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	v1
This version publication date	25 February 2016
First version publication date	19 June 2015

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 when co-administered with DTPa-IPV-Hib (Pediacel) (10Pn-PDC group) is non-inferior to co-administration with DTPa-HBV-IPV/Hib (Infanrix hexa) (10Pn-Hexa group), 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 GMC ratio between groups (10Pn-Hexa group over 10Pn-PDC 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	10Pn+DTPa-HBV-IPV/Hib Group

Arm description:

Subjects received 3 doses of 10Pn-PD-DiT (or GSK1024850A) vaccine co-administered with DTPa-HBV-IPV/Hib vaccine (Infanrix hexa by GSK Biologicals) 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 (10Pn-PD-DiT) or left (DTPa-HBV-IPV/Hib) 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	10Pn+DTPa-HBV-IPV/Hib Group

Arm description:

Subjects received 3 doses of 10Pn-PD-DiT (or GSK1024850A) vaccine co-administered with DTPa-IPV-Hib vaccine (Pediacel by Sanofi Pasteur MSD) 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 (10Pn-PD-DiT) or left (DTPa-IPV/Hib) 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	7Pn+DTPa-HBV-IPV/Hib Group

Arm description:

Subjects received 3 doses of 7Pn vaccine (or Prevenar by Pfizer [formerly Wyeth Lederle Vaccines S.A.]) co-administered with DTPa-IPV-Hib vaccine(Pediacel by Sanofi Pasteur MSD) 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 (7Pn) or left (DTPa-IPV-Hib; DTPa-HBV-IPV/Hib) 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	10Pn+DTPa-HBV-IPV/Hib Group	10Pn+DTPa-HBV-IPV/Hib Group	7Pn+DTPa-HBV-IPV/Hib 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	10Pn+DTPa-HBV-IPV/Hib Group

Arm description:

Subjects received 3 doses of 10Pn-PD-DiT (or GSK1024850A) vaccine co-administered with DTPa-HBV-IPV/Hib vaccine (Infanrix hexa by GSK Biologicals) 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 (10Pn-PD-DiT) or left (DTPa-HBV-IPV/Hib) 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	10Pn+DTPa-HBV-IPV/Hib Group

Arm description:

Subjects received 3 doses of 10Pn-PD-DiT (or GSK1024850A) vaccine co-administered with DTPa-IPV-Hib vaccine (Pediacel by Sanofi Pasteur MSD) 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 (10Pn-PD-DiT) or left (DTPa-IPV/Hib) 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	7Pn+DTPa-HBV-IPV/Hib Group

Arm description:

Subjects received 3 doses of 7Pn vaccine (or Prevenar by Pfizer [formerly Wyeth Lederle Vaccines S.A.]) co-administered with DTPa-IPV-Hib vaccine(Pediacel by Sanofi Pasteur MSD) 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 (10Pn; 7Pn) or left (DTPa-IPV-Hib; DTPa-HBV-IPV/Hib) 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]	10Pn+DTPa-HBV-IPV/Hib Group	10Pn+DTPa-HBV-IPV/Hib Group	7Pn+DTPa-HBV-IPV/Hib 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: 6 subjects did not join the study for the BST phase, 3 subjects from the 10Pn+DTPa-HBV-IPV/Hib Group, 1 subject from the 10Pn+DTPa-IPV-Hib Group and 2 subjects from the 7Pn+DTPa-IPV-Hib Group.

Baseline characteristics

Reporting groups	
Reporting group title	10Pn+DTPa-HBV-IPV/Hib Group
Reporting group description:	
Subjects received 3 doses of 10Pn-PD-DiT (or GSK1024850A) vaccine co-administered with DTPa-HBV-IPV/Hib vaccine (Infanrix hexa by GSK Biologicals) 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 (10Pn-PD-DiT) or left (DTPa-HBV-IPV/Hib) thigh or deltoid.	
Reporting group title	10Pn+DTPa-HBV-IPV/Hib Group
Reporting group description:	
Subjects received 3 doses of 10Pn-PD-DiT (or GSK1024850A) vaccine co-administered with DTPa-IPV-Hib vaccine (Pediacel by Sanofi Pasteur MSD) 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 (10Pn-PD-DiT) or left (DTPa-IPV/Hib) thigh or deltoid.	
Reporting group title	7Pn+DTPa-HBV-IPV/Hib Group
Reporting group description:	
Subjects received 3 doses of 7Pn vaccine (or Prevenar by Pfizer [formerly Wyeth Lederle Vaccines S.A.]) co-administered with DTPa-IPV-Hib vaccine(Pediacel by Sanofi Pasteur MSD) 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 (7Pn) or left (DTPa-IPV-Hib; DTPa-HBV-IPV/Hib) thigh or deltoid.	

Reporting group values	10Pn+DTPa-HBV-IPV/Hib Group	10Pn+DTPa-HBV-IPV/Hib Group	7Pn+DTPa-HBV-IPV/Hib Group
Number of subjects	260	260	260
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
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)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: weeks			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	384		
Male	396		

End points

End points reporting groups

Reporting group title	10Pn+DTPa-HBV-IPV/Hib Group

Reporting group description:

Subjects received 3 doses of 10Pn-PD-DiT (or GSK1024850A) vaccine co-administered with DTPa-HBV-IPV/Hib vaccine (Infanrix hexa by GSK Biologicals) 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 (10Pn-PD-DiT) or left (DTPa-HBV-IPV/Hib) thigh or deltoid.

Reporting group title	10Pn+DTPa-HBV-IPV/Hib Group

Reporting group description:

Subjects received 3 doses of 10Pn-PD-DiT (or GSK1024850A) vaccine co-administered with DTPa-IPV-Hib vaccine (Pediacel by Sanofi Pasteur MSD) 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 (10Pn-PD-DiT) or left (DTPa-IPV/Hib) thigh or deltoid.

Reporting group title	7Pn+DTPa-HBV-IPV/Hib Group

Reporting group description:

Subjects received 3 doses of 7Pn vaccine (or Prevenar by Pfizer [formerly Wyeth Lederle Vaccines S.A.]) co-administered with DTPa-IPV-Hib vaccine(Pediacel by Sanofi Pasteur MSD) 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 (7Pn) or left (DTPa-IPV-Hib; DTPa-HBV-IPV/Hib) thigh or deltoid.

Reporting group title	10Pn+DTPa-HBV-IPV/Hib Group

Reporting group description:

Subjects received 3 doses of 10Pn-PD-DiT (or GSK1024850A) vaccine co-administered with DTPa-HBV-IPV/Hib vaccine (Infanrix hexa by GSK Biologicals) 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 (10Pn-PD-DiT) or left (DTPa-HBV-IPV/Hib) thigh or deltoid.

Reporting group title	10Pn+DTPa-HBV-IPV/Hib Group

Reporting group description:

Subjects received 3 doses of 10Pn-PD-DiT (or GSK1024850A) vaccine co-administered with DTPa-IPV-Hib vaccine (Pediacel by Sanofi Pasteur MSD) 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 (10Pn-PD-DiT) or left (DTPa-IPV/Hib) thigh or deltoid.

Reporting group title	7Pn+DTPa-HBV-IPV/Hib Group

Reporting group description:

Subjects received 3 doses of 7Pn vaccine (or Prevenar by Pfizer [formerly Wyeth Lederle Vaccines S.A.]) co-administered with DTPa-IPV-Hib vaccine(Pediacel by Sanofi Pasteur MSD) 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 (10Pn; 7Pn) or left (DTPa-IPV-Hib; DTPa-HBV-IPV/Hib) 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)

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)

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 measure by 22F-inhibition Enzyme-Linked ImmunSorbent Assay (ELISA) Assay; calculated, expressed as geometric mean concentrations (GMCs) and tabulated. The seropositivity cut-off for the assay was >= 0.05 microgram per millilitre (microg/mL).

End point type	Primary

End point timeframe:

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

End point values	10Pn+DTPa-HBV-IPV/Hib Group	10Pn+DTPa-HBV-IPV/Hib Group	7Pn+DTPa-HBV-IPV/Hib Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	194	189	192	
Units: microg/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% CI of the geometric mean concentration (GMC) ratio between the 10Pn+DTPa-HBV-IPV/Hib and 10Pn+DTPa-IPV-Hib groups (10Pn+DTPa-HBV-IPV/Hib Group over 10Pn+DTPa-IPV-Hib 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	10Pn+DTPa-HBV-IPV/Hib Group v 10Pn+DTPa-HBV-IPV/Hib 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] - The non-inferiority objective was reached if the upper limit of the 2-sided 95% CI of the GMC ratio for between groups (10Pn+DTPa-HBV-IPV/Hib Group over 10Pn+DTPa-IPV-Hib Group), was lower than 2, for each of the 10 pneumococcal serotypes and protein D.

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 10Pn+DTPa-HBV-IPV/Hib and 10Pn+DTPa-IPV-Hib groups (10Pn+DTPa-HBV-IPV/Hib Group over 10Pn+DTPa-IPV-Hib 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	10Pn+DTPa-HBV-IPV/Hib Group v 10Pn+DTPa-HBV-IPV/Hib 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] - The non-inferiority objective was reached if the upper limit of the 2-sided 95% CI of the GMC ratio for between groups (10Pn+DTPa-HBV-IPV/Hib Group over 10Pn+DTPa-IPV-Hib Group), was lower than 2, for each of the 10 pneumococcal serotypes and protein D.

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 10Pn+DTPa-HBV-IPV/Hib and 10Pn+DTPa-IPV-Hib groups (10Pn+DTPa-HBV-IPV/Hib Group over 10Pn+DTPa-IPV-Hib 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	10Pn+DTPa-HBV-IPV/Hib Group v 10Pn+DTPa-HBV-IPV/Hib 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] - The non-inferiority objective was reached if the upper limit of the 2-sided 95% CI of the GMC ratio for between groups (10Pn+DTPa-HBV-IPV/Hib Group over 10Pn+DTPa-IPV-Hib Group), was lower than 2, for each of the 10 pneumococcal serotypes and protein D.

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 10Pn+DTPa-HBV-IPV/Hib and 10Pn+DTPa-IPV-Hib groups (10Pn+DTPa-HBV-IPV/Hib Group over 10Pn+DTPa-IPV-Hib 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	10Pn+DTPa-HBV-IPV/Hib Group v 10Pn+DTPa-HBV-IPV/Hib 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] - The non-inferiority objective was reached if the upper limit of the 2-sided 95% CI of the GMC ratio for between groups (10Pn+DTPa-HBV-IPV/Hib Group over 10Pn+DTPa-IPV-Hib Group), was lower than 2, for each of the 10 pneumococcal serotypes and protein D.

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 10Pn+DTPa-HBV-IPV/Hib and 10Pn+DTPa-IPV-Hib groups (10Pn+DTPa-HBV-IPV/Hib Group over 10Pn+DTPa-IPV-Hib 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	10Pn+DTPa-HBV-IPV/Hib Group v 10Pn+DTPa-HBV-IPV/Hib Group
Number of subjects included in analysis	383
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMC ratio
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	1.13

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

Statistical analysis description:

The 2-sided 95% CI of the geometric mean concentration (GMC) ratio between the 10Pn+DTPa-HBV-IPV/Hib and 10Pn+DTPa-IPV-Hib groups (10Pn+DTPa-HBV-IPV/Hib Group over 10Pn+DTPa-IPV-Hib 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	10Pn+DTPa-HBV-IPV/Hib Group v 10Pn+DTPa-HBV-IPV/Hib Group
Number of subjects included in analysis	383
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
Parameter estimate	GMC ratio
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	1.16

Notes:

[5] - The non-inferiority objective was reached if the upper limit of the 2-sided 95% CI of the GMC ratio for between groups (10Pn+DTPa-HBV-IPV/Hib Group over 10Pn+DTPa-IPV-Hib Group), was lower than 2, for each of the 10 pneumococcal serotypes and protein D.

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 10Pn+DTPa-HBV-IPV/Hib and 10Pn+DTPa-IPV-Hib groups (10Pn+DTPa-HBV-IPV/Hib Group over 10Pn+DTPa-IPV-Hib 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	10Pn+DTPa-HBV-IPV/Hib Group v 10Pn+DTPa-HBV-IPV/Hib Group
Number of subjects included in analysis	383
Analysis specification	Pre-specified
Analysis type	non-inferiority[6]
Parameter estimate	GMC ratio
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.21

Notes:

[6] - The non-inferiority objective was reached if the upper limit of the 2-sided 95% CI of the GMC ratio for between groups (10Pn+DTPa-HBV-IPV/Hib Group over 10Pn+DTPa-IPV-Hib Group), was lower than 2, for each of the 10 pneumococcal serotypes and protein D.

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 10Pn+DTPa-HBV-IPV/Hib and 10Pn+DTPa-IPV-Hib groups (10Pn+DTPa-HBV-IPV/Hib Group over 10Pn+DTPa-IPV-Hib 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 18C.

Comparison groups	10Pn+DTPa-HBV-IPV/Hib Group v 10Pn+DTPa-HBV-IPV/Hib Group

Number of subjects included in analysis	383
Analysis specification	Pre-specified
Analysis type	non-inferiority[7]
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:

[7] - The non-inferiority objective was reached if the upper limit of the 2-sided 95% CI of the GMC ratio for between groups (10Pn+DTPa-HBV-IPV/Hib Group over 10Pn+DTPa-IPV-Hib Group), was lower than 2, for each of the 10 pneumococcal serotypes and protein D.

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 10Pn+DTPa-HBV-IPV/Hib and 10Pn+DTPa-IPV-Hib groups (10Pn+DTPa-HBV-IPV/Hib Group over 10Pn+DTPa-IPV-Hib 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	10Pn+DTPa-HBV-IPV/Hib Group v 10Pn+DTPa-HBV-IPV/Hib Group
Number of subjects included in analysis	383
Analysis specification	Pre-specified
Analysis type	non-inferiority[8]
Parameter estimate	GMC ratio
Point estimate	0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	1.23

Notes:

[8] - The non-inferiority objective was reached if the upper limit of the 2-sided 95% CI of the GMC ratio for between groups (10Pn+DTPa-HBV-IPV/Hib Group over 10Pn+DTPa-IPV-Hib Group), was lower than 2, for each of the 10 pneumococcal serotypes and protein D.

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 10Pn+DTPa-HBV-IPV/Hib and 10Pn+DTPa-IPV-Hib groups (10Pn+DTPa-HBV-IPV/Hib Group over 10Pn+DTPa-IPV-Hib 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	10Pn+DTPa-HBV-IPV/Hib Group v 10Pn+DTPa-HBV-IPV/Hib Group
Number of subjects included in analysis	383
Analysis specification	Pre-specified
Analysis type	non-inferiority[9]
Parameter estimate	GMC ratio
Point estimate	0.92

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	1.23

Notes:

[9] - The non-inferiority objective was reached if the upper limit of the 2-sided 95% CI of the GMC ratio for between groups (10Pn+DTPa-HBV-IPV/Hib Group over 10Pn+DTPa-IPV-Hib Group), was lower than 2, for each of the 10 pneumococcal serotypes and protein D.

Primary: Antibody concentration against protein D (PD).

End point title	Antibody concentration against protein D (PD).

End point description:

Anti-PD antibody concentrations were calculated, expressed as geometric mean concentrations (GMCs) and tabulated. The seropositivity cut-off for the assay was >= 100 Enzyme-Linked ImmunoSobent Assay (ELISA) units per millilitre (EL.U/mL).

End point type	Primary

End point timeframe:

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

End point values	10Pn+DTPa-HBV-IPV/Hib Group	10Pn+DTPa-HBV-IPV/Hib Group	7Pn+DTPa-HBV-IPV/Hib 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 10Pn+DTPa-HBV-IPV/Hib and 10Pn+DTPa-IPV-Hib groups (10Pn+DTPa-HBV-IPV/Hib Group over 10Pn+DTPa-IPV-Hib 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	10Pn+DTPa-HBV-IPV/Hib Group v 10Pn+DTPa-HBV-IPV/Hib Group
Number of subjects included in analysis	384
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	GMC ratio
Point estimate	0.91

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.06

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms & Unsolicited AEs: During the 4-and 31-days period(s) post primary (PRI) or booster (BST) vaccinations, respectively; SAEs: from study start to study end

Adverse event reporting additional description:

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

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.0

Reporting groups

Reporting group title	10Pn+DTPa-HBV-IPV/Hib Group

Reporting group description:

Subjects received 3 doses of 10Pn-PD-DiT (or GSK1024850A) vaccine co-administered with DTPa-HBV-IPV/Hib vaccine (Infanrix hexa by GSK Biologicals) 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 (10Pn-PD-DiT) or left (DTPa-HBV-IPV/Hib) thigh or deltoid.

Reporting group title	10Pn+DTPa-IPV-Hib Group

Reporting group description:

Subjects received 3 doses of 10Pn-PD-DiT (or GSK1024850A) vaccine co-administered with DTPa-IPV-Hib vaccine (Pediacel by Sanofi Pasteur MSD) 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 (10Pn-PD-DiT) or left (DTPa-IPV/Hib) thigh or deltoid.

Reporting group title	7Pn+DTPa-HBV-IPV/Hib Group

Reporting group description:

Subjects received 3 doses of 7Pn vaccine (or Prevenar by Pfizer [formerly Wyeth Lederle Vaccines S.A.]) co-administered with DTPa-IPV-Hib vaccine (Pediacel by Sanofi Pasteur MSD) 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 (7Pn) or left (DTPa-IPV-Hib; DTPa-HBV-IPV/Hib) thigh or deltoid.

Serious adverse events	10Pn+DTPa-HBV-IPV/Hib Group	10Pn+DTPa-IPV-Hib Group	7Pn+DTPa-HBV-IPV/Hib Group
Total subjects affected by serious adverse events			
subjects affected / exposed	35 / 260 (13.46%)	26 / 260 (10.00%)	35 / 260 (13.46%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Concussion			
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			

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
Poisoning			
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			
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
Vascular disorders			
Haematoma			
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
Congenital, familial and genetic disorders			
Velo-cardio-facial syndrome			
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
Nervous system disorders			
Convulsion			
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			
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
Status epilepticus			
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

General disorders and administration site conditions			
Adhesion			
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
Pyrexia			
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
Blood and lymphatic system disorders			
Lymphadenitis			
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			
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
Gastrooesophageal reflux disease			
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
Intestinal obstruction			
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
Intestinal stenosis			
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
Intussusception			

subjects affected / exposed	0 / 260 (0.00%)	2 / 260 (0.77%)	0 / 260 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
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
Respiratory, thoracic and mediastinal disorders			
Apparent life threatening event			
subjects affected / exposed	2 / 260 (0.77%)	1 / 260 (0.38%)	0 / 260 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial hyperreactivity			
subjects affected / exposed	2 / 260 (0.77%)	1 / 260 (0.38%)	4 / 260 (1.54%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchospasm			
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			
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
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
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			
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			
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			
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			
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			
subjects affected / exposed	8 / 260 (3.08%)	4 / 260 (1.54%)	5 / 260 (1.92%)
occurrences causally related to treatment / all	0 / 8	0 / 4	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis adenovirus			
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 norovirus			
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
Gastroenteritis rotavirus			
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			
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			

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
Lower respiratory tract infection viral			
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
Mastoiditis			
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
Meningitis			
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
Oral herpes			
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
Otitis media			
subjects affected / exposed	3 / 260 (1.15%)	0 / 260 (0.00%)	1 / 260 (0.38%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 260 (0.38%)	2 / 260 (0.77%)	3 / 260 (1.15%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia primary atypical			
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
Pyelonephritis			

subjects affected / exposed	1 / 260 (0.38%)	0 / 260 (0.00%)	3 / 260 (1.15%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	5 / 260 (1.92%)	2 / 260 (0.77%)	5 / 260 (1.92%)
occurrences causally related to treatment / all	0 / 5	0 / 2	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			
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			
subjects affected / exposed	1 / 260 (0.38%)	1 / 260 (0.38%)	4 / 260 (1.54%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 260 (0.00%)	2 / 260 (0.77%)	0 / 260 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			
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
Metabolism and nutrition disorders			
Dehydration			
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
Feeding disorder neonatal			
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

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

Non-serious adverse events	10Pn+DTPa-HBV-IPV/Hib Group	10Pn+DTPa-IPV-Hib Group	7Pn+DTPa-HBV-IPV/Hib Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	241 / 260 (92.69%)	230 / 260 (88.46%)	235 / 260 (90.38%)
General disorders and administration site conditions			
Pyrexia - BST			
subjects affected / exposed[1]	16 / 257 (6.23%)	13 / 259 (5.02%)	21 / 258 (8.14%)
occurrences (all)	16	13	21
Pain - PRI			
alternative dictionary used: MedDRA 12.1			
alternative assessment type: Systematic			
subjects affected / exposed	205 / 260 (78.85%)	193 / 260 (74.23%)	178 / 260 (68.46%)
occurrences (all)	205	193	178
Redness - PRI			
alternative dictionary used: MedDRA 12.1			
alternative assessment type: Systematic			
subjects affected / exposed	197 / 260 (75.77%)	193 / 260 (74.23%)	184 / 260 (70.77%)
occurrences (all)	197	193	184
Swelling - PRI			
alternative dictionary used: MedDRA 12.1			
alternative assessment type: Systematic			
subjects affected / exposed	205 / 260 (78.85%)	199 / 260 (76.54%)	179 / 260 (68.85%)
occurrences (all)	205	199	179
Pain - BST			
alternative assessment type: Systematic			
subjects affected / exposed[2]	174 / 257 (67.70%)	161 / 259 (62.16%)	145 / 258 (56.20%)
occurrences (all)	174	161	145
Redness – BST			
alternative assessment type: Systematic			
subjects affected / exposed[3]	175 / 257 (68.09%)	144 / 259 (55.60%)	180 / 258 (69.77%)
occurrences (all)	175	144	180
Swelling - BST			
alternative assessment type: Systematic			

subjects affected / exposed[4]	185 / 257 (71.98%)	146 / 259 (56.37%)	160 / 258 (62.02%)
occurrences (all)	185	146	160
Drowsiness - PRI			
alternative dictionary used: MedDRA 12.1			
alternative assessment type: Systematic			
subjects affected / exposed	231 / 260 (88.85%)	220 / 260 (84.62%)	215 / 260 (82.69%)
occurrences (all)	231	220	215
Rectal Temperature >=38.0°C - PRI			
alternative dictionary used: MedDRA 12.1			
alternative assessment type: Systematic			
subjects affected / exposed	153 / 260 (58.85%)	124 / 260 (47.69%)	110 / 260 (42.31%)
occurrences (all)	153	124	110
Irritability - PRI			
alternative dictionary used: MedDRA 12.1			
alternative assessment type: Systematic			
subjects affected / exposed	241 / 260 (92.69%)	230 / 260 (88.46%)	235 / 260 (90.38%)
occurrences (all)	241	230	235
Loss of appetite - PRI			
alternative dictionary used: MedDRA 12.1			
alternative assessment type: Systematic			
subjects affected / exposed	155 / 260 (59.62%)	145 / 260 (55.77%)	153 / 260 (58.85%)
occurrences (all)	155	145	153
Drowsiness – BST			
alternative assessment type: Systematic			
subjects affected / exposed[5]	131 / 257 (50.97%)	118 / 259 (45.56%)	128 / 258 (49.61%)
occurrences (all)	131	118	128
Rectal Temperature >=38.0°C – BST			
alternative assessment type: Systematic			
subjects affected / exposed[6]	100 / 257 (38.91%)	100 / 259 (38.61%)	103 / 258 (39.92%)
occurrences (all)	100	100	103
Irritability – BST			
alternative assessment type: Systematic			
subjects affected / exposed[7]	167 / 257 (64.98%)	161 / 259 (62.16%)	166 / 258 (64.34%)
occurrences (all)	167	161	166

Loss of appetite - BST			
alternative assessment type: Systematic			
subjects affected / exposed[8]	93 / 257 (36.19%)	83 / 259 (32.05%)	111 / 258 (43.02%)
occurrences (all)	93	83	111
Gastrointestinal disorders			
Diarrhoea - PRI			
alternative dictionary used: MedDRA 12.1			
subjects affected / exposed	15 / 260 (5.77%)	14 / 260 (5.38%)	12 / 260 (4.62%)
occurrences (all)	15	14	12
Vomiting - PRI			
alternative dictionary used: MedDRA 12.1			
subjects affected / exposed	11 / 260 (4.23%)	13 / 260 (5.00%)	0 / 260 (0.00%)
occurrences (all)	11	13	0
Respiratory, thoracic and mediastinal disorders			
Wheezing - PRI			
alternative dictionary used: MedDRA 12.1			
subjects affected / exposed	15 / 260 (5.77%)	7 / 260 (2.69%)	10 / 260 (3.85%)
occurrences (all)	15	7	10
Skin and subcutaneous tissue disorders			
Eczema - PRI			
alternative dictionary used: MedDRA 12.1			
subjects affected / exposed	24 / 260 (9.23%)	15 / 260 (5.77%)	18 / 260 (6.92%)
occurrences (all)	24	15	18
Infections and infestations			
Upper respiratory tract infection - PRI			
alternative dictionary used: MedDRA 12.1			
subjects affected / exposed	99 / 260 (38.08%)	108 / 260 (41.54%)	111 / 260 (42.69%)
occurrences (all)	99	108	111
Gastroenteritis - PRI			
alternative dictionary used: MedDRA 12.1			
subjects affected / exposed	16 / 260 (6.15%)	13 / 260 (5.00%)	13 / 260 (5.00%)
occurrences (all)	16	13	13
Viral infection - BST			
subjects affected / exposed[9]	5 / 257 (1.95%)	17 / 259 (6.56%)	5 / 258 (1.94%)
occurrences (all)	5	17	5

Upper respiratory tract infection - BST			
subjects affected / exposed[10]	27 / 257 (10.51%)	32 / 259 (12.36%)	34 / 258 (13.18%)
occurrences (all)	27	32	34

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Assessment for this event for this specified phase was performed solely on subjects with available results.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Assessment for this event for this specified phase was performed solely on subjects with available results.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Assessment for this event for this specified phase was performed solely on subjects with available results.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Assessment for this event for this specified phase was performed solely on subjects with available results.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Assessment for this event for this specified phase was performed solely on subjects with available results.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Assessment for this event for this specified phase was performed solely on subjects with available results.

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Assessment for this event for this specified phase was performed solely on subjects with available results.

[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Assessment for this event for this specified phase was performed solely on subjects with available results.

[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Assessment for this event for this specified phase was performed solely on subjects with available results.

[10] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Assessment for this event for this specified phase was performed solely on subjects with available results.

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