Clinical trial results:
A phase III, controlled, partially-blind study to assess the reactogenicity, safety and immunogenicity of GSK Biologicals' 10-valent pneumococcal polysaccharide and non-typeable Haemophilus influenzae protein D conjugate vaccine (Synflorix) and 13-valent pneumococcal conjugate vaccine (Prevenar 13™) administered to children as a 2-dose primary vaccination at 2 and 4 months of age with either 10Pn-PD-DiT or Prevenar 13™ or with Prevenar 13™ and 10Pn-PD-DiT, respectively, followed by a Synflorix booster vaccination at 12-15 months of age.

Summary

EudraCT number	2013-003479-36
Trial protocol	Outside EU/EEA
Global end of trial date	07 May 2014

Results information

Result version number	v2
This version publication date	30 July 2016
First version publication date	10 July 2015
Version creation reason	• New data added to full data set Data for primary/secondary endpoints have been added.

Trial information

Trial identification

Sponsor protocol code	115992

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01641133
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Estrada dos Bandeirantes 8464, Rio de Janeiro, Brazil, Jacarepaguá CEP 2278
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	Yes

1901/2006 apply to this trial?	

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	31 May 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 May 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the reactogenicity of the 10Pn-PD-DiT vaccine and 13-valent pneumococcal conjugate vaccine (Prevenar 13™) in terms of the occurrence of adverse events with grade 3 intensity, after primary vaccination at 2 and 4 months of age with either 10Pn-PD-DiT or Prevenar 13™ or Prevenar 13™ and 10Pn-PD-DiT, respectively.

Protection of trial subjects:

All subjects were supervised for 30 min after vaccination/product administration with appropriate medical treatment readily available. 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 31 days after the last vaccination/product administration.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 September 2012
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	Mexico: 457
Worldwide total number of subjects	457
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	457

Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

457 subjects were enrolled in the study. Of these, 5 subjects were not included in the Total Vaccinated Cohort as study vaccine was not administered. In addition, 157 subjects enrolled at one center were excluded from analysis due to GCP deficiencies, and 1 subject from another center due to invalid Informed Consent form.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer

Blinding implementation details:

The study was conducted in a partially-blind manner. For the primary epoch, data were collected in an observer-blind manner and for the booster epoch, data collection was open. By observer-blind, it is meant that during the course of the study, the vaccine recipient and those responsible for the evaluation of any study endpoint were all unaware of which vaccine was administered.

Arms

Are arms mutually exclusive?	Yes
Arm title	SSS Group

Arm description:

Subjects received a 2-dose primary vaccination with 10Pn-PD-DiT vaccine at 2 and 4 months of age and a 10Pn-PD-DiT booster vaccination dose at 12-15 months of age.

Arm type	Experimental
Investigational medicinal product name	Synflorix™
Investigational medicinal product code	
Other name	10Pn-PD-DiT, GSK1024850A
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

2-dose primary vaccination with 10Pn-PD-DiT vaccine at 2 and 4 months of age and a 10Pn-PD-DiT booster vaccination dose at 12-15 months of age. The vaccine was administered intramuscularly into the right or left thigh for subjects at 2 and 4 months of age. For children ≥ 12 months, the vaccine was administered intramuscularly into the right or left thigh or in the deltoid if the muscle size is adequate, using a 25 mm (1 inch).

Arm title	PSS Group

Arm description:

Subjects received primary vaccination with Prev13 vaccine at 2 months of age and 10Pn-PD-DiT at 4 months of age and a 10Pn-PD-DiT booster vaccination dose at 12-15 months of age.

Arm type	Experimental
Investigational medicinal product name	Synflorix™
Investigational medicinal product code	
Other name	10Pn-PD-DiT, GSK1024850A
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

1-dose primary vaccination with 10Pn-PD-DiT vaccine at 4 months of age and a 10Pn-PD-DiT booster vaccination dose at 12-15 months of age. The vaccine was administered intramuscularly into the right or left thigh for subjects at 4 months of age. For children ≥ 12 months, the vaccine was administered

intramuscularly into the right or left thigh or in the deltoid if the muscle size is adequate, using a 25 mm (1 inch).

Investigational medicinal product name	Prevenar 13™
Investigational medicinal product code	
Other name	Prev13
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

1-dose primary vaccination with Prev13 vaccine at 2 months of age. The vaccine was administered intramuscularly into the right or left thigh.

Arm title	PPS Group

Arm description:

Subjects received a 2-dose primary vaccination with Prev13 vaccine at 2 and 4 months of age and a 10Pn-PD-DiT booster vaccination dose at 12-15 months of age.

Arm type	Experimental
Investigational medicinal product name	Synflorix™
Investigational medicinal product code	
Other name	10Pn-PD-DiT, GSK1024850A
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

10Pn-PD-DiT booster vaccination dose at 12-15 months of age. For children ≥ 12 months, the vaccine was administered intramuscularly into the right or left thigh or in the deltoid if the muscle size is adequate, using a 25 mm (1 inch).

Investigational medicinal product name	Prevenar 13™
Investigational medicinal product code	
Other name	Prev13
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

2-dose primary vaccination with Prev13 vaccine at 2 and 4 months of age. The vaccine was administered intramuscularly into the right or left thigh.

Number of subjects in period 1[1]	SSS Group	PSS Group	PPS Group
Started	97	99	98
Completed	87	90	90
Not completed	10	9	8
Consent withdrawn by subject	5	3	3
Adverse event, non-fatal	-	-	1
Migrated/moved from study area	5	3	1
Lost to follow-up	-	2	2
Protocol deviation	-	1	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 457 subjects were enrolled in the study. Of these, 5 subjects were not included in the Total Vaccinated Cohort as study vaccine was not administered. In addition, 157 subjects enrolled at one

center were excluded from analysis due to GCP deficiencies, and 1 subject from another center due to invalid Informed Consent form.

Baseline characteristics

Reporting groups	
Reporting group title	SSS Group
Reporting group description:	
Subjects received a 2-dose primary vaccination with 10Pn-PD-DiT vaccine at 2 and 4 months of age and a 10Pn-PD-DiT booster vaccination dose at 12-15 months of age.	
Reporting group title	PSS Group
Reporting group description:	
Subjects received primary vaccination with Prev13 vaccine at 2 months of age and 10Pn-PD-DiT at 4 months of age and a 10Pn-PD-DiT booster vaccination dose at 12-15 months of age.	
Reporting group title	PPS Group
Reporting group description:	
Subjects received a 2-dose primary vaccination with Prev13 vaccine at 2 and 4 months of age and a 10Pn-PD-DiT booster vaccination dose at 12-15 months of age.	

Reporting group values	SSS Group	PSS Group	PPS Group
Number of subjects	97	99	98
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	7.4	7.4
standard deviation	± 1.3	± 1.5	± 1.6
Gender categorical			
Units: Subjects			
Female	42	52	45
Male	55	47	53

Reporting group values	Total		
Number of subjects	294		
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	139		
Male	155		

End points

End points reporting groups

Reporting group title	SSS Group
Reporting group description:	
Subjects received a 2-dose primary vaccination with 10Pn-PD-DiT vaccine at 2 and 4 months of age and a 10Pn-PD-DiT booster vaccination dose at 12-15 months of age.	
Reporting group title	PSS Group
Reporting group description:	
Subjects received primary vaccination with Prev13 vaccine at 2 months of age and 10Pn-PD-DiT at 4 months of age and a 10Pn-PD-DiT booster vaccination dose at 12-15 months of age.	
Reporting group title	PPS Group
Reporting group description:	
Subjects received a 2-dose primary vaccination with Prev13 vaccine at 2 and 4 months of age and a 10Pn-PD-DiT booster vaccination dose at 12-15 months of age.	

Primary: Number of subjects with grade 3 Adverse Events (AEs) (solicited and unsolicited).

End point title	Number of subjects with grade 3 Adverse Events (AEs) (solicited and unsolicited).[1]
End point description:	
End point type	Primary
End point timeframe:	
Within 31-day (Day 0 - Day 30) after any dose of primary vaccination.	
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	SSS Group	PSS Group	PPS Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90	94	94	
Units: Subjects				
Any AE Dose 1 (N=90,94,94)	18	10	10	
Any AE Dose 2 (N=87,90,90)	12	11	6	
General AEs Dose 1 (N=90,94,94)	5	3	2	
General AEs Dose 2 (N=87,90,90)	8	4	2	
Local AEs Dose 1 (N=90,94,94)	17	8	9	
Local AEs Dose 2 (N=87,90,90)	7	9	4	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any and grade 3 solicited local symptoms.

End point title	Number of subjects reporting any and grade 3 solicited local

	symptoms.

End point description:

Solicited local symptoms assessed include pain, redness and swelling. Grade 3 pain was defined as crying when limb was moved/spontaneously painful. Grade 3 swelling/redness was defined as swelling/redness larger than (>) 30 millimeters (mm). "Any" is defined as incidence of the specified symptom regardless of intensity.

End point type	Secondary

End point timeframe:

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

End point values	SSS Group	PSS Group	PPS Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90	94	94	
Units: Subjects				
Any pain Dose 1 (N=90,94,94)	61	49	55	
Grade 3 pain Dose 1 (N=90,94,94)	14	8	9	
Any redness Dose 1 (N=90,94,94)	9	11	7	
Grade 3 redness Dose 1 (N=90,94,94)	1	0	0	
Any swelling Dose 1 (N=90,94,94)	16	12	10	
Grade 3 swelling Dose 1 (N=90,94,94)	3	0	0	
Any pain Dose 2 (N=87,90,90)	48	49	42	
Grade 3 pain Dose 2 (N=87,90,90)	6	9	4	
Any redness Dose 2 (N=87,90,90)	5	9	12	
Grade 3 redness Dose 2 (N=87,90,90)	1	0	0	
Any swelling Dose 2 (N=87,90,90)	5	9	11	
Grade 3 swelling Dose 2 (N=87,90,90)	0	0	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any and grade 3 solicited local symptoms.

End point title	Number of subjects reporting any and grade 3 solicited local symptoms.

End point description:

Solicited local symptoms assessed include pain, redness and swelling. Grade 3 pain was defined as crying when limb was moved/spontaneously painful. Grade 3 swelling/redness was defined as swelling/redness larger than (>) 30 millimeters (mm). "Any" is defined as incidence of the specified symptom regardless of intensity.

End point type	Secondary

End point timeframe:

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

End point values	SSS Group	PSS Group	PPS Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	86	87	85	
Units: Subjects				
Any pain	44	44	45	
Grade 3 pain	2	6	9	
Any redness	20	10	17	
Grade 3 redness	4	2	3	
Any swelling	12	14	19	
Grade 3 swelling	1	3	4	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any, grade 3 and related solicited general symptoms.

End point title	Number of subjects reporting any, grade 3 and related solicited general symptoms.

End point description:

Solicited general symptoms assessed include drowsiness, fever (defined as axillary temperature ≥ 37.5°C), irritability, and loss of appetite. Grade 3 drowsiness was defined as drowsiness which prevented normal everyday activities. Grade 3 fever was defined as fever (axillary temperature) above (>) 39.5 degree Celsius (°C). Grade 3 irritability was defined as crying that could not be comforted/preventing normal activity. Grade 3 loss of appetite was defined as the subject not eating at all. "Any" is defined as incidence of the specified symptom regardless of intensity or relationship to study

End point type	Secondary

End point timeframe:

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

End point values	SSS Group	PSS Group	PPS Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90	94	94	
Units: Subjects				
Any drowsiness Dose 1 (N=90,94,94)	35	36	45	
Grade 3 drowsiness Dose 1 (N=90,94,94)	1	1	2	
Related drowsiness Dose 1 (N=90,94,94)	35	32	42	
Any irritability Dose 1 (N=90,94,94)	48	46	53	
Grade 3 irritability Dose 1 (N=90,94,94)	5	2	2	
Related irritability Dose 1 (N=90,94,94)	46	41	49	
Any loss of appetite Dose 1 (N=90,94,94)	21	20	19	
Grade 3 loss of appetite Dose 1 (N=90,94,94)	1	0	0	
Related loss of appetite Dose 1 (N=90,94,94)	20	18	16	
Any fever Dose 1 (N=90,94,94)	18	12	11	

Grade 3 fever Dose 1 (N=90,94,94)	0	0	0	
Related fever Dose 1 (N=90,94,94)	17	11	10	
Any drowsiness Dose 2 (N=87,90,90)	27	24	31	
Grade 3 drowsiness Dose 2 (N=87,90,90)	1	1	0	
Related drowsiness Dose 2 (N=87,90,90)	25	23	31	
Any irritability Dose 2 (N=87,90,90)	39	52	41	
Grade 3 irritability Dose 2 (N=87,90,90)	4	1	1	
Related irritability Dose 2 (N=87,90,90)	37	51	39	
Any loss of appetite Dose 2 (N=87,90,90)	12	17	19	
Grade 3 loss of appetite Dose 2 (N=87,90,90)	0	0	0	
Related loss of appetite Dose 2 (N=87,90,90)	12	17	18	
Any fever Dose 2 (N=87,90,90)	15	14	17	
Grade 3 fever Dose 2 (N=87,90,90)	0	0	0	
Related fever Dose 2 (N=87,90,90)	15	14	16	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any, grade 3 and related solicited general symptoms.

End point title	Number of subjects reporting any, grade 3 and related solicited general symptoms.

End point description:

Solicited general symptoms assessed include drowsiness, fever (defined as axillary temperature ≥ 37.5°C), irritability, and loss of appetite. Grade 3 drowsiness was defined as drowsiness which prevented normal everyday activities. Grade 3 fever was defined as fever (axillary temperature) above (>) 39.5 degree Celsius (°C). Grade 3 irritability was defined as crying that could not be comforted/preventing normal activity. Grade 3 loss of appetite was defined as the subject not eating at all. “Any” is defined as incidence of the specified symptom regardless of intensity or relationship to study

End point type	Secondary

End point timeframe:

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

End point values	SSS Group	PSS Group	PPS Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	86	87	84	
Units: Subjects				
Any drowsiness	25	27	26	
Grade 3 drowsiness	1	0	3	
Related drowsiness	25	24	26	
Any irritability	33	39	45	
Grade 3 irritability	1	2	3	
Related irritability	33	36	44	
Any loss of appetite	24	22	17	

Grade 3 loss of appetite	0	1	0	
Related loss of appetite	22	21	17	
Any fever	9	11	11	
Grade 3 fever	0	0	0	
Related fever	9	8	10	

Statistical analyses

No statistical analyses for this end point

Secondary: Number (%) of subjects reporting any and grade 3 symptoms (solicited and unsolicited).

End point title	Number (%) of subjects reporting any and grade 3 symptoms (solicited and unsolicited).

End point description:

End point type	Secondary

End point timeframe:

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

End point values	SSS Group	PSS Group	PPS Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	86	87	85	
Units: Subjects				
Any symptom (N=86,87,85)	66	70	67	
Any grade 3 symptom (N=86,87,85)	10	12	14	
General symptom (N=86,87,84)	57	66	61	
Grade 3 general symptom (N=86,87,84)	4	5	4	
Local symptom (N=86,87,85)	50	47	47	
Grade 3 local symptom (N=86,87,85)	6	9	13	

Statistical analyses

No statistical analyses for this end point

Secondary: Number (%) of subjects with unsolicited adverse events.

End point title	Number (%) of subjects with unsolicited adverse events.

End point description:

An AE is any untoward medical occurrence in a clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. "Any" is defined an incidence of an unsolicited AE regardless of intensity or relationship to study vaccination.

End point type	Secondary

End point timeframe:

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

End point values	SSS Group	PSS Group	PPS Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	97	99	98	
Units: Subjects				
Any AE	55	58	61	

Statistical analyses

No statistical analyses for this end point

Secondary: Number (%) of subjects with unsolicited adverse events.

End point title	Number (%) of subjects with unsolicited adverse events.

End point description:

An AE is any untoward medical occurrence in a clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. "Any" is defined an incidence of an unsolicited AE regardless of intensity or relationship to study vaccination.

End point type	Secondary

End point timeframe:

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

End point values	SSS Group	PSS Group	PPS Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	86	88	87	
Units: Subjects				
Any AE	25	27	28	

Statistical analyses

No statistical analyses for this end point

Secondary: Number (%) of subjects with Serious Adverse Events (SAEs).

End point title	Number (%) of subjects with Serious Adverse Events (SAEs).

End point description:

End point type	Secondary

End point timeframe:

During the whole study period.

End point values	SSS Group	PSS Group	PPS Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	97	99	98	
Units: Subjects				
Any SAE	1	4	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against pneumococcal serotypes

End point title	Antibody concentrations against pneumococcal serotypes

End point description:

Antibodies assessed for this outcome measure were those against the vaccine/cross-reactive pneumococcal serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F (ANTI-1, -3, -4, -5, -6A, -6B, -7F, -9V, -14, -18C, -19A, -19F and -23F). Antibody concentrations were measured by 22F-inhibition enzyme-linked immunosorbent assay (ELISA), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The cut-off of the assay was an antibody concentration higher than or equal to (≥) 0.05 µg/mL.

End point type	Secondary

End point timeframe:

At study Month 3, e. g. one month after primary vaccination, at study Month 10, e.g. prior to booster vaccination and at study Month 11, e.g. one month after booster vaccination.

End point values	SSS Group	PSS Group	PPS Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	86	89	86	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-1 Month 3 (N=86, 89, 85)	2.74 (2.32 to 3.24)	3.12 (2.63 to 3.7)	4 (3.44 to 4.65)	
Anti-1 Month 10 (N=86, 86, 86)	0.34 (0.29 to 0.4)	0.53 (0.44 to 0.64)	0.62 (0.52 to 0.74)	
Anti-1 Month 11 (N=84, 82, 82)	4.61 (3.93 to 5.41)	4.2 (3.6 to 4.9)	5.22 (4.52 to 6.03)	
Anti-3 Month 3 (N=85, 86, 85)	0.06 (0.05 to 0.08)	0.84 (0.73 to 0.97)	2.48 (2.21 to 2.78)	
Anti-3 Month 10 (N=86, 86, 86)	0.09 (0.07 to 0.12)	0.21 (0.18 to 0.25)	0.37 (0.3 to 0.44)	
Anti-3 Month 11 (N=84, 82, 82)	0.1 (0.07 to 0.14)	0.21 (0.18 to 0.25)	0.33 (0.27 to 0.41)	
Anti-4 Month 3 (N=86, 89, 85)	3.54 (3.12 to 4.02)	2.73 (2.22 to 3.34)	2.74 (2.34 to 3.21)	
Anti-4 Month 10 (N=85, 86, 86)	0.57 (0.49 to 0.66)	0.56 (0.46 to 0.68)	0.39 (0.32 to 0.48)	

Anti-4 Month 11 (N=84, 82, 82)	6.76 (5.87 to 7.79)	4.7 (3.94 to 5.6)	8.77 (7.26 to 10.59)	
Anti-5 Month 3 (N=86, 89, 85)	4.55 (3.95 to 5.24)	2.59 (2.1 to 3.18)	4.89 (4.11 to 5.8)	
Anti-5 Month 10 (N=85, 86, 86)	0.96 (0.79 to 1.17)	0.77 (0.64 to 0.92)	1.05 (0.88 to 1.25)	
Anti-5 Month 11 (N=84, 82, 82)	8.31 (7.08 to 9.77)	5.27 (4.33 to 6.41)	6.15 (5.17 to 7.32)	
Anti-6A Month 3 (N=84, 85, 85)	0.22 (0.16 to 0.29)	0.36 (0.3 to 0.45)	3.35 (2.53 to 4.42)	
Anti-6A Month 10 (N=85, 84, 85)	0.25 (0.2 to 0.31)	0.28 (0.22 to 0.36)	0.67 (0.55 to 0.82)	
Anti-6A Month 11 (N=84, 82, 82)	1.3 (0.98 to 1.72)	0.93 (0.69 to 1.24)	1.97 (1.52 to 2.55)	
Anti-6B Month 3 (N=86, 88, 85)	0.96 (0.78 to 1.18)	0.21 (0.17 to 0.27)	0.38 (0.29 to 0.51)	
Anti-6B Month 10 (N=86, 86, 86)	0.48 (0.39 to 0.59)	0.3 (0.23 to 0.37)	0.24 (0.19 to 0.3)	
Anti-6B Month 11 (N=84, 82, 82)	3.53 (2.96 to 4.2)	1.92 (1.53 to 2.42)	3.03 (2.56 to 3.57)	
Anti-7F Month 3 (N=86, 88, 85)	3.36 (2.96 to 3.81)	2.74 (2.35 to 3.19)	4.83 (4.32 to 5.4)	
Anti-7F Month 10 (N=85, 85, 86)	1.16 (0.99 to 1.37)	1 (0.84 to 1.19)	1.24 (1.07 to 1.45)	
Anti-7F Month 11 (N=84, 82, 82)	7.63 (6.69 to 8.71)	5.07 (4.38 to 5.87)	5.83 (5.07 to 6.69)	
Anti-9V Month 3 (N=85, 87, 85)	2.67 (2.28 to 3.13)	1.34 (1.12 to 1.59)	2.96 (2.49 to 3.51)	
Anti-9V Month 10 (N=86, 86, 86)	0.86 (0.7 to 1.04)	0.49 (0.42 to 0.56)	0.53 (0.45 to 0.62)	
Anti-9V Month 11 (N=84, 82, 82)	7.04 (5.99 to 8.26)	2.48 (2.11 to 2.92)	2.84 (2.42 to 3.34)	
Anti-14 Month 3 (N=86, 89, 85)	4.74 (3.87 to 5.81)	3.45 (2.79 to 4.25)	4.99 (3.89 to 6.42)	
Anti-14 Month 10 (N=86, 86, 86)	1.15 (0.89 to 1.49)	1.05 (0.86 to 1.29)	1.78 (1.45 to 2.19)	
Anti-14 Month 11 (N=84, 82, 82)	10.04 (8.44 to 11.95)	8.1 (6.68 to 9.83)	7.62 (6.3 to 9.22)	
Anti-18C Month 3 (N=86, 89, 85)	3.3 (2.54 to 4.28)	3.22 (2.5 to 4.14)	3.24 (2.62 to 4)	
Anti-18C Month 10 (N=86, 86, 85)	0.81 (0.67 to 0.98)	0.65 (0.53 to 0.81)	0.56 (0.47 to 0.66)	
Anti-18C Month 11 (N=84, 82, 82)	25.18 (20.92 to 30.31)	19.39 (15.36 to 24.48)	19.27 (15.57 to 23.85)	
Anti-19A Month 3 (N=86, 89, 85)	0.24 (0.18 to 0.32)	0.72 (0.6 to 0.87)	2.43 (1.91 to 3.1)	
Anti-19A Month 10 (N=86, 86, 86)	0.19 (0.15 to 0.25)	0.36 (0.27 to 0.5)	0.34 (0.25 to 0.46)	
Anti-19A Month 11 (N=84, 82, 82)	1.64 (1.2 to 2.23)	1.67 (1.17 to 2.38)	2.17 (1.64 to 2.86)	
Anti-19F Month 3 (N=86, 89, 85)	4.62 (3.76 to 5.69)	5.67 (4.63 to 6.95)	4.17 (3.69 to 4.72)	
Anti-19F Month 10 (N=86, 86, 86)	1.19 (0.96 to 1.48)	1.39 (1.14 to 1.71)	0.53 (0.43 to 0.65)	
Anti-19F Month 11 (N=84, 82, 82)	14.43 (12.02 to 17.32)	13.57 (11.29 to 16.32)	13.81 (11.63 to 16.4)	
Anti-23F Month 3 (N=86, 88, 85)	1.43 (1.11 to 1.85)	0.53 (0.41 to 0.68)	1.74 (1.28 to 2.37)	
Anti-23F Month 10 (N=86, 86, 86)	0.53 (0.41 to 0.67)	0.24 (0.19 to 0.3)	0.36 (0.29 to 0.45)	
Anti-23F Month 11 (N=84, 82, 82)	4.16 (3.23 to 5.36)	1.76 (1.42 to 2.18)	2.76 (2.29 to 3.34)	

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Anti-PD antibody concentrations were measured by enzyme-linked immunosorbent assay (ELISA), expressed as geometric mean concentrations (GMCs), in ELISA Units per milliliter (EL.U/mL). The cut-off of the assay was an anti-PD antibody concentration higher than or equal to (≥) 100 EL.U/mL.

End point type	Secondary

End point timeframe:

At study Month 3, e. g. one month after primary vaccination and at study Month 11, e.g. one month after booster vaccination.

End point values	SSS Group	PSS Group	PPS Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	45	50	37	
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD Month 3 (N=45, 50, 37)	2025.1 (1601 to 2561.4)	117.2 (90.4 to 152.1)	143.2 (106.8 to 192.1)	
Anti-PD Month 11 (N=45, 42, 37)	3658.5 (2741.1 to 4882.8)	791 (576.2 to 1085.8)	219.7 (156.2 to 309.1)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited local and general symptoms during the 4-day post primary and booster vaccination period; Unsolicited AEs during the 31-day post primary and booster vaccination period; SAEs: during the whole study period.

Adverse event reporting additional description:

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

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	SSS Group

Reporting group description:

Subjects received a 2-dose primary vaccination with 10Pn-PD-DiT vaccine at 2 and 4 months of age and a 10Pn-PD-DiT booster vaccination dose at 12-15 months of age.

Reporting group title	PPS Group

Reporting group description:

Subjects received a 2-dose primary vaccination with Prev13 vaccine at 2 and 4 months of age and a 10Pn-PD-DiT booster vaccination dose at 12-15 months of age.

Reporting group title	PSS Group

Reporting group description:

Subjects received primary vaccination with Prev13 vaccine at 2 months of age and 10Pn-PD-DiT at 4 months of age and a 10Pn-PD-DiT booster vaccination dose at 12-15 months of age.

Serious adverse events	SSS Group	PPS Group	PSS Group
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 97 (3.09%)	1 / 98 (1.02%)	4 / 99 (4.04%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Convulsion			
subjects affected / exposed	0 / 97 (0.00%)	0 / 98 (0.00%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	0 / 97 (0.00%)	1 / 98 (1.02%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastroenteritis			
subjects affected / exposed	2 / 97 (2.06%)	0 / 98 (0.00%)	0 / 99 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 97 (0.00%)	0 / 98 (0.00%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	1 / 97 (1.03%)	0 / 98 (0.00%)	0 / 99 (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
Urinary tract infection			
subjects affected / exposed	0 / 97 (0.00%)	0 / 98 (0.00%)	1 / 99 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	SSS Group	PPS Group	PSS Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	69 / 97 (71.13%)	65 / 98 (66.33%)	68 / 99 (68.69%)
General disorders and administration site conditions			
Pain (primary phase)			
alternative assessment type: Systematic			
subjects affected / exposed[1]	69 / 90 (76.67%)	65 / 94 (69.15%)	63 / 94 (67.02%)
occurrences (all)	69	65	63
Redness (primary phase)			
alternative assessment type: Systematic			
subjects affected / exposed[2]	12 / 90 (13.33%)	15 / 94 (15.96%)	16 / 94 (17.02%)
occurrences (all)	12	15	16
Swelling (primary phase)			
alternative assessment type: Systematic			

subjects affected / exposed[3]	17 / 90 (18.89%)	14 / 94 (14.89%)	19 / 94 (20.21%)
occurrences (all)	17	14	19
Pain (booster phase)			
alternative assessment type: Systematic			
subjects affected / exposed[4]	44 / 86 (51.16%)	45 / 85 (52.94%)	44 / 87 (50.57%)
occurrences (all)	44	45	44
Redness (booster phase)			
alternative assessment type: Systematic			
subjects affected / exposed[5]	20 / 86 (23.26%)	17 / 85 (20.00%)	10 / 87 (11.49%)
occurrences (all)	20	17	10
Swelling (booster phase)			
alternative assessment type: Systematic			
subjects affected / exposed[6]	12 / 86 (13.95%)	19 / 85 (22.35%)	14 / 87 (16.09%)
occurrences (all)	12	19	14
Drowsiness (primary phase)			
alternative assessment type: Systematic			
subjects affected / exposed[7]	47 / 90 (52.22%)	55 / 94 (58.51%)	44 / 94 (46.81%)
occurrences (all)	47	55	44
Irritability (primary phase)			
alternative assessment type: Systematic			
subjects affected / exposed[8]	62 / 90 (68.89%)	62 / 94 (65.96%)	68 / 94 (72.34%)
occurrences (all)	62	62	68
Loss of appetite (primary phase)			
subjects affected / exposed[9]	28 / 90 (31.11%)	29 / 94 (30.85%)	31 / 94 (32.98%)
occurrences (all)	28	29	31
Fever (primary phase)			
subjects affected / exposed[10]	28 / 90 (31.11%)	25 / 94 (26.60%)	21 / 94 (22.34%)
occurrences (all)	28	25	21
Drowsiness (booster phase)			
alternative assessment type: Systematic			
subjects affected / exposed[11]	25 / 86 (29.07%)	26 / 84 (30.95%)	27 / 87 (31.03%)
occurrences (all)	25	26	27
Irritability (booster phase)			
alternative assessment type: Systematic			

subjects affected / exposed[12]	33 / 86 (38.37%)	45 / 84 (53.57%)	39 / 87 (44.83%)
occurrences (all)	33	45	39
Loss of appetite (booster phase)			
alternative assessment type: Systematic			
subjects affected / exposed[13]	24 / 86 (27.91%)	17 / 84 (20.24%)	22 / 87 (25.29%)
occurrences (all)	24	17	22
Fever (booster phase)			
alternative assessment type: Systematic			
subjects affected / exposed[14]	9 / 86 (10.47%)	11 / 84 (13.10%)	11 / 87 (12.64%)
occurrences (all)	9	11	11
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 97 (2.06%)	5 / 98 (5.10%)	3 / 99 (3.03%)
occurrences (all)	2	5	3
Constipation			
subjects affected / exposed	1 / 97 (1.03%)	2 / 98 (2.04%)	5 / 99 (5.05%)
occurrences (all)	1	2	5
Diarrhoea			
subjects affected / exposed[15]	1 / 86 (1.16%)	5 / 87 (5.75%)	1 / 88 (1.14%)
occurrences (all)	1	5	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 97 (2.06%)	5 / 98 (5.10%)	1 / 99 (1.01%)
occurrences (all)	2	5	1
Infections and infestations			
Nasopharyngits (primary phase)			
subjects affected / exposed	34 / 97 (35.05%)	31 / 98 (31.63%)	35 / 99 (35.35%)
occurrences (all)	34	31	35
Bronchiolitis			
subjects affected / exposed	6 / 97 (6.19%)	8 / 98 (8.16%)	8 / 99 (8.08%)
occurrences (all)	6	8	8
Pharyngitis			
subjects affected / exposed	2 / 97 (2.06%)	7 / 98 (7.14%)	3 / 99 (3.03%)
occurrences (all)	2	7	3
Conjunctivitis			

subjects affected / exposed	1 / 97 (1.03%)	5 / 98 (5.10%)	1 / 99 (1.01%)
occurrences (all)	1	5	1
Nasopharyngitis (booster phase)			
subjects affected / exposed[16]	13 / 86 (15.12%)	16 / 87 (18.39%)	13 / 88 (14.77%)
occurrences (all)	13	16	13
Gastroenteritis			
subjects affected / exposed[17]	7 / 86 (8.14%)	3 / 87 (3.45%)	3 / 88 (3.41%)
occurrences (all)	7	3	3

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis of the solicited symptom included only subjects with documented data.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis of the solicited symptom included only subjects with documented data.

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Justification: The analysis of the solicited symptom included only subjects with documented data.

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Justification: The analysis of the solicited symptom included only subjects with documented data.

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Justification: The analysis of the solicited symptom included only subjects with documented data.

[13] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis of the solicited symptom included only subjects with documented data.

[14] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis of the solicited symptom included only subjects with documented data.

[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: The analysis of the solicited symptom included only subjects with documented data.

[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.
Justification: The analysis of the solicited symptom included only subjects with documented data.

[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.
Justification: The analysis of the solicited symptom included only subjects with documented data.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 February 2012	Change in number of participating countries in this study. Initially this study was planned to be conducted in two countries and now it will be conducted in a single country.
13 June 2012	At the European Medicines Agency's (EMA) request, GSK Biologicals has updated its procedure for emergency unblinding during the conduct of a clinical study. According to the revised procedure, the responsibility and the decision to break the treatment code in emergency situations resides solely with the investigator and consequently, the investigator will have full authority to break the treatment code.
24 September 2013	In the past few months, GSK Biologicals has been investigating the quality of some serology assays used in clinical studies, including the Streptococcus pneumoniae opsonophagocytic activity (OPA) assay used in the present trial. This protocol amendment reflects the fact that delays in the availability of the assay results lead to changes in the analysis plan and scope of serological testing as follows: •The sequence of analysis has been modified to perform study analyses in 2 steps: in the first step – final analysis of safety and reactogenicity data from primary epoch excluding analysis of immunogenicity, and in the second step – final analysis of all immunogenicity data from primary and booster epochs and safety/reactogenicity data of booster epoch except for SAEs that will be analyzed throughout the study. •Cancellation of anti-protein D antibody testing at pre-booster time point, while testing at post-primary and post-booster time points will be performed as described previously in the study protocol. This has been considered sufficient to characterize immune response to protein D.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Opsonophagocytic activity results against pneumococcal serotypes were not available at the time of writing this summary. It will be updated when the results become available.

Notes: