Clinical trial results:
A phase IIIb open, controlled study to evaluate the immunogenicity, safety and reactogenicity of GlaxoSmithKline (GSK) Biologicals' 10-valent pneumococcal conjugate vaccine when given as a catch-up immunization in children older than 7 months of age or given as a 3-dose primary immunization in children before 6 months of age.

Summary

EudraCT number	2006-001482-42
Trial protocol	FI
Global end of trial date	15 November 2007

Results information

Result version number	v1
This version publication date	09 February 2016
First version publication date	14 June 2015

Trial information

Trial identification

Sponsor protocol code	107058

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00345358
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	29 April 2008
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 November 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the immunogenicity of GSK Biologicals' 10-valent pneumococcal conjugate vaccine, when given as a catch-up immunization in children older than 7 months of age (three age-groups with different schedules).

Protection of trial subjects:

All vaccines were observed closely for at least 30 minutes following the administration of vaccines, with appropriate medical treatment readily available in case of a rare anaphylactic reaction. 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. Subjects were followed-up for up to 31 days for adverse events after the last vaccination/product administration and during the entire study period for serious adverse events.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 September 2006
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	Finland: 600
Worldwide total number of subjects	600
EEA total number of subjects	600

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)	450
Children (2-11 years)	150
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 (all groups) and a booster (BST) phase (only 10Pn <6M and 10Pn 7-11M groups).

Pre-assignment

Screening details:

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

Period 1

Period 1 title	Primary Vaccination Phase
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	10Pn <6M Group

Arm description:

This group consisted of subjects up to 6 months of age at first vaccination who received 3 doses of 10Pn-PD-DiT (or 10Pn) vaccine co-administered with InfanrixTM IPV/Hib (DTPa-IPV/Hib) at 3, 4 and 5 months of age and a booster dose of the same vaccines at 12-15 months of age. Vaccines were administrated intramuscularly in the right (10Pn-PD-DiT) or the left (DTPa-IPV/Hib) thigh or deltoid region (deltoid region only for children >12 months of age if muscle size was adequate).

Arm type	Experimental
Investigational medicinal product name	10-valent streptococcus pneumoniae conjugate vaccine
Investigational medicinal product code	
Other name	10Pn-PD-DiT, 10Pn
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 primary doses administered at 3, 4 and 5 months of age followed by a booster dose at 12-15 months of age, all injected intramuscularly in the right thigh or deltoid region (deltoid region only for children >12 months of age if muscle size was adequate).

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

Dosage and administration details:

3 primary doses administered at 3, 4 and 5 months of age followed by a booster dose at 12-15 months of age, all injected intramuscularly in the left right thigh or deltoid region (deltoid region only for children >12 months of age if muscle size was adequate).

Arm title	10Pn 7-11M Group

Arm description:

This group consisted of subjects 7 to 11 months of age at first vaccination who received 2 doses of 10Pn-PD-DiT (10Pn), one first dose at enrolment followed by a second dose one month later, and a booster dose at 12-15 months of age. The 10PN-PD-DiT vaccine was administrated intramuscularly in the right thigh or deltoid region (deltoid region only for children >12 months of age if muscle size was adequate).

Arm type	Experimental
Investigational medicinal product name	10-valent streptococcus pneumoniae conjugate vaccine
Investigational medicinal product code	
Other name	10Pn-PD-DiT, 10Pn
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 doses, one first dose at enrolment followed by a second dose one month later, followed by a booster dose at 12-15 months of age., injected intramuscularly in the right thigh or deltoid region (deltoid region only for children >12 months of age if muscle size was adequate).

Arm title	10Pn 12-23M Group

Arm description:

This group consisted of subjects 12 to 23 months inclusive at first vaccination who received 2 doses of 10Pn-PD-DiT (10Pn), one first dose at enrolment followed by a second dose 2 months later. The 10PN-PD-DiT vaccine was administrated intramuscularly in the right thigh or deltoid region (deltoid region only for children >12 months of age if muscle size was adequate).

Arm type	Experimental
Investigational medicinal product name	IMP Name 10-valent streptococcus pneumoniae conjugate vaccine
Investigational medicinal product code	
Other name	10Pn-PD-DiT, 10Pn
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 doses of 10Pn-PD-DiT (10Pn), one first dose at enrolment followed by a second dose 2 months later, injected intramuscularly in the right thigh or deltoid region (deltoid region only for children >12 months of age if muscle size was adequate).

Arm title	10Pn >=24M Group

Arm description:

This group consisted of subjects aged between 24 months (inclusive) to 5 years (inclusive) at vaccination who received one dose of 10Pn-PD-DiT (10Pn). The 10PN-PD-DiT vaccine was administrated intramuscularly in the right thigh or deltoid region (deltoid region only for children >12 months of age if muscle size was adequate).

Arm type	Experimental
Investigational medicinal product name	10-valent streptococcus pneumoniae conjugate vaccine
Investigational medicinal product code	
Other name	10Pn-PD-DiT, 10Pn
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose administered when subject’s age was between 24 months (inclusive) to 5 years of age (inclusive) at vaccination, injected intramuscularly in the right thigh or deltoid region (deltoid region only for children >12 months of age if muscle size was adequate).

Number of subjects in period 1	10Pn <6M Group	10Pn 7-11M Group	10Pn 12-23M Group
Started	150	150	150
Completed	145	146	142
Not completed	5	4	8
Consent withdrawn by subject	1	2	4
Adverse event, non-fatal	3	1	1

Other reason (unspecified)	-	1	1
Lost to follow-up	1	-	2

Number of subjects in period 1	10Pn >=24M Group
Started	150
Completed	148
Not completed	2
Consent withdrawn by subject	-
Adverse event, non-fatal	-
Other reason (unspecified)	-
Lost to follow-up	2

Period 2

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

Arms

Are arms mutually exclusive?	Yes
Arm title	10Pn <6M Group

Arm description:

This group consisted of subjects up to 6 months of age at first vaccination who received 3 doses of 10Pn-PD-DiT (or 10Pn) vaccine co-administered with InfanrixTM IPV/Hib (DTPa-IPV/Hib) at 3, 4 and 5 months of age and a booster dose of the same vaccines at 12-15 months of age. Vaccines were administrated intramuscularly in the right (10Pn-PD-DiT) or the left (DTPa-IPV/Hib) thigh or deltoid region (deltoid region only for children >12 months of age if muscle size was adequate).

Arm type	Experimental
Investigational medicinal product name	10-valent streptococcus pneumoniae conjugate vaccine
Investigational medicinal product code	
Other name	10Pn-PD-DiT, 10Pn
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 primary doses administered at 3, 4 and 5 months of age followed by a booster dose at 12-15 months of age, all injected intramuscularly in the right thigh or deltoid region (deltoid region only for children >12 months of age if muscle size was adequate).

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

Dosage and administration details:

3 primary doses administered at 3, 4 and 5 months of age followed by a booster dose at 12-15 months of age, all injected intramuscularly in the left right thigh or deltoid region (deltoid region only for children >12 months of age if muscle size was adequate).

Arm title	10Pn 7-11M Group

Arm description:

This group consisted of subjects 7 to 11 months of age at first vaccination who received 2 doses of 10Pn-PD-DiT (10Pn), one first dose at enrolment followed by a second dose one month later, and a booster dose at 12-15 months of age. The 10PN-PD-DiT vaccine was administrated intramuscularly in the right thigh or deltoid region (deltoid region only for children >12 months of age if muscle size was adequate).

Arm type	Experimental
Investigational medicinal product name	10-valent streptococcus pneumoniae conjugate vaccine
Investigational medicinal product code	
Other name	10Pn-PD-DiT, 10Pn
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

2 doses, one first dose at enrolment followed by a second dose one month later, followed by a booster dose at 12-15 months of age., injected intramuscularly in the right thigh or deltoid region (deltoid region only for children >12 months of age if muscle size was adequate).

Number of subjects in period 2[1]	10Pn <6M Group	10Pn 7-11M Group
Started	145	145
Completed	141	145
Not completed	4	0
Consent withdrawn by subject	1	-
Lost to follow-up	3	-

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: One subject from the 10Pn 7-11M Group was not included in the Booster Phase of the study for not having received the booster vaccination dose.

Baseline characteristics

Reporting groups	
Reporting group title	10Pn <6M Group
Reporting group description:	
This group consisted of subjects up to 6 months of age at first vaccination who received 3 doses of 10Pn-PD-DiT (or 10Pn) vaccine co-administered with InfanrixTM IPV/Hib (DTPa-IPV/Hib) at 3, 4 and 5 months of age and a booster dose of the same vaccines at 12-15 months of age. Vaccines were administrated intramuscularly in the right (10Pn-PD-DiT) or the left (DTPa-IPV/Hib) thigh or deltoid region (deltoid region only for children >12 months of age if muscle size was adequate).	
Reporting group title	10Pn 7-11M Group
Reporting group description:	
This group consisted of subjects 7 to 11 months of age at first vaccination who received 2 doses of 10Pn-PD-DiT (10Pn), one first dose at enrolment followed by a second dose one month later, and a booster dose at 12-15 months of age. The 10PN-PD-DiT vaccine was administrated intramuscularly in the right thigh or deltoid region (deltoid region only for children >12 months of age if muscle size was adequate).	
Reporting group title	10Pn 12-23M Group
Reporting group description:	
This group consisted of subjects 12 to 23 months inclusive at first vaccination who received 2 doses of 10Pn-PD-DiT (10Pn), one first dose at enrolment followed by a second dose 2 months later. The 10PN-PD-DiT vaccine was administrated intramuscularly in the right thigh or deltoid region (deltoid region only for children >12 months of age if muscle size was adequate).	
Reporting group title	10Pn >=24M Group
Reporting group description:	
This group consisted of subjects aged between 24 months (inclusive) to 5 years (inclusive) at vaccination who received one dose of 10Pn-PD-DiT (10Pn). The 10PN-PD-DiT vaccine was administrated intramuscularly in the right thigh or deltoid region (deltoid region only for children >12 months of age if muscle size was adequate).	

Reporting group values	10Pn <6M Group	10Pn 7-11M Group	10Pn 12-23M Group
Number of subjects	150	150	150
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: months			
arithmetic mean	10.8	8.3	17.9
standard deviation	± 1.09	± 1.2	± 3.19
Gender categorical Units: Subjects			
Female	66	68	76
Male	84	82	74

Reporting group values	10Pn >=24M Group	Total	
Number of subjects	150	600	
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: months			
arithmetic mean	36.6		
standard deviation	± 11.87	-	
Gender categorical Units: Subjects			
Female	72	282	
Male	78	318	

End points

End points reporting groups

Reporting group title	10Pn <6M Group

Reporting group description:

This group consisted of subjects up to 6 months of age at first vaccination who received 3 doses of 10Pn-PD-DiT (or 10Pn) vaccine co-administered with InfanrixTM IPV/Hib (DTPa-IPV/Hib) at 3, 4 and 5 months of age and a booster dose of the same vaccines at 12-15 months of age. Vaccines were administrated intramuscularly in the right (10Pn-PD-DiT) or the left (DTPa-IPV/Hib) thigh or deltoid region (deltoid region only for children >12 months of age if muscle size was adequate).

Reporting group title	10Pn 7-11M Group

Reporting group description:

This group consisted of subjects 7 to 11 months of age at first vaccination who received 2 doses of 10Pn-PD-DiT (10Pn), one first dose at enrolment followed by a second dose one month later, and a booster dose at 12-15 months of age. The 10PN-PD-DiT vaccine was administrated intramuscularly in the right thigh or deltoid region (deltoid region only for children >12 months of age if muscle size was adequate).

Reporting group title	10Pn 12-23M Group

Reporting group description:

This group consisted of subjects 12 to 23 months inclusive at first vaccination who received 2 doses of 10Pn-PD-DiT (10Pn), one first dose at enrolment followed by a second dose 2 months later. The 10PN-PD-DiT vaccine was administrated intramuscularly in the right thigh or deltoid region (deltoid region only for children >12 months of age if muscle size was adequate).

Reporting group title	10Pn >=24M Group

Reporting group description:

This group consisted of subjects aged between 24 months (inclusive) to 5 years (inclusive) at vaccination who received one dose of 10Pn-PD-DiT (10Pn). The 10PN-PD-DiT vaccine was administrated intramuscularly in the right thigh or deltoid region (deltoid region only for children >12 months of age if muscle size was adequate).

Reporting group title	10Pn <6M Group

Reporting group description:

This group consisted of subjects up to 6 months of age at first vaccination who received 3 doses of 10Pn-PD-DiT (or 10Pn) vaccine co-administered with InfanrixTM IPV/Hib (DTPa-IPV/Hib) at 3, 4 and 5 months of age and a booster dose of the same vaccines at 12-15 months of age. Vaccines were administrated intramuscularly in the right (10Pn-PD-DiT) or the left (DTPa-IPV/Hib) thigh or deltoid region (deltoid region only for children >12 months of age if muscle size was adequate).

Reporting group title	10Pn 7-11M Group

Reporting group description:

This group consisted of subjects 7 to 11 months of age at first vaccination who received 2 doses of 10Pn-PD-DiT (10Pn), one first dose at enrolment followed by a second dose one month later, and a booster dose at 12-15 months of age. The 10PN-PD-DiT vaccine was administrated intramuscularly in the right thigh or deltoid region (deltoid region only for children >12 months of age if muscle size was adequate).

Primary: Number of subjects with anti-pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antibody concentrations >= 0.20 microgram per milliliter (µg/mL).

End point title	Number of subjects with anti-pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antibody concentrations >= 0.20 microgram per milliliter (µg/mL).[1]

End point description:

Anti-pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antibody concentrations were assessed by 22F-inhibition Enzyme-Linked Immuno-Sorbent Assay (ELISA) method. The >=0.20 microgram per milliliter (microg/mL) cut-off corresponded to the seroprotection cut-off as regards anti-pneumococcal serotypes antibody concentrations. Seropositivity status, defined as anti-pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antibody concentrations ≥ 0.05 microg/mL.

End point type	Primary

End point timeframe:

At one month after primary (10Pn <6M & 10Pn 7-11M groups) or after the full (10Pn 12-23M & 10Pn >=24M groups) vaccination course with 10Pn, that is Month (M)3 for 10Pn <6M & 12-23M groups, M2 for 10Pn 711M Group, & M1 for 10Pn >=24M Group,

Notes:

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

End point values	10Pn <6M Group	10Pn 7-11M Group	10Pn 12-23M Group	10Pn >=24M Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	131	135	133	140
Units: Subjects				
Anti-1 (N=131; 135; 133; 140)	128	135	132	135
Anti-4 (N=131; 135; 133; 140)	128	135	133	140
Anti-5(N=131; 135; 133; 138)	130	134	131	135
Anti-6B (N=131; 135; 133; 140)	95	69	108	96
Anti-7F (N=131; 135; 133; 140)	130	135	133	140
Anti-9V (N=131; 135; 133; 140)	128	129	130	132
Anti-14 (N=131; 135; 133; 139)	130	132	132	127
Anti-18C (N=131; 135; 133; 140)	127	135	133	140
Anti-19F (N=130; 135; 133; 140)	122	129	131	140
Anti-23F (N=131; 135; 133; 139)	114	95	122	93

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited & Unsolicited AEs: During the 4 & 31 days post PRI/BST vaccination; SAEs: during PRI and BST Phases. The occurrence of reported AEs (all/related) was not available and is encoded as equal to the number of subjects affected.

Adverse event reporting additional description:

Note that 1) SAEs for PRI Phase for 10Pn <6M & 10Pn 7-11M groups include SAEs reported up to BST dose not included; 2) BST Phase safety follow-up is not applicable to 10Pn 12-23M & 10Pn >=24M groups; to mark this, numbers of subjects for BST events for these groups are marked as equal to 1.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	11.0

Reporting groups

Reporting group title	10Pn <6M Group

Reporting group description:

This group consisted of subjects up to 6 months of age at first vaccination who received 3 doses of 10Pn-PD-DiT (or 10Pn) vaccine co-administered with InfanrixTM IPV/Hib (DTPa-IPV/Hib) at 3, 4 and 5 months of age and a booster dose of the same vaccines at 12-15 months of age. Vaccines were administrated intramuscularly in the right (10Pn-PD-DiT) or the left (DTPa-IPV/Hib) thigh or deltoid region (deltoid region only for children >12 months of age if muscle size was adequate).

Reporting group title	10Pn 7-11M Group

Reporting group description:

This group consisted of subjects 7 to 11 months of age at first vaccination who received 2 doses of 10Pn-PD-DiT (10Pn), one first dose at enrolment followed by a second dose one month later, and a booster dose at 12-15 months of age. The 10PN-PD-DiT vaccine was administrated intramuscularly in the right thigh or deltoid region (deltoid region only for children >12 months of age if muscle size was adequate).

Reporting group title	10Pn 12-23M Group

Reporting group description:

This group consisted of subjects 12 to 23 months inclusive at first vaccination who received 2 doses of 10Pn-PD-DiT (10Pn), one first dose at enrolment followed by a second dose 2 months later. The 10PN-PD-DiT vaccine was administrated intramuscularly in the right thigh or deltoid region (deltoid region only for children >12 months of age if muscle size was adequate).

Reporting group title	10Pn >=24M Group

Reporting group description:

This group consisted of subjects aged between 24 months (inclusive) to 5 years (inclusive) at vaccination who received one dose of 10Pn-PD-DiT (10Pn). The 10PN-PD-DiT vaccine was administrated intramuscularly in the right thigh or deltoid region (deltoid region only for children >12 months of age if muscle size was adequate).

Serious adverse events	10Pn <6M Group	10Pn 7-11M Group	10Pn 12-23M Group
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 150 (11.33%)	5 / 150 (3.33%)	2 / 150 (1.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Gastrointestinal disorders			
Abdominal pain upper - PRI			
alternative assessment type: Non-			

systematic			
subjects affected / exposed	1 / 150 (0.67%)	0 / 150 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Bronchitis chronic - PRI			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 150 (1.33%)	1 / 150 (0.67%)	0 / 150 (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
Psychiatric disorders			
Psychomotor retardation - PRI			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 150 (0.67%)	0 / 150 (0.00%)	0 / 150 (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			
Pneumonia - PRI			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 150 (1.33%)	2 / 150 (1.33%)	2 / 150 (1.33%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute - PRI			
alternative assessment type: Non-systematic			
subjects affected / exposed	4 / 150 (2.67%)	0 / 150 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis - PRI			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 150 (0.67%)	2 / 150 (1.33%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis rotavirus - PRI			
alternative assessment type: Non-			

systematic			
subjects affected / exposed	3 / 150 (2.00%)	0 / 150 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media - PRI			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 150 (0.00%)	2 / 150 (1.33%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Exanthema subitum - PRI			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 150 (0.67%)	0 / 150 (0.00%)	0 / 150 (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
Influenza - PRI			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 150 (0.67%)	0 / 150 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchiolitis - PRI			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 150 (0.67%)	0 / 150 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection - PRI			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 150 (0.67%)	0 / 150 (0.00%)	0 / 150 (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
Bacterial infection - BST			
alternative assessment type: Non-systematic			

subjects affected / exposed[1]	1 / 145 (0.69%)	0 / 145 (0.00%)	0 / 1 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis - BST			
alternative assessment type: Non-systematic			
subjects affected / exposed[2]	0 / 145 (0.00%)	1 / 145 (0.69%)	0 / 1 (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

Serious adverse events	10Pn >=24M Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 150 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Gastrointestinal disorders			
Abdominal pain upper - PRI			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 150 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Bronchitis chronic - PRI			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 150 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Psychomotor retardation - PRI			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 150 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia - PRI			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 150 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis acute - PRI				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 150 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis - PRI				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 150 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis rotavirus - PRI				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 150 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Otitis media - PRI				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 150 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Exanthema subitum - PRI				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 150 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Influenza - PRI				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 150 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Respiratory syncytial virus bronchiolitis - PRI				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 150 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory syncytial virus infection - PRI				
alternative assessment type: Non-systematic				
subjects affected / exposed	0 / 150 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bacterial infection - BST				
alternative assessment type: Non-systematic				
subjects affected / exposed[1]	0 / 1 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis - BST				
alternative assessment type: Non-systematic				
subjects affected / exposed[2]	0 / 1 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Notes:

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

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

Non-serious adverse events	10Pn <6M Group	10Pn 7-11M Group	10Pn 12-23M Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	143 / 150 (95.33%)	116 / 150 (77.33%)	113 / 150 (75.33%)
General disorders and administration site conditions			
Pain - PRI			

subjects affected / exposed[3]	89 / 149 (59.73%)	63 / 148 (42.57%)	113 / 149 (75.84%)
occurrences (all)	89	63	113
Redness - PRI			
subjects affected / exposed[4]	90 / 149 (60.40%)	95 / 148 (64.19%)	79 / 149 (53.02%)
occurrences (all)	90	95	79
Swelling - PRI			
subjects affected / exposed[5]	68 / 149 (45.64%)	66 / 148 (44.59%)	59 / 149 (39.60%)
occurrences (all)	68	66	59
Drowsiness – PRI Phase			
subjects affected / exposed[6]	122 / 149 (81.88%)	92 / 148 (62.16%)	90 / 149 (60.40%)
occurrences (all)	122	92	90
Rectal fever >= 38.5°C – PRI Phase			
subjects affected / exposed[7]	95 / 149 (63.76%)	55 / 148 (37.16%)	47 / 149 (31.54%)
occurrences (all)	95	55	47
Irritability – PRI Phase			
subjects affected / exposed[8]	143 / 149 (95.97%)	112 / 148 (75.68%)	107 / 149 (71.81%)
occurrences (all)	143	112	107
Loss of appetite – PRI Phase			
subjects affected / exposed[9]	70 / 149 (46.98%)	62 / 148 (41.89%)	62 / 149 (41.61%)
occurrences (all)	70	62	62
Pain – BST			
subjects affected / exposed[10]	91 / 144 (63.19%)	64 / 144 (44.44%)	0 / 1 (0.00%)
occurrences (all)	91	64	0
Redness – BST			
subjects affected / exposed[11]	80 / 144 (55.56%)	73 / 144 (50.69%)	0 / 1 (0.00%)
occurrences (all)	80	73	0
Swelling – BST			
subjects affected / exposed[12]	55 / 144 (38.19%)	45 / 144 (31.25%)	0 / 1 (0.00%)
occurrences (all)	55	45	0
Drowsiness – BST			
subjects affected / exposed[13]	73 / 144 (50.69%)	57 / 144 (39.58%)	0 / 1 (0.00%)
occurrences (all)	73	57	0
Rectal fever >= 38.5°C – BST			
subjects affected / exposed[14]	63 / 144 (43.75%)	33 / 144 (22.92%)	0 / 1 (0.00%)
occurrences (all)	63	33	0
Irritability – BST			

subjects affected / exposed[15]	109 / 144 (75.69%)	71 / 144 (49.31%)	0 / 1 (0.00%)
occurrences (all)	109	71	0
Loss of appetite – BST			
subjects affected / exposed[16]	57 / 144 (39.58%)	35 / 144 (24.31%)	0 / 1 (0.00%)
occurrences (all)	57	35	0
Injection site induration - PRI			
alternative assessment type: Non-systematic			
subjects affected / exposed	10 / 150 (6.67%)	10 / 150 (6.67%)	12 / 150 (8.00%)
occurrences (all)	10	10	12
Pyrexia - PRI			
alternative assessment type: Non-systematic			
subjects affected / exposed	11 / 150 (7.33%)	21 / 150 (14.00%)	19 / 150 (12.67%)
occurrences (all)	11	21	19
Pyrexia - BST			
alternative assessment type: Non-systematic			
subjects affected / exposed[17]	8 / 145 (5.52%)	12 / 145 (8.28%)	0 / 1 (0.00%)
occurrences (all)	8	12	0
Eye disorders			
Conjunctivitis - PRI			
alternative assessment type: Non-systematic			
subjects affected / exposed	6 / 150 (4.00%)	12 / 150 (8.00%)	4 / 150 (2.67%)
occurrences (all)	6	12	4
Gastrointestinal disorders			
Diarrhoea - PRI			
alternative assessment type: Non-systematic			
subjects affected / exposed	6 / 150 (4.00%)	14 / 150 (9.33%)	14 / 150 (9.33%)
occurrences (all)	6	14	14
Teething - PRI			
alternative assessment type: Non-systematic			
subjects affected / exposed	9 / 150 (6.00%)	17 / 150 (11.33%)	4 / 150 (2.67%)
occurrences (all)	9	17	4
Respiratory, thoracic and mediastinal disorders			
Cough - PRI			
alternative assessment type: Non-systematic			

subjects affected / exposed	5 / 150 (3.33%)	15 / 150 (10.00%)	20 / 150 (13.33%)
occurrences (all)	5	15	20
Infections and infestations			
Nasopharyngitis - PRI			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 150 (0.00%)	0 / 150 (0.00%)	11 / 150 (7.33%)
occurrences (all)	0	0	11
Otitis media - PRI			
alternative assessment type: Non-systematic			
subjects affected / exposed	6 / 150 (4.00%)	24 / 150 (16.00%)	21 / 150 (14.00%)
occurrences (all)	6	24	21
Rhinitis - PRI			
alternative assessment type: Non-systematic			
subjects affected / exposed	19 / 150 (12.67%)	31 / 150 (20.67%)	18 / 150 (12.00%)
occurrences (all)	19	31	18
Upper respiratory tract infection - PRI			
alternative assessment type: Non-systematic			
subjects affected / exposed	40 / 150 (26.67%)	35 / 150 (23.33%)	21 / 150 (14.00%)
occurrences (all)	40	35	21
Otitis media - BST			
alternative assessment type: Non-systematic			
subjects affected / exposed[18]	13 / 145 (8.97%)	8 / 145 (5.52%)	0 / 1 (0.00%)
occurrences (all)	13	8	0
Ear infection - BST			
alternative assessment type: Non-systematic			
subjects affected / exposed[19]	0 / 145 (0.00%)	9 / 145 (6.21%)	0 / 1 (0.00%)
occurrences (all)	0	9	0
Rhinitis - BST			
alternative assessment type: Non-systematic			
subjects affected / exposed[20]	24 / 145 (16.55%)	8 / 145 (5.52%)	0 / 1 (0.00%)
occurrences (all)	24	8	0
Upper respiratory tract infection - BST			
alternative assessment type: Non-systematic			

subjects affected / exposed[21]	25 / 145 (17.24%)	12 / 145 (8.28%)	0 / 1 (0.00%)
occurrences (all)	25	12	0

Non-serious adverse events	10Pn >=24M Group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	102 / 150 (68.00%)		
General disorders and administration site conditions			
Pain - PRI			
subjects affected / exposed[3]	102 / 148 (68.92%)		
occurrences (all)	102		
Redness - PRI			
subjects affected / exposed[4]	65 / 148 (43.92%)		
occurrences (all)	65		
Swelling - PRI			
subjects affected / exposed[5]	32 / 148 (21.62%)		
occurrences (all)	32		
Drowsiness – PRI Phase			
subjects affected / exposed[6]	55 / 148 (37.16%)		
occurrences (all)	55		
Rectal fever >= 38.5°C – PRI Phase			
subjects affected / exposed[7]	10 / 148 (6.76%)		
occurrences (all)	10		
Irritability – PRI Phase			
subjects affected / exposed[8]	62 / 148 (41.89%)		
occurrences (all)	62		
Loss of appetite – PRI Phase			
subjects affected / exposed[9]	41 / 148 (27.70%)		
occurrences (all)	41		
Pain – BST			
subjects affected / exposed[10]	0 / 1 (0.00%)		
occurrences (all)	0		
Redness – BST			
subjects affected / exposed[11]	0 / 1 (0.00%)		
occurrences (all)	0		
Swelling – BST			

subjects affected / exposed[12]	0 / 1 (0.00%)		
occurrences (all)	0		
Drowsiness – BST			
subjects affected / exposed[13]	0 / 1 (0.00%)		
occurrences (all)	0		
Rectal fever >= 38.5°C – BST			
subjects affected / exposed[14]	0 / 1 (0.00%)		
occurrences (all)	0		
Irritability – BST			
subjects affected / exposed[15]	0 / 1 (0.00%)		
occurrences (all)	0		
Loss of appetite – BST			
subjects affected / exposed[16]	0 / 1 (0.00%)		
occurrences (all)	0		
Injection site induration - PRI			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 150 (0.67%)		
occurrences (all)	1		
Pyrexia - PRI			
alternative assessment type: Non-systematic			
subjects affected / exposed	8 / 150 (5.33%)		
occurrences (all)	8		
Pyrexia - BST			
alternative assessment type: Non-systematic			
subjects affected / exposed[17]	0 / 1 (0.00%)		
occurrences (all)	0		
Eye disorders			
Conjunctivitis - PRI			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 150 (1.33%)		
occurrences (all)	2		
Gastrointestinal disorders			
Diarrhoea - PRI			
alternative assessment type: Non-systematic			

subjects affected / exposed	5 / 150 (3.33%)		
occurrences (all)	5		
Teething - PRI			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 150 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Cough - PRI			
alternative assessment type: Non-systematic			
subjects affected / exposed	5 / 150 (3.33%)		
occurrences (all)	5		
Infections and infestations			
Nasopharyngitis - PRI			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 150 (0.00%)		
occurrences (all)	0		
Otitis media - PRI			
alternative assessment type: Non-systematic			
subjects affected / exposed	10 / 150 (6.67%)		
occurrences (all)	10		
Rhinitis - PRI			
alternative assessment type: Non-systematic			
subjects affected / exposed	4 / 150 (2.67%)		
occurrences (all)	4		
Upper respiratory tract infection - PRI			
alternative assessment type: Non-systematic			
subjects affected / exposed	7 / 150 (4.67%)		
occurrences (all)	7		
Otitis media - BST			
alternative assessment type: Non-systematic			
subjects affected / exposed[18]	0 / 1 (0.00%)		
occurrences (all)	0		
Ear infection - BST			
alternative assessment type: Non-systematic			

subjects affected / exposed[19]	0 / 1 (0.00%)		
occurrences (all)	0		
Rhinitis - BST			
alternative assessment type: Non-systematic			
subjects affected / exposed[20]	0 / 1 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection - BST			
alternative assessment type: Non-systematic			
subjects affected / exposed[21]	0 / 1 (0.00%)		
occurrences (all)	0		

Notes:

[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 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.
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Justification: Assessment for this event for this phase was performed solely on subjects with available results.

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Justification: Assessment for this event for this phase was performed solely on subjects with available results.
[15] - 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 phase was performed solely on subjects with available results.
[16] - 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.
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[17] - 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.
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[18] - 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 phase was performed solely on subjects with available results.
[19] - 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 phase was performed solely on subjects with available results.
[20] - 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 phase was performed solely on subjects with available results.
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Justification: Assessment for this event for this 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
28 June 2006	The protocol was amended to clarify in the study title that the assessment of immunogenicity, safety and reactogenicity would be done in children older than 7 months of age and in children before 6 months of age. Furthermore, because the post-licensure surveillance of Prevenar in the United States had shown a decrease and an increase in invasive pneumococcal disease caused by the cross-reactive pneumococcal serotypes 6A and 19A, respectively, it was of interest to document the immune responses (Enzyme-Linked Immuno-Sorbent Assay [ELISA] and opsonophagocytic activity [OPA]) to these cross-reactive pneumococcal serotypes. Also a higher flexibility of the distribution of replacement vial/syringe for the 10Pn-PD-DiT vaccine at the study centres was allowed as in each group all the children would receive the same vaccine.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported