



Clinical trial results:

A phase III, randomized, open, controlled study to assess the immunogenicity, safety and reactogenicity of GlaxoSmithKline (GSK) Biologicals' 10-valent pneumococcal conjugate vaccine as a 3-dose primary immunization course at 6, 10 and 14 weeks of age in Sub-Saharan Africa, co-administered with GSK Biologicals' DTPw-HBV/Hib and OPV vaccines.

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

Summary

EudraCT number	2011-004650-25
Trial protocol	Outside EU/EEA
Global end of trial date	10 December 2009

Results information

Result version number	v2
This version publication date	07 April 2016
First version publication date	05 July 2015
Version creation reason	• Correction of full data set Data correction due to a system error in EudraCT – Results: categories issue. A few data (typos) were corrected in some endpoints.

Trial information

Trial identification

Sponsor protocol code	110521
-----------------------	--------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00678301
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, 44 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, 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	13 October 2010
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 December 2009
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 in Sub-Saharan Africa, one month post dose 3.

Protection of trial subjects:

All subjects were supervised closely for at least 30 minutes following vaccination with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccines. Subjects were followed up from the time the subject consented to participate in the study through consent by his/her parents/guardians until she/he was discharged.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 June 2008
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	Nigeria: 127
Country: Number of subjects enrolled	Mali: 238
Worldwide total number of subjects	365
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)	365

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:

At screening, the following steps occurred: check for inclusion/exclusion criteria, contraindications/precautions, medical and vaccination history of the subjects and signing or thumb-printing informed consent forms.

Pre-assignment period milestones

Number of subjects started	365
Number of subjects completed	357

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Subject not vaccinated: 8
----------------------------	---------------------------

Period 1

Period 1 title	Entire Study period (Months 0-3) (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	10Pn-PD-DiT/EPI Group

Arm description:

Subjects in this group received 3 doses of 10Pn-PD-DiT vaccine, GSK Biologicals' 10-valent pneumococcal conjugate 1024850A vaccine (later marketed as Synflorix) according to a 3-dose schedule at 6-10-14 weeks of age co-administered with 3 doses of Expanded Program on Immunization (EPI) vaccines Zilbrix™ Hib (or DTPw-HBV/Hib) and Polio Sabin™ (or OPV) according to the same schedule. The 10Pn-PD-DiT and DTPw-HBV/Hib vaccines were administered by intramuscular injection, in the right and left thigh respectively. The OPV vaccine was administered orally.

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

Dosage and administration details:

The 10Pn-PD-DiT vaccine was administered by intramuscular injection, in the right thigh, according to a 3-dose schedule at 6-10-14 weeks of age.

Investigational medicinal product name	Polio Sabin
Investigational medicinal product code	
Other name	OPV
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

The OPV vaccine was administered orally, according to a 3-dose schedule at 6-10-14 weeks of age.

Investigational medicinal product name	Zilbrix Hib
Investigational medicinal product code	
Other name	DTPw-HBV/Hib

Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The DTPw-HBV/Hib vaccine was administered by intramuscular injection, in the left thigh, according to a 3-dose schedule at 6-10-14 weeks of age.

Arm title	EPI Group
------------------	-----------

Arm description:

Subjects in this group received 3 doses of Expanded Program on Immunization (EPI) vaccines Zilbrix™ Hib (or DTPw-HBV/Hib) and Polio Sabin™ (or OPV) according to a 3-dose schedule at 6-10-14 weeks of age. The DTPw-HBV/Hib vaccine was administered by intramuscular injection, in the left thigh. The OPV vaccine was administered orally.

Arm type	Active comparator
Investigational medicinal product name	Polio Sabin
Investigational medicinal product code	
Other name	OPV
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

The OPV vaccine was administered orally, according to a 3-dose schedule at 6-10-14 weeks of age.

Investigational medicinal product name	Zilbrix Hib
Investigational medicinal product code	
Other name	DTPw-HBV/Hib
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The DTPw-HBV/Hib vaccine was administered by intramuscular injection, in the left thigh, according to a 3-dose schedule at 6-10-14 weeks of age.

Number of subjects in period 1^[1]	10Pn-PD-DiT/EPI Group	EPI Group
Started	239	118
Completed	231	116
Not completed	8	2
Consent withdrawn by subject	4	-
Adverse event, non-fatal	1	-
Lost to follow-up	3	1
Non-compliance with study procedures	-	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: 365 subjects were enrolled but 8 subjects didn't received vaccination.

Baseline characteristics

Reporting groups

Reporting group title	10Pn-PD-DiT/EPI Group
Reporting group description:	
Subjects in this group received 3 doses of 10Pn-PD-DiT vaccine, GSK Biologicals' 10-valent pneumococcal conjugate 1024850A vaccine (later marketed as Synflorix) according to a 3-dose schedule at 6-10-14 weeks of age co-administered with 3 doses of Expanded Program on Immunization (EPI) vaccines Zilbrix™ Hib (or DTPw-HBV/Hib) and Polio Sabin™ (or OPV) according to the same schedule. The 10Pn-PD-DiT and DTPw-HBV/Hib vaccines were administered by intramuscular injection, in the right and left thigh respectively. The OPV vaccine was administered orally.	
Reporting group title	EPI Group
Reporting group description:	
Subjects in this group received 3 doses of Expanded Program on Immunization (EPI) vaccines Zilbrix™ Hib (or DTPw-HBV/Hib) and Polio Sabin™ (or OPV) according to a 3-dose schedule at 6-10-14 weeks of age. The DTPw-HBV/Hib vaccine was administered by intramuscular injection, in the left thigh. The OPV vaccine was administered orally.	

Reporting group values	10Pn-PD-DiT/EPI Group	EPI Group	Total
Number of subjects	239	118	357
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	7.1	7	
standard deviation	± 1.15	± 1.18	-
Gender categorical			
Units: Subjects			
Female	119	62	181
Male	120	56	176

End points

End points reporting groups

Reporting group title	10Pn-PD-DiT/EPI Group
Reporting group description:	
Subjects in this group received 3 doses of 10Pn-PD-DiT vaccine, GSK Biologicals' 10-valent pneumococcal conjugate 1024850A vaccine (later marketed as Synflorix) according to a 3-dose schedule at 6-10-14 weeks of age co-administered with 3 doses of Expanded Program on Immunization (EPI) vaccines Zilbrix™ Hib (or DTPw-HBV/Hib) and Polio Sabin™ (or OPV) according to the same schedule. The 10Pn-PD-DiT and DTPw-HBV/Hib vaccines were administered by intramuscular injection, in the right and left thigh respectively. The OPV vaccine was administered orally.	
Reporting group title	EPI Group
Reporting group description:	
Subjects in this group received 3 doses of Expanded Program on Immunization (EPI) vaccines Zilbrix™ Hib (or DTPw-HBV/Hib) and Polio Sabin™ (or OPV) according to a 3-dose schedule at 6-10-14 weeks of age. The DTPw-HBV/Hib vaccine was administered by intramuscular injection, in the left thigh. The OPV vaccine was administered orally.	

Primary: Concentrations of antibodies against vaccine pneumococcal serotypes

End point title	Concentrations of antibodies against vaccine pneumococcal serotypes ^[1]
End point description:	
Pneumococcal serotypes assessed were vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. Seropositivity cut-off for the assay was an anti-pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antibody (Anti-1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) concentrations $\geq$ 0.05 microgram per milliliter ($\mu\text{g/mL}$).	
End point type	Primary
End point timeframe:	
At Month 3, one month after the administration of the third dose of 10Pn-PD-DiT vaccine	

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-PD-DiT/EPI Group	EPI Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	217	112		
Units: $\mu\text{g/mL}$				
geometric mean (confidence interval 95%)				
Anti-1 [N=217;108]	2.69 (2.42 to 2.99)	0.03 (0.03 to 0.03)		
Anti-4 [N=217;112]	3.44 (3.06 to 3.87)	0.03 (0.03 to 0.03)		
Anti-5 [N=217;109]	4.17 (3.75 to 4.63)	0.03 (0.03 to 0.04)		
Anti-6B [N=217;112]	0.95 (0.76 to 1.2)	0.03 (0.03 to 0.03)		
Anti-7F [N=217;110]	3.33 (2.99 to 3.71)	0.03 (0.03 to 0.04)		
Anti-9V [N=217;112]	2.39 (2.06 to 2.76)	0.04 (0.03 to 0.05)		

Anti-14 [N=217;112]	3.8 (3.24 to 4.46)	0.14 (0.11 to 0.17)		
Anti-18C [N=217;112]	10.01 (8.49 to 11.8)	0.03 (0.03 to 0.04)		
Anti-19F [N=217;111]	7.65 (6.55 to 8.93)	0.08 (0.07 to 0.1)		
Anti-23F [N=217;112]	1.1 (0.91 to 1.33)	0.03 (0.03 to 0.04)		

Statistical analyses

No statistical analyses for this end point

Primary: Antibody concentrations against protein D (anti-PD antibodies)

End point title	Antibody concentrations against protein D (anti-PD
-----------------	--

End point description:

Anti-PD antibody concentrations were tabulated, expressed in enzyme-linked immunorbent assay (ELISA) units per millilitre (EL.U/mL). Seropositivity cut-off for the assay was an anti-PD antibody concentrations ≥ 100 EL.U/mL.

End point type	Primary
----------------	---------

End point timeframe:

At Month 3, one month after the administration of the third dose of 10Pn-PD-DiT vaccine

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	10Pn-PD-DiT/EPI Group	EPI Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	217	112		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD	3791.8 (3448.4 to 4169.3)	85.4 (71.8 to 101.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A and -19A)

End point title	Concentrations of antibodies against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A and -19A)
-----------------	--

End point description:

Seropositivity status was defined as anti-pneumococcal cross-reactive serotypes 6A/19A antibody concentrations (Anti-6A/19A) ≥ 0.05 microgram per milliliter ($\mu\text{g/mL}$).

End point type	Secondary
----------------	-----------

End point timeframe:

At Month 3, one month after the administration of the third dose of 10Pn-PD-DiT vaccine

End point values	10Pn-PD-DiT/EPI Group	EPI Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	217	108		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-6A	0.09 (0.08 to 0.11)	0.04 (0.04 to 0.05)		
Anti-19A	0.15 (0.13 to 0.18)	0.06 (0.05 to 0.07)		

Statistical analyses

No statistical analyses for this end point

Secondary: Titers for opsonophagocytic activity (OPA) against vaccine pneumococcal serotypes

End point title	Titers for opsonophagocytic activity (OPA) against vaccine pneumococcal serotypes
-----------------	---

End point description:

Pneumococcal serotypes assessed were vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. Seropositivity status was defined as an opsonophagocytic activity against vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (OPA-1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) ≥ 8 .

End point type	Secondary
----------------	-----------

End point timeframe:

At Month 3, one month after the administration of the third dose of 10Pn-PD-DiT vaccine

End point values	10Pn-PD-DiT/EPI Group	EPI Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105	56		
Units: Titers				
geometric mean (confidence interval 95%)				
OPA-1 [N=105;56]	83 (61.7 to 111.7)	5 (3.8 to 6.4)		
OPA-4 [N=105;55]	892.5 (759.4 to 1049)	4.6 (3.9 to 5.5)		
OPA-5 [N=105;56]	82.7 (65.4 to 104.4)	4.5 (3.8 to 5.2)		
OPA-6B [N=103;54]	538.6 (346 to 838.3)	5.7 (4.1 to 7.9)		

OPA-7F [N=105;49]	2733 (2188.3 to 3413.3)	31.5 (15.5 to 64)		
OPA-9V [N=105;54]	1023.7 (784.8 to 1335.2)	8.4 (5.8 to 12.4)		
OPA-14 [N=104;53]	1079.2 (776 to 1500.9)	8.9 (5.7 to 14.1)		
OPA-18C [N=105;56]	617.6 (495.3 to 770)	4.4 (3.8 to 5.2)		
OPA-19F [N=105;56]	358.3 (269.9 to 475.5)	4.6 (3.8 to 5.7)		
OPA-23F [N=104;53]	881.8 (615 to 1264.4)	6.6 (4.2 to 10.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Titers for opsonophagocytic activity (OPA) against cross-reactive pneumococcal serotypes

End point title	Titers for opsonophagocytic activity (OPA) against cross-reactive pneumococcal serotypes
-----------------	--

End point description:

Pneumococcal serotypes assessed were cross-reactive pneumococcal serotypes 6A and 19A. Seropositivity status was defined as an opsonophagocytic activity against cross-reactive pneumococcal serotypes 6A and 19A (OPA-6A and 19A) ≥ 8 .

End point type	Secondary
----------------	-----------

End point timeframe:

At Month 3, one month after the administration of the third dose of 10Pn-PD-DiT vaccine

End point values	10Pn-PD-DiT/EPI Group	EPI Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105	56		
Units: Titres				
geometric mean (confidence interval 95%)				
OPA-6A [N=101;56]	14.1 (9.4 to 21.2)	6.1 (4.4 to 8.7)		
OPA-19A [N=105;56]	11 (8.3 to 14.6)	4.3 (4 to 4.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seropositive for antibodies against vaccine pneumococcal serotypes

End point title	Number of subjects seropositive for antibodies against vaccine pneumococcal serotypes
-----------------	---

End point description:

Pneumococcal serotypes assessed were vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. Seropositivity cut-off for the assay was an anti-pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antibody (Anti-1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) concentrations $\geq$ 0.05 microgram per milliliter ($\mu\text{g/mL}$).

End point type	Secondary
----------------	-----------

End point timeframe:

At Month 3, one month after the administration of the third dose of 10Pn-PD-DiT vaccine

End point values	10Pn-PD-DiT/EPI Group	EPI Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	217	108		
Units: Subjects				
Anti-1 [N=217;108]	217	14		
Anti-4 [N=217;112]	217	12		
Anti-5 [N=217;109]	217	18		
Anti-6B [N=217;112]	196	15		
Anti-7F [N=217;110]	217	19		
Anti-9V [N=217;112]	213	31		
Anti-14 [N=217;112]	217	91		
Anti-18C [N=217;112]	216	23		
Anti-19F [N=217;111]	217	73		
Anti-23F [N=217;112]	207	23		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroprotected as regards antibodies against vaccine pneumococcal serotypes

End point title	Number of subjects seroprotected as regards antibodies against vaccine pneumococcal serotypes
-----------------	---

End point description:

Pneumococcal serotypes assessed were vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. Seroprotection cut-off for the assay was an anti-pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antibody (Anti-1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) concentrations $\geq$ 0.2 microgram per milliliter ($\mu\text{g/mL}$).

End point type	Secondary
----------------	-----------

End point timeframe:

At Month 3, one month after the administration of the third dose of 10Pn-PD-DiT vaccine

End point values	10Pn-PD-DiT/EPI Group	EPI Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	217	112		
Units: Subjects				
Anti-1 [N=217;108]	217	2		
Anti-4 [N=217;112]	217	3		
Anti-5 [N=217;109]	217	4		
Anti-6B [N=217;112]	178	2		
Anti-7F [N=217;110]	216	2		
Anti-9V [N=217;112]	211	11		
Anti-14 [N=217;112]	215	40		
Anti-18C [N=217;112]	216	4		
Anti-19F [N=217;111]	214	25		
Anti-23F [N=217;112]	190	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seropositive as regards antibodies against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A and -19A).

End point title	Number of subjects seropositive as regards antibodies against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A and -19A).
-----------------	--

End point description:

Serotypes assessed were cross-reactive pneumococcal serotypes 6A and 19A. Seropositivity status was defined as anti-pneumococcal cross-reactive serotypes 6A/19A antibody concentrations (Anti-6A/19A) ≥ 0.05 microgram per milliliter ($\mu\text{g/mL}$).

End point type	Secondary
----------------	-----------

End point timeframe:

At Month 3, one month after the administration of the third dose of 10Pn-PD-DiT vaccine

End point values	10Pn-PD-DiT/EPI Group	EPI Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	217	108		
Units: Subjects				
Anti-6A	152	36		
Anti-19A	176	49		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroprotected as regards antibodies against cross-

reactive pneumococcal serotypes 6A and 19A (Anti-6A and -19A).

End point title	Number of subjects seroprotected as regards antibodies against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A and -19A).
-----------------	---

End point description:

Serotypes assessed were cross-reactive pneumococcal serotypes 6A and 19A. Seroprotection cut-off for the assay was an anti-6A/19A antibody concentrations ≥ 0.2 microgram per milliliter ($\mu\text{g/mL}$).

End point type	Secondary
----------------	-----------

End point timeframe:

At Month 3, one month after the administration of the third dose of 10Pn-PD-DiT vaccine

End point values	10Pn-PD-DiT/EPI Group	EPI Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	217	108		
Units: Subjects				
Anti-6A	56	8		
Anti-19A	95	15		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seropositive as regards antibodies against protein D (Anti-PD antibodies)

End point title	Number of subjects seropositive as regards antibodies against protein D (Anti-PD antibodies)
-----------------	--

End point description:

Seropositivity cut-off for the assay was an anti-PD antibody concentrations ≥ 100 EL.U/mL.

End point type	Secondary
----------------	-----------

End point timeframe:

At Month 3, one month after the administration of the third dose of 10Pn-PD-DiT vaccine

End point values	10Pn-PD-DiT/EPI Group	EPI Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	217	112		
Units: Subjects				
Anti-PD	217	34		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seropositive as regards opsonophagocytic activity against vaccine pneumococcal serotypes

End point title	Number of subjects seropositive as regards opsonophagocytic activity against vaccine pneumococcal serotypes
-----------------	---

End point description:

Pneumococcal serotypes assessed were vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F. Seropositivity status was defined as an opsonophagocytic activity against vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (OPA-1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) ≥ 8 .

End point type	Secondary
----------------	-----------

End point timeframe:

At Month 3, one month after the administration of the third dose of 10Pn-PD-DiT vaccine

End point values	10Pn-PD-DiT/EPI Group	EPI Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105	56		
Units: Subjects				
OPA-1 [N=105;56]	92	3		
OPA-4 [N=105;55]	105	3		
OPA-5 [N=105;56]	100	2		
OPA-6B [N=103;54]	88	5		
OPA-7F [N=105;49]	105	21		
OPA-9V [N=105;54]	103	13		
OPA-14 [N=104;53]	100	13		
OPA-18C [N=105;56]	103	2		
OPA-19F [N=105;56]	101	2		
OPA-23F [N=104;53]	97	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seropositive as regards opsonophagocytic activity against cross-reactive pneumococcal serotypes

End point title	Number of subjects seropositive as regards opsonophagocytic activity against cross-reactive pneumococcal serotypes
-----------------	--

End point description:

Pneumococcal serotypes assessed were cross-reactive pneumococcal serotypes 6A and 19A. Seropositivity status was defined as an opsonophagocytic activity against cross-reactive pneumococcal serotypes 6A and 19A (OPA-6A and 19A) ≥ 8 .

End point type	Secondary
----------------	-----------

End point timeframe:

At Month 3, one month after the administration of the third dose of 10Pn-PD-DiT vaccine

End point values	10Pn-PD-DiT/EPI Group	EPI Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105	56		
Units: Subjects				
OPA-6A [N=101;56]	31	6		
OPA-19A [N=105;56]	39	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-Bordetella pertussis (anti-BPT) antibody concentrations

End point title	Anti-Bordetella pertussis (anti-BPT) antibody concentrations
End point description:	
Anti-BPT antibody concentrations were measured, and tabulated in enzyme-linked immunosorbent assay (ELISA) unit per millilitre (EL.U/mL). Seropositivity cut-off for the assay was defined as an anti-BPT antibody concentrations ≥ 15 EL.U/mL	
End point type	Secondary
End point timeframe:	
At Month 3, one month after the administration of the third dose of DTPw-HBV/Hib vaccine	

End point values	10Pn-PD-DiT/EPI Group	EPI Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	111		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-BPT	111.9 (102 to 122.7)	124.9 (111.7 to 139.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seropositive as regards anti-Bordetella pertussis (anti-BPT) antibodies

End point title	Number of subjects seropositive as regards anti-Bordetella pertussis (anti-BPT) antibodies
End point description:	
Seropositivity cut-off for the assay was defined as an anti-BPT antibody concentration ≥ 15 enzyme-linked immunosorbent assay (ELISA) unit per millilitre (EL.U/mL).	

End point type	Secondary
End point timeframe:	
At Month 3, one month after the administration of the third dose of DTPw-HBV/Hib vaccine	

End point values	10Pn-PD-DiT/EPI Group	EPI Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	111		
Units: Subjects				
Anti-BPT	110	111		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-diphtheria (Anti-D) and anti-tetanus toxoids (Anti-TT) antibody concentrations

End point title	Anti-diphtheria (Anti-D) and anti-tetanus toxoids (Anti-TT) antibody concentrations
End point description:	
The seroprotection cut-off for the endpoint was an anti-diphtheria toxoid or anti-tetanus toxoid antibody concentrations ≥ 0.1 international unit per milliliter (IU/mL).	
End point type	Secondary
End point timeframe:	
At Month 3, one month after the administration of the third dose of DTPw-HBV/Hib vaccine	

End point values	10Pn-PD-DiT/EPI Group	EPI Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	112		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-D	4.103 (3.527 to 4.773)	3.13 (2.731 to 3.588)		
Anti-T	6.484 (5.511 to 7.628)	4.588 (3.88 to 5.426)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroprotected as regards anti-diphtheria (Anti D) and anti-tetanus toxoids (Anti TT) antibodies

End point title	Number of subjects seroprotected as regards anti-diphtheria (Anti D) and anti-tetanus toxoids (Anti TT) antibodies
End point description: A seroprotected subject as regards anti-D/-TT antibodies was defined as a subject with an Anti-D/-TT antibody concentration ≥ 0.1 international unit per milliliter (IU/mL).	
End point type	Secondary
End point timeframe: At Month 3, one month after the administration of the third dose of DTPw-HBV/Hib vaccine	

End point values	10Pn-PD-DiT/EPI Group	EPI Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	112		
Units: Subjects				
Anti-D	110	112		
Anti-T	110	112		

Statistical analyses

No statistical analyses for this end point

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

End point title	Anti-polyribosyl-ribitol-phosphate (Anti-PRP) antibody concentrations
End point description: Anti-PRP antibody concentrations were measured and tabulated in microgram per millilitre ($\mu\text{g/mL}$). Cut-off for the assay was $\geq 0.15 \mu\text{g/mL}$.	
End point type	Secondary
End point timeframe: At Month 3, one month after the administration of the third dose of DTPw-HBV/Hib vaccine	

End point values	10Pn-PD-DiT/EPI Group	EPI Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	112		
Units: $\mu\text{g/mL}$				
geometric mean (confidence interval 95%)				
Anti-PRP	18.461 (14.256 to 23.907)	10.137 (7.515 to 13.673)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroprotected as regards anti-polyribosyl-ribitol phosphate (anti-PRP) antibodies, for the ≥ 0.15 $\mu\text{g/mL}$ cut-off

End point title	Number of subjects seroprotected as regards anti-polyribosyl-ribitol phosphate (anti-PRP) antibodies, for the ≥ 0.15 $\mu\text{g/mL}$ cut-off
-----------------	--

End point description:

Anti-PRP antibody concentrations were measured and tabulated in microgram per millilitre ($\mu\text{g/mL}$). The seroprotection cut-off applied for this endpoint was ≥ 0.15 $\mu\text{g/mL}$.

End point type	Secondary
----------------	-----------

End point timeframe:

At Month 3, one month after the administration of the third dose of DTPw-HBV/Hib vaccine

End point values	10Pn-PD-DiT/EPI Group	EPI Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	112		
Units: Subjects				
Anti-PRP	110	111		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroprotected as regards anti-polyribosyl-ribitol phosphate (anti-PRP) antibodies, for the ≥ 1 $\mu\text{g/mL}$ cut-off

End point title	Number of subjects seroprotected as regards anti-polyribosyl-ribitol phosphate (anti-PRP) antibodies, for the ≥ 1 $\mu\text{g/mL}$ cut-off
-----------------	---

End point description:

Anti-PRP antibody concentrations were measured and tabulated in microgram per millilitre ($\mu\text{g/mL}$). The seroprotection cut-off applied for this endpoint was ≥ 1 $\mu\text{g/mL}$.

End point type	Secondary
----------------	-----------

End point timeframe:

At Month 3, one month after the administration of the third dose of DTPw-HBV/Hib vaccine

End point values	10Pn-PD-DiT/EPI Group	EPI Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	112		
Units: Subjects				
Anti-PRP	107	102		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

The seroprotection cut-off for the endpoint was an anti-HBs antibody concentration ≥ 10 milli-international units per milliliter (mIU/mL). Please note that a decrease in the specificity of the anti-HBs Enzyme-Linked ImmunoSorbent Assay (ELISA) assay had been observed in some studies for low levels of antibody (10-100 mIU/mL). The results presented are updated results following partial or complete retesting/reanalysis.

End point type	Secondary
----------------	-----------

End point timeframe:

At Month 3, one month after the administration of the third dose of DTPw-HBV/Hib vaccine

End point values	10Pn-PD-DiT/EPI Group	EPI Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	96		
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs	1835.1 (1384 to 2433.2)	1485.5 (1198.7 to 1840.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroprotected as regards anti-Hepatitis B surface antigen (HBs) antibodies.

End point title	Number of subjects seroprotected as regards anti-Hepatitis B surface antigen (HBs) antibodies.
-----------------	--

End point description:

The seroprotection cut-off values considered for this endpoint were an anti-HBs antibody concentration ≥ 10 and 100 milli-international units per milliliter (mIU/mL). This follows from that a decrease in the specificity of the anti-HBs Enzyme-Linked ImmunoSorbent Assay (ELISA) assay had been observed in some studies for low levels of antibody (10-100 mIU/mL). The results presented are updated results following partial or complete retesting/reanalysis.

End point type	Secondary
----------------	-----------

End point timeframe:

At Month 3, one month after the administration of the third dose of DTPw-HBV/Hib vaccine

End point values	10Pn-PD-DiT/EPI Group	EPI Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91	96		
Units: Subjects				
Anti-HBs >= 10 mIU/mL	89	96		
Anti-HBs >= 100 mIU/mL	89	94		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and any Grade 3 solicited local symptoms

End point title	Number of subjects with any and any 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:

Within the 4-day (Days 0 to 3) follow-up periods after each vaccination, across doses and across vaccines

End point values	10Pn-PD-DiT/EPI Group	EPI Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239	118		
Units: Subjects				
Any Pain	234	112		
Grade 3 Pain	8	3		
Any Redness	57	30		
Grade 3 Redness	0	0		
Any Swelling	173	83		
Grade 3 Swelling	22	11		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and any Grade 3 and related solicited

general symptoms

End point title	Number of subjects with any and any Grade 3 and related solicited general symptoms
-----------------	--

End point description:

Solicited general symptoms assessed include drowsiness, fever (defined as rectal temperature $\geq 38.0^{\circ}\text{C}$), irritability, and loss of appetite. "Any" is defined as incidence of the specified symptom regardless of intensity or relationship to study vaccination. Grade 3 drowsiness was defined as drowsiness which prevented normal everyday activities. Grade 3 fever was defined as fever (rectal temperature) above ($>$) 40.0°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.

End point type	Secondary
----------------	-----------

End point timeframe:

Within the 4-day (Days 0 to 3) follow-up periods after each vaccination, across doses and across vaccines

End point values	10Pn-PD-DiT/EPI Group	EPI Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239	118		
Units: Subjects				
Any Drowsiness	24	12		
Grade 3 Drowsiness	0	0		
Any Fever (Rectally)	207	105		
Grade 3 Fever (Rectally)	1	0		
Any Irritability	192	88		
Grade 3 Irritability	6	2		
Any Loss of appetite	37	15		
Grade 3 Loss of appetite	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with fever (temperature measured rectally $> 39.0^{\circ}\text{C}$)

End point title	Number of subjects with fever (temperature measured rectally $> 39.0^{\circ}\text{C}$)
-----------------	---

End point description:

The level of fever (fever being as rectal temperature $\geq 38.0^{\circ}\text{C}$) assessed for this endpoint was $> 39.0^{\circ}\text{C}$.

End point type	Secondary
----------------	-----------

End point timeframe:

Within the 4-day (Days 0 to 3) follow-up periods after each vaccination, across doses and across vaccines

End point values	10Pn-PD-DiT/EPI Group	EPI Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239	118		
Units: Subjects				
Fever >39.0°C	40	13		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point type	Secondary
----------------	-----------

End point timeframe:

Within the 31-day (Days 0-30) follow-up periods post vaccination, across doses and across vaccines

End point values	10Pn-PD-DiT/EPI Group	EPI Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239	118		
Units: Subjects				
Any AEs	176	92		

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:

Throughout the entire study period, from Month 0 to Month 3

End point values	10Pn-PD-DiT/EPI Group	EPI Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239	118		
Units: Subjects				
Any SAEs	5	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms and unsolicited AEs: During the 4-day (Days 0-3) and 31-day (Days 0-30) post vaccination follow-up periods, respectively, across doses and across vaccines. SAEs: throughout the entire study period, from Month 0 to Month 3.

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	12.0
--------------------	------

Reporting groups

Reporting group title	EPI Group
-----------------------	-----------

Reporting group description:

Subjects in this group received 3 doses of Expanded Program on Immunization (EPI) vaccines Zilbrix™ Hib (or DTPw-HBV/Hib) and Polio Sabin™ (or OPV) according to a 3-dose schedule at 6-10-14 weeks of age. The DTPw-HBV/Hib vaccine was administered by intramuscular injection, in the left thigh. The OPV vaccine was administered orally.

Reporting group title	10Pn-PD-DiT/EPI Group
-----------------------	-----------------------

Reporting group description:

Subjects in this group received 3 doses of 10Pn-PD-DiT vaccine, GSK Biologicals' 10-valent pneumococcal conjugate 1024850A vaccine (later marketed as Synflorix) according to a 3-dose schedule at 6-10-14 weeks of age co-administered with 3 doses of Expanded Program on Immunization (EPI) vaccines Zilbrix™ Hib (or DTPw-HBV/Hib) and Polio Sabin™ (or OPV) according to the same schedule. The 10Pn-PD-DiT and DTPw-HBV/Hib vaccines were administered by intramuscular injection, in the right and left thigh respectively. The OPV vaccine was administered orally.

Serious adverse events	EPI Group	10Pn-PD-DiT/EPI Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 118 (0.00%)	5 / 239 (2.09%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Vascular disorders			
Bronchopneumonia			
subjects affected / exposed	0 / 118 (0.00%)	4 / 239 (1.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma			
subjects affected / exposed	0 / 118 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	0 / 118 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Malaria			
subjects affected / exposed	0 / 118 (0.00%)	1 / 239 (0.42%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	EPI Group	10Pn-PD-DiT/EPI Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	112 / 118 (94.92%)	234 / 239 (97.91%)	
General disorders and administration site conditions			
Pain			
alternative assessment type: Systematic			
subjects affected / exposed	112 / 118 (94.92%)	234 / 239 (97.91%)	
occurrences (all)	112	234	
Redness			
alternative assessment type: Systematic			
subjects affected / exposed	30 / 118 (25.42%)	57 / 239 (23.85%)	
occurrences (all)	30	57	
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed	83 / 118 (70.34%)	173 / 239 (72.38%)	
occurrences (all)	83	173	
Drowsiness			
alternative assessment type: Systematic			
subjects affected / exposed	12 / 118 (10.17%)	24 / 239 (10.04%)	
occurrences (all)	12	24	
Fever (rectal temperature $\geq 38.5^{\circ}\text{C}$)			
alternative assessment type:			

Systematic			
subjects affected / exposed	105 / 118 (88.98%)	207 / 239 (86.61%)	
occurrences (all)	105	207	
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed	88 / 118 (74.58%)	192 / 239 (80.33%)	
occurrences (all)	88	192	
Loss of appetite			
alternative assessment type: Systematic			
subjects affected / exposed	15 / 118 (12.71%)	37 / 239 (15.48%)	
occurrences (all)	15	37	
Injection site erosion			
subjects affected / exposed	6 / 118 (5.08%)	1 / 239 (0.42%)	
occurrences (all)	6	1	
Injection site induration			
subjects affected / exposed	20 / 118 (16.95%)	22 / 239 (9.21%)	
occurrences (all)	20	22	
Eye disorders			
Conjunctivitis			
subjects affected / exposed	16 / 118 (13.56%)	35 / 239 (14.64%)	
occurrences (all)	16	35	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	22 / 118 (18.64%)	43 / 239 (17.99%)	
occurrences (all)	22	43	
Gastrointestinal disorder			
subjects affected / exposed	15 / 118 (12.71%)	25 / 239 (10.46%)	
occurrences (all)	15	25	
Stomatitis			
subjects affected / exposed	4 / 118 (3.39%)	13 / 239 (5.44%)	
occurrences (all)	4	13	
Respiratory, thoracic and mediastinal disorders			
Allergic bronchitis			
subjects affected / exposed	46 / 118 (38.98%)	83 / 239 (34.73%)	
occurrences (all)	46	83	
Infections and infestations			

Bronchitis		
subjects affected / exposed	6 / 118 (5.08%)	12 / 239 (5.02%)
occurrences (all)	6	12
Ear infection		
subjects affected / exposed	21 / 118 (17.80%)	42 / 239 (17.57%)
occurrences (all)	21	42
Gastroenteritis		
subjects affected / exposed	32 / 118 (27.12%)	61 / 239 (25.52%)
occurrences (all)	32	61
Pharyngitis		
subjects affected / exposed	5 / 118 (4.24%)	14 / 239 (5.86%)
occurrences (all)	5	14
Respiratory tract infection		
subjects affected / exposed	11 / 118 (9.32%)	17 / 239 (7.11%)
occurrences (all)	11	17
Rhinitis		
subjects affected / exposed	42 / 118 (35.59%)	85 / 239 (35.56%)
occurrences (all)	42	85
Skin infection		
subjects affected / exposed	16 / 118 (13.56%)	16 / 239 (6.69%)
occurrences (all)	16	16
Urinary tract infection		
subjects affected / exposed	8 / 118 (6.78%)	3 / 239 (1.26%)
occurrences (all)	8	3

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 February 2008	Amendment 1 was made in response to comments of the Ethics Committee of Mali and included the following changes: 1) Data and related publications on invasive pneumococcal disease in Mali were included; 2) Update on the presentation and administration of the OPV vaccine (Polio Sabin); 3) Update in the statistical analysis of safety; 4) Clarification on recording in the clinical report form (CRF) of administered vaccines other than the study vaccines; 5) Correction in the reference to the standard operating procedure (SOP) on destruction of used/unused vaccine vials/syringes/containers.
17 March 2009	Amendment 2 was made to include the following changes: 1) Planning of an interim analysis on all cleaned demographic, reactogenicity and immunogenicity data pertaining to Malian subjects enrolled by 31 December 2008; 2) Change in coordinating author and contributing authors.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported