Clinical trial results:
A phase II, randomized, controlled, observer-blind study to evaluate the impact of two formulations of GlaxoSmithKline (GSK) Biologicals' combined 10-valent pneumococcal polysaccharide and non-typeable Haemophilus influenzae protein D conjugate and pneumococcal protein vaccine on nasopharyngeal carriage, safety and immunogenicity when co-administered with routine EPI vaccines in infants following safety assessment in children aged 2-4 years in The Gambia.

Summary

EudraCT number	2012-002727-15
Trial protocol	Outside EU/EEA
Global end of trial date	18 March 2013

Results information

Result version number	v1
This version publication date	01 March 2016
First version publication date	26 July 2015

Trial information

Trial identification

Sponsor protocol code	114174

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01262872
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 February 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 March 2013
Global end of trial reached?	Yes
Global end of trial date	18 March 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

• To assess the safety and reactogenicity of GSK Biologicals' combined 10Pn-PD-DiT and pneumococcal protein vaccine (10Pn-PD-DiT-dPly-PhtD) when administered as a one-dose schedule to children aged 2-4 years, in terms of occurrence of grade 3 related solicited and unsolicited adverse events and related serious adverse events (Cohort 1)
• To assess the impact of 10Pn-PD-DiT-dPly-PhtD on nasopharyngeal carriage of non-vaccine S. pneumoniae serotypes when co-administered with routine EPI vaccines as a 3-dose vaccination course (Cohort 2).

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 consents to participate in the study until she/he is discharged.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 February 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Gambia: 1320
Worldwide total number of subjects	1320
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)	1200
Children (2-11 years)	120
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:

Cohort 1 subjects participated in Step 1 (duration of about 6 months). Cohort 2 subjects participated in Step 2 (duration of about 10 months). Enrolment for Step 2 was conditional upon successful results of a post-vaccination safety evaluation of all children enrolled in Cohort 1 by an Independent Data Monitoring Committee.

Pre-assignment

Screening details:

During the screening the following steps occurred: check for inclusion/exclusion criteria, contraindications/precautions, medical history of the subjects and signing informed consent forms.

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

Blinding implementation details:

Step 1 of the study was conducted in an observer-blind manner. Step 2 was conducted in an observed-blind manner inside each defined vaccination schedule and open between schedules. 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 (e.g., carriage, safety, reactogenicity and immunogenicity) were all unaware of which vaccine was administered.

Arms

Are arms mutually exclusive?	Yes
Arm title	10PP-LD 3+0d Group

Arm description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received 3 doses of the GSK 2189242A (or 10PP) vaccine in its low-dose (LD) formulation and EPI vaccines according to a 3+0 Schedule. That is, subjects received 3 doses of the 10PP vaccine, LD formulation, co-administered with Tritanrix™-HepB/Hib and Polio Sabin™ at 2-3-4 months of age (Day 0, Month 1 and Month 2), followed by one dose of each of the M-Vac™, Stamaril™ and Polio Sabin™ vaccines administered at approximately 9 months of age. The 10PP vaccine was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Arm type	Experimental
Investigational medicinal product name	Pneumococcal vaccine GSK 2189242A (LD formulation 1)
Investigational medicinal product code	
Other name	10PP, LD Formulation
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection (IM) into the right thigh.

Investigational medicinal product name	Tritanrix™-HepB/Hib
Investigational medicinal product code	
Other name	DTPw-HBV/Hib
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection (IM)administered into the left thigh.

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

Dosage and administration details:

The vaccine was administered orally.

Investigational medicinal product name	M-Vac™
Investigational medicinal product code	
Other name	Measles
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered into the left thigh.

Investigational medicinal product name	Stamaril™
Investigational medicinal product code	
Other name	Yellow Fever Vaccine (YFV)
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered into the left thigh.

Arm title	10PP-HD 3+0d Group

Arm description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received 3 doses of the GSK 2189242A (or 10PP) vaccine in its high-dose (HD) formulation and EPI vaccines according to a 3+0 Schedule. That is, subjects received 3 doses of the 10PP vaccine, HD formulation, co-administered with the Tritanrix™-HepB/Hib and Polio Sabin™ at 2-3-4 months of age (Day 0, Month 1 and Month 2), followed by one dose of each of the M-Vac™, Stamaril™ and Polio Sabin™ vaccines administered at approximately 9 months of age. The 10PP vaccine was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Arm type	Experimental
Investigational medicinal product name	Pneumococcal vaccine GSK 2189242A (HD formulation 2)
Investigational medicinal product code	
Other name	10PP, HD Formulation
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection (IM) into the right thigh.

Investigational medicinal product name	Tritanrix™-HepB/Hib
Investigational medicinal product code	
Other name	DTPw-HBV/Hib
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered into the left thigh.

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

Dosage and administration details:

The vaccine was administered orally.

Investigational medicinal product name	M-Vac™
Investigational medicinal product code	
Other name	Measles
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered into the left thigh.

Investigational medicinal product name	Stamaril™
Investigational medicinal product code	
Other name	Yellow Fever Vaccine (YFV)
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered into the left thigh.

Arm title	Synflorix 3+0d Group

Arm description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received 3 doses of Synflorix™ and EPI vaccines according to a 3+0 Schedule. That is, subjects received 3 doses of the Synflorix™, co-administered with Tritanrix™-HepB/Hib and Polio Sabin™ at 2-3-4 months of age (Day 0, Month 1 and Month 2), followed by one dose of each of the M-Vac™, Stamaril™ and Polio Sabin™ vaccines administered at approximately 9 months of age. Synflorix™ was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Arm type	Active comparator
Investigational medicinal product name	Synflorix™
Investigational medicinal product code	
Other name	10Pn-PD-DiT vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection (IM) into the right thigh.

Investigational medicinal product name	Tritanrix™-HepB/Hib
Investigational medicinal product code	
Other name	DTPw-HBV/Hib
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered into the left thigh.

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

Dosage and administration details:

The vaccine was administered orally.

Investigational medicinal product name	M-Vac™
Investigational medicinal product code	
Other name	Measles
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered into the left thigh.

Investigational medicinal product name	Stamaril™
Investigational medicinal product code	
Other name	Yellow Fever Vaccine (YFV)
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered into the left thigh.

Arm title	Prevnar13 3+0d Group

Arm description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received 3 doses of Prevnar 13™ and EPI vaccines according to a 3+0 Schedule. That is, subjects received 3 doses of Prevnar 13™, co-administered with Tritanrix™-HepB/Hib and Polio Sabin™ at 2-3-4 months of age (Day 0, Month 1 and Month 2), followed by one dose of each of the M-Vac™, Stamaril™ and Polio Sabin™ vaccines administered at approximately 9 months of age. Prevnar 13™ was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Arm type	Active comparator
Investigational medicinal product name	Prevnar13™
Investigational medicinal product code	
Other name	Prev13
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection (IM) into the right thigh.

Investigational medicinal product name	Tritanrix™-HepB/Hib
Investigational medicinal product code	
Other name	DTPw-HBV/Hib
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered into the left thigh.

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

Dosage and administration details:

The vaccine was administered orally.

Investigational medicinal product name	M-Vac™
Investigational medicinal product code	
Other name	Measles
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered into the left thigh.

Investigational medicinal product name	Stamaril™
Investigational medicinal product code	
Other name	Yellow Fever Vaccine (YFV)
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered into the left thigh.

Arm title	10PP-HD 2+1d Group

Arm description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received the GSK 2189242A (or 10PP) vaccine, in its high-dose (HD) formulation, and EPI vaccines according to a 2+1 Schedule. That is, subjects received 2 doses of the 10PP vaccine, HD formulation co-administered with Tritanrix™-Hep B/Hib and Polio Sabin™ at 2-4 months of age (at Day 0 and Month 2), followed by a third dose of the same formulation co-administered with M-Vac™, Stamaril™ and Polio Sabin™ at approximately 9 months of age.. The 2nd doses of Tritanrix™-Hep B/Hib and Polio Sabin™ in EPI vaccines were administered without any pneumococcal vaccine at 3 months of age. The 10PP vaccine was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Arm type	Experimental
Investigational medicinal product name	Pneumococcal vaccine GSK 2189242A (HD formulation 2)
Investigational medicinal product code	
Other name	10PP, HD Formulation
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection (IM) into the right thigh.

Investigational medicinal product name	Tritanrix™-HepB/Hib
Investigational medicinal product code	
Other name	DTPw-HBV/Hib
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered into the left thigh.

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

Dosage and administration details:

The vaccine was administered orally.

Investigational medicinal product name	M-Vac™
Investigational medicinal product code	
Other name	Measles
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered into the left thigh.

Investigational medicinal product name	Stamaril™
Investigational medicinal product code	
Other name	Yellow Fever Vaccine (YFV)
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered into the left thigh.

Arm title	Synflorix 2+1d Group

Arm description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received Synflorix™ and EPI vaccines according to a 2+1 Schedule. That is, subjects received 2 doses of the Synflorix™ co-administered with Tritanrix™-Hep B/Hib and Polio Sabin™ at 2-4 months of age (at Day 0 and Month 2), followed by a third dose of Synflorix™ co-administered with M-

Vac™, Stamaril™ and Polio Sabin™ at approximately 9 months of age. The 2nd doses of Tritanrix™-Hep B/Hib and Polio Sabin™ in EPI vaccines were administered without any pneumococcal vaccine at 3 months of age. Synflorix™ was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Arm type	Active comparator
Investigational medicinal product name	Synflorix™
Investigational medicinal product code	
Other name	10Pn-PD-DiT vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection (IM) into the right thigh.

Investigational medicinal product name	Tritanrix™-HepB/Hib
Investigational medicinal product code	
Other name	DTPw-HBV/Hib
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered into the left thigh.

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

Dosage and administration details:

The vaccine was administered orally.

Investigational medicinal product name	M-Vac™
Investigational medicinal product code	
Other name	Measles
Pharmaceutical forms	Powder and suspension for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered into the left thigh.

Investigational medicinal product name	Stamaril™
Investigational medicinal product code	
Other name	Yellow Fever Vaccine (YFV)
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered into the left thigh.

Arm title	10PP-HD 1d Group

Arm description:

This group consisted in children aged 2-4 years at vaccination enrolled as part of the Cohort 1/Step 1 of the study who received a single dose of the GSK 2189242A (or 10PP) vaccine in its high-dose (HD) formulation at Day 0. The 10PP vaccine was administered intramuscularly in the non-dominant deltoid.

Arm type	Experimental
Investigational medicinal product name	Pneumococcal vaccine GSK 2189242A (LD formulation 1)
Investigational medicinal product code	
Other name	10PP, LD Formulation
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection (IM) into the deltoid region of the non-dominant arm.

Arm title	Prevnar13 1d Group

Arm description:

This group consisted in children aged 2-4 years at vaccination enrolled as part of the Cohort 1/Step 1 of the study who received a single dose of Prevnar 13™ at Day 0. Prevnar 13™ was administered intramuscularly in the non-dominant deltoid.

Arm type	Active comparator
Investigational medicinal product name	Prevnar13™
Investigational medicinal product code	
Other name	Prev13
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection (IM) into the deltoid region of the non-dominant arm.

Number of subjects in period 1	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group
Started	200	200	200
Completed	191	190	195
Not completed	9	10	5
Other reason undisclosed	9	10	5

Number of subjects in period 1	Prevnar13 3+0d Group	10PP-HD 2+1d Group	Synflorix 2+1d Group
Started	200	200	200
Completed	191	191	194
Not completed	9	9	6
Other reason undisclosed	9	9	6

Number of subjects in period 1	10PP-HD 1d Group	Prevnar13 1d Group
Started	60	60
Completed	60	60
Not completed	0	0
Other reason undisclosed	-	-

Reporting groups

Reporting group title	10PP-LD 3+0d Group

Reporting group description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received 3 doses of the GSK 2189242A (or 10PP) vaccine in its low-dose (LD) formulation and EPI vaccines according to a 3+0 Schedule. That is, subjects received 3 doses of the 10PP vaccine, LD formulation, co-administered with Tritanrix™-HepB/Hib and Polio Sabin™ at 2-3-4 months of age (Day 0, Month 1 and Month 2), followed by one dose of each of the M-Vac™, Stamaril™ and Polio Sabin™ vaccines administered at approximately 9 months of age. The 10PP vaccine was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Reporting group title	10PP-HD 3+0d Group

Reporting group description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received 3 doses of the GSK 2189242A (or 10PP) vaccine in its high-dose (HD) formulation and EPI vaccines according to a 3+0 Schedule. That is, subjects received 3 doses of the 10PP vaccine, HD formulation, co-administered with the Tritanrix™-HepB/Hib and Polio Sabin™ at 2-3-4 months of age (Day 0, Month 1 and Month 2), followed by one dose of each of the M-Vac™, Stamaril™ and Polio Sabin™ vaccines administered at approximately 9 months of age. The 10PP vaccine was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Reporting group title	Synflorix 3+0d Group

Reporting group description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received 3 doses of Synflorix™ and EPI vaccines according to a 3+0 Schedule. That is, subjects received 3 doses of the Synflorix™, co-administered with Tritanrix™-HepB/Hib and Polio Sabin™ at 2-3-4 months of age (Day 0, Month 1 and Month 2), followed by one dose of each of the M-Vac™, Stamaril™ and Polio Sabin™ vaccines administered at approximately 9 months of age. Synflorix™ was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Reporting group title	Prevnar13 3+0d Group

Reporting group description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received 3 doses of Prevnar 13™ and EPI vaccines according to a 3+0 Schedule. That is, subjects received 3 doses of Prevnar 13™, co-administered with Tritanrix™-HepB/Hib and Polio Sabin™ at 2-3-4 months of age (Day 0, Month 1 and Month 2), followed by one dose of each of the M-Vac™, Stamaril™ and Polio Sabin™ vaccines administered at approximately 9 months of age. Prevnar 13™ was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Reporting group title	10PP-HD 2+1d Group

Reporting group description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received the GSK 2189242A (or 10PP) vaccine, in its high-dose (HD) formulation, and EPI vaccines according to a 2+1 Schedule. That is, subjects received 2 doses of the 10PP vaccine, HD formulation co-administered with Tritanrix™-Hep B/Hib and Polio Sabin™ at 2-4 months of age (at Day 0 and Month 2), followed by a third dose of the same formulation co-administered with M-Vac™, Stamaril™ and Polio Sabin™ at approximately 9 months of age.. The 2nd doses of Tritanrix™-Hep B/Hib and Polio Sabin™ in EPI vaccines were administered without any pneumococcal vaccine at 3 months of age. The 10PP vaccine was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Reporting group title	Synflorix 2+1d Group

Reporting group description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received Synflorix™ and EPI vaccines according to a 2+1 Schedule. That is, subjects received 2 doses of the Synflorix™ co-administered with Tritanrix™-Hep B/Hib and Polio Sabin™ at 2-4 months of age (at Day 0 and Month 2), followed by a third dose of Synflorix™ co-administered with M-

Vac™, Stamaril™ and Polio Sabin™ at approximately 9 months of age. The 2nd doses of Tritanrix™-Hep B/Hib and Polio Sabin™ in EPI vaccines were administered without any pneumococcal vaccine at 3 months of age. Synflorix™ was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Reporting group title	10PP-HD 1d Group

Reporting group description:

This group consisted in children aged 2-4 years at vaccination enrolled as part of the Cohort 1/Step 1 of the study who received a single dose of the GSK 2189242A (or 10PP) vaccine in its high-dose (HD) formulation at Day 0. The 10PP vaccine was administered intramuscularly in the non-dominant deltoid.

Reporting group title	Prevnar13 1d Group

Reporting group description:

This group consisted in children aged 2-4 years at vaccination enrolled as part of the Cohort 1/Step 1 of the study who received a single dose of Prevnar 13™ at Day 0. Prevnar 13™ was administered intramuscularly in the non-dominant deltoid.

Reporting group values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group
Number of subjects	200	200	200
Age categorical Units: Subjects			
Infants and toddlers (28 days-23 months)	200	200	200
Children (2-11 years)	0	0	0
Gender categorical Units: Subjects			
Female	105	98	103
Male	95	102	97

Reporting group values	Prevnar13 3+0d Group	10PP-HD 2+1d Group	Synflorix 2+1d Group
Number of subjects	200	200	200
Age categorical Units: Subjects			
Infants and toddlers (28 days-23 months)	200	200	200
Children (2-11 years)	0	0	0
Gender categorical Units: Subjects			
Female	103	103	97
Male	97	97	103

Reporting group values	10PP-HD 1d Group	Prevnar13 1d Group	Total
Number of subjects	60	60	1320
Age categorical Units: Subjects			
Infants and toddlers (28 days-23 months)	0	0	1200
Children (2-11 years)	60	60	120
Gender categorical Units: Subjects			
Female	41	26	676
Male	19	34	644

End points

End points reporting groups

Reporting group title	10PP-LD 3+0d Group

Reporting group description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received 3 doses of the GSK 2189242A (or 10PP) vaccine in its low-dose (LD) formulation and EPI vaccines according to a 3+0 Schedule. That is, subjects received 3 doses of the 10PP vaccine, LD formulation, co-administered with Tritanrix™-HepB/Hib and Polio Sabin™ at 2-3-4 months of age (Day 0, Month 1 and Month 2), followed by one dose of each of the M-Vac™, Stamaril™ and Polio Sabin™ vaccines administered at approximately 9 months of age. The 10PP vaccine was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Reporting group title	10PP-HD 3+0d Group

Reporting group description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received 3 doses of the GSK 2189242A (or 10PP) vaccine in its high-dose (HD) formulation and EPI vaccines according to a 3+0 Schedule. That is, subjects received 3 doses of the 10PP vaccine, HD formulation, co-administered with the Tritanrix™-HepB/Hib and Polio Sabin™ at 2-3-4 months of age (Day 0, Month 1 and Month 2), followed by one dose of each of the M-Vac™, Stamaril™ and Polio Sabin™ vaccines administered at approximately 9 months of age. The 10PP vaccine was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Reporting group title	Synflorix 3+0d Group

Reporting group description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received 3 doses of Synflorix™ and EPI vaccines according to a 3+0 Schedule. That is, subjects received 3 doses of the Synflorix™, co-administered with Tritanrix™-HepB/Hib and Polio Sabin™ at 2-3-4 months of age (Day 0, Month 1 and Month 2), followed by one dose of each of the M-Vac™, Stamaril™ and Polio Sabin™ vaccines administered at approximately 9 months of age. Synflorix™ was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Reporting group title	Prevnar13 3+0d Group

Reporting group description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received 3 doses of Prevnar 13™ and EPI vaccines according to a 3+0 Schedule. That is, subjects received 3 doses of Prevnar 13™, co-administered with Tritanrix™-HepB/Hib and Polio Sabin™ at 2-3-4 months of age (Day 0, Month 1 and Month 2), followed by one dose of each of the M-Vac™, Stamaril™ and Polio Sabin™ vaccines administered at approximately 9 months of age. Prevnar 13™ was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Reporting group title	10PP-HD 2+1d Group

Reporting group description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received the GSK 2189242A (or 10PP) vaccine, in its high-dose (HD) formulation, and EPI vaccines according to a 2+1 Schedule. That is, subjects received 2 doses of the 10PP vaccine, HD formulation co-administered with Tritanrix™-Hep B/Hib and Polio Sabin™ at 2-4 months of age (at Day 0 and Month 2), followed by a third dose of the same formulation co-administered with M-Vac™, Stamaril™ and Polio Sabin™ at approximately 9 months of age.. The 2nd doses of Tritanrix™-Hep B/Hib and Polio Sabin™ in EPI vaccines were administered without any pneumococcal vaccine at 3 months of age. The 10PP vaccine was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Reporting group title	Synflorix 2+1d Group

Reporting group description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received Synflorix™ and EPI vaccines according to a 2+1 Schedule. That is, subjects received 2 doses of the Synflorix™ co-administered with Tritanrix™-Hep B/Hib and Polio Sabin™ at 2-4 months of age (at Day 0 and Month 2), followed by a third dose of Synflorix™ co-administered with M-

Vac™, Stamaril™ and Polio Sabin™ at approximately 9 months of age. The 2nd doses of Tritanrix™-Hep B/Hib and Polio Sabin™ in EPI vaccines were administered without any pneumococcal vaccine at 3 months of age. Synflorix™ was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Reporting group title	10PP-HD 1d Group

Reporting group description:

This group consisted in children aged 2-4 years at vaccination enrolled as part of the Cohort 1/Step 1 of the study who received a single dose of the GSK 2189242A (or 10PP) vaccine in its high-dose (HD) formulation at Day 0. The 10PP vaccine was administered intramuscularly in the non-dominant deltoid.

Reporting group title	Prevnar13 1d Group

Reporting group description:

This group consisted in children aged 2-4 years at vaccination enrolled as part of the Cohort 1/Step 1 of the study who received a single dose of Prevnar 13™ at Day 0. Prevnar 13™ was administered intramuscularly in the non-dominant deltoid.

Primary: Number of subjects with any and Grade 3 solicited local symptoms and Grade 3 solicited local symptoms with relationship to vaccination – For Step 1/Cohort 1 subjects

End point title	Number of subjects with any and Grade 3 solicited local symptoms and Grade 3 solicited local symptoms with relationship to vaccination – For Step 1/Cohort 1 subjects[1][2]

End point description:

Assessed local symptoms were pain, redness and swelling. Any = Occurrence of the specified solicited local symptom, regardless of intensity. Grade 3 Pain = Crying when limb was moved/spontaneously painful. Grade 3 Redness/Swelling = Redness/swelling at injection site larger than (>) 30 millimeters (mm). All solicited local symptoms were systematically considered by the investigators as causally related to vaccination. Primary results correspond to results for occurrences of Grade 3 symptoms. This outcome concerns subjects enrolled in Cohort 1/Step 1.

End point type	Primary

End point timeframe:

Within the 4-day (Days 0-3) period post vaccination with pneumococcal vaccine (10PP vaccine or Prevnar 13™)

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.
[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 1d Group	Prevnar13 1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	60		
Units: Subjects				
Any Pain	0	0		
Grade 3 Pain	0	0		
Any Redness	0	0		
Grade 3 Redness	0	0		
Any Swelling	1	0		
Grade 3 Swelling	1	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with any and Grade 3 solicited general symptoms with and without relationship to vaccination – For Step 1/Cohort 1 subjects

End point title	Number of subjects with any and Grade 3 solicited general symptoms with and without relationship to vaccination – For Step 1/Cohort 1 subjects[3][4]

End point description:

Assessed solicited general symptoms were Drowsiness, Fever (axillary temperature higher than [≥] 37.5 degrees Celsius [°C]), Irritability/Fussiness and Loss of appetite. Any = Occurrence of the specified solicited general symptom, regardless of intensity and relationship to vaccination. Related = Occurrence of the specified symptom assessed by the investigator as causally related to vaccination. Grade 3 Drowsiness = Drowsiness that prevented normal activity. Grade 3 Fever = Axillary temperature higher than (>) 39.5°C. Grade 3 Irritability/fussiness = Crying that could not be comforted/prevented normal activity. Grade 3 Loss of appetite = Subject did not eat at all. Primary results correspond to results for occurrences of Grade 3 symptoms assessed as related to vaccination. This outcome concerns subjects enrolled in Cohort 1/Step 1.

End point type	Primary

End point timeframe:

Within the 4-day (Days 0-3) period post vaccination with pneumococcal vaccine (10PP vaccine or Prevnar 13™)

Notes:

[3] - 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.
[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 1d Group	Prevnar13 1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	60		
Units: Subjects				
Any Drowsiness	0	0		
Grade 3 Drowsiness	0	0		
Related Drowsiness	0	0		
Grade 3 & Related Drowsiness	0	0		
Any Fever	4	2		
Grade 3 Fever	0	0		
Related Fever	1	1		
Grade 3 & Related Fever	0	0		
Any Irritability/Fussiness	0	0		
Grade 3 Irritability/Fussiness	0	0		
Related Irritability/Fussiness	0	0		
Grade 3 & Related Irritability/Fussiness	0	0		

Any Loss of appetite	1	0		
Grade 3 Loss of appetite	0	0		
Related Loss of appetite	0	0		
Grade 3 & Related Loss of appetite	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with any and Grade 3 unsolicited adverse events (AEs) with and without relationship to vaccination - In Step 1/Cohort 1 subjects

End point title	Number of subjects with any and Grade 3 unsolicited adverse events (AEs) with and without relationship to vaccination - In Step 1/Cohort 1 subjects[5][6]

End point description:

An unsolicited 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. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. For marketed medicinal products, this also includes failure to produce expected benefits (i.e. lack of efficacy), abuse or misuse. Any = Occurrence of AE, regardless of intensity or relationship to vaccination. Grade 3 = Occurrence of AE which prevented normal activities. Related = Occurrence of AE assessed by the investigator as causally related to vaccination. Primary results correspond to results for occurrences of Grade 3 unsolicited AE(s) assessed as related to vaccination. This outcome concerns subjects enrolled in Cohort 1/Step 1.

End point type	Primary

End point timeframe:

Within the 31-day (Days 0-30) period post vaccination with pneumococcal vaccine (10PP vaccine or Prevnar 13™)

Notes:

[5] - 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.
[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 1d Group	Prevnar13 1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	60		
Units: Subjects				
Any unsolicited AE(s)	13	7		
Grade 3 unsolicited AE(s)	0	0		
Related unsolicited AE(s)	0	0		
Grade 3 and related unsolicited AE(s)	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with any serious adverse events (SAEs) and with SAE(s) with relationship to vaccination - In Step 1/Cohort 1 subjects

End point title	Number of subjects with any serious adverse events (SAEs) and with SAE(s) with relationship to vaccination - In Step 1/Cohort 1 subjects[7][8]

End point description:

SAEs assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization, result in disability/incapacity. These should also be considered serious: invasive or malignant cancers, intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that do not result in hospitalisation. Any = Occurrence of an SAE, regardless of relationship to vaccination. Related = Occurrence of an SAE assessed by the investigator as causally related to vaccination. Primary results correspond to results for occurrences of SAE(s) assessed as related to vaccination. This outcome concerns subjects enrolled in Cohort 1/Step 1.

End point type	Primary

End point timeframe:

From Day 0 to Month 1

Notes:

[7] - 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.
[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 1d Group	Prevnar13 1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	60		
Units: Subjects				
Any SAE(s)	0	0		
SAE(s) related to vaccination	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with haematological or biochemical abnormalities with respect to normal laboratory ranges – For Cohort 1/Step 1 subjects

End point title	Number of subjects with haematological or biochemical abnormalities with respect to normal laboratory ranges – For Cohort 1/Step 1 subjects[9]

End point description:

Assessed biochemical and haematological parameters were: Haemoglobin (Hgb), White cell count (WBC), Platelet counts, Alanine aminotransferase (ALT) and Creatinine (CREA). Per parameter, it was assessed whether subjects had laboratory values below normal, normal, or above normal range. Below = value below the laboratory reference range defined for the specified time point and laboratory parameter. Within = value within the laboratory reference range defined for the specified time point and laboratory parameter. Above = value above the laboratory reference range defined for the specified time point and laboratory parameter. Unknown = value unknown for the specified time point and laboratory parameter. This outcome concerns subjects enrolled in Cohort 1/Step 1.

End point type	Secondary

End point timeframe:

At Month 1, or 1 month post vaccination with pneumococcal vaccine (10PP vaccine or Prevnar 13™)

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 1d Group	Prevnar13 1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	60		
Units: Subjects				
ALT – Status: Unknown	0	0		
ALT – Status: Below	0	0		
ALT – Status: Within	60	57		
ALT – Status: Above	0	3		
CREA – Status: Unknown	0	0		
CREA – Status: Below	0	0		
CREA – Status: Within	60	60		
CREA – Status: Above	0	0		
Hgb – Status: Unknown	0	0		
Hgb – Status: Below	2	2		
Hgb – Status: Within	57	56		
Hgb – Status: Above	1	2		
Platelets – Status: Unknown	0	0		
Platelets – Status: Below	0	0		
Platelets – Status: Within	59	60		
Platelets – Status: Above	1	0		
WBC – Status: Unknown	0	0		
WBC – Status: Below	0	0		
WBC – Status: Within	60	60		
WBC – Status: Above	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs) – For Step 1/Cohort 1 subjects

End point title	Number of subjects with serious adverse events (SAEs) – For Step 1/Cohort 1 subjects[10]

End point description:

SAEs assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization, result in disability/incapacity. These should also be considered serious: invasive or malignant cancers, intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that do not result in hospitalisation. Any = Occurrence of an SAE, regardless of relationship to vaccination. This outcome concerns subjects enrolled in Cohort 1/Step 1.

End point type	Secondary

End point timeframe:

From Day 0 to Month 6

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 1d Group	Prevnar13 1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	60		
Units: Subjects				
Any SAE(s)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against pneumococcal pneumolysin toxoid (Ply) and pneumococcal histidine triad protein D (PhtD) proteins – For Cohort 1/Step 1 subjects

End point title	Antibody concentrations against pneumococcal pneumolysin toxoid (Ply) and pneumococcal histidine triad protein D (PhtD) proteins – For Cohort 1/Step 1 subjects[11]

End point description:

Anti-Ply and anti-PhtD antibody concentrations were measured by Multiplex immunoassay and expressed as geometric mean concentrations (GMCs), in Luminex Units per milliliter (LU/mL). Cut-off of the assay were concentrations higher than or equal to (≥) 599 LU/mL for anti-Ply antibodies and ≥ 391 LU/mL for anti-PhtD antibodies. This outcome concerns subjects enrolled in Cohort 1/Step 1. At Month 1, or 1 month post vaccination with pneumococcal vaccine (10PP vaccine or Prevnar 13™)

End point type	Secondary

End point timeframe:

At Month 1, or 1 month post vaccination with pneumococcal vaccine (10PP vaccine or Prevnar 13™)

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 1d Group	Prevnar13 1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	51		
Units: LU/mL				
geometric mean (confidence interval 95%)				
Anti-Ply	22794.9 (17570.1 to 29573.3)	8510.3 (6668.5 to 10860.8)		

Anti-PhtD	31326.3 (26293.9 to 37321.8)	16810 (13516.3 to 20906.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against Protein D (PD) – For Cohort 1/Step 1 subjects

End point title	Antibody concentrations against Protein D (PD) – For Cohort 1/Step 1 subjects[12]

End point description:

Anti-PD antibody concentrations were measured by Multiplex immunoassay, expressed as geometric mean concentrations (GMCs), in Luminex Units per milliliter (LU/mL). The cut-off of the assay was an anti-PD antibody concentration higher than or equal to (≥) 112 LU/mL. This outcome concerns subjects enrolled in Cohort 1/Step 1.

End point type	Secondary

End point timeframe:

At Month 1, or 1 month post vaccination with pneumococcal vaccine (10PP vaccine or Prevnar 13™)

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 1d Group	Prevnar13 1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	51		
Units: LU/mL				
geometric mean (confidence interval 95%)				
Anti-PD	137.5 (108.4 to 174.4)	65.1 (58.2 to 72.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against vaccine serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F – For Cohort 1/Step 1 subjects

End point title	Antibody concentrations against vaccine serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F – For Cohort 1/Step 1 subjects[13]

End point description:

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. This outcome concerns subjects enrolled in Cohort 1/Step 1.

End point type	Secondary

End point timeframe:

At Month 1, or 1 month post vaccination with pneumococcal vaccine (10PP vaccine or Prevnar 13™)

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 1d Group	Prevnar13 1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	51		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-1 antibodies	1.71 (1.33 to 2.22)	3.12 (2.44 to 4.01)		
Anti-4 antibodies	4.8 (3.75 to 6.14)	4.17 (3.33 to 5.21)		
Anti-5 antibodies	1.17 (0.88 to 1.55)	1.47 (1.08 to 1.99)		
Anti-6B antibodies	0.5 (0.34 to 0.73)	1.57 (0.98 to 2.51)		
Anti-7F antibodies	2.44 (1.99 to 2.98)	6.11 (4.44 to 8.41)		
Anti-9V antibodies	0.89 (0.71 to 1.12)	2.41 (1.87 to 3.26)		
Anti-14 antibodies	1.88 (1.39 to 2.53)	3.77 (2.61 to 5.43)		
Anti-18C antibodies	7.58 (5.43 to 10.57)	4.82 (3.46 to 6.71)		
Anti-19F antibodies	7.82 (5.84 to 10.46)	5.95 (4.48 to 7.9)		
Anti-23F antibodies	0.31 (0.21 to 0.46)	1.11 (0.74 to 1.67)		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against vaccine serotypes 3, 6A and 19A – For Cohort 1/Step 1 subjects

End point title	Antibody concentrations against vaccine serotypes 3, 6A and 19A – For Cohort 1/Step 1 subjects[14]

End point description:

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. This outcome concerns subjects enrolled in Cohort 1/Step 1.

End point type	Secondary

End point timeframe:

At Month 1, or 1 month post vaccination with pneumococcal vaccine (10PP vaccine or Prevnar 13™)

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 1d Group	Prevnar13 1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	51		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-3 antibodies	0.25 (0.14 to 0.46)	2.35 (1.77 to 3.12)		
Anti-6A antibodies	0.18 (0.12 to 0.27)	1.36 (0.96 to 1.93)		
Anti-19A antibodies	1.38 (0.91 to 2.1)	5.51 (4.02 to 7.55)		

Statistical analyses

No statistical analyses for this end point

Secondary: Titers for opsonophagocytic activity against vaccine serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F – For Cohort 1/Step 1 subjects

End point title	Titers for opsonophagocytic activity against vaccine serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F – For Cohort 1/Step 1 subjects[15]

End point description:

The cut-off of the assay was a titer for opsonophagocytic activity higher than or equal to (≥) 8. This outcome concerns subjects enrolled in Cohort 1/Step 1.

End point type	Secondary

End point timeframe:

At Month 1, or 1 month post vaccination with pneumococcal vaccine (10PP vaccine or Prevnar 13™)

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 1d Group	Prevnar13 1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	51		
Units: Titers				
geometric mean (confidence interval 95%)				
OPSONO-1 (N=52;50)	17.2 (11.2 to 26.4)	112.8 (71.9 to 177)		

OPSONO-4 (N=52;51)	2818.9 (2009.7 to 3953.8)	4162.3 (3123.9 to 5545.9)		
OPSONO-5 (N=52;49)	9 (6.4 to 12.7)	89.8 (55.8 to 144.5)		
OPSONO-6B (N=50;51)	345.3 (171.4 to 695.5)	5082.5 (3700.2 to 6981.2)		
OPSONO-7F (N=52;51)	6214 (5217.1 to 7401.4)	17781 (14034.2 to 22528)		
OPSONO-9V (N=52;51)	2880.8 (2264.8 to 3664.5)	12687.8 (9188.2 to 17520.2)		
OPSONO-14 (N=51;51)	1116.1 (715.5 to 1741)	5985.9 (4313.1 to 8307.4)		
OPSONO-18C (N=52;49)	3955.4 (3027.7 to 5167.2)	2799.8 (1931.1 to 4059.2)		
OPSONO-19F (N=52;51)	862.9 (529.2 to 1407)	452.8 (276.2 to 742.2)		
OPSONO-23F (N=51;51)	2756.7 (1638 to 4639.5)	12652.4 (8076 to 19822.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Titers for opsonophagocytic activity against vaccine serotypes 3, 6A and 19A – For Cohort 1/Step 1 subjects

End point title	Titers for opsonophagocytic activity against vaccine serotypes 3, 6A and 19A – For Cohort 1/Step 1 subjects[16]

End point description:

The cut-off of the assay was a titer for opsonophagocytic activity higher than or equal to (≥) 8. This outcome concerns subjects enrolled in Cohort 1/Step 1.

End point type	Secondary

End point timeframe:

At Month 1, or 1 month post vaccination with pneumococcal vaccine (10PP vaccine or Prevnar 13™)

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 1d Group	Prevnar13 1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	51		
Units: Titers				
geometric mean (confidence interval 95%)				
OPSONO-3 (N=51;51)	10.1 (6.5 to 15.8)	152.5 (120.4 to 193.2)		

OPSONO-6A (N=47;51)	212.7 (110.4 to 410)	8488.8 (5984.2 to 12041.8)		
OPSONO-19A (N=49;50)	461.7 (277.2 to 769)	970.3 (701 to 1342.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies inhibiting pneumococcal pneumolysin toxoid (Ply) haemolysis activity, or Hem-dPly antibodies – For Cohort 1/Step 1 subjects

End point title	Concentrations of antibodies inhibiting pneumococcal pneumolysin toxoid (Ply) haemolysis activity, or Hem-dPly antibodies – For Cohort 1/Step 1 subjects[17]

End point description:

Concentrations of Hem-dPly antibodies were expressed as geometric mean titers . The cut-off of the assay was an Hem-dPly antibody titer ≥ 140. This outcome concerns subjects enrolled in Cohort 1/Step 1.

End point type	Secondary

End point timeframe:

At Month 1, or 1 month post vaccination with pneumococcal vaccine (10PP vaccine or Prevnar 13™)

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 1d Group	Prevnar13 1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	51		
Units: Titers				
geometric mean (confidence interval 95%)				
Hem-dPly antibodies	682.3 (562.8 to 827.3)	534 (439.4 to 648.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and Grade 3 solicited local symptoms – For Cohort2/Step 2 subjects receiving the 3+0 Schedule.

End point title	Number of subjects with any and Grade 3 solicited local symptoms – For Cohort2/Step 2 subjects receiving the 3+0 Schedule.[18]

End point description:

Assessed local symptoms were pain, redness and swelling. Any = Occurrence of the specified solicited local symptom, regardless of intensity. Grade 3 Pain = Crying when limb was moved/spontaneously

painful. Grade 3 Redness/Swelling = Redness/swelling at injection site larger than (>) 30 millimeters (mm). This outcome concerns Cohort2/Step 2 subjects receiving the 3+0 Schedule.

End point type	Secondary

End point timeframe:

Within the 4-day (Days 0-3) periods post vaccination with 3 doses of pneumococcal vaccine (10PP vaccine, Synflorix™ or Prevnar 13™), across doses

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group	Prevnar13 3+0d Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	200	200	200	200
Units: Subjects				
Any pain	108	121	123	115
Grade 3 pain	0	1	0	0
Any redness	8	7	9	5
Grade 3 redness	0	1	1	0
Any swelling	30	45	40	37
Grade 3 swelling	7	10	17	7

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and Grade 3 solicited local symptoms – For Cohort2/Step 2 subjects receiving the 2+1 Schedule.

End point title	Number of subjects with any and Grade 3 solicited local symptoms – For Cohort2/Step 2 subjects receiving the 2+1 Schedule.[19]

End point description:

Assessed local symptoms were pain, redness and swelling. Any = Occurrence of the specified solicited local symptom, regardless of intensity. Grade 3 Pain = Crying when limb was moved/spontaneously painful. Grade 3 Redness/Swelling = Redness/swelling at injection site larger than (>) 30 millimeters (mm). This outcome concerns Cohort2/Step 2 subjects receiving the 2+1 Schedule.

End point type	Secondary

End point timeframe:

Within the 4-day (Days 0-3) periods post vaccination with the 2 first doses of pneumococcal vaccine (10PP vaccine or Synflorix™), across doses

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 2+1d Group	Synflorix 2+1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	200	200		
Units: Subjects				
Any pain	97	102		
Grade 3 pain	1	1		
Any redness	3	5		
Grade 3 redness	0	0		
Any swelling	35	31		
Grade 3 swelling	9	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and Grade 3 solicited local symptoms – For Cohort2/Step 2 subjects receiving the 2+1 Schedule.

End point title	Number of subjects with any and Grade 3 solicited local symptoms – For Cohort2/Step 2 subjects receiving the 2+1 Schedule.[20]

End point description:

Assessed local symptoms were pain, redness and swelling. Any = Occurrence of the specified solicited local symptom, regardless of intensity. Grade 3 Pain = Crying when limb was moved/spontaneously painful. Grade 3 Redness/Swelling = Redness/swelling at injection site larger than (>) 30 millimeters (mm). This outcome concerns Cohort2/Step 2 subjects receiving the 2+1 Schedule.

End point type	Secondary

End point timeframe:

Within the 4-day (Days 0-3) period post vaccination with Dose 3 of pneumococcal vaccine (10PP vaccine or Synflorix™)

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 2+1d Group	Synflorix 2+1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	191	195		
Units: Subjects				
Any pain	21	26		
Grade 3 pain	0	0		
Any redness	0	0		
Grade 3 redness	0	0		
Any swelling	4	8		
Grade 3 swelling	1	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and Grade 3 solicited general symptoms and with solicited general symptoms with relationship to vaccination – For Step 2/Cohort 2 subjects receiving the 3+0 Schedule

End point title	Number of subjects with any and Grade 3 solicited general symptoms and with solicited general symptoms with relationship to vaccination – For Step 2/Cohort 2 subjects receiving the 3+0 Schedule[21]

End point description:

Assessed solicited general symptoms were Drowsiness, Fever (axillary temperature higher than [≥] 37.5 degrees Celsius [°C]), Irritability/Fussiness and Loss of appetite. Any = Occurrence of the specified solicited general symptom, regardless of intensity. Related = Occurrence of the specified symptom assessed by the investigators as causally related to vaccination. Grade 3 Drowsiness = Drowsiness that prevented normal activity. Grade 3 Fever = Axillary temperature higher than (>) 39.5°C. Grade 3 Irritability/fussiness = Crying that could not be comforted/prevented normal activity. Grade 3 Loss of appetite = Subject did not eat at all. This outcome concerns Step 2/Cohort 2 subjects receiving the 3+0 Schedule.

End point type	Secondary

End point timeframe:

Within the 4-day (Days 0-3) periods post vaccination with 3 doses of pneumococcal vaccine (10PP vaccine, Synflorix™ or Prevnar 13™), across doses

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group	Prevnar13 3+0d Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	200	200	200	200
Units: Subjects				
Any Drowsiness	43	46	38	44
Grade 3 Drowsiness	0	0	0	0
Related Drowsiness	43	45	38	43
Any Irritability/fussiness	139	133	141	136
Grade 3 Irritability/fussiness	6	4	4	7
Related Irritability/fussiness	138	132	138	136
Any Loss of appetite	32	30	27	34
Grade 3 Loss of appetite	0	0	1	0
Related Loss of appetite	32	29	26	34
Any Fever	104	100	105	106
Grade 3 Fever	0	0	0	0
Related Fever	102	100	104	104

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and Grade 3 solicited general symptoms and with solicited general symptoms with relationship to vaccination – For Step 2/Cohort 2 subjects receiving the 2+1 Schedule

End point title	Number of subjects with any and Grade 3 solicited general symptoms and with solicited general symptoms with relationship to vaccination – For Step 2/Cohort 2 subjects receiving the 2+1 Schedule[22]

End point description:

Assessed solicited general symptoms were Drowsiness, Fever (axillary temperature higher than [≥] 37.5 degrees Celsius [°C]), Irritability/Fussiness and Loss of appetite. Any = Occurrence of the specified solicited general symptom, regardless of intensity. Related = Occurrence of the specified symptom assessed by the investigators as causally related to vaccination. Grade 3 Drowsiness = Drowsiness that prevented normal activity. Grade 3 Fever = Axillary temperature higher than (>) 39.5°C. Grade 3 Irritability/fussiness = Crying that could not be comforted/prevented normal activity. Grade 3 Loss of appetite = Subject did not eat at all. This outcome concerns Step 2/Cohort 2 subjects receiving the 2+1 Schedule.

End point type	Secondary

End point timeframe:

Within the 4-day (Days 0-3) periods post vaccination with the 2 first doses of pneumococcal vaccine (10PP vaccine or Synflorix™), across doses

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 2+1d Group	Synflorix 2+1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	200	200		
Units: Subjects				
Any Drowsiness	47	44		
Grade 3 Drowsiness	0	0		
Related Drowsiness	46	43		
Any Fever	92	84		
Grade 3 Fever	0	0		
Related Fever	89	84		
Any Irritability/fussiness	131	128		
Grade 3 Irritability/fussiness	1	2		
Related Irritability/fussiness	128	126		
Any Loss of appetite	24	25		
Grade 3 Loss of appetite	0	0		
Related Loss of appetite	24	24		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and Grade 3 solicited general symptoms and with solicited general symptoms with relationship to vaccination – For Step 2/Cohort 2 subjects receiving the 2+1 Schedule

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

	relationship to vaccination – For Step 2/Cohort 2 subjects receiving the 2+1 Schedule[23]

End point description:

Assessed solicited general symptoms were Drowsiness, Fever (axillary temperature higher than [≥] 37.5 degrees Celsius [°C]), Irritability/Fussiness and Loss of appetite. Any = Occurrence of the specified solicited general symptom, regardless of intensity. Related = Occurrence of the specified symptom assessed by the investigators as causally related to vaccination. Grade 3 Drowsiness = Drowsiness that prevented normal activity. Grade 3 Fever = Axillary temperature higher than (>) 39.5°C. Grade 3 Irritability/fussiness = Crying that could not be comforted/prevented normal activity. Grade 3 Loss of appetite = Subject did not eat at all. This outcome concerns Step 2/Cohort 2 subjects receiving the 2+1 Schedule.

End point type	Secondary

End point timeframe:

Within the 4-day (Days 0-3) period post vaccination with Dose 3 of pneumococcal vaccine (10PP vaccine or Synflorix™)

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 2+1d Group	Synflorix 2+1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	191	195		
Units: Subjects				
Any Drowsiness	12	4		
Grade 3 Drowsiness	0	0		
Related Drowsiness	12	4		
Any Fever	32	27		
Grade 3 Fever	0	1		
Related Fever	30	25		
Any Irritability/fussiness	27	19		
Grade 3 Irritability/fussiness	0	0		
Related Irritability/fussiness	27	19		
Any Loss of appetite	3	5		
Grade 3 Loss of appetite	0	0		
Related Loss of appetite	3	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any unsolicited adverse events (AEs) – For Step 2/Cohort 2 subjects receiving the 3+0 Schedule

End point title	Number of subjects with any unsolicited adverse events (AEs) – For Step 2/Cohort 2 subjects receiving the 3+0 Schedule[24]

End point description:

An unsolicited 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. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. For marketed medicinal products, this also includes failure to produce expected

benefits (i.e. lack of efficacy), abuse or misuse. Any = Occurrence of an unsolicited AE, regardless of intensity or relationship to vaccination. This outcome concerns Step 2/Cohort 2 subjects receiving the 3+0 Schedule.

End point type	Secondary

End point timeframe:

Within the 31-day (Days 0-30) periods post vaccination with 3 doses of pneumococcal vaccine (10PP vaccine, Synflorix™ or Prevnar 13™), across doses

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-LD 3+0d Group	10PP-HD 3+0d Group	Synflorix 3+0d Group	Prevnar13 3+0d Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	200	200	200	200
Units: Subjects				
Any AE(s)	113	114	123	114

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any unsolicited adverse events (AEs) – For Step 2/Cohort 2 subjects receiving the 2+1 Schedule

End point title	Number of subjects with any unsolicited adverse events (AEs) – For Step 2/Cohort 2 subjects receiving the 2+1 Schedule[25]

End point description:

An unsolicited 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. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. For marketed medicinal products, this also includes failure to produce expected benefits (i.e. lack of efficacy), abuse or misuse. Any = Occurrence of an unsolicited AE, regardless of intensity or relationship to vaccination. This outcome concerns Step 2/Cohort 2 subjects receiving the 2+1 Schedule.

End point type	Secondary

End point timeframe:

Within the 31-day (Days 0-30) periods post vaccination with the 2 first doses of pneumococcal vaccine (10PP vaccine or Synflorix™), across doses

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Cohort 1 subjects participated in Step 1 . Cohort 2 subjects participated in Step 2. Please, refer to the title of the endpoint: Statistics are presented only for the groups belonging to the concerned Cohort/Step and the vaccination schedule.

End point values	10PP-HD 2+1d Group	Synflorix 2+1d Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	200	200		
Units: Subjects				
Any AE(s)	84	95		

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms during the 4-day post-vaccination period in Cohort 1 and 2. Unsolicited AEs during 31-day post-vaccination period and SAEs from Month 0 to Month 1 and to Month 6 in Cohort 1.

Adverse event reporting additional description:

Data for unsolicited AEs and SAEs for Cohort 2 are not presented (n affected are marked as 0). Detailed data for these events are still blinded as the study is still ongoing.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	10PP-HD 1d Group

Reporting group description:

Group This group consisted in children aged 2-4 years at vaccination enrolled as part of the Cohort 1/Step 1 of the study who received a single dose of the GSK 2189242A (or 10PP) vaccine in its high-dose (HD) formulation at Day 0. The 10PP vaccine was administered intramuscularly in the non-dominant deltoid.

Reporting group title	Prevnar 13 1d Group

Reporting group description:

This group consisted in children aged 2-4 years at vaccination enrolled as part of the Cohort 1/Step 1 of the study who received a single dose of Prevnar 13™ at Day 0. Prevnar 13™ was administered intramuscularly in the non-dominant deltoid.

Reporting group title	10PP-LD 3+0d Group

Reporting group description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received 3 doses of the GSK 2189242A (or 10PP) vaccine in its low-dose (LD) formulation and EPI vaccines according to a 3+0 Schedule. That is, subjects received 3 doses of the 10PP vaccine, LD formulation, co-administered with Tritanrix™-HepB/Hib and Polio Sabin™ at 2-3-4 months of age (Day 0, Month 1 and Month 2), followed by one dose of each of the M-Vac™, Stamaril™ and Polio Sabin™ vaccines administered at approximately 9 months of age. The 10PP vaccine was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Reporting group title	10PP-HD 3+0d Group

Reporting group description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received 3 doses of the GSK 2189242A (or 10PP) vaccine in its high-dose (HD) formulation and EPI vaccines according to a 3+0 Schedule. That is, subjects received 3 doses of the 10PP vaccine, HD formulation, co-administered with the Tritanrix™-HepB/Hib and Polio Sabin™ at 2-3-4 months of age (Day 0, Month 1 and Month 2), followed by one dose of each of the M-Vac™, Stamaril™ and Polio Sabin™ vaccines administered at approximately 9 months of age. The 10PP vaccine was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Reporting group title	Synflorix 3+0d Group

Reporting group description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received 3 doses of Synflorix™ and EPI vaccines according to a 3+0 Schedule. That is, subjects received 3 doses of the Synflorix™, co-administered with Tritanrix™-HepB/Hib and Polio Sabin™ at 2-3-4 months of age (Day 0, Month 1 and Month 2), followed by one dose of each of the M-Vac™, Stamaril™ and Polio Sabin™ vaccines administered at approximately 9 months of age. Synflorix™ was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Reporting group title	Prevnar 13 3+0d Group

Reporting group description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received 3 doses of Prevnar 13™ and EPI vaccines according to a 3+0 Schedule. That

is, subjects received 3 doses of Prevnar 13™, co-administered with Tritanrix™-HepB/Hib and Polio Sabin™ at 2-3-4 months of age (Day 0, Month 1 and Month 2), followed by one dose of each of the M-Vac™, Stamaril™ and Polio Sabin™ vaccines administered at approximately 9 months of age. Prevnar 13™ was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Reporting group title	10PP-HD 2+1d Group

Reporting group description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received the GSK 2189242A (or 10PP) vaccine, in its high-dose (HD) formulation, and EPI vaccines according to a 2+1 Schedule. That is, subjects received 2 doses of the 10PP vaccine, HD formulation co-administered with Tritanrix™-Hep B/Hib and Polio Sabin™ at 2-4 months of age (at Day 0 and Month 2), followed by a third dose of the same formulation co-administered with M-Vac™, Stamaril™ and Polio Sabin™ at approximately 9 months of age.. The 2nd doses of Tritanrix™-Hep B/Hib and Polio Sabin™ in EPI vaccines were administered without any pneumococcal vaccine at 3 months of age. The 10PP vaccine was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Reporting group title	Synflorix 2+1d Group

Reporting group description:

This group consisted in infants aged 8-10 weeks at first vaccination enrolled as part the Cohort 2/Step 2 of the study who received Synflorix™ and EPI vaccines according to a 2+1 Schedule. That is, subjects received 2 doses of the Synflorix™ co-administered with Tritanrix™-Hep B/Hib and Polio Sabin™ at 2-4 months of age (at Day 0 and Month 2), followed by a third dose of Synflorix™ co-administered with M-Vac™, Stamaril™ and Polio Sabin™ at approximately 9 months of age. The 2nd doses of Tritanrix™-Hep B/Hib and Polio Sabin™ in EPI vaccines were administered without any pneumococcal vaccine at 3 months of age. Synflorix™ was administered intramuscularly into the right thigh; Tritanrix™-HepB/Hib, M-Vac™ and Stamaril™ were administered intramuscularly into the left thigh; Polio Sabin™ was administered orally.

Serious adverse events	10PP-HD 1d Group	Prevnar 13 1d Group	10PP-LD 3+0d Group
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 60 (0.00%)	0 / 60 (0.00%)	0 / 200 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	10PP-HD 3+0d Group	Synflorix 3+0d Group	Prevnar 13 3+0d Group
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 200 (0.00%)	0 / 200 (0.00%)	0 / 200 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	10PP-HD 2+1d Group	Synflorix 2+1d Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 200 (0.00%)	0 / 200 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	10PP-HD 1d Group	Prevnar 13 1d Group	10PP-LD 3+0d Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 60 (8.33%)	2 / 60 (3.33%)	139 / 200 (69.50%)
General disorders and administration site conditions			
Fever (axillary temperature ≥ 37.5° C) (1 dose Group)			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 60 (6.67%)	2 / 60 (3.33%)	0 / 200 (0.00%)
occurrences (all)	4	2	0
Pain (3+0 dose Group)			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 60 (0.00%)	0 / 60 (0.00%)	108 / 200 (54.00%)
occurrences (all)	0	0	108
Swelling (3+0 dose Group)			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 60 (0.00%)	0 / 60 (0.00%)	30 / 200 (15.00%)
occurrences (all)	0	0	30
Pain (2+1 dose Group)			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 60 (0.00%)	0 / 60 (0.00%)	0 / 200 (0.00%)
occurrences (all)	0	0	0
Swelling (2+1 dose Group)			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 60 (0.00%)	0 / 60 (0.00%)	0 / 200 (0.00%)
occurrences (all)	0	0	0
Pain (after dose 3)			
alternative assessment type: Systematic			
subjects affected / exposed[1]	0 / 60 (0.00%)	0 / 60 (0.00%)	0 / 200 (0.00%)
occurrences (all)	0	0	0

Drowsiness (3+0 dose Group)			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 60 (0.00%)	0 / 60 (0.00%)	43 / 200 (21.50%)
occurrences (all)	0	0	43
Irritability/fussiness (3+0 dose Group)			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 60 (0.00%)	0 / 60 (0.00%)	139 / 200 (69.50%)
occurrences (all)	0	0	139
Loss of appetite (3+0 dose Group)			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 60 (0.00%)	0 / 60 (0.00%)	32 / 200 (16.00%)
occurrences (all)	0	0	32
Fever (axillary temperature ≥37.5° C) (3+0 dose Group)			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 60 (0.00%)	0 / 60 (0.00%)	104 / 200 (52.00%)
occurrences (all)	0	0	104
Drowsiness (2+1 dose Group)			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 60 (0.00%)	0 / 60 (0.00%)	0 / 200 (0.00%)
occurrences (all)	0	0	0
Irritability/fussiness (2+1 dose Group)			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 60 (0.00%)	0 / 60 (0.00%)	0 / 200 (0.00%)
occurrences (all)	0	0	0
Loss of appetite (2+1 dose Group)			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 60 (0.00%)	0 / 60 (0.00%)	0 / 200 (0.00%)
occurrences (all)	0	0	0
Fever (axillary temperature ≥37.5° C) (2+1 dose Group)			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 60 (0.00%)	0 / 60 (0.00%)	0 / 200 (0.00%)
occurrences (all)	0	0	0
Drowsiness (after dose 3)			

alternative assessment type: Systematic			
subjects affected / exposed[2]	0 / 60 (0.00%)	0 / 60 (0.00%)	0 / 200 (0.00%)
occurrences (all)	0	0	0
Irritability/fussiness (after dose 3)			
alternative assessment type: Systematic			
subjects affected / exposed[3]	0 / 60 (0.00%)	0 / 60 (0.00%)	0 / 200 (0.00%)
occurrences (all)	0	0	0
Fever (axillary temperature ≥ 37.5° C) (after dose 3)			
alternative assessment type: Systematic			
subjects affected / exposed[4]	0 / 60 (0.00%)	0 / 60 (0.00%)	0 / 200 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Respiratory tract infection			
subjects affected / exposed	5 / 60 (8.33%)	1 / 60 (1.67%)	0 / 200 (0.00%)
occurrences (all)	5	1	0

Non-serious adverse events	10PP-HD 3+0d Group	Synflorix 3+0d Group	Prevnar 13 3+0d Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	133 / 200 (66.50%)	141 / 200 (70.50%)	136 / 200 (68.00%)
General disorders and administration site conditions			
Fever (axillary temperature ≥ 37.5° C) (1 dose Group)			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 200 (0.00%)	0 / 200 (0.00%)	0 / 200 (0.00%)
occurrences (all)	0	0	0
Pain (3+0 dose Group)			
alternative assessment type: Systematic			
subjects affected / exposed	121 / 200 (60.50%)	123 / 200 (61.50%)	115 / 200 (57.50%)
occurrences (all)	121	123	115
Swelling (3+0 dose Group)			
alternative assessment type: Systematic			
subjects affected / exposed	45 / 200 (22.50%)	40 / 200 (20.00%)	37 / 200 (18.50%)
occurrences (all)	45	40	37
Pain (2+1 dose Group)			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 200 (0.00%)	0 / 200 (0.00%)	0 / 200 (0.00%)
occurrences (all)	0	0	0
Swelling (2+1 dose Group)			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 200 (0.00%)	0 / 200 (0.00%)	0 / 200 (0.00%)
occurrences (all)	0	0	0
Pain (after dose 3)			
alternative assessment type: Systematic			
subjects affected / exposed[1]	0 / 200 (0.00%)	0 / 200 (0.00%)	0 / 200 (0.00%)
occurrences (all)	0	0	0
Drowsiness (3+0 dose Group)			
alternative assessment type: Systematic			
subjects affected / exposed	46 / 200 (23.00%)	38 / 200 (19.00%)	44 / 200 (22.00%)
occurrences (all)	46	38	44
Irritability/fussiness (3+0 dose Group)			
alternative assessment type: Systematic			
subjects affected / exposed	133 / 200 (66.50%)	141 / 200 (70.50%)	136 / 200 (68.00%)
occurrences (all)	133	141	136
Loss of appetite (3+0 dose Group)			
alternative assessment type: Systematic			
subjects affected / exposed	30 / 200 (15.00%)	27 / 200 (13.50%)	34 / 200 (17.00%)
occurrences (all)	30	27	34
Fever (axillary temperature ≥37.5° C) (3+0 dose Group)			
alternative assessment type: Systematic			
subjects affected / exposed	100 / 200 (50.00%)	105 / 200 (52.50%)	106 / 200 (53.00%)
occurrences (all)	100	105	106
Drowsiness (2+1 dose Group)			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 200 (0.00%)	0 / 200 (0.00%)	0 / 200 (0.00%)
occurrences (all)	0	0	0
Irritability/fussiness (2+1 dose Group)			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 200 (0.00%)	0 / 200 (0.00%)	0 / 200 (0.00%)
occurrences (all)	0	0	0
Loss of appetite (2+1 dose Group)			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 200 (0.00%)	0 / 200 (0.00%)	0 / 200 (0.00%)
occurrences (all)	0	0	0
Fever (axillary temperature ≥37.5° C) (2+1 dose Group)			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 200 (0.00%)	0 / 200 (0.00%)	0 / 200 (0.00%)
occurrences (all)	0	0	0
Drowsiness (after dose 3)			
alternative assessment type: Systematic			
subjects affected / exposed[2]	0 / 200 (0.00%)	0 / 200 (0.00%)	0 / 200 (0.00%)
occurrences (all)	0	0	0
Irritability/fussiness (after dose 3)			
alternative assessment type: Systematic			
subjects affected / exposed[3]	0 / 200 (0.00%)	0 / 200 (0.00%)	0 / 200 (0.00%)
occurrences (all)	0	0	0
Fever (axillary temperature ≥ 37.5° C) (after dose 3)			
alternative assessment type: Systematic			
subjects affected / exposed[4]	0 / 200 (0.00%)	0 / 200 (0.00%)	0 / 200 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Respiratory tract infection			
subjects affected / exposed	0 / 200 (0.00%)	0 / 200 (0.00%)	0 / 200 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	10PP-HD 2+1d Group	Synflorix 2+1d Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	131 / 200 (65.50%)	128 / 200 (64.00%)	
General disorders and administration site conditions			
Fever (axillary temperature ≥ 37.5° C) (1 dose Group)			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 200 (0.00%)	0 / 200 (0.00%)	
occurrences (all)	0	0	
Pain (3+0 dose Group)			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 200 (0.00%)	0 / 200 (0.00%)	
occurrences (all)	0	0	
Swelling (3+0 dose Group)			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 200 (0.00%)	0 / 200 (0.00%)	
occurrences (all)	0	0	
Pain (2+1 dose Group)			
alternative assessment type: Systematic			
subjects affected / exposed	97 / 200 (48.50%)	102 / 200 (51.00%)	
occurrences (all)	97	102	
Swelling (2+1 dose Group)			
alternative assessment type: Systematic			
subjects affected / exposed	35 / 200 (17.50%)	31 / 200 (15.50%)	
occurrences (all)	35	31	
Pain (after dose 3)			
alternative assessment type: Systematic			
subjects affected / exposed[1]	21 / 191 (10.99%)	26 / 195 (13.33%)	
occurrences (all)	21	26	
Drowsiness (3+0 dose Group)			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 200 (0.00%)	0 / 200 (0.00%)	
occurrences (all)	0	0	
Irritability/fussiness (3+0 dose Group)			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 200 (0.00%)	0 / 200 (0.00%)	
occurrences (all)	0	0	
Loss of appetite (3+0 dose Group)			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 200 (0.00%)	0 / 200 (0.00%)	
occurrences (all)	0	0	

Fever (axillary temperature ≥37.5° C) (3+0 dose Group) alternative assessment type: Systematic			
subjects affected / exposed	0 / 200 (0.00%)	0 / 200 (0.00%)	
occurrences (all)	0	0	
Drowsiness (2+1 dose Group) alternative assessment type: Systematic			
subjects affected / exposed	47 / 200 (23.50%)	44 / 200 (22.00%)	
occurrences (all)	47	44	
Irritability/fussiness (2+1 dose Group) alternative assessment type: Systematic			
subjects affected / exposed	131 / 200 (65.50%)	128 / 200 (64.00%)	
occurrences (all)	131	128	
Loss of appetite (2+1 dose Group) alternative assessment type: Systematic			
subjects affected / exposed	24 / 200 (12.00%)	25 / 200 (12.50%)	
occurrences (all)	24	25	
Fever (axillary temperature ≥37.5° C) (2+1 dose Group) alternative assessment type: Systematic			
subjects affected / exposed	92 / 200 (46.00%)	84 / 200 (42.00%)	
occurrences (all)	92	84	
Drowsiness (after dose 3) alternative assessment type: Systematic			
subjects affected / exposed[2]	12 / 191 (6.28%)	4 / 195 (2.05%)	
occurrences (all)	12	4	
Irritability/fussiness (after dose 3) alternative assessment type: Systematic			
subjects affected / exposed[3]	27 / 191 (14.14%)	19 / 195 (9.74%)	
occurrences (all)	27	19	
Fever (axillary temperature ≥ 37.5° C) (after dose 3) alternative assessment type: Systematic			
subjects affected / exposed[4]	32 / 191 (16.75%)	27 / 195 (13.85%)	
occurrences (all)	32	27	
Infections and infestations			

Respiratory tract infection subjects affected / exposed occurrences (all)	0 / 200 (0.00%) 0	0 / 200 (0.00%) 0	

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.

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

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: 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
04 October 2010	• Following comments from Scientific Committee in the Gambia the inclusion/exclusion criteria were modified as follows: The criterion of gestational age has been removed from the inclusion criteria as the exact duration of pregnancy is difficult to retrieve in this population Reference to HIV infection has been removed from the exclusion criteria • In addition follow-up period of solicited adverse events has been shortened from 7 days (Day 0 - Day 6) to 4 days (Day 0 - Day 3) following vaccination in order to adjust to the scheduled field workers' visits and due to the difficulty to collect information in this population retrospectively for day 4 and day 5, when no field worker visit is performed. Consequently, field worker visits at day 6 have been removed.
10 March 2011	Following advice from IDMC, the following change has been implemented: Safety analysis that will lead to a decision to begin enrolment in Cohort 2 will be done on all enrolled children from cohort 1 (approximately 120 subjects) instead of the first 60 enrolled subjects.In addition, the following changes have been included:OPA assay testing techniques have been broadened by inclusion of OPA multiplex to OPA standard testing. Multiplex assay will be used in this study and future studies as it allows multiple measurements in one single test, so it would result in reduction in sera volume needed for OPA in future studies. Likewise, a multiplex immunochemistry assay with equivalent characteristics to the 22F-inhibition ELISA assay and bridged to the 22F-inhibition ELISA might be used in this study.As a result of assay qualification, the cut-off for the functional assay measuring the inhibition of pneumolysin haemolysis activity was changed to 140 instead of 6.The use of one multidose container of oral polio vaccine will be allowed for up to 20 subjects per day.The naming for the first blood sampling timepoint in Cohort 1 has been added in Table 7.The volume of blood to be drawn from children in Cohort 1 (6 ml) was specified in Appendix A in addition to the volume of blood to be drawn from infants in Cohort 2.The type of swab to be used during this study was removed from the protocol. The choice of the type of swab is only specified in the Study Procedure Manual.Quantitative serotype-specific PCR was added to the list of bacterial diagnosis testing on the nasopharyngeal swabs that may be done if specific validated assays become available in the GSK Biologicals laboratory or a validated laboratory designated by GSK Biologicals or deemed necessary should the results of this study and/or another study require it or for development of new assays regarding the diseases or vaccines under evaluation.The control vaccine to be administered to the Prev_C group in Cohort
03 October 2011	• In order to comply with the national immunisation program, a dose of OPV will be administered to subject from Cohort 2, at the time of Visit 5 (at approximately 9 months of age). • Vaccines such as Polio, Measles or Meningococcal Vaccines that are recommended as part of a national campaigns for immunisation are now allowed to be administered at any time during the study. • Complementary analysis of immunogenicity of co-administered vaccines depending on number of received doses has been envisaged. • In the microbiological assessment section the possibility to perform additional testing on the nasopharyngeal swabs for viral pathogens has been added. • Some inconsistencies in protocol wording that could lead to misinterpretation have been clarified throughout the document.

19 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. • The anti-PD, anti-dPly, anti-PhtD Luminex assay has been initially developed and qualified using sera samples from subjects having natural immunity against these 3 proteins. The assay has been evaluated in phase I - II studies and in SPNG005 cohort 1. During re-qualification with standard based on post- vaccination serum, assay consistency was found to be insufficient. Therefore, the Luminex 3-plex anti-PD, -dPly, -PhtD was replaced by 3 qualified individual ELISAs. • In addition, the list of contributing authors has been updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported