



Clinical trial results:

A phase III, open, controlled study to evaluate the immunogenicity, safety and reactogenicity of GSK Biologicals' 10- valent pneumococcal conjugate vaccine administered to children with sickle cell disease between 8 weeks and 2 years of age, as compared to healthy children.

Summary

EudraCT number	2012-000254-64
Trial protocol	Outside EU/EEA
Global end of trial date	23 May 2013

Results information

Result version number	v3 (current)
This version publication date	31 March 2023
First version publication date	25 July 2015
Version creation reason	<ul style="list-style-type: none">• Correction of full data set Correction of full data set and alignment between registries.

Trial information

Trial identification

Sponsor protocol code	114056
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01175083
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)	Yes
EMA paediatric investigation plan number(s)	EMA-000673-PIP01-09
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	04 August 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 May 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the immunogenicity of GSK Biologicals' 10-valent pneumococcal conjugate vaccine when co-administered with DTPw-HBV/Hib and OPV vaccines in children with sickle cell disease, one month after completion of the 3-dose primary vaccination course before 6 months of age

Protection of trial subjects:

All subjects were supervised after vaccination/product administration 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.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 June 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Burkina Faso: 300
Worldwide total number of subjects	300
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)	300
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

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	Primary Epoch
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Tritanrix-HepB/Hib+Polio Sabin <6S Group

Arm description:

Children below (<) 6 months of age at time of enrolment, diagnosed with sickle cell disease (S), who received a 3-dose primary vaccination at Study Months 0, 1 and 2 with Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines, followed by a booster vaccination at Study Month 8.

Arm type	Experimental
Investigational medicinal product name	GSK1024850A (Synflorix)
Investigational medicinal product code	
Other name	GSK Biologicals' 10-valent pneumococcal polysaccharide and non-typeable Haemophilus influenzae (H. influenzae) protein D conjugate vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 intramuscular vaccine doses were administered intramuscularly into the right thigh.

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

Dosage and administration details:

Intramuscular injection, 4 doses in the left thigh.

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

Dosage and administration details:

4 doses administered orally.

Investigational medicinal product name	Hiberix
Investigational medicinal product code	
Other name	Hib
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

White frozen dried pellet in monodose vial to be reconstituted with DTPw-HBV vaccine, intramuscular injection 4 doses in the left thigh.

Arm title	Tritanrix-HepB/Hib+Polio Sabin <6NS Group
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Arm description:

Healthy children, below (<) 6 months of age at time of enrolment, who received a 3-dose primary vaccination at Study Months 0, 1 and 2 with Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines, followed by a booster vaccination at Study Month 8.

Arm type	Active comparator
Investigational medicinal product name	GSK1024850A (Synflorix)
Investigational medicinal product code	
Other name	GSK Biologicals' 10-valent pneumococcal polysaccharide and non-typeable Haemophilus influenzae (H. influenzae) protein D conjugate vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 intramuscular vaccine doses were administered intramuscularly into the right thigh.

Investigational medicinal product name	Tritanrix-HB
Investigational medicinal product code	
Other name	DTPw-HB
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Intramuscular injection, 4 doses in the left thigh.

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

Dosage and administration details:

4 doses administered orally.

Investigational medicinal product name	Hiberix
Investigational medicinal product code	
Other name	Hib
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

White frozen dried pellet in monodose vial to be reconstituted with DTPw-HBV vaccine, intramuscular injection 4 doses in the left thigh.

Arm title	Synflorix 7-11S Group
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Arm description:

Children between 7-11 months of age at time of enrolment, diagnosed with sickle cell disease (S), who received a 2-dose primary vaccination at Study Months 0 and 1 with Synflorix vaccine, followed by a booster vaccination at Study Month 3.

Arm type	Experimental
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Investigational medicinal product name	GSK1024850A (Synflorix)
Investigational medicinal product code	
Other name	GSK Biologicals' 10-valent pneumococcal polysaccharide and non-typeable Haemophilus influenzae (H. influenzae) protein D conjugate vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
2 intramuscular vaccine doses were administered intramuscularly into the right thigh.	
Arm title	Synflorix 7-11NS Group
Arm description:	
Healthy children between 7-11 months of age at time of enrolment, who received a 2-dose primary vaccination at Study Months 0 and 1 with Synflorix vaccine, followed by a booster vaccination at Study Month 3.	
Arm type	Active comparator
Investigational medicinal product name	GSK1024850A (Synflorix)
Investigational medicinal product code	
Other name	GSK Biologicals' 10-valent pneumococcal polysaccharide and non-typeable Haemophilus influenzae (H. influenzae) protein D conjugate vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
2 intramuscular vaccine doses were administered intramuscularly into the right thigh.	
Arm title	Synflorix 12-23S Group
Arm description:	
Children between 12-23 months of age at time of enrolment, diagnosed with sickle cell disease (S), who received a 2-dose vaccination with Synflorix vaccine, at Study Months 0 and 2.	
Arm type	Experimental
Investigational medicinal product name	GSK1024850A (Synflorix)
Investigational medicinal product code	
Other name	GSK Biologicals' 10-valent pneumococcal polysaccharide and non-typeable Haemophilus influenzae (H. influenzae) protein D conjugate vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
2 intramuscular vaccine doses were administered intramuscularly into the right thigh.	
Arm title	Synflorix 12-23NS Group
Arm description:	
Healthy children between 12-23 months of age at time of enrolment, who received a 2-dose vaccination with Synflorix vaccine, at Study Months 0 and 2.	
Arm type	Active comparator
Investigational medicinal product name	GSK1024850A (Synflorix)
Investigational medicinal product code	
Other name	GSK Biologicals' 10-valent pneumococcal polysaccharide and non-typeable Haemophilus influenzae (H. influenzae) protein D conjugate vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
2 intramuscular vaccine doses were administered intramuscularly into the right thigh.	

Number of subjects in period 1	Tritanrix-HepB/Hib+Polio Sabin <6S Group	Tritanrix-HepB/Hib+Polio Sabin <6NS Group	Synflorix 7-11S Group
Started	50	50	50
Completed	50	50	50
Not completed	0	0	0
Consent withdrawn by subject	-	-	-
Lost to follow-up	-	-	-

Number of subjects in period 1	Synflorix 7-11NS Group	Synflorix 12-23S Group	Synflorix 12-23NS Group
Started	50	50	50
Completed	50	50	47
Not completed	0	0	3
Consent withdrawn by subject	-	-	2
Lost to follow-up	-	-	1

Period 2

Period 2 title	Booster Epoch
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Tritanrix-HepB/Hib+Polio Sabin <6S Group

Arm description:

Children below (<) 6 months of age at time of enrolment, diagnosed with sickle cell disease (S), who received a 3-dose primary vaccination at Study Months 0, 1 and 2 with Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines, followed by a booster vaccination at Study Month 8.

Arm type	Experimental
Investigational medicinal product name	GSK1024850A (Synflorix)
Investigational medicinal product code	
Other name	GSK Biologicals' 10-valent pneumococcal polysaccharide and non-typeable Haemophilus influenzae (H. influenzae) protein D conjugate vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 intramuscular vaccine doses were administered intramuscularly into the right thigh.

Investigational medicinal product name	Tritanrix-HB
Investigational medicinal product code	
Other name	DTPw-HBV
Pharmaceutical forms	Suspension for injection

Routes of administration	Intramuscular use
Dosage and administration details:	
Intramuscular injection, 4 doses in the left thigh.	
Investigational medicinal product name	Polio Sabin
Investigational medicinal product code	
Other name	OPV
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use
Dosage and administration details:	
4 doses administered orally.	
Investigational medicinal product name	Hiberix
Investigational medicinal product code	
Other name	Hib
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
White frozen dried pellet in monodose vial to be reconstituted with DTPw-HBV vaccine, intramuscular injection 4 doses in the left thigh.	
Arm title	Tritanrix-HepB/Hib+Polio Sabin <6NS Group
Arm description:	
Healthy children, below (<) 6 months of age at time of enrolment, who received a 3-dose primary vaccination at Study Months 0, 1 and 2 with Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines, followed by a booster vaccination at Study Month 8.	
Arm type	Experimental
Investigational medicinal product name	GSK1024850A (Synflorix)
Investigational medicinal product code	
Other name	GSK Biologicals' 10-valent pneumococcal polysaccharide and non-typeable Haemophilus influenzae (H. influenzae) protein D conjugate vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
3 intramuscular vaccine doses were administered intramuscularly into the right thigh.	
Investigational medicinal product name	Tritanrix-HB
Investigational medicinal product code	
Other name	DTPw-HBV
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Intramuscular injection, 4 doses in the left thigh.	
Investigational medicinal product name	Polio Sabin
Investigational medicinal product code	
Other name	OPV
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use
Dosage and administration details:	
4 doses administered orally.	
Investigational medicinal product name	Hiberix
Investigational medicinal product code	
Other name	Hib
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

White frozen dried pellet in monodose vial to be reconstituted with DTPw-HBV vaccine, intramuscular injection 4 doses in the left thigh.

Arm title	Synflorix 7-11S Group
Arm description:	
Children between 7-11 months of age at time of enrolment, diagnosed with sickle cell disease (S), who received a 2-dose primary vaccination at Study Months 0 and 1 with Synflorix vaccine, followed by a booster vaccination at Study Month 3.	
Arm type	Experimental
Investigational medicinal product name	GSK1024850A (Synflorix)
Investigational medicinal product code	
Other name	GSK Biologicals' 10-valent pneumococcal polysaccharide and non-typeable Haemophilus influenzae (H. influenzae) protein D conjugate vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 intramuscular vaccine doses were administered intramuscularly into the right thigh.

Arm title	Synflorix 7-11NS Group
Arm description:	
Healthy children between 7-11 months of age at time of enrolment, who received a 2-dose primary vaccination at Study Months 0 and 1 with Synflorix vaccine, followed by a booster vaccination at Study Month 3.	
Arm type	Active comparator
Investigational medicinal product name	GSK1024850A (Synflorix)
Investigational medicinal product code	
Other name	GSK Biologicals' 10-valent pneumococcal polysaccharide and non-typeable Haemophilus influenzae (H. influenzae) protein D conjugate vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 intramuscular vaccine doses were administered intramuscularly into the right thigh.

Number of subjects in period 2^[1]	Tritanrix-HepB/Hib+Polio Sabin <6S Group	Tritanrix-HepB/Hib+Polio Sabin <6NS Group	Synflorix 7-11S Group
Started	49	49	50
Completed	49	49	49
Not completed	0	0	1
Consent withdrawn by subject	-	-	-
Death	-	-	1

Number of subjects in period 2^[1]	Synflorix 7-11NS Group
Started	50
Completed	49
Not completed	1

Consent withdrawn by subject	1
Death	-

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: One subject died between both Epochs and hence did not participate in the Booster Epoch.

Baseline characteristics

Reporting groups

Reporting group title	Tritanrix-HepB/Hib+Polio Sabin <6S Group
Reporting group description: Children below (<) 6 months of age at time of enrolment, diagnosed with sickle cell disease (S), who received a 3-dose primary vaccination at Study Months 0, 1 and 2 with Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines, followed by a booster vaccination at Study Month 8.	
Reporting group title	Tritanrix-HepB/Hib+Polio Sabin <6NS Group
Reporting group description: Healthy children, below (<) 6 months of age at time of enrolment, who received a 3-dose primary vaccination at Study Months 0, 1 and 2 with Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines, followed by a booster vaccination at Study Month 8.	
Reporting group title	Synflorix 7-11S Group
Reporting group description: Children between 7-11 months of age at time of enrolment, diagnosed with sickle cell disease (S), who received a 2-dose primary vaccination at Study Months 0 and 1 with Synflorix vaccine, followed by a booster vaccination at Study Month 3.	
Reporting group title	Synflorix 7-11NS Group
Reporting group description: Healthy children between 7-11 months of age at time of enrolment, who received a 2-dose primary vaccination at Study Months 0 and 1 with Synflorix vaccine, followed by a booster vaccination at Study Month 3.	
Reporting group title	Synflorix 12-23S Group
Reporting group description: Children between 12-23 months of age at time of enrolment, diagnosed with sickle cell disease (S), who received a 2-dose vaccination with Synflorix vaccine, at Study Months 0 and 2.	
Reporting group title	Synflorix 12-23NS Group
Reporting group description: Healthy children between 12-23 months of age at time of enrolment, who received a 2-dose vaccination with Synflorix vaccine, at Study Months 0 and 2.	

Reporting group values	Tritanrix-HepB/Hib+Polio Sabin <6S Group	Tritanrix-HepB/Hib+Polio Sabin <6NS Group	Synflorix 7-11S Group
Number of subjects	50	50	50
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	50	50	50
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	21	29	26
Male	29	21	24

Reporting group values	Synflorix 7-11NS Group	Synflorix 12-23S Group	Synflorix 12-23NS Group
Number of subjects	50	50	50
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	50	50	50
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	32	15	24
Male	18	35	26

Reporting group values	Total		
Number of subjects	300		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	300		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Gender categorical Units: Subjects			
Female	147		
Male	153		

End points

End points reporting groups

Reporting group title	Tritanrix-HepB/Hib+Polio Sabin <6S Group
Reporting group description: Children below (<) 6 months of age at time of enrolment, diagnosed with sickle cell disease (S), who received a 3-dose primary vaccination at Study Months 0, 1 and 2 with Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines, followed by a booster vaccination at Study Month 8.	
Reporting group title	Tritanrix-HepB/Hib+Polio Sabin <6NS Group
Reporting group description: Healthy children, below (<) 6 months of age at time of enrolment, who received a 3-dose primary vaccination at Study Months 0, 1 and 2 with Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines, followed by a booster vaccination at Study Month 8.	
Reporting group title	Synflorix 7-11S Group
Reporting group description: Children between 7-11 months of age at time of enrolment, diagnosed with sickle cell disease (S), who received a 2-dose primary vaccination at Study Months 0 and 1 with Synflorix vaccine, followed by a booster vaccination at Study Month 3.	
Reporting group title	Synflorix 7-11NS Group
Reporting group description: Healthy children between 7-11 months of age at time of enrolment, who received a 2-dose primary vaccination at Study Months 0 and 1 with Synflorix vaccine, followed by a booster vaccination at Study Month 3.	
Reporting group title	Synflorix 12-23S Group
Reporting group description: Children between 12-23 months of age at time of enrolment, diagnosed with sickle cell disease (S), who received a 2-dose vaccination with Synflorix vaccine, at Study Months 0 and 2.	
Reporting group title	Synflorix 12-23NS Group
Reporting group description: Healthy children between 12-23 months of age at time of enrolment, who received a 2-dose vaccination with Synflorix vaccine, at Study Months 0 and 2.	
Reporting group title	Tritanrix-HepB/Hib+Polio Sabin <6S Group
Reporting group description: Children below (<) 6 months of age at time of enrolment, diagnosed with sickle cell disease (S), who received a 3-dose primary vaccination at Study Months 0, 1 and 2 with Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines, followed by a booster vaccination at Study Month 8.	
Reporting group title	Tritanrix-HepB/Hib+Polio Sabin <6NS Group
Reporting group description: Healthy children, below (<) 6 months of age at time of enrolment, who received a 3-dose primary vaccination at Study Months 0, 1 and 2 with Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines, followed by a booster vaccination at Study Month 8.	
Reporting group title	Synflorix 7-11S Group
Reporting group description: Children between 7-11 months of age at time of enrolment, diagnosed with sickle cell disease (S), who received a 2-dose primary vaccination at Study Months 0 and 1 with Synflorix vaccine, followed by a booster vaccination at Study Month 3.	
Reporting group title	Synflorix 7-11NS Group
Reporting group description: Healthy children between 7-11 months of age at time of enrolment, who received a 2-dose primary vaccination at Study Months 0 and 1 with Synflorix vaccine, followed by a booster vaccination at Study Month 3.	

Primary: Concentrations of antibodies against vaccine pneumococcal serotypes for subjects receiving Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines

End point title	Concentrations of antibodies against vaccine pneumococcal serotypes for subjects receiving Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines ^{[1][2]}
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End point description:

Antibodies have been assessed against the following vaccine pneumococcal serotypes: 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (Anti-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F). Antibody concentrations were measured by 22F enzyme-linked immunosorbent assay (ELISA), presented as geometric mean concentrations (GMCs) and expressed in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration greater than or equal to (≥) 0.05 micrograms per milliliter (µg/mL). Antibody concentrations below than (<) 0.05 µg/mL were given an arbitrary value of half the cut-off for the purpose of GMC calculation.

End point type	Primary
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End point timeframe:

One month after primary vaccination (Month 3)

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: This endpoint is only reporting values for the Tritanrix-HepB/Hib+Polio Sabin <6S Group and the Tritanrix-HepB/Hib+Polio Sabin <6NS Group.

End point values	Tritanrix-HepB/Hib+Polio Sabin <6S Group	Tritanrix-HepB/Hib+Polio Sabin <6NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	46		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-1 [Month 3] (N=48,46)	3.51 (2.77 to 4.44)	3.63 (2.91 to 4.53)		
Anti-4 [Month 3] (N=47,46)	4.25 (3.18 to 5.67)	3.51 (2.73 to 4.51)		
Anti-5 [Month 3] (N=47,46)	5.15 (4.07 to 6.51)	5.94 (4.91 to 7.18)		
Anti-6B [Month 3] (N=48,46)	1.29 (0.83 to 1.99)	1.13 (0.74 to 1.72)		
Anti-7F [Month 3] (N=48,46)	4.91 (3.84 to 6.28)	4.28 (3.49 to 5.26)		
Anti-9V [Month 3] (N=47,46)	4.56 (3.51 to 5.92)	4.59 (3.7 to 5.7)		
Anti-14 [Month 3] (N=46,46)	4.3 (3.08 to 6)	5.95 (4.27 to 8.29)		
Anti-18C [Month 3] (N=47,45)	14.6 (11.01 to 19.36)	11.33 (8.47 to 15.17)		
Anti-19F [Month 3] (N=47,46)	11.87 (9.05 to 15.57)	9.78 (7.01 to 13.64)		
Anti-23F [Month 3] (N=48,46)	1.32 (0.9 to 1.93)	1.41 (0.95 to 2.11)		

Statistical analyses

No statistical analyses for this end point

Primary: Concentrations of antibodies against protein D (PD) for subjects receiving Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines

End point title	Concentrations of antibodies against protein D (PD) for subjects receiving Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines ^{[3][4]}
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End point description:

Anti-PD antibody concentrations were measured by enzyme-linked immunosorbent assay (ELISA), presented as geometric mean concentrations (GMCs) and expressed in ELISA units per milliliter (EL.U/mL). The seropositivity cut-off of the assay was an antibody concentration ≥ 100 EL.U/mL. Antibody concentrations < 100 EL.U/mL were given an arbitrary value of half the cut-off for the purpose of GMC calculation.

End point type	Primary
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End point timeframe:

One month after the primary vaccination (Month 3)

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: This endpoint is only reporting values for the Tritanrix-HepB/Hib+Polio Sabin <6S Group and the Tritanrix-HepB/Hib+Polio Sabin <6NS Group.

End point values	Tritanrix-HepB/Hib+Polio Sabin <6S Group	Tritanrix-HepB/Hib+Polio Sabin <6NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	46		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD [Month 3] (N=47,46)	2789.09 (2313.89 to 3361.87)	3065.4 (2530.54 to 3713.31)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and Grade 3 solicited local symptoms during the primary vaccination phase

End point title	Number of subjects with any and Grade 3 solicited local symptoms during the primary vaccination phase
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End point description:

Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = cried when limb was moved/spontaneously painful. Grade 3 redness/swelling = redness/swelling spreading beyond 30 millimeters (mm) of injection site.

End point type	Secondary
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End point timeframe:

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

End point values	Tritanrix- HepB/Hib+Polio Sabin <6S Group	Tritanrix- HepB/Hib+Polio Sabin <6NS Group	Synflorix 7-11S Group	Synflorix 7- 11NS Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	50	50	50
Units: Subjects				
Any Pain, Dose 1	8	12	7	10
Grade 3 Pain, Dose 1	0	0	0	0
Any Redness, Dose 1	0	0	0	0
Grade 3 Redness, Dose 1	0	0	0	0
Any Swelling, Dose 1	0	0	0	0
Grade 3 Swelling, Dose 1	0	0	0	0
Any Pain, Dose 2	7	7	5	7
Grade 3 Pain, Dose 2	0	0	0	0
Any Redness, Dose 2	0	0	0	0
Grade 3 Redness, Dose 2	0	0	0	0
Any Swelling, Dose 2	0	1	0	1
Grade 3 Swelling, Dose 2	0	0	0	0
Any Pain, Dose 3	4	6	0	0
Grade 3 Pain, Dose 3	0	0	0	0
Any Redness, Dose 3	0	0	0	0
Grade 3 Redness, Dose 3	0	0	0	0
Any Swelling, Dose 3	0	0	0	0
Grade 3 Swelling, Dose 3	0	0	0	0
Any Pain, Across	17	23	12	15
Grade 3 Pain, Across	0	0	0	0
Any Redness, Across	0	0	0	0
Grade 3 Redness, Across	0	0	0	0
Any Swelling, Across	0	1	0	1
Grade 3 Swelling, Across	0	0	0	0

End point values	Synflorix 12- 23S Group	Synflorix 12- 23NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: Subjects				
Any Pain, Dose 1	9	6		
Grade 3 Pain, Dose 1	0	0		
Any Redness, Dose 1	0	0		
Grade 3 Redness, Dose 1	0	0		
Any Swelling, Dose 1	1	1		
Grade 3 Swelling, Dose 1	0	0		
Any Pain, Dose 2	5	3		
Grade 3 Pain, Dose 2	0	0		
Any Redness, Dose 2	0	0		

Grade 3 Redness, Dose 2	0	0		
Any Swelling, Dose 2	0	0		
Grade 3 Swelling, Dose 2	0	0		
Any Pain, Dose 3	0	0		
Grade 3 Pain, Dose 3	0	0		
Any Redness, Dose 3	0	0		
Grade 3 Redness, Dose 3	0	0		
Any Swelling, Dose 3	0	0		
Grade 3 Swelling, Dose 3	0	0		
Any Pain, Across	13	9		
Grade 3 Pain, Across	0	0		
Any Redness, Across	0	0		
Grade 3 Redness, Across	0	0		
Any Swelling, Across	1	1		
Grade 3 Swelling, Across	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any, grade 3 and related solicited general symptoms during the primary vaccination phase

End point title	Number of subjects with any, grade 3 and related solicited general symptoms during the primary vaccination phase
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End point description:

Assessed solicited general symptoms were drowsiness, irritability, loss of appetite and fever [defined as rectal temperature equal to or above (\geq) 38 degrees Celsius ($^{\circ}$ C)]. Any = occurrence of the symptom regardless of intensity grade. Grade 3 symptom = symptom that prevented normal activity. Grade 3 fever = fever $> 40.0^{\circ}$ C. Related = symptom assessed by the investigator as related to the vaccination.

End point type	Secondary
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End point timeframe:

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

End point values	Tritanrix-HepB/Hib+Polio Sabin <6S Group	Tritanrix-HepB/Hib+Polio Sabin <6NS Group	Synflorix 7-11S Group	Synflorix 7-11NS Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	50	50	50
Units: Subjects				
Any Drowsiness, Dose 1	0	0	0	1
Grade 3 Drowsiness, Dose 1	0	0	0	0
Related Drowsiness, Dose 1	0	0	0	1
Any Irritability, Dose 1	0	2	0	0
Grade 3 Irritability, Dose 1	0	0	0	0
Related Irritability, Dose 1	0	0	0	0
Any Loss of appetite, Dose 1	0	0	0	0
Grade 3 Loss of appetite, Dose 1	0	0	0	0
Related Loss of appetite, Dose 1	0	0	0	0

Any Fever, Dose 1	34	31	22	26
Grade 3 Fever, Dose 1	0	0	0	0
Related Fever, Dose 1	31	29	19	22
Any Drowsiness, Dose 2	0	0	0	0
Grade 2 Drowsiness, Dose 2	0	0	0	0
Related Drowsiness, Dose 2	0	0	0	0
Any Irritability, Dose 2	0	0	0	0
Grade 3 Irritability, Dose 2	0	0	0	0
Related Irritability, Dose 2	0	0	0	0
Any Loss of appetite, Dose 2	0	0	0	0
Grade 3 Loss of appetite, Dose 2	0	0	0	0
Related Loss of appetite, Dose 2	0	0	0	0
Any Fever, Dose 2	40	30	22	11
Grade 3 Fever, Dose 2	0	0	0	0
Related Fever, Dose 2	38	28	20	9
Any Drowsiness, Dose 3	0	0	0	0
Grade 3 Drowsiness, Dose 3	0	0	0	0
Related Drowsiness, Dose 3	0	0	0	0
Any Irritability, Dose 3	3	4	0	0
Grade 3 Irritability, Dose 3	0	0	0	0
Related Irritability, Dose 3	3	3	0	0
Any Loss of appetite, Dose 3	0	1	0	0
Grade 3 Loss of appetite, Dose 3	0	0	0	0
Related Loss of appetite, Dose 3	0	0	0	0
Any Fever, Dose 3	30	30	0	0
Grade 3 Fever, Dose 3	0	0	0	0
Related Fever, Dose 3	26	28	0	0
Any Drowsiness, Across Doses	0	0	0	1
Grade 3 Drowsiness, Across Doses	0	0	0	0
Related Drowsiness, Across Doses	0	0	0	1
Any Irritability, Across Doses	3	6	0	0
Grade 3 Irritability, Across Doses	0	0	0	0
Related Irritability, Across Doses	3	3	0	0
Any Loss of appetite, Across Doses	0	1	0	0
Grade 3 Loss of appetite, Across Doses	0	0	0	0
Related Loss of appetite, Across Doses	0	0	0	0
Any Fever, Across Doses	48	43	31	29
Grade 3 Fever, Across Doses	0	0	0	0
Related Fever, Across Doses	46	43	29	25

End point values	Synflorix 12-23S Group	Synflorix 12-23NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: Subjects				
Any Drowsiness, Dose 1	0	0		
Grade 3 Drowsiness, Dose 1	0	0		
Related Drowsiness, Dose 1	0	0		
Any Irritability, Dose 1	1	0		

Grade 3 Irritability, Dose 1	0	0		
Related Irritability, Dose 1	1	0		
Any Loss of appetite, Dose 1	0	1		
Grade 3 Loss of appetite, Dose 1	0	0		
Related Loss of appetite, Dose 1	0	1		
Any Fever, Dose 1	21	15		
Grade 3 Fever, Dose 1	0	0		
Related Fever, Dose 1	21	13		
Any Drowsiness, Dose 2	0	0		
Grade 2 Drowsiness, Dose 2	0	0		
Related Drowsiness, Dose 2	0	0		
Any Irritability, Dose 2	1	0		
Grade 3 Irritability, Dose 2	0	0		
Related Irritability, Dose 2	1	0		
Any Loss of appetite, Dose 2	0	0		
Grade 3 Loss of appetite, Dose 2	0	0		
Related Loss of appetite, Dose 2	0	0		
Any Fever, Dose 2	12	12		
Grade 3 Fever, Dose 2	0	0		
Related Fever, Dose 2	10	9		
Any Drowsiness, Dose 3	0	0		
Grade 3 Drowsiness, Dose 3	0	0		
Related Drowsiness, Dose 3	0	0		
Any Irritability, Dose 3	0	0		
Grade 3 Irritability, Dose 3	0	0		
Related Irritability, Dose 3	0	0		
Any Loss of appetite, Dose 3	0	0		
Grade 3 Loss of appetite, Dose 3	0	0		
Related Loss of appetite, Dose 3	0	0		
Any Fever, Dose 3	0	0		
Grade 3 Fever, Dose 3	0	0		
Related Fever, Dose 3	0	0		
Any Drowsiness, Across Doses	0	0		
Grade 3 Drowsiness, Across Doses	0	0		
Related Drowsiness, Across Doses	0	0		
Any Irritability, Across Doses	2	0		
Grade 3 Irritability, Across Doses	0	0		
Related Irritability, Across Doses	2	0		
Any Loss of appetite, Across Doses	0	1		
Grade 3 Loss of appetite, Across Doses	0	0		
Related Loss of appetite, Across Doses	0	1		
Any Fever, Across Doses	29	20		
Grade 3 Fever, Across Doses	0	0		
Related Fever, Across Doses	28	17		

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects with any unsolicited adverse events (AEs)
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End point description:

An unsolicited AE covers 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 and reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any was defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination.

End point type	Secondary
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End point timeframe:

Within the 31-day (Days 0-30) post-primary and post-booster vaccination period
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End point values	Tritanrix-HepB/Hib+Polio Sabin <6S Group	Tritanrix-HepB/Hib+Polio Sabin <6NS Group	Synflorix 7-11S Group	Synflorix 7-11NS Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	50	50	50
Units: Subjects				
Any AEs post primary vaccination [N=50,50,50,50]	37	34	32	37
Any AEs post-booster vaccination [N=49,49,50,50]	8	17	18	12

End point values	Synflorix 12-23S Group	Synflorix 12-23NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: Subjects				
Any AEs post primary vaccination [N=50,50,50,50]	23	25		
Any AEs post-booster vaccination [N=49,49,50,50]	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs)

End point title	Number of subjects with serious adverse events (SAEs)
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End point description:

Serious adverse events (SAEs) assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity.

End point type	Secondary
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End point timeframe:

During the entire study period from Month 0 to Month 9
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End point values	Tritanrix-HepB/Hib+Polio Sabin <6S Group	Tritanrix-HepB/Hib+Polio Sabin <6NS Group	Synflorix 7-11S Group	Synflorix 7-11NS Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	50	50	50
Units: Subjects				
Any SAEs	3	9	3	4

End point values	Synflorix 12-23S Group	Synflorix 12-23NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: Subjects				
Any SAEs	2	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and grade 3 solicited local symptoms during the booster vaccination phase

End point title	Number of subjects with any and grade 3 solicited local symptoms during the booster vaccination phase
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End point description:

Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = cried when limb was moved/spontaneously painful. Grade 3 redness/swelling = redness/swelling spreading beyond 30 millimeters (mm) of injection site.

End point type	Secondary
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End point timeframe:

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

End point values	Tritanrix-HepB/Hib+Polio Sabin <6S Group	Tritanrix-HepB/Hib+Polio Sabin <6NS Group	Synflorix 7-11S Group	Synflorix 7-11NS Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	49	50	50
Units: Subjects				
Any Pain	11	6	3	0
Grade 3 Pain	0	0	0	0
Any Redness	0	0	0	0
Grade 3 Redness	0	0	0	0

Any Swelling	1	0	1	0
Grade 3 Swelling	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any, grade 3 and related solicited general symptoms during the booster vaccination phase

End point title	Number of subjects with any, grade 3 and related solicited general symptoms during the booster vaccination phase
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End point description:

Assessed solicited general symptoms were drowsiness, irritability, loss of appetite and fever [defined as rectal temperature equal to or above (\geq) 38 degrees Celsius ($^{\circ}$ C)]. Any = occurrence of the symptom regardless of intensity grade. Grade 3 symptom = symptom that prevented normal activity. Grade 3 fever = fever $> 40.0^{\circ}$ C. Related = symptom assessed by the investigator as related to the vaccination.

End point type	Secondary
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End point timeframe:

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

End point values	Tritanrix-HepB/Hib+Polio Sabin <6S Group	Tritanrix-HepB/Hib+Polio Sabin <6NS Group	Synflorix 7-11S Group	Synflorix 7-11NS Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	49	50	50
Units: Subjects				
Any Drowsiness	0	0	0	0
Grade 3 Drowsiness	0	0	0	0
Related Drowsiness	0	0	0	0
Any Irritability	6	0	0	0
Grade 3 Irritability	0	0	0	0
Related Irritability	5	0	0	0
Any Loss of appetite	0	0	0	0
Grade 3 Loss of appetite	0	0	0	0
Related Loss of appetite	0	0	0	0
Any Fever	38	31	14	13
Grade 3 Fever	0	0	0	0
Related Fever	35	28	13	13

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against cross-reactive pneumococcal

serotypes for subjects receiving Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines

End point title	Concentrations of antibodies against cross-reactive pneumococcal serotypes for subjects receiving Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines ^[5]
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End point description:

Antibody concentrations against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A, -19A) were measured by 22F enzyme-linked immunosorbent assay (ELISA), presented as geometric mean concentrations (GMCs) and expressed in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 micrograms per milliliter (µg/mL). Antibody concentrations < 0.05 µg/mL were given an arbitrary value of half the cut-off for the purpose of GMC calculation.

End point type	Secondary
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End point timeframe:

Prior to (Month 0) and one month after primary vaccination (Month 3), prior to (Month 8) and one month after (Month 9) booster vaccination

Notes:

[5] - 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: This endpoint is only reporting values for the Tritanrix-HepB/Hib+Polio Sabin <6S Group and the Tritanrix-HepB/Hib+Polio Sabin <6NS Group.

End point values	Tritanrix-HepB/Hib+Polio Sabin <6S Group	Tritanrix-HepB/Hib+Polio Sabin <6NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	45		
Units: Titer				
geometric mean (confidence interval 95%)				
Anti-6A [Month 0] (N=47,41)	0.10 (0.07 to 0.14)	0.15 (0.1 to 0.23)		
Anti-6A [Month 3] (N=46,43)	0.12 (0.08 to 0.17)	0.10 (0.07 to 0.13)		
Anti-6A [Month 8] (N=37,30)	0.40 (0.27 to 0.61)	0.18 (0.1 to 0.3)		
Anti-6A [Month 9] (N=36,29)	0.48 (0.31 to 0.74)	0.36 (0.23 to 0.55)		
Anti-19A [Month 0] (N=47,44)	0.24 (0.17 to 0.36)	0.23 (0.16 to 0.33)		
Anti-19A [Month 3] (N=48,45)	0.26 (0.17 to 0.39)	0.25 (0.17 to 0.37)		
Anti-19A [Month 8] (N=44,38)	0.23 (0.15 to 0.37)	0.21 (0.13 to 0.35)		
Anti-19A [Month 9] (N=44,37)	1.09 (0.65 to 1.83)	0.85 (0.5 to 1.43)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against vaccine pneumococcal serotypes for subjects who received a two-dose primary vaccination followed by a booster dose

End point title	Concentrations of antibodies against vaccine pneumococcal
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End point description:

Antibodies have been assessed against the following vaccine pneumococcal serotypes: 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (Anti-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F). Antibody concentrations were measured by 22F enzyme-linked immunosorbent assay (ELISA), presented as geometric mean concentrations (GMCs) and expressed in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 micrograms per milliliter (µg/mL). Antibody concentrations < 0.05 µg/mL were given an arbitrary value of half the cut-off for the purpose of GMC calculation.

End point type Secondary

End point timeframe:

Prior to (Month 0) and one month after (Month 2) primary vaccination, prior to (Month 3) and one month after (Month 4) booster vaccination

Notes:

[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: This endpoint is only reporting values for Synflorix 7-11S Group and the Synflorix 7-11NS Group.

End point values	Synflorix 7-11S Group	Synflorix 7-11NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-1 [Month 0] (N=48,46)	0.03 (0.03 to 0.03)	0.04 (0.03 to 0.05)		
Anti-1 [Month 2] (N=50,48)	5.48 (4.34 to 6.93)	3.99 (3.24 to 4.91)		
Anti-1 [Month 3] (N=50,49)	2.68 (2.12 to 3.39)	2.44 (1.99 to 2.98)		
Anti-1 [Month 4] (N=49,48)	5.51 (4.27 to 7.1)	4.92 (3.74 to 6.48)		
Anti-4 [Month 0] (N=49,50)	0.03 (0.03 to 0.04)	0.03 (0.02 to 0.04)		
Anti-4 [Month 2] (N=49,47)	10.88 (8.94 to 13.24)	7.55 (6 to 9.5)		
Anti-4 [Month 3] (N=50,48)	5.72 (4.66 to 7.03)	4.32 (3.51 to 5.32)		
Anti-4 [Month 4] (N=49,48)	9.75 (7.67 to 12.39)	7.88 (6.28 to 9.89)		
Anti-5 [Month 0] (N=48,50)	0.04 (0.03 to 0.06)	0.06 (0.05 to 0.08)		
Anti-5 [Month 2] (N=50,47)	6.76 (5.14 to 8.89)	4.59 (3.58 to 5.88)		
Anti-5 [Month 3] (N=50,49)	3.68 (2.87 to 4.73)	3.4 (2.66 to 4.33)		
Anti-5 [Month 4] (N=49,48)	7.75 (6.05 to 9.92)	7.87 (6.02 to 10.29)		
Anti-6B [Month 0] (N=49,46)	0.03 (0.02 to 0.03)	0.03 (0.02 to 0.03)		
Anti-6B [Month 2] (N=49,49)	1.61 (1.03 to 2.52)	1.48 (1.02 to 2.13)		
Anti-6B [Month 3] (N=50,49)	1.51 (1.06 to 2.15)	1.35 (0.98 to 1.87)		
Anti-6B [Month 4] (N=49,48)	3.12 (2.1 to 4.64)	2.93 (2.17 to 3.95)		
Anti-7F [Month 0] (N=50,50)	0.04 (0.03 to 0.05)	0.04 (0.03 to 0.05)		

Anti-7F [Month 2] (N=49,49)	8.51 (6.94 to 10.42)	6.67 (5.44 to 8.19)		
Anti-7F [Month 3] (N=50,49)	5.46 (4.37 to 6.83)	4.68 (3.76 to 5.81)		
Anti-7F [Month 4] (N=48,48)	11.08 (8.9 to 13.81)	10.29 (7.92 to 13.37)		
Anti-9V [Month 0] (N=49,48)	0.04 (0.03 to 0.05)	0.04 (0.03 to 0.05)		
Anti-9V [Month 2] (N=49,49)	2.55 (1.86 to 3.49)	1.67 (1.21 to 2.29)		
Anti-9V [Month 3] (N=50,49)	1.9 (1.42 to 2.56)	1.52 (1.16 to 2)		
Anti-9V [Month 4] (N=49,48)	4.73 (3.4 to 6.58)	3.76 (2.67 to 5.3)		
Anti-14 [Month 0] (N=47,48)	0.08 (0.06 to 0.12)	0.07 (0.05 to 0.1)		
Anti-14 [Month 2] (N=50,46)	4.91 (3.48 to 6.95)	4.81 (3.67 to 6.29)		
Anti-14 [Month 3] (N=50,49)	4.71 (3.45 to 6.43)	4.98 (4.01 to 6.2)		
Anti-14 [Month 4] (N=49,48)	10.24 (7.96 to 13.18)	10.69 (8.34 to 13.71)		
Anti-18C [Month 0] (N=50,49)	0.03 (0.03 to 0.03)	0.03 (0.03 to 0.04)		
Anti-18C [Month 2] (N=49,47)	12.92 (9.93 to 16.82)	14.62 (11.61 to 18.4)		
Anti-18C [Month 3] (N=50,49)	8.43 (6.53 to 10.88)	11.49 (9.24 to 14.29)		
Anti-18C [Month 4] (N=49,48)	23.57 (18.38 to 30.22)	31.88 (25.34 to 40.11)		
Anti-19F [Month 0] (N=49,48)	0.05 (0.04 to 0.06)	0.04 (0.04 to 0.06)		
Anti-19F [Month 2] (N=50,49)	11.13 (7.97 to 15.54)	9.77 (6.16 to 15.48)		
Anti-19F [Month 3] (N=50,49)	6.54 (4.79 to 8.92)	7.39 (5.04 to 10.81)		
Anti-19F [Month 4] (N=49,48)	15.59 (11.24 to 21.62)	15.85 (10.52 to 23.89)		
Anti-23F [Month 0] (N=48,48)	0.03 (0.03 to 0.04)	0.04 (0.03 to 0.05)		
Anti-23F [Month 2] (N=50,48)	1.29 (0.79 to 2.1)	0.93 (0.6 to 1.45)		
Anti-23F [Month 3] (N=50,48)	1 (0.65 to 1.56)	1.08 (0.74 to 1.56)		
Anti-23F [Month 4] (N=49,48)	3.11 (1.85 to 5.24)	3.17 (2.04 to 4.91)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against cross-reactive pneumococcal serotypes for subjects who received a two-dose primary vaccination followed by a booster dose

End point title	Concentrations of antibodies against cross-reactive pneumococcal serotypes for subjects who received a two-dose primary vaccination followed by a booster dose ^[7]
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End point description:

Antibody concentrations against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A, -19A) were measured by 22F enzyme-linked immunosorbent assay (ELISA), presented as geometric mean concentrations (GMCs) and expressed in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 micrograms per milliliter (µg/mL). Antibody concentrations < 0.05 µg/mL were given an arbitrary value of half the cut-off for the purpose of GMC calculation.

End point type	Secondary
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End point timeframe:

Prior to (Month 0) and one month after (Month 2) primary vaccination, prior to (Month 3) and one month after (Month 4) booster vaccination

Notes:

[7] - 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: This endpoint is only reporting values for Synflorix 7-11S Group and the Synflorix 7-11NS Group.

End point values	Synflorix 7-11S Group	Synflorix 7-11NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	49		
Units: Titer				
geometric mean (confidence interval 95%)				
Anti-6A [Month 0] (N=47,44)	0.03 (0.03 to 0.04)	0.03 (0.03 to 0.04)		
Anti-6A [Month 2] (N=48,46)	0.18 (0.11 to 0.3)	0.16 (0.11 to 0.24)		
Anti-6A [Month3] (N=50,47)	0.23 (0.14 to 0.37)	0.22 (0.16 to 0.32)		
Anti-6A [Month 4] (N=48,48)	0.44 (0.28 to 0.7)	0.43 (0.3 to 0.62)		
Anti-19A [Month 0] (N=48,49)	0.04 (0.03 to 0.06)	0.06 (0.04 to 0.1)		
Anti-19A [Month 2] (N=50,49)	0.46 (0.28 to 0.76)	0.77 (0.5 to 1.18)		
Anti-19A [Month3] (N=50,48)	0.44 (0.27 to 0.7)	0.77 (0.51 to 1.17)		
Anti-19A [Month 4] (N=49,48)	1.49 (0.93 to 2.38)	2.35 (1.5 to 3.67)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of antibodies against vaccine pneumococcal serotypes for subjects who received a two-dose primary vaccination without any booster dose

End point title	Concentration of antibodies against vaccine pneumococcal serotypes for subjects who received a two-dose primary vaccination without any booster dose ^[8]
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End point description:

Antibodies have been assessed against the following vaccine pneumococcal serotypes: 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (Anti-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F). Antibody concentrations were measured by 22F enzyme-linked immunosorbent assay (ELISA), presented as geometric mean concentrations (GMCs) and expressed in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 micrograms per milliliter (µg/mL). Antibody concentrations < 0.05 µg/mL were given an arbitrary value of half the cut-off for the

purpose of GMC calculation.

End point type	Secondary
End point timeframe:	
Prior to (Month 0) the first vaccine dose, prior to (Month 2) and one month after (Month 3) the second vaccine dose	

Notes:

[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: This endpoint is only reporting values for the Synflorix 12-23S Group and the Synflorix 12-23NS Group.

End point values	Synflorix 12-23S Group	Synflorix 12-23NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	47		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-1 [Month 0] (N=47,45)	0.04 (0.03 to 0.05)	0.04 (0.03 to 0.05)		
Anti-1 [Month 2] (N=48,47)	1.39 (1.07 to 1.8)	1.49 (1.18 to 1.89)		
Anti-1 [Month 3] (N=48,46)	4.67 (3.75 to 5.81)	4.26 (3.38 to 5.37)		
Anti-4 [Month 0] (N=48,47)	0.04 (0.03 to 0.05)	0.04 (0.03 to 0.05)		
Anti-4 [Month 2] (N=47,47)	4.22 (3.23 to 5.51)	3.74 (2.96 to 4.72)		
Anti-4 [Month 3] (N=47,46)	8.87 (7.03 to 11.19)	7.02 (5.85 to 8.43)		
Anti-5 [Month 0] (N=48,47)	0.06 (0.04 to 0.08)	0.08 (0.06 to 0.11)		
Anti-5 [Month 2] (N=48,47)	1.06 (0.77 to 1.47)	1.1 (0.83 to 1.44)		
Anti-5 [Month 3] (N=48,46)	5.52 (4.23 to 7.2)	4.07 (3.06 to 5.42)		
Anti-6B [Month 0] (N=48,47)	0.03 (0.03 to 0.04)	0.04 (0.03 to 0.05)		
Anti-6B [Month 2] (N=48,47)	0.41 (0.28 to 0.62)	0.34 (0.24 to 0.48)		
Anti-6B [Month 3] (N=48,46)	1.37 (0.91 to 2.07)	1.25 (0.87 to 1.79)		
Anti-7F [Month 0] (N=48,47)	0.07 (0.05 to 0.11)	0.05 (0.04 to 0.07)		
Anti-7F [Month 2] (N=48,47)	2.74 (2.13 to 3.52)	3.17 (2.56 to 3.93)		
Anti-7F [Month 3] (N=48,46)	6.81 (5.32 to 8.7)	6.36 (5.25 to 7.69)		
Anti-9V [Month 0] (N=48,47)	0.08 (0.05 to 0.12)	0.05 (0.04 to 0.07)		
Anti-9V [Month 2] (N=48,47)	0.99 (0.72 to 1.34)	0.83 (0.62 to 1.11)		
Anti-9V [Month 3] (N=48,46)	2.35 (1.85 to 3)	1.72 (1.31 to 2.25)		
Anti-14 [Month 0] (N=47,46)	0.11 (0.07 to 0.16)	0.09 (0.06 to 0.12)		
Anti-14 [Month 2] (N=48,47)	1.87 (1.46 to 2.4)	1.24 (0.92 to 1.66)		
Anti-14 [Month 3] (N=47,45)	7.59 (5.84 to 9.87)	5.75 (4.33 to 7.62)		

Anti-18C [Month 0] (N=48,47)	0.04 (0.03 to 0.06)	0.05 (0.04 to 0.07)		
Anti-18C [Month 2] (N=48,47)	6.21 (4.77 to 8.1)	6.12 (4.56 to 8.21)		
Anti-18C [Month 3] (N=47,45)	25.52 (20.66 to 31.53)	22.64 (18.14 to 28.26)		
Anti-19F [Month 0] (N=48,47)	0.06 (0.04 to 0.09)	0.08 (0.05 to 0.12)		
Anti-19F [Month 2] (N=48,47)	5.88 (4.44 to 7.8)	5.12 (3.79 to 6.94)		
Anti-19F [Month 3] (N=48,46)	18 (13.97 to 23.2)	14.46 (10.81 to 19.34)		
Anti-23F [Month 0] (N=48,47)	0.03 (0.03 to 0.04)	0.05 (0.03 to 0.07)		
Anti-23F [Month 2] (N=48,47)	0.5 (0.32 to 0.77)	0.35 (0.25 to 0.49)		
Anti-23F [Month 3] (N=47,46)	1.95 (1.32 to 2.87)	1.4 (1.05 to 1.87)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of antibodies against cross-reactive pneumococcal serotypes for subjects who received a two-dose primary vaccination without any booster dose

End point title	Concentration of antibodies against cross-reactive pneumococcal serotypes for subjects who received a two-dose primary vaccination without any booster dose ^[9]
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End point description:

Antibody concentrations against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A, -19A) were measured by 22F enzyme-linked immunosorbent assay (ELISA), presented as geometric mean concentrations (GMCs) and expressed in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 micrograms per milliliter (µg/mL). Antibody concentrations < 0.05 µg/mL were given an arbitrary value of half the cut-off for the purpose of GMC calculation.

End point type	Secondary
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End point timeframe:

Prior to (Month 0) the first vaccine dose, prior to (Month 2) and one month after (Month 3) the second vaccine dose

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: This endpoint is only reporting values for the Synflorix 12-23S Group and the Synflorix 12-23NS Group.

End point values	Synflorix 12-23S Group	Synflorix 12-23NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	47		
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-6A [Month 0] (N=45,44)	0.03 (0.03 to 0.03)	0.04 (0.03 to 0.05)		
Anti-6A [Month 2] (N=47,47)	0.15 (0.1 to 0.23)	0.12 (0.08 to 0.18)		

Anti-6A [Month 3] (N=47,46)	0.39 (0.23 to 0.66)	0.31 (0.2 to 0.48)		
Anti-19A [Month 0] (N=47,45)	0.06 (0.04 to 0.09)	0.07 (0.04 to 0.11)		
Anti-19A [Month 2] (N=48,47)	0.77 (0.5 to 1.17)	0.75 (0.47 to 1.19)		
Anti-19A [Month 3] (N=48,46)	3.15 (2.13 to 4.65)	2.79 (1.93 to 4.05)		

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic titers against vaccine pneumococcal serotypes for subjects receiving Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines

End point title	Opsonophagocytic titers against vaccine pneumococcal serotypes for subjects receiving Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines ^[10]
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End point description:

Opsonophagocytic activity has been assessed against vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (Opsono-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F) and presented as geometric mean titers (GMTs). The seropositivity cut-off for the assay was ≥ 8 . Antibody titers < 8 were given an arbitrary value of half the cut-off for the purpose of GMT calculation.

End point type	Secondary
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End point timeframe:

Prior to (Month 0) and one month after (Month 3) primary vaccination, prior to (Month 8) and one month after (Month 9) booster vaccination

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: This endpoint is only reporting values for the Tritanrix-HepB/Hib+Polio Sabin <6S Group and the Tritanrix-HepB/Hib+Polio Sabin <6NS Group.

End point values	Tritanrix-HepB/Hib+Polio Sabin <6S Group	Tritanrix-HepB/Hib+Polio Sabin <6NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	46	41		
Units: Titer				
geometric mean (confidence interval 95%)				
Opsono-1 Month 3 (N=45,41)	106.4 (56 to 202.2)	94.6 (49.9 to 179.5)		
Opsono-1 Month 8 (N=41,33)	11.7 (6.8 to 20.1)	10.9 (6 to 20.1)		
Opsono-1 Month 9 (N=41,35)	930.5 (606.3 to 1427.9)	750.4 (401.4 to 1403)		
Opsono-4 Month 3 (N=44,38)	1316.6 (1014 to 1709.7)	992.5 (680 to 1448.4)		
Opsono-4 Month 8 (N=40,31)	222.1 (130.6 to 377.8)	108.3 (51.6 to 227.6)		
Opsono-4 Month 9 (N=41,33)	2064.2 (1625.3 to 2621.8)	2079.3 (1425.7 to 3032.7)		

Opsono-5 Month 3 (N=44,41)	106.9 (66.8 to 171.2)	119.4 (81.4 to 175.2)		
Opsono-5 Month 8 (N=40,33)	14.9 (8.9 to 24.9)	15.8 (9.6 to 26.1)		
Opsono-5 Month 9 (N=41,33)	273.2 (200.6 to 372)	277.5 (168.8 to 456.1)		
Opsono-6B Month 3 (N=41,37)	1043.3 (605.3 to 1798.3)	446.2 (207.4 to 960)		
Opsono-6B Month 8 (N=39,32)	285.3 (150.1 to 542.1)	245.6 (115 to 524.3)		
Opsono-6B Month 9 (N=40,33)	952.2 (638.8 to 1419.3)	989.2 (530.6 to 1843.9)		
Opsono-7F Month 3 (N=42,37)	4644.1 (3519.3 to 6128.4)	4924.2 (3430.2 to 7068.8)		
Opsono-7F Month 8 (N=40,32)	1747.2 (1225.4 to 2491.3)	1585.7 (1133.8 to 2217.8)		
Opsono-7F Month 9 (N=39,32)	7262.9 (5257.6 to 10033.1)	8120.3 (5802.1 to 11364.8)		
Opsono-9V Month 3 (N=46,39)	1438.6 (1084 to 1909.3)	1116.8 (679.6 to 1835.2)		
Opsono-9V Month 8 (N=38,32)	215.5 (97.5 to 476.1)	244.5 (123.9 to 482.2)		
Opsono-9V Month 9 (N=40,32)	2062.3 (1569 to 2710.8)	2987.2 (2149.4 to 4151.6)		
Opsono-14 Month 3 (N=44,41)	1689.9 (1090.7 to 2618.2)	1062.3 (562.8 to 2005.2)		
Opsono-14 Month 8 (N=39,26)	215.9 (113.6 to 410.1)	132.5 (60.3 to 291.5)		
Opsono-14 Month 9 (N=40,33)	1571.5 (1114.2 to 2216.4)	1454.1 (741.8 to 2850.5)		
Opsono-18C Month 3 (N=40,37)	873.8 (591.7 to 1290.4)	524.7 (319.6 to 861.6)		
Opsono-18C Month 8 (N=39,30)	46.5 (28.5 to 75.7)	28.7 (17.5 to 47.3)		
Opsono-18C Month 9 (N=39,31)	1246 (776.7 to 1999)	1011.8 (686.4 to 1491.4)		
Opsono-19F Month 3 (N=43,39)	558.9 (376.3 to 830.2)	266.1 (148.2 to 477.8)		
Opsono-19F Month 8 (N=41,32)	60.7 (37.1 to 99.3)	43.4 (22.6 to 83.2)		
Opsono-19F Month 9 (N=40,33)	652.9 (413.3 to 1031.5)	486.7 (278.9 to 849.4)		
Opsono-23F Month 3 (N=44,37)	705.1 (309.2 to 1607.8)	759.7 (326.7 to 1766.6)		
Opsono-23F Month 8 (N=36,31)	85.2 (27.5 to 264.4)	41.6 (14.6 to 118.9)		
Opsono-23F Month 9 (N=39,33)	4231.2 (2793.7 to 6408.3)	1454 (736.1 to 2872.3)		

Statistical analyses

Secondary: Opsonophagocytic titers against cross-reactive pneumococcal serotypes for subjects receiving Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines

End point title	Opsonophagocytic titers against cross-reactive pneumococcal serotypes for subjects receiving Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines ^[11]
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End point description:

Opsonophagocytic activity has been assessed for cross-reactive vaccine pneumococcal serotypes 6A and 19A (Opsono-6A, Opsono-19A) and presented as geometric mean titers (GMTs). The seropositivity cut-off for the assay was ≥ 8 . Antibody titers < 8 were given an arbitrary value of half the cut-off for the purpose of GMT calculation.

End point type	Secondary
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End point timeframe:

Prior to (Month 0) and one month after (Month 3) primary vaccination, prior to (Month 8) and one month after (Month 9) booster vaccination

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: This endpoint is only reporting values for the Tritanrix-HepB/Hib+Polio Sabin <6S Group and the Tritanrix-HepB/Hib+Polio Sabin <6NS Group.

End point values	Tritanrix-HepB/Hib+Polio Sabin <6S Group	Tritanrix-HepB/Hib+Polio Sabin <6NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	41		
Units: Titers				
geometric mean (confidence interval 95%)				
Opsono-6A [Month 3] (N=42,41)	24.73 (11.46 to 53.37)	9.45 (5.32 to 16.75)		
Opsono-6A [Month 8] (N=40,33)	18.23 (8.97 to 37.09)	17.59 (8.08 to 38.3)		
Opsono-6A [Month 9] (N=38,32)	35.35 (15.6 to 80.12)	30.7 (12.14 to 77.64)		
Opsono-19A [Month 3] (N=38,34)	9.42 (5.65 to 15.7)	5.04 (3.83 to 6.63)		
Opsono-19A [Month 8] (N=34,23)	6.31 (4.28 to 9.32)	5.83 (3.95 to 8.61)		
Opsono-19A [Month 9] (N=26,28)	22.06 (9.49 to 51.3)	19.44 (10.25 to 36.86)		

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic titers against cross-reactive pneumococcal serotypes for subjects who received a two-dose primary vaccination followed by a booster dose

End point title	Opsonophagocytic titers against cross-reactive pneumococcal serotypes for subjects who received a two-dose primary
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End point description:

Opsonophagocytic activity has been assessed for cross-reactive vaccine pneumococcal serotypes 6A and 19A (Opsono-6A, Opsono-19A) and presented as geometric mean titers (GMTs). The seropositivity cut-off for the assay was ≥ 8 . Antibody titers < 8 were given an arbitrary value of half the cut-off for the purpose of GMT calculation.

End point type

Secondary

End point timeframe:

Prior to (Month 0) and one month after (Month 2) primary vaccination, prior to (Month 3) and one month after (Month 4) booster vaccination

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: This endpoint is only reporting values for Synflorix 7-11S Group and the Synflorix 7-11NS Group.

End point values	Synflorix 7-11S Group	Synflorix 7-11NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	45		
Units: Titers				
geometric mean (confidence interval 95%)				
Opsono-6A [Month 2] (N=49,39)	40.59 (19.11 to 86.23)	51.23 (22.85 to 114.88)		
Opsono-6A [Month 3] (N=44,45)	38.11 (17.04 to 85.21)	36.27 (16.89 to 77.89)		
Opsono-6A [Month 4] (N=45,43)	77.09 (35.58 to 167.04)	98.18 (43.05 to 223.96)		
Opsono-19A [Month 2] (N=40,31)	15.21 (7.95 to 29.08)	108.31 (49.55 to 236.78)		
Opsono-19A [Month 3] (N=37,26)	14.65 (7.71 to 27.81)	19.4 (8.04 to 46.82)		
Opsono-19A [Month 4] (N=31,29)	76.09 (30.5 to 189.83)	449.06 (170.05 to 1185.87)		
Opsono-6A [Month 0] (N=46,40)	4.81 (3.71 to 6.24)	5.02 (3.64 to 6.90)		
Opsono-19A [Month 0] (N=41,40)	4.49 (3.91 to 5.16)	4.33 (3.68 to 5.10)		

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic titers against vaccine pneumococcal serotypes for subjects who received a two-dose primary vaccination without any booster dose

End point title

Opsonophagocytic titers against vaccine pneumococcal serotypes for subjects who received a two-dose primary vaccination without any booster dose^[13]

End point description:

Opsonophagocytic activity has been assessed against vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (Opsono-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F) and presented as geometric mean titers (GMTs). The seropositivity cut-off for the assay was ≥ 8 . Antibody titers < 8 were given an arbitrary value of half the cut-off for the purpose of GMT calculation.

End point type

Secondary

End point timeframe:

Prior to (Month 0) the first vaccine dose, prior to (Month 2) and one month after (Month 3) the second vaccine dose

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: This endpoint is only reporting values for the Synflorix 12-23S Group and the Synflorix 12-23NS Group.

End point values	Synflorix 12-23S Group	Synflorix 12-23NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	47	45		
Units: Titer				
geometric mean (confidence interval 95%)				
Opsono-1 Month 2 (N=46,45)	9.3 (6.1 to 14.3)	10.9 (6.8 to 17.4)		
Opsono-1 Month 3 (N=45,43)	195.7 (119.9 to 319.3)	115.1 (64 to 206.8)		
Opsono-4 Month 2 (N=44,43)	1086.3 (758.4 to 1555.9)	1539.4 (1128.4 to 2100.1)		
Opsono-4 Month 3 (N=44,43)	2089.7 (1635 to 2670.8)	3193.9 (2241.3 to 4551.4)		
Opsono-5 Month 2 (N=45,45)	9.8 (7.1 to 13.7)	9.6 (6.6 to 13.7)		
Opsono-5 Month 3 (N=44,44)	151.3 (99.8 to 229.2)	84 (53.5 to 131.8)		
Opsono-6B Month 2 (N=41,42)	345.1 (172.4 to 690.7)	278.4 (131.8 to 588.4)		
Opsono-6B Month 3 (N=43,43)	748.4 (425.9 to 1315)	866.4 (511.8 to 1466.7)		
Opsono-7F Month 2 (N=44,45)	5462.3 (4108.9 to 7261.4)	5802.2 (4678.6 to 7195.6)		
Opsono-7F Month 3 (N=44,42)	10279.4 (7836.7 to 13483.6)	10131.4 (8303.7 to 12361.6)		
Opsono-9V Month 2 (N=43,44)	1976.2 (1392.6 to 2804.4)	2359 (1514.3 to 3674.9)		
Opsono-9V Month 3 (N=44,43)	3778.2 (2880 to 4956.4)	4276.8 (3122.3 to 5858.3)		
Opsono-14 Month 2 (N=42,40)	711.2 (400.7 to 1262.4)	865.6 (583.2 to 1284.9)		
Opsono-14 Month 3 (N=45,40)	2704.5 (1856.4 to 3940)	2737.5 (1890 to 3965.1)		
Opsono-18C Month 2 (N=32,34)	1035.5 (507.6 to 2112.5)	449.2 (222.8 to 905.9)		
Opsono-18C Month 3 (N=40,40)	2873.1 (2070 to 3987.6)	2126.8 (1509.7 to 2996.3)		
Opsono-19F Month 2 (N=44,43)	229.1 (132.9 to 395)	248 (143 to 430.1)		
Opsono-19F Month 3 (N=45,43)	1845.3 (1169.3 to 2912.1)	1271.4 (825.4 to 1958.3)		

Opsono-23F Month 2 (N=44,44)	2572.2 (1264.1 to 5233.9)	2433.6 (1309.7 to 4522)		
Opsono-23F Month 3 (N=42,41)	5016.6 (3176.6 to 7922.4)	5325.4 (2857.8 to 9923.9)		
Opsono-1 Month 0 (N=47,43)	6.9 (4.5 to 10.8)	5.6 (4.2 to 7.6)		
Opsono-4 Month 0 (N=46,44)	8.0 (4.7 to 13.6)	7.3 (4.3 to 12.3)		
Opsono-5 Month 0 (N=47,45)	5.5 (4.2 to 7.4)	4.4 (3.6 to 5.4)		
Opsono-6B Month 0 (N=41,38)	13.6 (6.7 to 27.6)	9.9 (5.2 to 18.7)		
Opsono-7F Month 0 (N=44,36)	1436.6 (1014.4 to 2034.6)	1228.1 (783.3 to 1925.5)		
Opsono-9V Month 0 (N=40,37)	119.5 (50.4 to 283.2)	81.3 (35.7 to 185.0)		
Opsono-14 Month 0 (N=40,34)	16.3 (8.3 to 31.8)	12.0 (5.3 to 27.0)		
Opsono-18C Month 0 (N=44,40)	4.9 (4.0 to 6.0)	4.0 (4.0 to 4.0)		
Opsono-19F Month 0 (N=46,42)	5.5 (5.5 to 7.3)	4.0 (4.0 to 4.0)		
Opsono-23F Month 0 (N=39,38)	68.1 (21.1 to 219.6)	37.6 (12.3 to 114.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic titers against cross-reactive pneumococcal serotypes for subjects who received a two-dose primary vaccination without any booster dose

End point title	Opsonophagocytic titers against cross-reactive pneumococcal serotypes for subjects who received a two-dose primary vaccination without any booster dose ^[14]
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End point description:

Opsonophagocytic activity has been assessed for cross-reactive vaccine pneumococcal serotypes 6A and 19A (Opsono-6A, Opsono-19A) and presented as geometric mean titers (GMTs). The seropositivity cut-off for the assay was ≥ 8 . Antibody titers < 8 were given an arbitrary value of half the cut-off for the purpose of GMT calculation.

End point type	Secondary
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End point timeframe:

Prior to (Month 0) the first vaccine dose, prior to (Month 2) and one month after (Month 3) the second vaccine dose

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: This endpoint is only reporting values for the Synflorix 12-23S Group and the Synflorix 12-23NS Group.

End point values	Synflorix 12-23S Group	Synflorix 12-23NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	42		
Units: Titers				
geometric mean (confidence interval 95%)				
Opsono-6A [Month 2] (N=44,42)	82.82 (40.27 to 170.33)	77.25 (31.81 to 187.64)		
Opsono-6A [Month 3] (N=40,39)	147.91 (63.11 to 346.68)	157.37 (59.23 to 418.11)		
Opsono-19A [Month 2] (N=23,27)	28.37 (11.84 to 67.98)	25.68 (11.6 to 56.84)		
Opsono-19A [Month 3] (N=19,23)	214.17 (75.58 to 606.93)	321.14 (144.75 to 712.5)		
Opsono-6A [Month 0] (N=44,40)	9.26 (5.76 to 14.89)	6.35 (4.02 to 10.02)		
Opsono-19A [Month 0] (N=44,40)	5.85 (4.27 to 8.01)	6.32 (4.09 to 9.76)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of antibodies against protein D (PD) for subjects who received a two-dose primary vaccination followed by a booster dose

End point title	Concentration of antibodies against protein D (PD) for subjects who received a two-dose primary vaccination followed by a booster dose ^[15]
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End point description:

Anti-PD antibody concentrations were measured by enzyme-linked immunosorbent assay (ELISA), presented as geometric mean concentrations (GMCs) and expressed in ELISA units per milliliter (EL.U/mL). The seropositivity cut-off of the assay was an antibody concentration ≥ 100 EL.U/mL. Antibody concentrations < 100 EL.U/mL were given an arbitrary value of half the cut-off for the purpose of GMC calculation.

End point type	Secondary
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End point timeframe:

Prior to (Month 0) and one month after (Month 2) primary vaccination, prior to (Month 3) and one month after (Month 4) booster vaccination

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: This endpoint is only reporting values for Synflorix 7-11S Group and the Synflorix 7-11NS Group.

End point values	Synflorix 7-11S Group	Synflorix 7-11NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD [Month 0] (N=47,48)	72.73 (57.23 to 92.42)	88.74 (70.85 to 111.13)		

Anti-PD [Month 2] (N=50,50)	1313.39 (1014.3 to 1700.67)	1489.78 (1171.98 to 1893.76)		
Anti-PD [Month 3] (N=50,49)	932.52 (732.63 to 1186.96)	1063.54 (844.52 to 1339.37)		
Anti-PD [Month 4] (N=49,48)	2695.5 (2150.74 to 3378.24)	2638.27 (2049.91 to 3395.49)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of antibodies against protein D (PD) for subjects who received a two-dose primary vaccination without any booster dose

End point title	Concentration of antibodies against protein D (PD) for subjects who received a two-dose primary vaccination without any booster dose ^[16]
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End point description:

Anti-PD antibody concentrations were measured by enzyme-linked immunosorbent assay (ELISA), presented as geometric mean concentrations (GMCs) and expressed in ELISA units per milliliter (EL.U/mL). The seropositivity cut-off of the assay was an antibody concentration ≥ 100 EL.U/mL. Antibody concentrations < 100 EL.U/mL were given an arbitrary value of half the cut-off for the purpose of GMC calculation.

End point type	Secondary
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End point timeframe:

Prior to (Month 0) the first vaccine dose, prior to (Month 2) and one month after (Month 3) the second vaccine dose

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: This endpoint is only reporting values for the Synflorix 12-23S Group and the Synflorix 12-23NS Group.

End point values	Synflorix 12-23S Group	Synflorix 12-23NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	47		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD [Month 0] (N=47,46)	79.59 (62.08 to 102.04)	76.22 (61.39 to 94.63)		
Anti-PD [Month 2] (N=48,47)	199.23 (150.51 to 263.72)	184.34 (140.21 to 242.35)		
Anti-PD [Month 3] (N=48,46)	1376.56 (1020.71 to 1856.46)	760.99 (553.23 to 1046.77)		

Statistical analyses

Secondary: Concentration of antibodies against diphtheria toxoid (DT) and tetanus toxoid (TT) for subjects who were co-administered Tritanrix-HepB/Hib vaccine

End point title	Concentration of antibodies against diphtheria toxoid (DT) and tetanus toxoid (TT) for subjects who were co-administered Tritanrix-HepB/Hib vaccine ^[17]
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End point description:

Anti-DT and anti-TT antibody concentrations are presented as geometric mean concentrations (GMCs) and expressed in international units per milliliter (IU/mL). Seroprotection status was defined as anti-DT or anti-TT antibody concentration \geq than 0.1 IU/mL.

End point type	Secondary
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End point timeframe:

Prior to (Month 0) and one month after (Month 3) primary vaccination, prior to (Month 8) and one month after (Month 9) booster vaccination

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: This endpoint is only reporting values for the Tritanrix-HepB/Hib+Polio Sabin <6S Group and the Tritanrix-HepB/Hib+Polio Sabin <6NS Group.

End point values	Tritanrix-HepB/Hib+Polio Sabin <6S Group	Tritanrix-HepB/Hib+Polio Sabin <6NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	46		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-DT Month 0 (N=48,45)	0.07 (0.05 to 0.08)	0.06 (0.05 to 0.07)		
Anti-DT Month 3 (N=48,46)	3.22 (2.59 to 4)	3.5 (2.82 to 4.34)		
Anti-DT Month 8 (N=44,37)	0.62 (0.5 to 0.77)	0.9 (0.72 to 1.12)		
Anti-DT Month 9 (N=44,38)	6.58 (5.44 to 7.97)	7.55 (6.11 to 9.32)		
Anti-TT Month 0 (N=48,46)	1.54 (1.13 to 2.09)	1.22 (0.85 to 1.76)		
Anti-TT Month 3 (N=48,46)	4.04 (3.26 to 5.01)	4.13 (3.27 to 5.22)		
Anti-TT Month 8 (N=44,38)	1.19 (0.96 to 1.48)	1.33 (1.08 to 1.63)		
Anti-TT Month 9 (N=44,38)	10.88 (9.24 to 12.81)	11.11 (9.62 to 12.83)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against Bordetella pertussis (BPT) for subjects who were co-administered Tritanrix-HepB/Hib vaccine

End point title	Concentrations of antibodies against Bordetella pertussis (BPT) for subjects who were co-administered Tritanrix-HepB/Hib
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End point description:

Anti-BPT antibody concentrations are presented as geometric mean concentrations (GMCs) and expressed in enzyme-linked immunosorbent assay (ELISA) units per milliliter (EL.U/mL). The seropositivity cut-off of the assay was an antibody concentration ≥ 15 EL.U/mL.

End point type

Secondary

End point timeframe:

Prior to (Month 0) and one month after (Month 3) primary vaccination, prior to (Month 8) and one month after (Month 9) booster vaccination

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: This endpoint is only reporting values for the Tritanrix-HepB/Hib+Polio Sabin <6S Group and the Tritanrix-HepB/Hib+Polio Sabin <6NS Group.

End point values	Tritanrix-HepB/Hib+Polio Sabin <6S Group	Tritanrix-HepB/Hib+Polio Sabin <6NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	48	46		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-BPT Month 0 (N=48,46)	7.71 (7.29 to 8.16)	7.77 (7.39 to 8.17)		
Anti-BPT Month 3 (N=48,46)	105.61 (86.93 to 128.3)	101.74 (84.56 to 122.42)		
Anti-BPT Month 8 (N=44,38)	22.67 (17.45 to 29.45)	22.69 (17.88 to 28.8)		
Anti-BPT Month 9 (N=44,38)	177.87 (152.1 to 207.99)	190.58 (167.67 to 216.63)		

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic titers against vaccine pneumococcal serotypes for subjects who received a two-dose primary vaccination followed by a booster dose

End point title

Opsonophagocytic titers against vaccine pneumococcal serotypes for subjects who received a two-dose primary vaccination followed by a booster dose^[19]

End point description:

Opsonophagocytic activity has been assessed against vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (Opsono-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F) and presented as geometric mean titers (GMTs). The seropositivity cut-off for the assay was ≥ 8 . Antibody titers < 8 were given an arbitrary value of half the cut-off for the purpose of GMT calculation.

End point type

Secondary

End point timeframe:

Prior to (Month 0) and one month after (Month 2) primary vaccination, prior to (Month 3) and one month after (Month 4) booster vaccination

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: This endpoint is only reporting values for Synflorix 7-11S Group and the Synflorix 7-11NS Group.

End point values	Synflorix 7-11S Group	Synflorix 7-11NS Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	49	47		
Units: Titers				
geometric mean (confidence interval 95%)				
Opsono-1 Month 0 (N=47,43)	4.9 (3.8 to 6.3)	4.5 (3.6 to 5.7)		
Opsono-1 Month 2 (N=48,45)	134.7 (83.6 to 216.9)	88.1 (53.7 to 144.6)		
Opsono-1 Month 3 (N=48,46)	74.2 (42.6 to 129.3)	48 (26.6 to 86.7)		
Opsono-1 Month 4 (N=48,44)	516.0 (307.6 to 865.7)	511.3 (293.2 to 891.8)		
Opsono-4 Month 0 (N=44,44)	5.1 (3.6 to 7.2)	11.8 (5.7 to 24.5)		
Opsono-4 Month 2 (N=49,44)	1636.3 (1217.5 to 2199.2)	1771.1 (1359.0 to 2308.2)		
Opsono-4 Month 3 (N=45,45)	812.7 (584.5 to 1130.1)	1048.3 (790.4 to 1390.3)		
Opsono-4 Month 4 (N=48,43)	2130.5 (1639.1 to 2769.2)	2415.5 (1686.5 to 3459.8)		
Opsono-5 Month 0 (N=47,44)	4.4 (3.8 to 5.1)	4.0 (4.0 to 4.0)		
Opsono-5 Month 2 (N=49,46)	105.7 (67.7 to 165.1)	85.8 (59.4 to 124.0)		
Opsono-5 Month 3 (N=47,47)	54.1 (34.9 to 83.6)	49.2 (31.7 to 76.3)		
Opsono-5 Month 4 (N=48,43)	277.4 (180.7 to 425.7)	289.6 (190.9 to 439.3)		
Opsono-6B Month 0 (N=43,41)	7.9 (4.6 to 13.8)	8.5 (4.7 to 15.4)		
Opsono-6B Month 2 (N=48,43)	702.5 (413.2 to 1194.2)	696.6 (388.5 to 1249.2)		
Opsono-6B Month 3 (N=44,45)	708.3 (422.9 to 1186.1)	615.5 (337.3 to 1123.1)		
Opsono-6B Month 4 (N=46,43)	1360.0 (860.2 to 2150.3)	1305.4 (731.9 to 2328.4)		
Opsono-7F Month 0 (N=41,40)	215.3 (91.2 to 508.1)	643.5 (293.4 to 1411.7)		
Opsono-7F Month 2 (N=47,40)	6694.3 (5055.1 to 8864.9)	10452.0 (7782.7 to 14036.6)		
Opsono-7F Month 3 (N=46,46)	7776.9 (6000.8 to 10078.7)	9336.3 (6752.4 to 12908.9)		
Opsono-7F Month 4 (N=47,39)	10854.8 (9051.6 to 13017.2)	9362.8 (6882.3 to 12737.3)		
Opsono-9V Month 0 (N=42,44)	16.9 (8.3 to 34.5)	20.3 (9.2 to 44.5)		
Opsono-9V Month 2 (N=48,42)	2858.2 (1875.3 to 4356.2)	2667.9 (1677.9 to 4242.0)		

Opsono-9V Month 3 (N=44,46)	1982.9 (1192.1 to 3298.2)	1986.2 (1167.8 to 3378.2)		
Opsono-9V Month 4 (N=48,41)	3047.9 (2389.7 to 3887.3)	2719.2 (1681.0 to 4398.9)		
Opsono-14 Month 0 (N=40,39)	5.5 (3.8 to 8.1)	5.9 (3.8 to 9.1)		
Opsono-14 Month 2 (N=44,43)	2109.5 (1299.0 to 3425.9)	4009.9 (2501.9 to 6426.7)		
Opsono-14 Month 3 (N=46,46)	1431.6 (865.2 to 2368.6)	2128.3 (1477.5 to 3065.9)		
Opsono-14 Month 4 (N=46,40)	3414.9 (2237.4 to 5211.9)	3717.3 (2403.9 to 5748.5)		
Opsono-18C Month 0 (N=44,43)	4.1 (3.9 to 4.5)	4.6 (3.4 to 6.2)		
Opsono-18C Month 2 (N=39,37)	744.4 (393.3 to 1409.2)	1605.6 (937.1 to 2751.1)		
Opsono-18C Month 3 (N=40,42)	411.4 (214.4 to 789.7)	746.4 (430.5 to 1294.1)		
Opsono-18C Month 4 (N=44,40)	2218.9 (1577.5 to 3121.2)	3238.7 (1874.7 to 5595.0)		
Opsono-19F Month 0 (N=44,43)	4.2 (3.8 to 4.7)	4.0 (4.0 to 4.0)		
Opsono-19F Month 2 (N=47,43)	393.4 (393.4 to 722.0)	491.5 (256.8 to 940.6)		
Opsono-19F Month 3 (N=45,46)	160.2 (86.8 to 295.6)	279.5 (161.1 to 484.9)		
Opsono-19F Month 4 (N=47,41)	1347.7 (813.6 to 2232.3)	1174.4 (605.6 to 2277.3)		
Opsono-23F Month 0 (N=43,40)	7.6 (4.1 to 13.9)	15.3 (6.4 to 36.6)		
Opsono-23F Month 2 (N=46,44)	1545.1 (788.3 to 3028.2)	2107.5 (1155.0 to 3845.5)		
Opsono-23F Month 3 (N=40,46)	1168.8 (560.8 to 2435.8)	1026.2 (458.3 to 2298.0)		
Opsono-23F Month 4 (N=47,43)	2038.8 (977.1 to 4254.4)	3525.1 (1974.2 to 6294.4)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited local and general symptoms: during the 4-day (Days 0-3) period following each vaccination dose; Unsolicited AEs: within the 31-day (Days 0-30) period following each vaccination; SAEs: throughout the study, from Day 0 up to Month 9.

Adverse event reporting additional description:

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

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.0
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Reporting groups

Reporting group title	Tritanrix-HepB/Hib+Polio Sabin <6S Group
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Reporting group description:

Children below (<) 6 months of age at time of enrolment, diagnosed with sickle cell disease (S), who received a 3-dose primary vaccination at Study Months 0, 1 and 2 with Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines, followed by a booster vaccination at Study Month 8

Reporting group title	Tritanrix-HepB/Hib+Polio Sabin <6NS Group
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Reporting group description:

Healthy children, below (<) 6 months of age at time of enrolment, who received a 3-dose primary vaccination at Study Months 0, 1 and 2 with Synflorix vaccine co-administered with Tritanrix-HepB/Hib and Polio Sabin vaccines, followed by a booster vaccination at Study Month 8.

Reporting group title	Synflorix 7-11S Group
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Reporting group description:

Children between 7-11 months of age at time of enrolment, diagnosed with sickle cell disease (S), who received a 2-dose primary vaccination at Study Months 0 and 1 with Synflorix vaccine, followed by a booster vaccination at Study Month 3.

Reporting group title	Synflorix 7-11NS Group
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Reporting group description:

Healthy children between 7-11 months of age at time of enrolment, who received a 2-dose primary vaccination at Study Months 0 and 1 with Synflorix vaccine, followed by a booster vaccination at Study Month 3.

Reporting group title	Synflorix 12-23S Group
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Reporting group description:

Children between 12-23 months of age at time of enrolment, diagnosed with sickle cell disease (S), who received a 2-dose vaccination with Synflorix vaccine, at Study Months 0 and 2.

Reporting group title	Synflorix 12-23NS Group
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Reporting group description:

Healthy children between 12-23 months of age at time of enrolment, who received a 2-dose vaccination with Synflorix vaccine, at Study Months 0 and 2.

Serious adverse events	Tritanrix-HepB/Hib+Polio Sabin <6S Group	Tritanrix-HepB/Hib+Polio Sabin <6NS Group	Synflorix 7-11S Group
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 50 (6.00%)	9 / 50 (18.00%)	3 / 50 (6.00%)
number of deaths (all causes)	1	1	1
number of deaths resulting from			

adverse events			
General disorders and administration site conditions			
Pyrexia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Gastrointestinal disorders			
Enteritis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 50 (2.00%)	6 / 50 (12.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 1	0 / 6	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaria			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 50 (6.00%)	3 / 50 (6.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bronchitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis rotavirus			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis Salmonella			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Osteomyelitis acute			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Malnutrition			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0

Serious adverse events	Synflorix 7-11NS Group	Synflorix 12-23S Group	Synflorix 12-23NS Group
Total subjects affected by serious			

adverse events			
subjects affected / exposed	4 / 50 (8.00%)	2 / 50 (4.00%)	2 / 50 (4.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
General disorders and administration site conditions			
Pyrexia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Enteritis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 50 (4.00%)	0 / 50 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaria			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 50 (2.00%)	1 / 50 (2.00%)	2 / 50 (4.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	1 / 50 (2.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis rotavirus			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis Salmonella			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis acute			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Malnutrition			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 50 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Tritanrix-HepB/Hib+Polio Sabin <6S Group	Tritanrix-HepB/Hib+Polio Sabin <6NS Group	Synflorix 7-11S Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	50 / 50 (100.00%)	49 / 50 (98.00%)	47 / 50 (94.00%)
Congenital, familial and genetic disorders			
Sickle cell anaemia with crisis			
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	3 / 50 (6.00%)
occurrences (all)	1	0	5
General disorders and administration site conditions			
Pain			
subjects affected / exposed	23 / 50 (46.00%)	26 / 50 (52.00%)	15 / 50 (30.00%)
occurrences (all)	30	31	17
Pyrexia			
subjects affected / exposed	49 / 50 (98.00%)	47 / 50 (94.00%)	37 / 50 (74.00%)
occurrences (all)	143	123	63
Eye disorders			
Conjunctivitis			
subjects affected / exposed	2 / 50 (4.00%)	3 / 50 (6.00%)	1 / 50 (2.00%)
occurrences (all)	2	3	1
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	8 / 50 (16.00%)	6 / 50 (12.00%)	4 / 50 (8.00%)
occurrences (all)	8	6	4
Enteritis			
subjects affected / exposed	2 / 50 (4.00%)	5 / 50 (10.00%)	7 / 50 (14.00%)
occurrences (all)	2	5	7
Abdominal pain			
subjects affected / exposed	3 / 50 (6.00%)	1 / 50 (2.00%)	2 / 50 (4.00%)
occurrences (all)	3	1	2
Respiratory, thoracic and mediastinal			

disorders Cough subjects affected / exposed occurrences (all)	4 / 50 (8.00%) 4	5 / 50 (10.00%) 5	3 / 50 (6.00%) 3
Psychiatric disorders Irritability subjects affected / exposed occurrences (all)	9 / 50 (18.00%) 9	6 / 50 (12.00%) 6	0 / 50 (0.00%) 0
Infections and infestations Malaria subjects affected / exposed occurrences (all)	10 / 50 (20.00%) 10	13 / 50 (26.00%) 14	18 / 50 (36.00%) 19
Bronchitis subjects affected / exposed occurrences (all)	9 / 50 (18.00%) 10	10 / 50 (20.00%) 12	6 / 50 (12.00%) 6
Gastroenteritis subjects affected / exposed occurrences (all)	6 / 50 (12.00%) 6	6 / 50 (12.00%) 7	3 / 50 (6.00%) 3
Rhinitis subjects affected / exposed occurrences (all)	4 / 50 (8.00%) 4	7 / 50 (14.00%) 7	5 / 50 (10.00%) 6
Nasopharyngitis subjects affected / exposed occurrences (all)	7 / 50 (14.00%) 7	5 / 50 (10.00%) 6	3 / 50 (6.00%) 3
Gastrointestinal fungal infection subjects affected / exposed occurrences (all)	4 / 50 (8.00%) 5	6 / 50 (12.00%) 6	3 / 50 (6.00%) 3
Ear infection subjects affected / exposed occurrences (all)	3 / 50 (6.00%) 3	2 / 50 (4.00%) 2	0 / 50 (0.00%) 0

Non-serious adverse events	Synflorix 7-11NS Group	Synflorix 12-23S Group	Synflorix 12-23NS Group
Total subjects affected by non-serious adverse events subjects affected / exposed	47 / 50 (94.00%)	41 / 50 (82.00%)	31 / 50 (62.00%)
Congenital, familial and genetic disorders Sickle cell anaemia with crisis			

subjects affected / exposed occurrences (all)	0 / 50 (0.00%) 0	10 / 50 (20.00%) 13	0 / 50 (0.00%) 0
General disorders and administration site conditions			
Pain			
subjects affected / exposed	15 / 50 (30.00%)	14 / 50 (28.00%)	9 / 50 (18.00%)
occurrences (all)	17	16	9
Pyrexia			
subjects affected / exposed	35 / 50 (70.00%)	29 / 50 (58.00%)	21 / 50 (42.00%)
occurrences (all)	52	33	28
Eye disorders			
Conjunctivitis			
subjects affected / exposed	1 / 50 (2.00%)	2 / 50 (4.00%)	0 / 50 (0.00%)
occurrences (all)	1	2	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	4 / 50 (8.00%)	1 / 50 (2.00%)	1 / 50 (2.00%)
occurrences (all)	4	1	1
Enteritis			
subjects affected / exposed	4 / 50 (8.00%)	0 / 50 (0.00%)	1 / 50 (2.00%)
occurrences (all)	4	0	1
Abdominal pain			
subjects affected / exposed	0 / 50 (0.00%)	0 / 50 (0.00%)	0 / 50 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 50 (4.00%)	1 / 50 (2.00%)	0 / 50 (0.00%)
occurrences (all)	2	1	0
Psychiatric disorders			
Irritability			
subjects affected / exposed	0 / 50 (0.00%)	2 / 50 (4.00%)	0 / 50 (0.00%)
occurrences (all)	0	2	0
Infections and infestations			
Malaria			
subjects affected / exposed	18 / 50 (36.00%)	10 / 50 (20.00%)	8 / 50 (16.00%)
occurrences (all)	20	10	8
Bronchitis			

subjects affected / exposed	9 / 50 (18.00%)	1 / 50 (2.00%)	4 / 50 (8.00%)
occurrences (all)	10	1	4
Gastroenteritis			
subjects affected / exposed	7 / 50 (14.00%)	1 / 50 (2.00%)	5 / 50 (10.00%)
occurrences (all)	7	1	5
Rhinitis			
subjects affected / exposed	4 / 50 (8.00%)	3 / 50 (6.00%)	4 / 50 (8.00%)
occurrences (all)	4	3	4
Nasopharyngitis			
subjects affected / exposed	8 / 50 (16.00%)	4 / 50 (8.00%)	5 / 50 (10.00%)
occurrences (all)	8	4	5
Gastrointestinal fungal infection			
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	0 / 50 (0.00%)
occurrences (all)	1	0	0
Ear infection			
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	1 / 50 (2.00%)
occurrences (all)	1	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 April 2010	The oral polio vaccine was to be provided in multidose vials Changes in the randomization of treatment Inconsistencies regarding the age for booster vaccination in the 7-11 month groups Changes in the priority ranking of immunological assays Changes in the definition of the Epochs Update of Rationale of the study
03 September 2010	<ul style="list-style-type: none">•For clarification, the inclusion criteria for children with sickle cell disease have been further detailed.•An additional blood sample for SCD testing was planned to be taken at the pre-vaccination timepoint from subjects aged 7-11 and 12-23 months without hemoglobin status confirmed by electrophoresis available.•Presentation of oral polio vaccine that was to be used has changed: 10- or 20-dose vials were used. In addition, the use of one 10- or 20-dose vial to vaccinate up to 10 or 20 subjects, respectively, on the same day was allowed.•The immunogenicity objectives related to the co-administered OPV have been removed since there are no plans to test poliovirus immune response.•The contact details for the emergency code break have been clarified.
08 May 2012	The main changes and their rationale are the following: <ul style="list-style-type: none">•Additional information was given about administration of vaccines through the local EPI program.•Extension of the recruitment period due to a lower enrolment rate than expected.•Additional exclusion criterion for children of the <6S and <6NS groups to clarify differences between groups with regard to administration of vaccines included in the EPI program either as study vaccines or outside the study.•Additional exclusion criterion for all groups, i.e. exclusion of subjects being heterozygous or carriers of abnormal haemoglobin (e.g. haemoglobin S, haemoglobin C) who are not considered to have SCD, to avoid potential bias and to keep homogeneity of the examined groups.
09 April 2013	In the past few months, GSK Biologicals has been investigating the quality of some serology assays used in clinical studies, including the Streptococcus pneumonia opsonophagocytic activity (OPA) assay used in the present trial. This protocol amendment reflected the fact that delays in the availability of the assay results would lead to changes in the analysis plan. Therefore, the sequence of analysis has been modified to perform study analysis in one final step on all immunogenicity and safety data obtained up to one month after administration of the last dose of study vaccine for all study groups. The results of this final analysis were presented in a final clinical study report.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported