	383
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	GMC ratio
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.15

Notes:

[3] - Non-inferiority criteria: The upper limit (UL) of the 2-sided 95% CI of the GMC ratio for between groups (Synflorix + Infanrix hexa Group over Synflorix + Pediacel Group), was lower than 2 for the pneumococcal vaccine serotype 5.

Statistical analysis title	Immune response non-inferiority - serotype 6B

Statistical analysis description:

The 2-sided 95% CI of the geometric mean concentration (GMC) ratio between the Synflorix + Infanrix hexa and Synflorix + Pediacel groups (Synflorix + Infanrix hexa Group over Synflorix + Pediacel Group), at one month after Dose 3 of pneumococcal vaccine, was computed for each of the 10 pneumococcal vaccine serotypes and protein D. This statistical method concerns pneumococcal vaccine serotype 6B.

Comparison groups	Synflorix + Infanrix hexa Group v Synflorix + Pediacel Group
Number of subjects included in analysis	383
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Parameter estimate	GMC ratio
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	1.26

Notes:

[4] - Non-inferiority criteria: The upper limit (UL) of the 2-sided 95% CI of the GMC ratio for between groups (Synflorix + Infanrix hexa Group over Synflorix + Pediacel Group), was lower than 2 for the pneumococcal vaccine serotype 6B.

Statistical analysis title	Immune response non-inferiority - serotype 7F

Statistical analysis description:

The 2-sided 95% CI of the geometric mean concentration (GMC) ratio between the Synflorix + Infanrix hexa and Synflorix + Pediacel Group groups (Synflorix + Infanrix hexa Group over Synflorix + Pediacel Group), at one month after Dose 3 of pneumococcal vaccine, was computed for each of the 10 pneumococcal vaccine serotypes and protein D. This statistical method concerns pneumococcal vaccine serotype 7F.

Comparison groups	Synflorix + Infanrix hexa Group v Synflorix + Pediacel Group
Number of subjects included in analysis	383
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
Parameter estimate	GMC ratio
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	1.13

Notes:

[5] - Non-inferiority criteria: The upper limit of the 2-sided 95% CI of the GMC ratio for between groups (Synflorix + Infanrix hexa Group over Synflorix + Pediacel Group Group), was lower than 2 for the pneumococcal vaccine serotype 7F.

Statistical analysis title	Immune response non-inferiority - serotype 9V

Statistical analysis description:

The 2-sided 95% CI of the geometric mean concentration (GMC) ratio between the Synflorix + Infanrix hexa and Synflorix + Pediacel groups (Synflorix + Infanrix hexa Group over Synflorix + Pediacel Group), at one month after Dose 3 of pneumococcal vaccine, was computed for each of the 10 pneumococcal vaccine serotypes and protein D. This statistical method concerns pneumococcal vaccine serotype 9V.

Comparison groups	Synflorix + Infanrix hexa Group v Synflorix + Pediacel Group
Number of subjects included in analysis	383
Analysis specification	Pre-specified
Analysis type	non-inferiority[6]
Parameter estimate	GMC ratio
Point estimate	0.95

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	1.16

Notes:

[6] - Non-inferiority criteria: The upper limit (UL) of the 2-sided 95% CI of the GMC ratio for between groups (Synflorix + Infanrix hexa Group over Synflorix + Pediacel Group), was lower than 2 for the pneumococcal vaccine serotype 9V.

Statistical analysis title	Immune response non-inferiority - serotype 14

Statistical analysis description:

The 2-sided 95% CI of the geometric mean concentration (GMC) ratio between the Synflorix + Infanrix hexa and Synflorix + Pediacel groups (Synflorix + Infanrix hexa Group over Synflorix + Pediacel Group), at one month after Dose 3 of pneumococcal vaccine, was computed for each of the 10 pneumococcal vaccine serotypes and protein D. This statistical method concerns pneumococcal vaccine serotype 14.

Comparison groups	Synflorix + Infanrix hexa Group v Synflorix + Pediacel Group
Number of subjects included in analysis	383
Analysis specification	Pre-specified
Analysis type	non-inferiority[7]
Parameter estimate	GMC ratio
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.21

Notes:

[7] - Non-inferiority criteria: The upper limit (UL) of the 2-sided 95% CI of the GMC ratio for between groups (Synflorix + Infanrix hexa Group over Synflorix + Pediacel Group), was lower than 2 for the pneumococcal vaccine serotype 14.

Statistical analysis title	Immune response non-inferiority - serotype 18C

Statistical analysis description:

The 2-sided 95% CI of the geometric mean concentration (GMC) ratio between the Synflorix + Infanrix hexa and Synflorix + Pediacel groups (Synflorix + Infanrix hexa Group over), at one month after Dose 3 of pneumococcal vaccine, was computed for each of the 10 pneumococcal vaccine serotypes and protein D. This statistical method concerns pneumococcal vaccine serotype 18C.

Comparison groups	Synflorix + Infanrix hexa Group v Synflorix + Pediacel Group
Number of subjects included in analysis	383
Analysis specification	Pre-specified
Analysis type	non-inferiority[8]
Method	Regression, Cox
Parameter estimate	GMC ratio
Point estimate	1.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.28
upper limit	2.03

Notes:

[8] - Non-inferiority criteria: The upper limit (UL) of the 2-sided 95% CI of the GMC ratio for between groups (Synflorix + Infanrix hexa Group over Synflorix + Pediacel Group), was lower than 2 for the pneumococcal vaccine serotype 18C.

Statistical analysis title	Immune response non-inferiority - serotype 19F

Statistical analysis description:

The 2-sided 95% CI of the geometric mean concentration (GMC) ratio between the Synflorix + Infanrix hexa and Synflorix + Pediacel groups (Synflorix + Infanrix hexa Group over Synflorix + Pediacel Group), at one month after Dose 3 of pneumococcal vaccine, was computed for each of the 10 pneumococcal vaccine serotypes and protein D. This statistical method concerns pneumococcal vaccine serotype 19F.

Comparison groups	Synflorix + Infanrix hexa Group v Synflorix + Pediacel Group
Number of subjects included in analysis	383
Analysis specification	Pre-specified
Analysis type	non-inferiority[9]
Parameter estimate	GMC ratio
Point estimate	1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	1.36

Notes:

[9] - Non-inferiority criteria: The upper limit (UL) of the 2-sided 95% CI of the GMC ratio for between groups (Synflorix + Infanrix hexa Group over Synflorix + Pediacel Group), was lower than 2 for the pneumococcal vaccine serotype 19F.

Statistical analysis title	Immune response non-inferiority - serotype 23F

Statistical analysis description:

The 2-sided 95% CI of the geometric mean concentration (GMC) ratio between the Synflorix + Infanrix hexa Group and Synflorix + Pediacel groups (Synflorix + Infanrix hexa Group Group over Synflorix + Pediacel Group), at one month after Dose 3 of pneumococcal vaccine, was computed for each of the 10 pneumococcal vaccine serotypes and protein D. This statistical method concerns pneumococcal vaccine serotype 23F.

Comparison groups	Synflorix + Infanrix hexa Group v Synflorix + Pediacel Group
Number of subjects included in analysis	383
Analysis specification	Pre-specified
Analysis type	non-inferiority[10]
Parameter estimate	GMC ratio
Point estimate	0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	1.23

Notes:

[10] - Non-inferiority criteria: The upper limit (UL) of the 2-sided 95% CI of the GMC ratio for between groups (Synflorix + Infanrix hexa Group Group over Synflorix + Pediacel Group), was lower than 2 for the pneumococcal vaccine serotype 23F.

Primary: Antibody concentration against protein D (PD) - Primary vaccination

End point title	Antibody concentration against protein D (PD) - Primary vaccination

End point description:

Anti-PD antibody concentrations were presented as geometric mean concentrations (GMCs) and expressed in ELISA units per milliliter (EL.U/mL). The seropositivity cut-off for the assay was ≥ 100 EL.U/mL.
The Primary ATP cohort for immunogenicity included all evaluable subjects for whom data concerning immunogenicity outcome measures were available. This included subjects for whom assay results were available for antibodies against at least one study vaccine antigen component post-dose III.

End point type	Primary

End point timeframe:

At Month 3, one month after the administration of the third dose of pneumococcal conjugate vaccine

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	195	189	182	
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD	1580 (1409.5 to 1771.1)	1743 (1560.2 to 1947.2)	69.7 (63 to 77.1)	

Statistical analyses

Statistical analysis title	Immune response non-inferiority - protein D

Statistical analysis description:

The 2-sided 95% CI of the geometric mean concentration (GMC) ratio between the Synflorix + Infanrix hexa and Synflorix + Pediacel groups (Synflorix + Infanrix hexa Group over Synflorix + Pediacel Group), at one month after Dose 3 of pneumococcal vaccine, was computed for each of the 10 pneumococcal vaccine serotypes and protein D. This statistical method concerns protein D.

Comparison groups	Synflorix + Infanrix hexa Group v Synflorix + Pediacel Group
Number of subjects included in analysis	384
Analysis specification	Pre-specified
Analysis type	non-inferiority[11]
Parameter estimate	GMC ratio
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.06

Notes:

[11] - Non-inferiority criteria: The upper limit (UL) of the 2-sided 95% CI of the GMC ratio for between groups (Synflorix + Infanrix hexa Group over Synflorix + Pediacel Group), was lower than 2 for protein D.

Secondary: Number of subjects with antibody concentrations against 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) ≥ 0.2 µg/mL - Primary vaccination

End point title	Number of subjects with antibody concentrations against 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) ≥ 0.2 µg/mL - Primary vaccination

End point description:

Antibody concentrations against the pneumococcal serotypes were assessed by 22F-inhibition ELISA.
The reference cut-off value of the assay was an antibody concentration greater than or equal to (≥) 0.02 µg/mL.
The Primary ATP cohort for immunogenicity included all evaluable subjects for whom data concerning immunogenicity outcome measures were available. This included subjects for whom assay results were available for antibodies against at least one study vaccine antigen component post-dose III.

End point type	Secondary

End point timeframe:

At Month 3, one month after the administration of the third vaccine dose

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	194	189	192	
Units: Subjects				
Anti-1 (N=181;178;178)	174	176	5	
Anti-4 (N=192;185;191)	188	180	189	
Anti-5 (N=187;181;178)	187	179	0	
Anti-6B (N=177;174;180)	122	113	124	
Anti-7F (N=192;187;183)	190	186	11	
Anti-9V (N=185;186;187)	176	181	184	
Anti-14 (N=192;187;192)	191	187	192	
Anti-18C (N=194;189;191)	183	178	187	
Anti-19F (N=189;183;189)	180	174	189	
Anti-23F (N=179;175;184)	134	133	171	

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic activity (OPA) titers against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F - Primary vaccination

End point title	Opsonophagocytic activity (OPA) titers against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F - Primary vaccination

End point description:

Titers were presented as geometric mean titers (GMTs), for the seropositivity cut-off value of 8.
The Primary ATP cohort for immunogenicity included all evaluable subjects for whom data concerning immunogenicity outcome measures were available. This included subjects for whom assay results were available for antibodies against at least one study vaccine antigen component post-dose III.

End point type	Secondary

End point timeframe:

At Month 3, one month after the administration of the third vaccine dose

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	139	135	132	
Units: Titers				
geometric mean (confidence interval 95%)				
Opsono-1 (N=132;126;125)	20.7 (15.6 to 27.6)	20.8 (15.8 to 27.4)	4.7 (4.1 to 5.2)	
Opsono-4 (N=133;132;129)	592.9 (475.9 to 738.7)	600.4 (492.2 to 732.3)	838.4 (718.7 to 978.2)	
Opsono-5 (N=138;134;132)	54.8 (44 to 68.4)	60.1 (48.2 to 74.8)	4.2 (3.9 to 4.6)	
Opsono-6B (N=129;130;123)	261.3 (176 to 388)	296.4 (198 to 443.7)	633 (419 to 956.4)	
Opsono-7F (N=130;127;114)	2063.3 (1691.7 to 2516.6)	2136.1 (1707.9 to 2671.5)	18.4 (12.1 to 28)	
Opsono-9V (N=132;129;125)	863.6 (687.6 to 1084.7)	1277.7 (1053.3 to 1550.1)	1194 (1009.5 to 1412.1)	
Opsono-14 (N=134;135;127)	990.4 (820.6 to 1195.5)	1086.4 (899.6 to 1311.9)	1373.3 (1040.4 to 1812.7)	
Opsono-18C (N=133;129;129)	122.6 (89.4 to 168.2)	84.2 (60.9 to 116.5)	213.6 (163.6 to 278.8)	
Opsono-19F (N=137;133;130)	133 (98.1 to 180.2)	143.8 (108.6 to 190.3)	39.2 (30.6 to 50.4)	
Opsono-23F (N=139;133;130)	847.4 (626.5 to 1146.3)	1089 (800.2 to 1482)	3703.4 (3119.4 to 4396.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with antibody concentrations against pneumococcal cross-reactive serotypes 6A and 19A (Anti-6A and 19A) ≥ 0.2 µg/mL - Primary vaccination

End point title	Number of subjects with antibody concentrations against pneumococcal cross-reactive serotypes 6A and 19A (Anti-6A and 19A) ≥ 0.2 µg/mL - Primary vaccination

End point description:

Antibody concentrations against the cross- reactive pneumococcal serotypes were assessed by 22F-inhibition ELISA. The reference cut-off value of the assay was an antibody concentration greater than or equal to (≥) 0.02 µg/mL.
The Primary ATP cohort for immunogenicity included all evaluable subjects for whom data concerning immunogenicity outcome measures were available. This included subjects for whom assay results were available for antibodies against at least one study vaccine antigen component post-dose III.

End point type	Secondary

End point timeframe:

At Month 3, one month after the administration of the third vaccine dose

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	185	177	183	
Units: Subjects				
Anti-6A (N=185;176;183)	58	51	41	
Anti-19A (N=180;177;180	56	50	40	

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against pneumococcal cross-reactive serotypes 6A and 19A (Anti-6A and 19A) - Primary vaccination

End point title	Antibody concentrations against pneumococcal cross-reactive serotypes 6A and 19A (Anti-6A and 19A) - Primary vaccination

End point description:

Anti-pneumococcal cross-reactive serotypes 6A and 19A antibody concentrations (Anti-6A and -19A) were measured by 22F-inhibition ELISA; presented as geometric mean concentrations (GMCs) and expressed in micrograms per milliliter (µg/mL). The seropositivity cut-off for the assay was ≥ 0.05 µg/mL.
The Primary ATP cohort for immunogenicity included all evaluable subjects for whom data concerning immunogenicity outcome measures were available. This included subjects for whom assay results were available for antibodies against at least one study vaccine antigen component post-dose III.

End point type	Secondary

End point timeframe:

At Month 3, one month after the administration of the third vaccine dose

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	185	177	183	
Units: µg/mL				
geometric mean (confidence interval 65%)				
Anti-6A (N=185;176;183)	0.1 (0.08 to 0.12)	0.1 (0.09 to 0.12)	0.08 (0.06 to 0.09)	
Anti-19A (N=180;177;180)	0.1 (0.09 to 0.13)	0.09 (0.08 to 0.11)	0.08 (0.07 to 0.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic activity (OPA) titers against pneumococcal cross-reactive serotypes 6A and 19A - Primary vaccination

End point title	Opsonophagocytic activity (OPA) titers against pneumococcal cross-reactive serotypes 6A and 19A - Primary vaccination

End point description:

Titers were presented as geometric mean titers (GMTs), for the seropositivity cut-off of 8.
The Primary ATP cohort for immunogenicity included all evaluable subjects for whom data concerning immunogenicity outcome measures were available. This included subjects for whom assay results were available for antibodies against at least one study vaccine antigen component post-dose III.

End point type	Secondary

End point timeframe:

At Month 3, one month after the administration of the third vaccine dose

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	135	129	130	
Units: Titres				
geometric mean (confidence interval 95%)				
Opsono-6A (N=128;120;121)	23.2 (16.1 to 33.6)	25.4 (17.1 to 37.8)	33 (21.4 to 50.8)	
Opsono-19A (N=135;129;130)	9 (6.9 to 11.7)	8 (6.3 to 10.2)	4.9 (4.4 to 5.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against diphtheria and tetanus toxoids (anti-D and T) - Primary vaccination

End point title	Concentrations of antibodies against diphtheria and tetanus toxoids (anti-D and T) - Primary vaccination

End point description:

Anti-D and anti-T antibody concentrations were presented as geometric mean concentrations (GMCs) and expressed in international units per milliliter (IU/mL). The seropositivity cut-off value was greater than or equal to (≥) 0.1 IU/mL.
The Primary ATP cohort for immunogenicity included all evaluable subjects for whom data concerning immunogenicity outcome measures were available. This included subjects for whom assay results were available for antibodies against at least one study vaccine antigen component post-dose III.

End point type	Secondary

End point timeframe:

At Month 3, one month after the administration of the third vaccine dose

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	187	180	189	
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-diphteria (N=185;176;187)	1.475 (1.307 to 1.664)	1.078 (0.939 to 1.237)	1.077 (0.949 to 1.222)	
Anti-tetanus (N=187;180;189)	2.873 (2.622 to 3.147)	1.702 (1.528 to 1.897)	0.934 (0.837 to 1.043)	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-polyribosyl-ribitol phosphate (anti-PRP) antibody concentrations - Primary vaccination

End point title	Anti-polyribosyl-ribitol phosphate (anti-PRP) antibody concentrations - Primary vaccination

End point description:

Anti-PRP antibody concentrations were presented as geometric mean concentrations (GMCs) and expressed in micrograms per milliliter (µg/mL). The seropositivity cut-off value was ≥ 0.15 µg/mL. The Primary ATP cohort for immunogenicity included all evaluable subjects for whom data concerning immunogenicity outcome measures were available. This included subjects for whom assay results were available for antibodies against at least one study vaccine antigen component post-dose III.

End point type	Secondary

End point timeframe:

At Month 3, one month after the administration of the third vaccine dose

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	189	179	188	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PRP (N=189;179;188)	2.139 (1.766 to 2.59)	4.796 (3.829 to 6.007)	2.219 (1.724 to 2.857)	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) antibody concentrations - Primary vaccination

End point title	Anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) antibody concentrations - Primary vaccination

End point description:

Anti-PT, anti-FHA and anti-PRN antibody concentrations were presented as geometric mean concentrations (GMCs) and expressed in ELISA units per milliliter (EL.U/mL). The seropositivity cut-off value was ≥ 5 EL.U/mL.
The Primary ATP cohort for immunogenicity included all evaluable subjects for whom data concerning immunogenicity outcome measures were available. This included subjects for whom assay results were available for antibodies against at least one study vaccine antigen component post-dose III.

End point type	Secondary

End point timeframe:

At Month 3, one month after the administration of the third vaccine dose

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	187	180	188	
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PT (N=187;180;188)	42.7 (39.1 to 46.6)	36.4 (33.4 to 39.8)	40.1 (37 to 43.6)	
Anti-FHA (N=183;172;183)	145.6 (130.4 to 162.5)	100.8 (89.6 to 113.5)	100.5 (89.9 to 112.4)	
Anti-PRN (N=187;180;188)	97.6 (86.8 to 109.7)	40.1 (34.8 to 46.1)	45.1 (39.3 to 51.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-hepatitis B surface antigen (anti-HBs) antibody concentrations - Primary vaccination

End point title	Anti-hepatitis B surface antigen (anti-HBs) antibody concentrations - Primary vaccination

End point description:

Antibody concentrations were presented as GMCs and expressed in mIU/mL. A seroprotected subject was a subject whose antibody ChemiLuminescence ImmunoAssay(CLIA) concentration was ≥10 mIU/mL. Note: investigations on the quality of some serology assays revealed that the anti-HBs ELISA overestimated concentration between 10-100 mIU/mL while values >100 mIU/mL were confirmed valid. All available samples at one month post-dose III and month post-dose IV timepoints for which the anti-HBs antibody concentration was between 10-100 mIU/mL by in-house ELISA, were retested by the commercial assay Centaur, an FDA-approved and CE-marked CLIA with a cut-off defining seropositivity of 6.2 mIU/mL. Anti-HBs seroprotection was redefined as in-house ELISA concentration >100 mIU/mL or CLIA concentration >10 mIU/mL.
The Primary ATP cohort for immunogenicity included all evaluable subjects for whom data concerning immunogenicity outcome measures were available.

End point type	Secondary

End point timeframe:

At Month 3, one month after the administration of the third vaccine dose

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	111	112	113	
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs (N=111;112;113)	356.9 (279.4 to 455.8)	14 (11.6 to 16.9)	11.5 (9.8 to 13.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-polio types 1, 2 and 3 titers - Primary vaccination

End point title	Anti-polio types 1, 2 and 3 titers - Primary vaccination

End point description:

Anti-polio 1, -polio 2, -polio 3 antibody titers were presented as geometric mean titers (GMTs), for the seropositivity cut-off value ≥ 8.
The Primary ATP cohort for immunogenicity included all evaluable subjects for whom data concerning immunogenicity outcome measures were available. This included subjects for whom assay results were available for antibodies against at least one study vaccine antigen component post-dose III.

End point type	Secondary

End point timeframe:

At Month 3, one month after the administration of the third vaccine dose

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	150	149	
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-polio 1 (N=155;150;149)	27.2 (21.7 to 34.1)	16 (13 to 19.7)	18.1 (14.8 to 22.1)	
Anti-polio 2 (N=156;149;149)	37.1 (29.1 to 47.4)	29 (23 to 36.6)	23.2 (18.5 to 29.1)	
Anti-polio 3 (N=156;148;149)	47.3 (35.8 to 62.4)	34.2 (27 to 43.4)	26.7 (21.5 to 33)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with antibody concentrations against 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) ≥ 0.2 µg/mL - Booster vaccination

End point title	Number of subjects with antibody concentrations against 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) ≥ 0.2 µg/mL - Booster vaccination

End point description:

Antibody concentrations against the pneumococcal serotypes were assessed by 22F-inhibition ELISA. The reference cut-off value of the assay was an antibody concentration greater than or equal to (≥) 0.02 µg/mL.
The Booster ATP cohort for immunogenicity included all evaluable subjects, for whom assay results were available for antibodies against at least one study vaccine antigen component after booster vaccination.
The Booster ATP cohort for immunogenicity included all evaluable subjects, for whom assay results were available for antibodies against at least one study vaccine antigen component after booster vaccination.

End point type	Secondary

End point timeframe:

Prior to (PRE/Month 9) and one month after the administration of the booster dose (POST/Month 10)

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	190	198	202	
Units: Subjects				
Anti-1, PRE(N=178;185;198)	84	92	6	
Anti-4, PRE (N=174;181;194)	136	147	148	
Anti-5, PRE (N=181;181;198)	142	152	3	
Anti-6B, PRE (N=175;180;192)	117	127	62	
Anti-7F, PRE(N=176;181;195)	165	164	5	
Anti-9V, PRE(N=180;180;196)	168	168	176	
Anti-14, PRE (N=183;184;199)	170	172	190	
Anti-18C, PRE (N=179;181;194)	152	143	151	
Anti-19F, PRE(N=172;177;197)	149	157	109	
Anti-23F, PRE (N=180;182;196)	123	140	108	
Anti-1, POST(N=187;196;199)	187	195	7	
Anti-4, POST (N=187;194;198)	187	194	198	
Anti-5, POST (N=186;191;195)	185	191	4	
Anti-6B, POST (N=186;193;199)	176	181	192	
Anti-7F, POST (N=189;198;199)	189	198	8	
Anti-9V, POST (N=188;197;202)	188	197	202	
Anti-14, POST (N=190;198;201)	190	197	198	
Anti-18C, POST (N=189;197;200)	188	196	200	
Anti-19F, POST(N=183;194;196)	180	191	196	
Anti-23F, POST (N=185;194;199)	179	190	194	

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against 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) - Booster vaccination

End point title	Antibody concentrations against 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) - Booster vaccination

End point description:

Anti-pneumococcal serotype 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antibody concentrations were assessed by 22F-inhibition ELISA, presented as geometric mean concentrations (GMCs) and expressed in micrograms per milliliter (µg/mL). The seropositivity cut-off value was ≥ 0.05 µg/mL.
The Booster ATP cohort for immunogenicity included all evaluable subjects, for whom assay results were available for antibodies against at least one study vaccine antigen component after booster vaccination.

End point type	Secondary

End point timeframe:

Prior to (PRE/Month 9) and one month after the administration of the booster dose (POST/Month 10)

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	190	198	202	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-1, PRE(N=178;185;198)	0.2 (0.17 to 0.22)	0.22 (0.19 to 0.26)	0.03 (0.03 to 0.04)	
Anti-4, PRE (N=174;181;194)	0.39 (0.34 to 0.46)	0.43 (0.37 to 0.5)	0.38 (0.34 to 0.43)	
Anti-5, PRE (N=181;181;198)	0.41 (0.36 to 0.47)	0.42 (0.37 to 0.48)	0.03 (0.03 to 0.04)	
Anti-6B, PRE (N=175;180;192)	0.3 (0.25 to 0.36)	0.32 (0.27 to 0.38)	0.13 (0.11 to 0.16)	
Anti-7F, PRE(N=176;181;195)	0.6 (0.54 to 0.68)	0.62 (0.55 to 0.71)	0.03 (0.03 to 0.03)	
Anti-9V, PRE(N=180;180;196)	0.68 (0.6 to 0.78)	0.76 (0.66 to 0.89)	0.55 (0.49 to 0.62)	
Anti-14, PRE (N=183;184;199)	1.06 (0.9 to 1.26)	1.14 (0.95 to 1.36)	1.55 (1.35 to 1.79)	
Anti-18C, PRE (N=179;181;194)	0.58 (0.49 to 0.68)	0.43 (0.36 to 0.5)	0.4 (0.35 to 0.45)	
Anti-19F, PRE(N=172;177;197)	0.79 (0.64 to 0.99)	0.9 (0.73 to 1.11)	0.31 (0.25 to 0.37)	
Anti-23F, PRE (N=180;182;196)	0.33 (0.27 to 0.39)	0.38 (0.32 to 0.46)	0.26 (0.22 to 0.3)	
Anti-1, POST(N=187;196;199)	2.16 (1.89 to 2.46)	2.5 (2.19 to 2.86)	0.03 (0.03 to 0.04)	
Anti-4, POST (N=187;194;198)	3.04 (2.7 to 3.42)	3.29 (2.89 to 3.73)	4.01 (3.53 to 4.56)	
Anti-5, POST (N=186;191;195)	3.27 (2.9 to 3.7)	3.27 (2.9 to 3.68)	0.04 (0.03 to 0.04)	
Anti-6B, POST (N=186;193;199)	1.45 (1.23 to 1.71)	1.41 (1.19 to 1.67)	2.52 (2.15 to 2.96)	

Anti-7F, POST (N=189;198;199)	3.79 (3.4 to 4.23)	4.06 (3.63 to 4.54)	0.03 (0.03 to 0.04)	
Anti-9V, POST (N=188;197;202)	3.96 (3.58 to 4.39)	4.23 (3.78 to 4.74)	6.05 (5.38 to 6.8)	
Anti-14, POST (N=190;198;201)	4.59 (4.06 to 5.19)	4.95 (4.38 to 5.6)	7.31 (6.37 to 8.39)	
Anti-18C, POST (N=189;197;200)	6.36 (5.56 to 7.27)	4.63 (4.09 to 5.25)	5.08 (4.47 to 5.78)	
Anti-19F, POST(N=183;194;196)	5.45 (4.72 to 6.3)	5.8 (5.04 to 6.68)	2.4 (2.14 to 2.7)	
Anti-23F, POST (N=185;194;199)	2.32 (1.98 to 2.71)	2.6 (2.24 to 3.02)	5.32 (4.49 to 6.31)	

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic activity (OPA) titers against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F - Booster vaccination

End point title	Opsonophagocytic activity (OPA) titers against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F - Booster vaccination

End point description:

Titers were presented as geometric mean titers (GMTs), for the seropositivity cut-off value of 8.
The Booster ATP cohort for immunogenicity included all evaluable subjects, for whom assay results were available for antibodies against at least one study vaccine antigen component after booster vaccination.

End point type	Secondary

End point timeframe:

Prior to (PRE/Month 9) and one month after the administration of the booster dose (POST/Month 10)

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	156	154	168	
Units: Titers				
geometric mean (confidence interval 95%)				
Opsono-1, PRE (N=149;152;168)	5.5 (4.7 to 6.4)	5.6 (4.7 to 6.7)	5 (4.4 to 5.8)	
Opsono-4, PRE (N=145;150;164)	11.3 (8.6 to 14.9)	15.3 (11.3 to 20.6)	12.3 (9.3 to 16.2)	
Opsono-5, PRE (N=148;151;166)	7.2 (6.1 to 8.5)	7 (6 to 8.1)	4.3 (4 to 4.6)	
Opsono-6B, PRE (N=141;138;153)	52 (34.8 to 77.7)	96.7 (63.1 to 148)	27.4 (18.6 to 40.3)	
Opsono-7F, PRE (N=146;150;146)	818.9 (642.2 to 1044.3)	754.3 (598.4 to 950.8)	138.1 (91.2 to 209.2)	
Opsono-9V, PRE (N=143;147;159)	267.2 (212.7 to 335.8)	338.7 (264.8 to 433.2)	149.5 (112.4 to 198.9)	
Opsono-14, PRE (N=143;144;161)	117.3 (82.9 to 165.9)	142.5 (101.3 to 200.4)	156 (114.5 to 212.5)	
Opsono-18C, PRE (N=139;148;162)	8.2 (6.2 to 10.8)	6.8 (5.3 to 8.5)	7 (5.7 to 8.7)	

Opsono-19F, PRE (N=149;149;167)	13.8 (10.6 to 18.1)	15.4 (11.8 to 20.2)	7.8 (6.2 to 9.9)	
Opsono-23F, PRE (N=143;143;162)	314.1 (198.6 to 496.7)	350.4 (229.8 to 534.2)	338.9 (219.9 to 522.3)	
Opsono-1, POST (N=156;154;164)	208.8 (160.6 to 271.7)	221.4 (165.1 to 297)	4.6 (4.2 to 5.1)	
Opsono-4, POST (N=155;152;164)	1046.8 (865.8 to 1265.7)	1121.6 (909.4 to 1383.3)	2335.8 (1946.3 to 2803.3)	
Opsono-5, POST (N=152;151;164)	149.3 (119.2 to 187)	132.4 (103.8 to 168.9)	4.1 (4 to 4.3)	
Opsono-6B, POST (N=153;149;160)	681.4 (514.6 to 902.1)	763.3 (581.9 to 1001.3)	1807.5 (1408 to 2320.3)	
Opsono-7F, POST (N=154;152;153)	3936.5 (3413.2 to 4540)	3976 (3390.2 to 4663.1)	129.1 (85.9 to 193.9)	
Opsono-9V, POST (N=153;151;163)	2512.9 (2213.1 to 2853.2)	2257.6 (1974.3 to 2581.5)	3889.5 (3260.1 to 4640.2)	
Opsono-14, POST (N=154;154;164)	1534.2 (1290.9 to 1823.3)	1896.3 (1591.3 to 2259.7)	1867.9 (1540.5 to 2265.1)	
Opsono-18C, POST (N=153;152;159)	720.7 (597.5 to 869.4)	385.9 (303.5 to 490.8)	660.4 (520.9 to 837.3)	
Opsono-19F, POST (N=153;149;164)	435.7 (336.3 to 564.5)	475.4 (377.8 to 598.1)	123.2 (95.9 to 158.2)	
Opsono-23F, POST (N=152;154;164)	2895.4 (2276.1 to 3683.1)	2895.3 (2419.3 to 3465)	12418.7 (10171.8 to 15161.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with antibody concentrations against pneumococcal cross-reactive serotypes 6A and 19A (Anti-6A and 19A) ≥ 0.2 µg/mL - Booster vaccination

End point title	Number of subjects with antibody concentrations against pneumococcal cross-reactive serotypes 6A and 19A (Anti-6A and 19A) ≥ 0.2 µg/mL - Booster vaccination

End point description:

Antibody concentrations against the cross-reactive pneumococcal serotypes were assessed by 22F-inhibition ELISA. The reference cut-off value of the assay was an antibody concentration greater than or equal to (≥) 0.02 µg/mL.
The Booster ATP cohort for immunogenicity included all evaluable subjects, for whom assay results were available for antibodies against at least one study vaccine antigen component after booster vaccination.

End point type	Secondary

End point timeframe:

Prior to (PRE/Month 9) and one month after the administration of the booster dose (POST/Month 10)

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	187	196	201	
Units: Subjects				
Anti-6A, PRE (N=181;185;193)	50	56	28	
Anti-19A, PRE (N=182;184;199)	61	63	29	
Anti-6A, POST (N=187;196;201)	135	142	160	
Anti-19A, POST (N=187;195;200)	130	139	97	

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against pneumococcal cross-reactive serotypes 6A and 19A (Anti-6A and 19A) - Booster vaccination

End point title	Antibody concentrations against pneumococcal cross-reactive serotypes 6A and 19A (Anti-6A and 19A) - Booster vaccination

End point description:

Anti-pneumococcal cross-reactive serotype 6A and 19A antibody concentrations were assessed by 22F-inhibition ELISA, presented as geometric mean concentrations (GMCs) and expressed in micrograms per milliliter (µg/mL). The seropositivity cut-off value was ≥ 0.05 µg/mL.
The Booster ATP cohort for immunogenicity included all evaluable subjects, for whom assay results were available for antibodies against at least one study vaccine antigen component after booster vaccination.

End point type	Secondary

End point timeframe:

Prior to (PRE/Month 9) and one month after the administration of the booster dose (POST/Month 10)

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	187	196	201	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-6A, PRE (N=181;185;193)	0.1 (0.09 to 0.12)	0.11 (0.09 to 0.13)	0.06 (0.05 to 0.07)	
Anti-19A, PRE (N=182;184;199)	0.12 (0.1 to 0.15)	0.12 (0.09 to 0.14)	0.06 (0.05 to 0.07)	
Anti-6A, POST (N=187;196;201)	0.45 (0.36 to 0.55)	0.49 (0.4 to 0.61)	0.71 (0.58 to 0.88)	
Anti-19A, POST (N=187;195;200)	0.5 (0.39 to 0.63)	0.52 (0.41 to 0.66)	0.21 (0.17 to 0.25)	

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic activity (OPA) titers against pneumococcal cross-reactive serotypes 6A and 19A - Booster vaccination

End point title	Opsonophagocytic activity (OPA) titers against pneumococcal cross-reactive serotypes 6A and 19A - Booster vaccination

End point description:

Titers were presented as geometric mean titers (GMTs), for the seropositivity cut-off value of 8.
The Booster ATP cohort for immunogenicity included all evaluable subjects, for whom assay results were available for antibodies against at least one study vaccine antigen component after booster vaccination.

End point type	Secondary

End point timeframe:

Prior to (PRE/Month 9) and one month after the administration of the booster dose (POST/Month 10)

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	151	148	167	
Units: Titers				
geometric mean (confidence interval 95%)				
Opsono-6A, PRE (N=128;135;151)	23.3 (15.7 to 34.6)	30.7 (20.8 to 45.2)	15.5 (11.1 to 21.6)	
Opsono-19A, PRE (N=148;148;167)	5.7 (4.6 to 7)	5.5 (4.6 to 6.5)	5.5 (4.6 to 6.5)	
Opsono-6A, POST (N=145;142;160)	143.3 (99.1 to 207.3)	197.1 (138 to 281.3)	493.3 (357.1 to 681.6)	
Opsono-19A, POST (N=151;148;162)	34.9 (24.8 to 49.2)	24.6 (17.7 to 34.3)	7.7 (6.2 to 9.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against protein D (Anti-PD) - Booster vaccination

End point title	Concentrations of antibodies against protein D (Anti-PD) - Booster vaccination

End point description:

Anti-PD antibody concentrations were presented as geometric mean concentrations (GMCs) and expressed in ELISA units per milliliter (EL.U/mL). The seropositivity cut-off for the assay was ≥ 100 EL.U/mL.
The Booster ATP cohort for immunogenicity included all evaluable subjects, for whom assay results were available for antibodies against at least one study vaccine antigen component after booster vaccination.

End point type	Secondary

End point timeframe:

Prior to (PRE/Month 9) and one month after the administration of the booster dose (POST/Month 10)

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	189	198	201	
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD, PRE (N=182;189;195)	421 (370.3 to 478.5)	520.5 (455.8 to 594.3)	80.8 (73.1 to 89.4)	
Anti-PD, POST (N=189;198;201)	1715 (1510.3 to 1947.5)	1936.8 (1710.5 to 2193.2)	84.1 (76 to 93.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against diphtheria and tetanus toxoids (anti-D and T) - Booster vaccination

End point title	Concentrations of antibodies against diphtheria and tetanus toxoids (anti-D and T) - Booster vaccination

End point description:

Anti-D and anti-T antibody concentrations were presented as geometric mean concentrations (GMCs) and expressed in international units per milliliter (IU/mL). The seropositivity cut-off value was greater than or equal to (≥) 0.1 IU/mL.
The Booster ATP cohort for immunogenicity included all evaluable subjects, for whom assay results were available for antibodies against at least one study vaccine antigen component after booster vaccination.

End point type	Secondary

End point timeframe:

Prior to (PRE/Month 9) and one month after the administration of the booster dose (POST/Month 10)

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	186	194	197	
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-diphteria, PRE (N=175;179;192)	0.235 (0.205 to 0.27)	0.232 (0.203 to 0.264)	0.266 (0.235 to 0.301)	
Anti-tetanus, PRE (N=175;180;193)	0.728 (0.656 to 0.809)	0.536 (0.477 to 0.603)	0.232 (0.202 to 0.267)	
Anti-diphteria, POST (N=186;194;197)	4.061 (3.601 to 4.58)	3.226 (2.866 to 3.632)	4.882 (4.425 to 5.386)	
Anti-tetanus, POST (N=186;194;197)	8.628 (7.867 to 9.462)	5.989 (5.461 to 6.568)	3.248 (2.859 to 3.69)	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-polyribosyl-ribitol phosphate (anti-PRP) antibody concentrations - Booster vaccination

End point title	Anti-polyribosyl-ribitol phosphate (anti-PRP) antibody concentrations - Booster vaccination

End point description:

Anti-PRP antibody concentrations were presented as geometric mean concentrations (GMCs) and expressed in micrograms per milliliter (µg/mL). The seropositivity cut-off value was ≥ 0.15 µg/mL.
The Booster ATP cohort for immunogenicity included all evaluable subjects, for whom assay results were available for antibodies against at least one study vaccine antigen component after booster vaccination.

End point type	Secondary

End point timeframe:

Prior to (PRE/Month 9) and one month after the administration of the booster dose (POST/Month 10)

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	184	192	197	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PRP, PRE (N=174;179;193)	0.475 (0.386 to 0.585)	0.855 (0.682 to 1.072)	0.371 (0.298 to 0.461)	
Anti-PRP, POST (N=184;192;197)	19.331 (16.144 to 23.147)	39.383 (32.617 to 47.551)	23.676 (18.944 to 29.591)	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) antibody concentrations - Booster vaccination

End point title	Anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) antibody concentrations - Booster vaccination

End point description:

Anti-PT, anti-FHA and anti-PRN antibody concentrations were presented as geometric mean concentrations (GMCs) and expressed in ELISA units per milliliter (EL.U/mL). The seropositivity cut-off value was ≥ 5 EL.U/mL.
The Booster ATP cohort for immunogenicity included all evaluable subjects, for whom assay results were available for antibodies against at least one study vaccine antigen component after booster vaccination.

End point type	Secondary

End point timeframe:

Prior to (PRE/Month 9) and one month after the administration of the booster dose (POST/Month 10)

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	186	194	197	
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PT, PRE (N=174;176;189)	7.4 (6.6 to 8.4)	6 (5.4 to 6.7)	6.6 (5.9 to 7.3)	
Anti-FHA, PRE (N=175;179;191)	34 (29.4 to 39.4)	35.3 (30.8 to 40.6)	34.7 (30.1 to 39.9)	
Anti-PRN, PRE (N=175;179;192)	14.1 (12.3 to 16.2)	6.8 (5.9 to 7.9)	8.6 (7.4 to 10)	
Anti-PT, POST (N=186;194;196)	53.5 (48.3 to 59.2)	47.4 (42.9 to 52.5)	54.8 (48.9 to 61.4)	
Anti-FHA, POST (N=184;192;194)	343.5 (308 to 383.1)	135.7 (121.2 to 151.9)	140 (123.2 to 159.1)	
Anti-PRN, POST (N=186;193;197)	281.7 (247.2 to 321)	97.8 (85.4 to 112)	106.4 (91.5 to 123.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-hepatitis B surface antigen (anti-HBs) antibody concentrations - Booster vaccination

End point title	Anti-hepatitis B surface antigen (anti-HBs) antibody concentrations - Booster vaccination

End point description:

Antibody concentrations were presented as GMCs and expressed in mIU/mL. A seroprotected subject was a subject whose antibody CLIA concentration was ≥10 mIU/mL. Note: investigations on the quality of some serology assays revealed that the anti-HBs ELISA overestimated concentration between 10-100 mIU/mL while values >100 mIU/mL were confirmed valid. Therefore, all available samples at one month post-dose III and one month post-dose IV timepoints for which the anti-HBs antibody concentration was between 10-100 mIU/mL by in-house ELISA, were retested by the commercial assay Centaur, an FDA-approved and CE-marked CLIA with a cut-off defining seropositivity of 6.2 mIU/mL. Anti-HBs seroprotection was redefined as in-house ELISA concentration >100 mIU/mL or CLIA concentration >10 mIU/mL.
The Booster ATP cohort for immunogenicity included all evaluable subjects, for whom assay results were available for antibodies against at least one study vaccine antigen component after booster vaccination.

End point type	Secondary

End point timeframe:

Prior to (PRE/Month 9) and one month after the administration of the booster dose (POST/Month 10)

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	125	124	135	
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs, PRE (121;124;135)	142.1 (113.4 to 178.1)	9.9 (8.8 to 11.2)	9.9 (8.8 to 11.2)	
Anti-HBs, POST (125;123;135)	1981 (1552 to 2528.7)	8.6 (7.6 to 9.9)	8.5 (7.6 to 9.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-polio types 1, 2 and 3 titers - Booster vaccination

End point title	Anti-polio types 1, 2 and 3 titers - Booster vaccination

End point description:

Anti-polio 1, -polio 2, -polio 3 antibody titers were presented as geometric mean titers (GMTs), for the seropositivity cut-off value ≥ 8.
The Booster ATP cohort for immunogenicity included all evaluable subjects, for whom assay results were available for antibodies against at least one study vaccine antigen component after booster vaccination.

End point type	Secondary

End point timeframe:

Prior to (PRE/Month 9) and one month after the administration of the booster dose (POST/Month 10)

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	167	173	182	
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-polio 1, PRE (N=156;166;182)	8.3 (7 to 10)	7.3 (6.3 to 8.4)	7 (6.1 to 8)	
Anti-polio 2, PRE (N=156;164;182)	13.4 (10.8 to 16.6)	10.6 (8.8 to 12.7)	10.4 (8.9 to 12.2)	
Anti-polio 3, PRE (N=156;166;180)	11.3 (9.3 to 13.9)	9 (7.5 to 10.7)	8.7 (7.4 to 10.3)	
Anti-polio 1, POST (N=166;173;170)	370.7 (289.8 to 474.2)	177.5 (135.8 to 231.9)	221.2 (171.5 to 285.3)	
Anti-polio 2, POST (N=167;173;169)	710.8 (588 to 859.3)	338.8 (272.7 to 420.8)	481.4 (391 to 592.7)	
Anti-polio 3, POST (N=167;172;170)	631.5 (495.7 to 804.4)	311.9 (240.4 to 404.6)	348.3 (263.6 to 460.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with booster vaccine response against pertussis toxoid (PT), filamentous haemagglutinin (FHA) and pertactin (PRN) antibodies - Booster vaccination

End point title	Number of subjects with booster vaccine response against pertussis toxoid (PT), filamentous haemagglutinin (FHA) and pertactin (PRN) antibodies - Booster vaccination

End point description:

A booster responder to PT/FHA/PRN was defined as a subject with antibodies concentration ≥ 5 EL.U/mL against PT/FHA/PRN in subjects who were initially seronegative for anti-PT/FHA/PRN antibodies (i.e., subjects with anti-PT/FHA/PRN antibody concentrations < 5 EL.U/mL), or antibody concentration ≥ 2 fold the pre-vaccination antibody concentration in subjects who were initially seropositive (i.e., subjects with anti-PT/FHA/PRN antibody concentrations ≥ 5 EL.U/mL).
All evaluable subjects, for whom assay results were available for the respective antigen both before and after booster vaccination. For Anti-PT and anti-FHA antigens, evaluable data were not available for 1 participant (Synflorix + Infanrix Hexa), 2 and 1 participants respectively (Synflorix + Pediacel), 2 and 3 participants (Prevenar + Pediacel).

End point type	Secondary

End point timeframe:

One month after (Month 10) the administration of the booster dose

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	140	145	155	
Units: Subjects				
Anti-PT, S- seronegative (N=40;48;48)	40	47	48	
Anti-PT, S+ seropositive (N=99;95;105)	95	94	98	
Anti-FHA, S- seronegative (N=4;1;2)	4	1	2	
Anti-FHA, S+ seropositive (N=135;143;150)	128	119	125	
Anti-PRN, S- seronegative (N=18;56;53)	18	56	51	
Anti-PRN, S+ seropositive (N=122;89;102)	122	88	101	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with antibody concentrations against 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) ≥ 0.2 µg/mL - 12 months after booster dose

End point title	Number of subjects with antibody concentrations against 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) ≥ 0.2 µg/mL - 12 months after booster dose

End point description:

Antibody concentrations against the pneumococcal serotypes were assessed by 22F-inhibition ELISA. The reference cut-off value of the assay was an antibody concentration greater than or equal to (≥) 0.02 µg/mL.
The Booster ATP cohort for immunogenicity included all evaluable subjects, for whom assay results were available for antibodies against at least one study vaccine antigen component after booster vaccination.

End point type	Secondary

End point timeframe:

At Month 21, 12 months after the administration of the booster dose (at 23-25 months of age) (M12)

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	166	169	177	
Units: Subjects				
Anti-1, M12 (N=163;166;173)	106	108	6	
Anti-4, M12 (N=163;167;173)	101	102	130	
Anti-5, M12 (N=163;163;170)	129	129	10	
Anti-6B, M12 (N=162;164;173)	94	96	133	
Anti-7F, M12 (N=163;165;170)	157	157	15	
Anti-9V, M12 (N=165;168;173)	155	157	160	
Anti-14, M12 (N=166;169;177)	149	156	173	
Anti-18C, M12 (N=164;167;174)	160	155	161	
Anti-19F, M12 (N=164;165;171)	158	158	134	
Anti-23F, M12(N=162;166;172)	123	126	153	

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against 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) - 12 months after booster dose

End point title	Antibody concentrations against 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) - 12 months after booster dose

End point description:

Anti-pneumococcal serotype 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antibody concentrations were assessed by 22F-inhibition ELISA, presented as geometric mean concentrations (GMCs) and expressed in micrograms per milliliter (µg/mL). The seropositivity cut-off value was ≥ 0.05 µg/mL.
The Booster ATP cohort for immunogenicity included all evaluable subjects, for whom assay results were available for antibodies against at least one study vaccine antigen component after booster vaccination.

End point type	Secondary

End point timeframe:

At Month 21, 12 months after the administration of the booster dose (at 23-25 months of age) (M12)

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	166	169	177	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-1, M12 (N=163;166;173)	0.3 (0.26 to 0.35)	0.32 (0.28 to 0.38)	0.04 (0.03 to 0.04)	
Anti-4, M12 (N=163;167;173)	0.25 (0.22 to 0.29)	0.29 (0.25 to 0.34)	0.36 (0.32 to 0.42)	
Anti-5, M12 (N=163;163;170)	0.45 (0.39 to 0.53)	0.47 (0.39 to 0.55)	0.05 (0.04 to 0.05)	
Anti-6B, M12 (N=162;164;173)	0.3 (0.25 to 0.36)	0.32 (0.26 to 0.4)	0.46 (0.38 to 0.56)	
Anti-7F, M12 (N=163;165;170)	0.72 (0.63 to 0.81)	0.73 (0.64 to 0.84)	0.04 (0.03 to 0.05)	
Anti-9V, M12 (N=165;168;173)	0.74 (0.63 to 0.88)	0.78 (0.66 to 0.91)	0.81 (0.7 to 0.94)	
Anti-14, M12 (N=166;169;177)	0.73 (0.62 to 0.86)	0.85 (0.73 to 0.99)	1.28 (1.1 to 1.48)	
Anti-18C, M12 (N=164;167;174)	1.03 (0.89 to 1.19)	0.64 (0.56 to 0.74)	0.66 (0.59 to 0.75)	
Anti-19F, M12 (N=164;165;171)	1.48 (1.22 to 1.8)	1.46 (1.2 to 1.78)	0.76 (0.59 to 0.98)	
Anti-23F, M12(N=162;166;172)	0.51 (0.41 to 0.63)	0.52 (0.42 to 0.63)	1.01 (0.83 to 1.24)	

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic activity (OPA) titers against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F - 12 months after booster dose

End point title	Opsonophagocytic activity (OPA) titers against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F - 12 months after booster dose

End point description:

Antibody concentrations against the cross-reactive pneumococcal serotypes were assessed by 22F-inhibition ELISA. The reference cut-off value of the assay was an antibody concentration greater than or equal to (≥) 0.02 µg/mL.
The Booster ATP cohort for immunogenicity included all evaluable subjects, for whom assay results were available for antibodies against at least one study vaccine antigen component after booster vaccination.

End point type	Secondary

End point timeframe:

At Month 21, 12 months after the administration of the booster dose (at 23-25 months of age) (M12)

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	159	152	165	
Units: Titers				
geometric mean (confidence interval 95%)				
Opsono-1, M12 (N=159;150;162)	10.9 (8.5 to 14.1)	9.9 (7.8 to 12.5)	4.3 (3.9 to 4.7)	
Opsono-4, M12 (N=154;147;160)	12 (9.1 to 15.9)	15.5 (11 to 21.7)	45.2 (30.8 to 66.5)	
Opsono-5, M12 (N=159;152;165)	12.9 (10.4 to 16)	13.7 (11 to 17.1)	4.1 (3.9 to 4.3)	
Opsono-6B, M12 (N=139;137;152)	77.7 (48.8 to 123.8)	137.6 (83.5 to 226.6)	220 (145.4 to 332.8)	
Opsono-7F, M12 (N=142;136;143)	1982.9 (1568.8 to 2506.2)	2205.6 (1833.4 to 2653.4)	738.1 (549.8 to 990.7)	
Opsono-9V, M12 (N=143;135;147)	465.9 (324.2 to 669.5)	470 (325.8 to 677.9)	476.2 (317.8 to 713.5)	
Opsono-14, M12 (N=128;121;149)	93.1 (60 to 144.4)	151.6 (97.7 to 235.4)	238.7 (163.5 to 348.6)	
Opsono-18C, M12 (N=135;133;151)	21.6 (15.2 to 30.6)	12.5 (8.9 to 17.6)	15.3 (10.9 to 21.3)	
Opsono-19F, M12 (N=148;150;162)	31.1 (22.6 to 42.8)	32.9 (23.8 to 45.4)	15.1 (11 to 20.6)	
Opsono-23F, M12 (N=146;140;161)	366.5 (218.3 to 615.3)	706.1 (443.5 to 1124.3)	3879.8 (2774.4 to 5425.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with antibody concentrations against pneumococcal cross-reactive serotypes 6A and 19A (Anti-6A and 19A) ≥ 0.2 µg/mL - 12 months after booster dose

End point title	Number of subjects with antibody concentrations against pneumococcal cross-reactive serotypes 6A and 19A (Anti-6A and 19A) ≥ 0.2 µg/mL - 12 months after booster dose

End point description:

Antibody concentrations against the cross-reactive pneumococcal serotypes were assessed by 22F-inhibition ELISA. The reference cut-off value of the assay was an antibody concentration greater than or equal to (≥) 0.02 µg/mL.
The Booster ATP cohort for immunogenicity included all evaluable subjects, for whom assay results were available for antibodies against at least one study vaccine antigen component after booster vaccination.

End point type	Secondary

End point timeframe:

At Month 21, 12 months after the administration of the booster dose (at 23-25 months of age) (M12)

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	165	166	176	
Units: Subjects				
Anti-6A, M12 (N=163;166;174)	54	57	92	
Anti-19A, M12 (N=165;166;176)	120	97	80	

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against pneumococcal cross-reactive serotypes 6A and 19A (Anti-6A and 19A) - 12 months after booster dose

End point title	Antibody concentrations against pneumococcal cross-reactive serotypes 6A and 19A (Anti-6A and 19A) - 12 months after booster dose

End point description:

Anti-pneumococcal cross-reactive serotype 6A and 19A antibody concentrations were assessed by 22F-inhibition ELISA, presented as geometric mean concentrations (GMCs) and expressed in micrograms per milliliter (µg/mL). The seropositivity cut-off value was ≥ 0.05 µg/mL.
The Booster ATP cohort for immunogenicity included all evaluable subjects, for whom assay results were available for antibodies against at least one study vaccine antigen component after booster vaccination.

End point type	Secondary

End point timeframe:

At Month 21, 12 months after the administration of the booster dose (at 23-25 months of age) (M12)

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	165	166	176	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-6A, M12 (N=163;166;174)	0.14 (0.12 to 0.17)	0.15 (0.12 to 0.19)	0.22 (0.18 to 0.27)	
Anti-19A, M12 (N=165;166; 176)	0.43 (0.35 to 0.53)	0.29 (0.23 to 0.36)	0.21 (0.16 to 0.27)	

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic activity (OPA) titers against pneumococcal cross-reactive serotypes 6A and 19A - 12 months after booster dose

End point title	Opsonophagocytic activity (OPA) titers against pneumococcal

	cross-reactive serotypes 6A and 19A - 12 months after booster dose

End point description:

Titers were presented as geometric mean titers (GMTs), for the seropositivity cut-off value of 8.
The Booster ATP cohort for immunogenicity included all evaluable subjects, for whom assay results were available for antibodies against at least one study vaccine antigen component after booster vaccination.

End point type	Secondary

End point timeframe:

At Month 21, 12 months after the administration of the booster dose (at 23-25 months of age) (M12)

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	150	146	158	
Units: Titers				
geometric mean (confidence interval 95%)				
Opsono-6A, M12 (N=126;129;148)	21.6 (14.1 to 33.1)	24.8 (15.5 to 39.5)	56.5 (36.4 to 87.7)	
Opsono-19A, M12 (N=150;146;158)	12.6 (9.5 to 16.7)	9.1 (7 to 11.9)	9.6 (7.1 to 12.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against protein D (Anti-PD) - 12 months after booster dose

End point title	Concentrations of antibodies against protein D (Anti-PD) - 12 months after booster dose

End point description:

Anti-PD antibody concentrations were presented as geometric mean concentrations (GMCs) and expressed in ELISA units per milliliter (EL.U/mL). The seropositivity cut-off for the assay was ≥ 100 EL.U/mL.
The Booster ATP cohort for immunogenicity included all evaluable subjects, for whom assay results were available for antibodies against at least one study vaccine antigen component after booster vaccination.

End point type	Secondary

End point timeframe:

At Month 21, 12 months after the administration of the booster dose (at 23-25 months of age) (M12)

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	168	170	178	
Units: EL.U/mL				
geometric mean (confidence interval				

95%)				
Anti-PD, M12 (N=168;170;178)	332 (287.1 to 384)	423 (359.9 to 497.1)	81.4 (73.1 to 90.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with positive cultures of Haemophilus Influenzae and/or Streptococcus Pneumoniae in the nasopharynx - Primary vaccination

End point title	Number of subjects with positive cultures of Haemophilus Influenzae and/or Streptococcus Pneumoniae in the nasopharynx - Primary vaccination

End point description:

Positive cultures of H. influenzae* (HI) and S. pneumoniae (SP) identified in the nasopharynx at each swab time point: one month post-Dose III (M3), M9 (11-13 months of age), M12 (14-16 months of age), M16 (18-20 months of age) and M21 (23-25 months of age). *Data presented only include results from samples confirmed as positive for H. influenzae / Non-typeable H. influenzae after differentiation from H. haemolyticus by Polymerase Chain Reaction (PCR) assay.
The Primary Total Vaccinated cohort included all vaccinated subjects who received at least one primary dose.

End point type	Secondary

End point timeframe:

One month after the third dose (Month 3), prior to the booster dose (Month 9), 3 months after the booster dose (Month 12), 7 months after the booster dose (Month 16) and 12 months after the booster dose (Month 21)

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	260	259	259	
Units: Subjects				
Any SP, Month 3 [N=260;259;259]	102	109	100	
Any SP, Month 9 [N=255;259;258]	115	134	119	
Any SP, Month 12 [N=256;258;257]	121	131	126	
Any SP, Month 16 [N=256;258;258]	151	135	148	
Any SP, Month 21 [N=255;257;257]	154	139	131	
Any HI, Month 3 [N=259;258;258]	94	91	85	
Any HI, Month 9 [N=254;258;256]	152	155	144	
Any HI, Month 12 [N=260;258;257]	159	160	165	
Any HI, Month 16 [N=252;258;256]	185	169	162	
Any HI, Month 21 [N=254;255;254]	192	192	177	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with positive cultures of Streptococcus Pneumoniae vaccine seroptypes (VS), cross-reactive serotypes (CRS) or other serotypes (OS) in the nasopharynx - Primary vaccination

End point title	Number of subjects with positive cultures of Streptococcus Pneumoniae vaccine seroptypes (VS), cross-reactive serotypes (CRS) or other serotypes (OS) in the nasopharynx - Primary vaccination

End point description:

Positive cultures of S. pneumoniae (SP) identified in the nasopharynx at each swab time point: one month post-Dose III (M3), pre-booster vaccination (11-13 months of age), M12 (14-16 months of age), M16 (18-20 months of age) and M21 (23-25 months of age).
The Primary Total Vaccinated cohort included all vaccinated subjects who received at least one primary dose.

End point type	Secondary

End point timeframe:

One month after the third dose (Month 3), prior to the booster dose (Month 9), 3 months after the booster dose (Month 12), 7 months after the booster dose (Month 16) and 12 months after the booster dose (Month 21)

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	260	259	259	
Units: Subjects				
S. pneumoniae, VS - M3 [N=260;259;259]	18	25	21	
S. pneumoniae, VS - M9 [N=255;259;257]	16	20	18	
S. pneumoniae, VS - M12 [N=256;258;257]	11	18	13	
S. pneumoniae, VS - M16 [N=256;258;258]	15	12	12	
S. pneumoniae, VS - M21 [N=255;257;257]	8	8	8	
S. pneumoniae, CRS - M3 [N=260;259;259]	25	32	20	
S. pneumoniae, CRS - M9 [N=255;259;257]	15	30	25	
S. pneumoniae, CRS - M12 [N=256;258;257]	25	26	27	
S. pneumoniae, CRS - M16 [N=256;258;258]	33	33	31	
S. pneumoniae, CRS - M21 [N=255;257;257]	28	13	25	
S. pneumoniae, OS - M3 [N=260;259;259]	45	40	51	
S. pneumoniae, OS - M9 [N=255;259;257]	69	61	60	
S. pneumoniae, OS - M12 [N=256;258;257]	74	69	70	
S. pneumoniae, OS - M16 [N=256;258;258]	86	67	89	

S. pneumoniae, OS - M21 [N=255;257;257]	97	81	80	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with acquisition of new Streptococcus pneumoniae and Haemophilus Influenzae strains identified in nasopharyngeal swabs - Primary vaccination

End point title	Number of subjects with acquisition of new Streptococcus pneumoniae and Haemophilus Influenzae strains identified in nasopharyngeal swabs - Primary vaccination

End point description:

Acquisition of new H. influenzae* (HI) and S. pneumoniae (SP) strains, identified in the nasopharynx at each swab time point: pre-booster vaccination (11-13 months of age), M12 (14-16 months of age), M16 (18-20 months of age) and M21 (23-25 months of age). *Data presented only include results from samples confirmed as positive for H. influenzae / Non-typeable H. influenzae after differentiation from H. haemolyticus by Polymerase Chain Reaction (PCR) assay.
The Primary Total Vaccinated cohort included all vaccinated subjects who received at least one primary dose.

End point type	Secondary

End point timeframe:

Prior to the booster dose (Month 9), 3 months after the booster dose (Month 12), 7 months after the booster dose (Month 16) and 12 months after the booster dose (Month 21)

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	256	259	258	
Units: Subjects				
Any SP, M9 [N=255;259;258]	103	114	107	
Any SP, M12 [N=256;258;257]	86	95	90	
Any SP, M16 [N=256;258;258]	128	105	125	
Any SP, M21 [N=255;257;257]	132	113	110	
Any HI, M9 [N=254;258;256]	88	84	83	
Any HI, M12 [N=256;258;257]	47	48	58	
Any HI, M16 [N=252;258;256]	71	55	64	
Any HI, M21 [N=254;255;254]	73	75	71	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with acquisition of new Streptococcus pneumoniae

vaccine serotypes (VS), cross-reactive serotypes (CRS) or other serotypes (OS) identified in nasopharyngeal swabs - Primary vaccination

End point title	Number of subjects with acquisition of new Streptococcus pneumoniae vaccine serotypes (VS), cross-reactive serotypes (CRS) or other serotypes (OS) identified in nasopharyngeal swabs - Primary vaccination

End point description:

Acquisition of new S. pneumonia (SP) strains, identified in the nasopharynx at each swab time point: pre-booster vaccination (11-13 months of age), M12 (14-16 months of age), M16 (18-20 months of age) and M21 (23-25 months of age).
The Primary Total Vaccinated cohort included all vaccinated subjects who received at least one primary dose.

End point type	Secondary

End point timeframe:

Prior to the booster dose (Month 9), 3 months after the booster dose (Month 12), 7 months after the booster dose (Month 16) and 12 months after the booster dose (Month 21)

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	256	259	258	
Units: Subjects				
S. pneumoniae, VS - M9 [N=255;259;257]	14	11	15	
S. pneumoniae, VS - M12 [N=256;258;257]	8	9	8	
S. pneumoniae, VS - M16 [N=256;258;258]	13	7	9	
S. pneumoniae, VS - M21 [N=255;257;257]	4	7	6	
S. pneumoniae, CRS - M9 [N=255;259;257]	13	26	20	
S. pneumoniae, CRS - M12 [N=256;258;257]	19	15	20	
S. pneumoniae, CRS - M16 [N=256;258;258]	27	25	24	
S. pneumoniae, CRS - M21 [N=255;257;257]	22	8	18	
S. pneumoniae, OS - M9 [N=255;259;257]	64	55	57	
S. pneumoniae, OS - M12 [N=256;258;257]	52	59	52	
S. pneumoniae, OS - M16 [N=256;258;258]	74	55	77	
S. pneumoniae, OS - M21 [N=255;257;257]	87	69	69	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited local symptoms - Primary vaccination

End point title	Number of subjects with solicited local symptoms - Primary vaccination

End point description:

Solicited local symptoms assessed were pain, redness and swelling. Any was defined as any occurrence of the specified symptom regardless of intensity. Grade 3 pain was defined as cried when limb was moved/spontaneously painful. Grade 3 redness/swelling was defined as redness/swelling spreading beyond (>) 30 millimeters from injection site.
The Primary Total Vaccinated cohort included all vaccinated subjects who received at least one primary dose.

End point type	Secondary

End point timeframe:

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

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	260	260	260	
Units: Subjects				
Any Pain, Dose 1 [N=260;260;260]	168	159	142	
Grade 3 Pain, Dose 1 [N=260;260;260]	30	31	22	
Any Redness, Dose 1 [N=260;260;260]	105	134	120	
Grade 3 Redness, Dose 1 [N=260;260;260]	7	21	15	
Any Swelling, Dose 1 [N=260;260;260]	140	145	113	
Grade 3 Swelling, Dose 1 [N=260;260;260]	12	18	15	
Any Pain, Dose 2 [N=259;260;260]	130	120	104	
Grade 3 Pain, Dose 2 [N=259;260;260]	11	12	13	
Any Redness, Dose 2 [N=259;260;260]	125	131	121	
Grade 3 Redness, Dose 2 [N=259;260;260]	4	8	4	
Any Swelling, Dose 2 [N=259;260;260]	143	135	125	
Grade 3 Swelling, Dose 2 [N=259;260;260]	7	8	8	
Any Pain, Dose 3 [N=260;259;260]	100	87	73	
Grade 3 Pain, Dose 3 [N=260;259;260]	9	4	5	
Any Redness, Dose 3 [N=260;259;260]	141	119	121	
Grade 3 Redness, Dose 3 [N=260;259;260]	1	1	1	
Any Swelling, Dose 3 [N=260;259;260]	142	133	118	
Grade 3 Swelling, Dose 3 [N=260;259;260]	4	7	10	
Any Pain, Across doses [N=260;260;260]	205	193	178	
Grade 3 Pain, Across doses [N=260;260;260]	42	40	29	
Any Redness, Across doses [N=260;260;260]	197	193	184	
Grade 3 Redness, Across doses [N=260;260;260]	12	26	19	
Any Swelling, Across doses [N=260;260;260]	205	199	179	
Grade 3 Swelling, Across doses [N=260;260;260]	18	29	24	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited general symptoms - Primary vaccination

End point title	Number of subjects with solicited general symptoms - Primary vaccination

End point description:

Solicited general symptoms assessed include drowsiness, fever (defined as rectal temperature ≥ 38.0°C), irritability, and loss of appetite. Any was defined as incidence of the specified symptom regardless of intensity. Grade 3 drowsiness was defined as drowsiness which prevented normal everyday activities. Grade 3 fever was defined as fever (rectal temperature) above (>) 40.0 degree Celsius (°C). Grade 3 irritability was defined as crying that could not be comforted/preventing normal activity. Grade 3 loss of appetite was defined as the subject not eating at all. Related symptom was defined as a general symptom assessed by the investigator as causally related to study vaccination.
The Primary Total Vaccinated cohort included all vaccinated subjects who received at least one primary dose.

End point type	Secondary

End point timeframe:

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

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	260	260	260	
Units: Subjects				
Any Drowsiness, Dose 1 [N=260;260;260]	183	164	164	
Grade 3 Drowsiness, Dose 1 [N=260;260;260]	4	6	6	
Related Drowsiness, Dose 1 [N=260;260;260]	178	160	160	
Any Temperature, Dose 1 [N=260;260;260]	88	40	40	
Grade 3 Temperature, Dose 1 [N=260;260;260]	0	0	0	
Related Temperature, Dose 1 [N=260;260;260]	88	40	40	
Any Irritability, Dose 1 [N=260;260;260]	190	180	180	
Grade 3 Irritability, Dose 1 [N=260;260;260]	18	8	8	
Related Irritability, Dose 1 [N=260;260;260]	186	173	173	
Any Loss of appetite, Dose 1 [N=260;260;260]	88	87	87	

Grade 3 Loss of appetite, Dose 1 [N=260;260;260]	3	1	1	
Related Loss of appetite, Dose 1 [N=260;260;260]	65	84	84	
Any Drowsiness, Dose 2 [N=259;260;260]	157	143	143	
Grade 3 Drowsiness, Dose 2 [N=259;260;260]	5	1	1	
Related Drowsiness, Dose 2 [N=259;260;260]	152	141	141	
Any Temperature, Dose 2 [N=259;260;260]	82	60	60	
Grade 3 Temperature, Dose 2 [N=259;260;260]	0	0	0	
Related Temperature, Dose 2 [N=259;260;260]	81	59	59	
Any Irritability, Dose 2 [N=259;260;260]	181	165	165	
Grade 3 Irritability, Dose 2 [N=259;260;260]	14	5	5	
Related Irritability, Dose 2 [N=259;260;260]	177	154	154	
Any Loss of appetite, Dose 2 [N=259;260;260]	82	85	85	
Grade 3 Loss of appetite, Dose 2 [N=259;260;260]	1	0	0	
Related Loss of appetite, Dose 2 [N=259;260;260]	80	81	81	
Any Drowsiness, Dose 3 [N=259;260;260]	127	118	118	
Grade 3 Drowsiness, Dose 3 [N=260;259;260]	7	1	1	
Related Drowsiness, Dose 3 [N=260;259;260]	124	115	115	
Any Temperature, Dose 3 [N=260;259;260]	70	38	38	
Grade 3 Temperature, Dose 3 [N=260;259;260]	0	0	0	
Related Temperature, Dose 3 [N=260;259;260]	67	34	34	
Any Irritability, Dose 3 [N=260;259;260]	138	138	138	
Grade 3 Irritability, Dose 3 [N=260;259;260]	19	5	5	
Related Irritability, Dose 3 [N=260;259;260]	132	133	133	
Any Loss of appetite, Dose 3 [N=260;259;260]	63	59	59	
Grade 3 Loss of appetite, Dose 3 [N=260;260;260]	0	0	0	
Related Loss of appetite, Dose 3 [N=260;259;260]	58	54	54	
Any Drowsiness, Across doses [N=260;260;260]	231	215	215	
Grade 3 Drowsiness, Across doses [N=260;260;260]	14	7	7	
Related Drowsiness, Across doses [N=260;260;260]	227	213	213	
Any Temperature, Across doses [N=260;260;260]	153	110	110	
Grade 3 Temperature, Across doses [N=260;260;260]	0	0	0	

Related Temperature, Across doses [N=260;260;260]	149	106	106	
Any Irritability, Across doses [N=260;260;260]	241	235	235	
Grade 3 Irritability, Across doses [N=260;260;260	42	16	16	
Related Irritability, Across doses [N=260;260;260]	238	232	232	
Any Loss of appetite, Across doses [N=260;260;260]	155	153	153	
Grade 3 Loss of appetite, Across doses [N=260;260;	4	1	1	
Related Loss of appetite, Across doses [N=260;260;	152	148	148	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited adverse events (AEs) - Primary vaccination

End point title	Number of subjects with unsolicited adverse events (AEs) - Primary vaccination

End point description:

An AE is 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. "Any" is defined an incidence of an unsolicited AE regardless of intensity or relationship to study vaccination. The Primary Total Vaccinated cohort included all vaccinated subjects who received at least one primary dose.

End point type	Secondary

End point timeframe:

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

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	260	260	260	
Units: Subjects	181	177	185	

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects with 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, results in disability/incapacity or are a congenital

anomaly/birth defect in the offspring of a study subjects.
The Primary Total Vaccinated cohort included all vaccinated subjects who received at least one primary dose.

End point type	Secondary

End point timeframe:

Throughout the entire study period (up to Month 21)

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	260	260	260	
Units: Subjects				
Subject(s) with SAE(s)	35	26	35	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited local symptoms -Booster vaccination

End point title	Number of subjects with solicited local symptoms -Booster vaccination

End point description:

Solicited local symptoms assessed were pain, redness and swelling. Any was defined as any occurrence of the specified symptom regardless of intensity. Grade 3 pain was defined as cried when limb was moved/spontaneously painful. Grade 3 redness/swelling was defined as redness/swelling > 30 millimeters from injection site.
The Booster Total Vaccinated cohort included all subjects vaccinated with the booster dose.

End point type	Secondary

End point timeframe:

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

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	257	258	258	
Units: Subjects				
Any Pain (N=257;258; 258)	174	161	145	
Grade 3 Pain (N=257;258; 258)	21	21	7	
Any Redness (N=257;258; 258)	175	144	180	
Grade 3 Redness (N=257;258; 258)	22	10	10	
Any Swelling (N=257;258; 258)	185	146	160	
Grade 3 Swelling (N=257;258; 258)	27	15	11	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited general symptoms - Booster vaccination

End point title	Number of subjects with solicited general symptoms - Booster vaccination

End point description:

Solicited general symptoms assessed include drowsiness, fever (defined as rectal temperature ≥ 38.0°C), irritability, and loss of appetite. Any was defined as incidence of the specified symptom regardless of intensity. Grade 3 drowsiness was defined as drowsiness which prevented normal everyday activities. Grade 3 fever was defined as fever (rectal temperature) above (>) 40.0 degree Celsius (°C). Grade 3 irritability was defined as crying that could not be comforted/preventing normal activity. Grade 3 loss of appetite was defined as the subject not eating at all. Related symptom was defined as a general symptom assessed by the investigator as causally related to study vaccination.
The Booster Total Vaccinated cohort included all subjects vaccinated with the booster dose.

End point type	Secondary

End point timeframe:

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

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	256	258	258	
Units: Subjects				
Any Drowsiness	131	118	128	
Grade 3 Drowsiness	6	5	3	
Related Drowsiness	126	110	121	
Any Temperature	100	100	103	
Grade 3 Temperature	1	2	1	
Related Temperature	95	89	93	
Any Irritability	167	161	166	
Grade 3 Irritability	11	8	1	
Related Irritability	161	147	159	
Any Loss of appetite	93	83	111	
Grade 3 Loss of appetite	5	0	2	
Related Loss of appetite	89	72	101	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited adverse events (AEs) - Booster vaccination

End point title	Number of subjects with unsolicited adverse events (AEs) - Booster vaccination

End point description:

An AE is 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. "Any" was defined an incidence of an unsolicited AE regardless of intensity or relationship to study vaccination. The Booster Total Vaccinated cohort included all subjects vaccinated with the booster dose.

End point type	Secondary

End point timeframe:

Within the 31-day (Days 0-30) after booster vaccination

End point values	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	257	259	258	
Units: Subjects	106	105	105	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

xSolicited local and general symptoms: during the 4-day (Days 0-3) post-primary and post-booster vaccination; Unsolicited AEs: during the 31-day (Days 0-30) post-primary and post-booster vaccination; SAEs: during the entire study period (up to Month 21).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.1

Reporting groups

Reporting group title	Synflorix + Infanrix hexa Group

Reporting group description:

Subjects received 3 doses of Synflorix vaccine co-administered with Infanrix hexa at 2, 3 and 4 months of age (Study Months 0, 1, 2) and received a booster dose of each vaccine between 11 and 13 months of age (Study Month 9). All vaccines were administered intramuscularly in the right (Synflorix) or left (Infanrix hexa) thigh or deltoid.

Reporting group title	Synflorix + Pediacel Group

Reporting group description:

Subjects received 3 doses of Synflorix vaccine co-administered with Pediacel at 2, 3 and 4 months of age (Study Months 0, 1, 2) and received a booster dose of each vaccine between 11 and 13 months of age (Study Month 9). All vaccines were administered intramuscularly in the right (Synflorix) or left (Pediacel) thigh or deltoid.

Reporting group title	Prevenar + Pediacel Group

Reporting group description:

Subjects received 3 doses of Prevenar co-administered with Pediacel vaccine at 2, 3 and 4 months of age (Study Months 0, 1, 2) and received a booster dose of each vaccine between 11 and 13 months of age (Study Month 9). All vaccines were administered intramuscularly in the right (Prevenar) or left (Pediacel) thigh or deltoid.

Serious adverse events	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group
Total subjects affected by serious adverse events			
subjects affected / exposed	35 / 260 (13.46%)	35 / 260 (13.46%)	26 / 260 (10.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Concussion			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 260 (1.15%)	2 / 260 (0.77%)	2 / 260 (0.77%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Greenstick fracture			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 260 (0.00%)	0 / 260 (0.00%)	1 / 260 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Poisoning			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 260 (0.38%)	0 / 260 (0.00%)	0 / 260 (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
Thermal burn			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 260 (0.00%)	1 / 260 (0.38%)	0 / 260 (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
Vascular disorders			
Haematoma			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 260 (0.00%)	0 / 260 (0.00%)	1 / 260 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Velo-cardio-facial syndrome			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 260 (0.00%)	1 / 260 (0.38%)	0 / 260 (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
Nervous system disorders			
Convulsion			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 260 (0.00%)	1 / 260 (0.38%)	1 / 260 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile convulsion			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 260 (0.00%)	1 / 260 (0.38%)	0 / 260 (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
Status epilepticus			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 260 (0.00%)	0 / 260 (0.00%)	1 / 260 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Adhesion			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 260 (0.00%)	0 / 260 (0.00%)	1 / 260 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 260 (0.38%)	0 / 260 (0.00%)	1 / 260 (0.38%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Lymphadenitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 260 (0.38%)	0 / 260 (0.00%)	0 / 260 (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
Gastrointestinal disorders			
Coeliac disease			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 260 (0.00%)	1 / 260 (0.38%)	0 / 260 (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
Gastrooesophageal reflux disease			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 260 (0.38%)	1 / 260 (0.38%)	0 / 260 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 260 (0.00%)	0 / 260 (0.00%)	1 / 260 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal stenosis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 260 (0.00%)	0 / 260 (0.00%)	1 / 260 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intussusception			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 260 (0.00%)	0 / 260 (0.00%)	2 / 260 (0.77%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 260 (0.00%)	0 / 260 (0.00%)	1 / 260 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Apparent life threatening event			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 260 (0.77%)	0 / 260 (0.00%)	1 / 260 (0.38%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial hyperreactivity			
alternative assessment type: Non-systematic			

subjects affected / exposed	2 / 260 (0.77%)	4 / 260 (1.54%)	1 / 260 (0.38%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchospasm			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 260 (0.38%)	0 / 260 (0.00%)	0 / 260 (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
Status asthmaticus			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 260 (0.00%)	1 / 260 (0.38%)	0 / 260 (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
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 260 (0.38%)	0 / 260 (0.00%)	0 / 260 (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			
Bronchiolitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 260 (1.15%)	1 / 260 (0.38%)	1 / 260 (0.38%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 260 (0.38%)	0 / 260 (0.00%)	0 / 260 (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
Cellulitis			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 260 (0.38%)	0 / 260 (0.00%)	0 / 260 (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
Enterovirus infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 260 (0.38%)	1 / 260 (0.38%)	0 / 260 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
alternative assessment type: Non-systematic			
subjects affected / exposed	8 / 260 (3.08%)	5 / 260 (1.92%)	4 / 260 (1.54%)
occurrences causally related to treatment / all	0 / 8	0 / 5	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis adenovirus			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 260 (0.38%)	0 / 260 (0.00%)	1 / 260 (0.38%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis norovirus			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 260 (0.00%)	0 / 260 (0.00%)	1 / 260 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis rotavirus			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 260 (0.38%)	2 / 260 (0.77%)	2 / 260 (0.77%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 260 (0.00%)	1 / 260 (0.38%)	1 / 260 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Intervertebral discitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 260 (0.00%)	1 / 260 (0.38%)	0 / 260 (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
Lower respiratory tract infection viral			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 260 (0.00%)	1 / 260 (0.38%)	0 / 260 (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
Mastoiditis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 260 (0.00%)	1 / 260 (0.38%)	0 / 260 (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			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 260 (0.00%)	0 / 260 (0.00%)	1 / 260 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oral herpes			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 260 (0.38%)	1 / 260 (0.38%)	0 / 260 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 260 (1.15%)	1 / 260 (0.38%)	0 / 260 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 260 (0.38%)	3 / 260 (1.15%)	2 / 260 (0.77%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia primary atypical			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 260 (0.00%)	1 / 260 (0.38%)	0 / 260 (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
Pyelonephritis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 260 (0.38%)	3 / 260 (1.15%)	0 / 260 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchiolitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	5 / 260 (1.92%)	5 / 260 (1.92%)	2 / 260 (0.77%)
occurrences causally related to treatment / all	0 / 5	0 / 5	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 260 (0.38%)	0 / 260 (0.00%)	0 / 260 (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
Upper respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 260 (0.38%)	4 / 260 (1.54%)	1 / 260 (0.38%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 260 (0.00%)	0 / 260 (0.00%)	2 / 260 (0.77%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 260 (0.00%)	1 / 260 (0.38%)	0 / 260 (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			
Dehydration			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 260 (0.00%)	0 / 260 (0.00%)	1 / 260 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Feeding disorder neonatal			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 260 (0.00%)	0 / 260 (0.00%)	1 / 260 (0.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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	Synflorix + Infanrix hexa Group	Synflorix + Pediacel Group	Prevenar + Pediacel Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	260 / 260 (100.00%)	260 / 260 (100.00%)	260 / 260 (100.00%)
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	195 / 260 (75.00%)	179 / 260 (68.85%)	164 / 260 (63.08%)
occurrences (all)	364	297	275
Pain			
subjects affected / exposed	227 / 260 (87.31%)	219 / 260 (84.23%)	208 / 260 (80.00%)
occurrences (all)	573	527	464
Erythema			

subjects affected / exposed	231 / 260 (88.85%)	210 / 260 (80.77%)	222 / 260 (85.38%)
occurrences (all)	546	528	542
Swelling			
subjects affected / exposed	232 / 260 (89.23%)	220 / 260 (84.62%)	211 / 260 (81.15%)
occurrences (all)	610	559	516
Somnolence			
subjects affected / exposed	240 / 260 (92.31%)	237 / 260 (91.15%)	225 / 260 (86.54%)
occurrences (all)	598	544	553
Irritability			
subjects affected / exposed	252 / 260 (96.92%)	242 / 260 (93.08%)	247 / 260 (95.00%)
occurrences (all)	676	659	649
Decreased appetite			
subjects affected / exposed	182 / 260 (70.00%)	174 / 260 (66.92%)	191 / 260 (73.46%)
occurrences (all)	326	309	342
Injection site haematoma			
subjects affected / exposed	12 / 260 (4.62%)	16 / 260 (6.15%)	7 / 260 (2.69%)
occurrences (all)	15	16	8
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	22 / 260 (8.46%)	21 / 260 (8.08%)	15 / 260 (5.77%)
occurrences (all)	25	24	17
Vomiting			
subjects affected / exposed	10 / 260 (3.85%)	13 / 260 (5.00%)	16 / 260 (6.15%)
occurrences (all)	10	14	20
Enteritis			
subjects affected / exposed	17 / 260 (6.54%)	8 / 260 (3.08%)	12 / 260 (4.62%)
occurrences (all)	17	9	12
Respiratory, thoracic and mediastinal disorders			
Wheezing			
subjects affected / exposed	19 / 260 (7.31%)	10 / 260 (3.85%)	17 / 260 (6.54%)
occurrences (all)	21	11	17
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	25 / 260 (9.62%)	16 / 260 (6.15%)	18 / 260 (6.92%)
occurrences (all)	25	17	19
Infections and infestations			

Upper respiratory tract infection			
subjects affected / exposed	117 / 260 (45.00%)	125 / 260 (48.08%)	133 / 260 (51.15%)
occurrences (all)	153	160	170
Gastroenteritis			
subjects affected / exposed	23 / 260 (8.85%)	17 / 260 (6.54%)	17 / 260 (6.54%)
occurrences (all)	24	17	17
Viral infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	10 / 260 (3.85%)	10 / 260 (3.85%)	24 / 260 (9.23%)
occurrences (all)	12	10	24
Otitis media			
subjects affected / exposed	22 / 260 (8.46%)	14 / 260 (5.38%)	10 / 260 (3.85%)
occurrences (all)	22	14	11

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 November 2007	A first amendment was made to the protocol in response to comments from the Dutch Authorities to clarify that this study was a single-centre study.
30 January 2008	On request of the Dutch Authorities, a second amendment to the protocol was made. Changes concerned the study design: 1) Before vaccination at Visit 1 no blood sample was to be collected; 2) The priority ranking for testing of opsonophagocytic activity (OPA) activity against the 10 pneumococcal vaccine serotypes in case of insufficient blood sample volume was changed; 3) Testing of OPA activity against the 10 pneumococcal vaccine serotypes was to be done for all subjects i.e. all subjects for which the amount of remaining/available serum is sufficient; 4) The sample size was increased.
14 August 2008	Changes concerned the study design: 1) To collect information about factors that could potentially influence nasopharyngeal carriage of Streptococcus (S.). pneumoniae and Haemophilus (H.) influenzae, it was planned that the subjects' parents/ guardian(s) would be asked some questions at Visits 4, 5, 7, 8 and 9; 2) The recruitment period was changed to 9 months.
22 March 2010	The following changes were introduced: 1) Due to the H1N1 influenza pandemic, the children were offered H1N1 influenza vaccine as part of a national pandemic prevention plan. Thus, the age range for the booster vaccination visit and subsequent visits was extended; 2) Further details on microbiological testing were included; 3) A second Interim Analysis was added to evaluate carriage (at 3 timepoints) using classical methods for bacterial identification / typing, additional microbiological techniques for H. influenzae/H. haemolyticus discrimination and quantitative molecular techniques for H. influenzae carriage; 4) The back-up contact details for reporting SAEs were updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported