Clinical trial results:
A phase III, open study in children previously enrolled in study 10PN-PD-DIT-037 (111188) to assess the immunogenicity, safety and reactogenicity of GlaxoSmithKline (GSK) Biologicals' 10-valent pneumococcal conjugate vaccine when administered as a booster dose at either 9-18 or 15-18 months of age in primed children or when administered as a catch-up vaccination (2+1 schedule) in unprimed children during the second year of life.

Summary

EudraCT number	2011-002140-27
Trial protocol	Outside EU/EEA
Global end of trial date	19 August 2011

Results information

Result version number	v3 (current)
This version publication date	15 December 2022
First version publication date	24 May 2015
Version creation reason	• Correction of full data set Correction of full data set and alingment between registries.

Trial information

Trial identification

Sponsor protocol code	112909

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01030822
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 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)	EMEA-000673-PIP01-09
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No	No

1901/2006 apply to this trial?	

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	22 March 2012
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 August 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the immune responses following vaccination with a booster dose of the 10Pn-PD-DiT vaccine administered at either 9-12 or 15-18 months of age in children previously vaccinated with the 10Pn-PD-DiT vaccine in study 10PN-PD-DIT-037 (111188) according to a 3-dose primary vaccination at 6, 10 and 14 weeks of age.

Protection of trial subjects:

All subjects were supervised closely for at least 30 minutes following vaccination with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccines. Subjects were followed-up for one month (minimum 30 days) following administration of the last dose of study vaccines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 April 2010
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	India: 287
Worldwide total number of subjects	287
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)	287

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:

A total of 287 participants were randomized, but 2 participants withdrew their consent and 3 participants moved away from the study area, therefore only 282 received a study vaccine.

Period 1

Period 1 title	Overall period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Synflorix 1 Group

Arm description:

Subjects who were previously primed with a 3-dose primary vaccination of Synflorix vaccine in the 10PN-PD-DIT-037 (111188) study, received a booster dose of Synflorix vaccine, administered intramuscularly in the right or left thigh, at 9-18 months of age.

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

Dosage and administration details:

1 booster dose at 9-18 months of age, administered in in the right or left thigh.

Arm title	Synflorix 2 Group

Arm description:

Subjects who were previously primed with a 3-dose primary vaccination of Synflorix vaccine in the 10PN-PD-DIT-037 (111188) study, received a booster dose of Synflorix vaccine, administered intramuscularly in the right or left thigh, at 15-18 months of age.

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

Dosage and administration details:

1 booster dose at 15-18 months of age, administered in in the right or left thigh.

Arm title	Tritanrix-HepB+Hiberix Group

Arm description:

Unprimed subjects who were previously vaccinated with Tritanrix-HepB and Hiberix vaccines in the Control Group of the 10PN-PD-DIT-037 (111188) study, received a catch-up vaccination with Synflorix vaccine (2 primary doses +1 booster dose), administered intramuscularly in the right or left thigh, during their second year of life: 2+1 catch-up vaccination starting at 12-18 months of age with an interval of at least 8 weeks (56-118 days) between primary doses; the booster dose was administered at 18-24 months of age.

Arm type	Active comparator

Investigational medicinal product name	Synflorix
Investigational medicinal product code	
Other name	10Pn-PD-DiT
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 booster dose at 15-18 months of age, administered in in the right or left thigh.

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

Dosage and administration details:

Unprimed subjects previously vaccinated with 3 doses of TritanrixTM-HepB vaccines in the Control Group of study 10PN-PD-DIT-037.

Investigational medicinal product name	Hiberix
Investigational medicinal product code	
Other name	Hib
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Unprimed subjects previously vaccinated with 3 doses of Hiberix vaccines in the Control Group of study 10PN-PD-DIT-037.

Number of subjects in period 1[1]	Synflorix 1 Group	Synflorix 2 Group	Tritanrix-HepB+Hiberix Group
Started	100	95	87
Completed	69	71	61
Not completed	31	24	26
Consent withdrawn by subject	16	13	16
Lost to follow-up	9	4	7
Moved/migrated from study area	6	7	3

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: A total of 287 participants were randomized, but 2 participants withdrew their consent and 3 participants moved away from the study area, therefore only 282 received a study vaccine.

Baseline characteristics

Reporting groups	
Reporting group title	Synflorix 1 Group
Reporting group description:	
Subjects who were previously primed with a 3-dose primary vaccination of Synflorix vaccine in the 10PN-PD-DIT-037 (111188) study, received a booster dose of Synflorix vaccine, administered intramuscularly in the right or left thigh, at 9-18 months of age.	
Reporting group title	Synflorix 2 Group
Reporting group description:	
Subjects who were previously primed with a 3-dose primary vaccination of Synflorix vaccine in the 10PN-PD-DIT-037 (111188) study, received a booster dose of Synflorix vaccine, administered intramuscularly in the right or left thigh, at 15-18 months of age.	
Reporting group title	Tritanrix-HepB+Hiberix Group
Reporting group description:	
Unprimed subjects who were previously vaccinated with Tritanrix-HepB and Hiberix vaccines in the Control Group of the 10PN-PD-DIT-037 (111188) study, received a catch-up vaccination with Synflorix vaccine (2 primary doses +1 booster dose), administered intramuscularly in the right or left thigh, during their second year of life: 2+1 catch-up vaccination starting at 12-18 months of age with an interval of at least 8 weeks (56-118 days) between primary doses; the booster dose was administered at 18-24 months of age.	

Reporting group values	Synflorix 1 Group	Synflorix 2 Group	Tritanrix-HepB+Hiberix Group
Number of subjects	100	95	87
Age categorical			
Units: Subjects			
Age continuous			
Units: months			
arithmetic mean	12.5	15.6	16.1
standard deviation	± 2.74	± 1.27	± 1.18
Gender categorical			
Units: Subjects			
Female	39	50	48
Male	61	45	39

Reporting group values	Total		
Number of subjects	282		
Age categorical			
Units: Subjects			
Age continuous			
Units: months			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	137		
Male	145		

End points

End points reporting groups

Reporting group title	Synflorix 1 Group

Reporting group description:

Subjects who were previously primed with a 3-dose primary vaccination of Synflorix vaccine in the 10PN-PD-DIT-037 (111188) study, received a booster dose of Synflorix vaccine, administered intramuscularly in the right or left thigh, at 9-18 months of age.

Reporting group title	Synflorix 2 Group

Reporting group description:

Subjects who were previously primed with a 3-dose primary vaccination of Synflorix vaccine in the 10PN-PD-DIT-037 (111188) study, received a booster dose of Synflorix vaccine, administered intramuscularly in the right or left thigh, at 15-18 months of age.

Reporting group title	Tritanrix-HepB+Hiberix Group

Reporting group description:

Unprimed subjects who were previously vaccinated with Tritanrix-HepB and Hiberix vaccines in the Control Group of the 10PN-PD-DIT-037 (111188) study, received a catch-up vaccination with Synflorix vaccine (2 primary doses +1 booster dose), administered intramuscularly in the right or left thigh, during their second year of life: 2+1 catch-up vaccination starting at 12-18 months of age with an interval of at least 8 weeks (56-118 days) between primary doses; the booster dose was administered at 18-24 months of age.

Primary: Concentrations of antibodies against vaccine pneumococcal serotypes

End point title	Concentrations of antibodies against vaccine pneumococcal serotypes[1][2]

End point description:

Antibodies assessed for this outcome measure were those against the 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), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration greater than or equal to (≥) 0.05 µg/mL. Antibody concentrations lower 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

End point timeframe:

Prior to booster vaccination (PRE), one month after booster vaccination (Month 1) and at approximately 24 months of age: at Month 15 for the Synflorix 1 Group and at Month 9 for Synflorix 2 Group [24 months (mths) of age]

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 Synflorix 1 Group and the Synflorix 2 Group.

End point values	Synflorix 1 Group	Synflorix 2 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	71		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-1 PRE (N=88;69)	0.37 (0.29 to 0.48)	0.31 (0.23 to 0.41)		

Anti-1 Month 1 (N=80;61)	4.78 (3.87 to 5.91)	5.98 (4.54 to 7.9)		
Anti-1 24 mths of age (N=59;55)	0.96 (0.68 to 1.37)	1.37 (1 to 1.87)		
Anti-4 PRE (N=88;68)	0.76 (0.58 to 1)	0.58 (0.44 to 0.75)		
Anti-4 Month 1 (N=81;63)	7.28 (5.41 to 9.79)	11.56 (7.96 to 16.79)		
Anti-4 24 mths of age (N=59;55)	1.24 (0.9 to 1.7)	2.29 (1.53 to 3.42)		
Anti-5 PRE (N=88;69)	0.5 (0.4 to 0.63)	0.38 (0.29 to 0.48)		
Anti-5 Month 1 (N=81;62)	5.86 (4.69 to 7.32)	7.2 (5.25 to 9.86)		
Anti-5 24 mths of age (N=59;55)	1.19 (0.86 to 1.65)	2.03 (1.43 to 2.86)		
Anti-6B PRE (N=88;71)	0.65 (0.5 to 0.85)	0.49 (0.37 to 0.64)		
Anti-6B Month 1 (N=81;64)	2.82 (2.16 to 3.68)	2.98 (2.05 to 4.32)		
Anti-6B 24 mths of age (N=59;55)	0.78 (0.54 to 1.11)	0.9 (0.61 to 1.32)		
Anti-7F PRE (N=88;70)	1.12 (0.92 to 1.38)	0.93 (0.73 to 1.19)		
Anti-7F Month 1 (N=81;63)	6.3 (4.8 to 8.25)	7.89 (5.91 to 10.54)		
Anti-7F 24 mths of age (N=59;55)	1.3 (0.96 to 1.76)	1.98 (1.43 to 2.75)		
Anti-9V PRE (N=88;71)	1.2 (0.94 to 1.52)	0.96 (0.74 to 1.25)		
Anti-9V Month 1 (N=81;64)	8.03 (6.03 to 10.69)	9.76 (7.08 to 13.44)		
Anti-9V 24 mths of age (N=58;55)	1.7 (1.2 to 2.41)	2.27 (1.64 to 3.14)		
Anti-14 PRE (N=89;70)	1.76 (1.22 to 2.53)	1.52 (1.08 to 2.15)		
Anti-14 Month 1 (N=81;64)	10.18 (7.6 to 13.65)	11.85 (8.15 to 17.22)		
Anti-14 24 mths of age (N=59;55)	3.02 (2.09 to 4.37)	4.11 (2.98 to 5.67)		
Anti-18C PRE (N=89;71)	2.51 (1.94 to 3.23)	1.55 (1.19 to 2.03)		
Anti-18C Month 1 (N=81;63)	33.39 (24.73 to 45.08)	42.43 (31.48 to 57.2)		
Anti-18C 24 mths of age (N=59;55)	5.56 (3.84 to 8.05)	10.04 (6.55 to 15.37)		
Anti-19F PRE (N=89;70)	1.78 (1.34 to 2.36)	1.23 (0.97 to 1.57)		
Anti-19F Month 1 (N=81;64)	13.68 (9.86 to 18.97)	13.64 (9.42 to 19.76)		
Anti-19F 24 mths of age (N=59;55)	2.57 (1.81 to 3.65)	4.15 (2.88 to 5.98)		
Anti-23F PRE (N=88;70)	0.73 (0.55 to 0.97)	0.65 (0.48 to 0.89)		
Anti-23F Month 1 (N=81;63)	5.54 (4.02 to 7.63)	6.48 (4.69 to 8.96)		
Anti-23F 24 mths of age (N=59;55)	1.3 (0.88 to 1.91)	1.38 (0.96 to 1.98)		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against vaccine pneumococcal serotypes

End point title	Concentrations of antibodies against vaccine pneumococcal serotypes[3]

End point description:

Antibodies assessed for this outcome measure were those against the 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), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 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 vaccination (PRE), one month post-Dose 2 (Month 3), prior to (Month 6) and one month after the third (booster) vaccine dose (Month 7)

Notes:

[3] - 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+Hiberix Group.

End point values	Tritanrix-HepB+Hiberix Group			
Subject group type	Reporting group			
Number of subjects analysed	81			
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-1 PRE (N=81)	0.04 (0.03 to 0.04)			
Anti-1 Month 3 (N=69)	2.5 (1.93 to 3.24)			
Anti-1 Month 6 (N=65)	1.03 (0.82 to 1.29)			
Anti-1 Month 7 (N=54)	3.32 (2.69 to 4.1)			
Anti-4 PRE (N=80)	0.04 (0.03 to 0.05)			
Anti-4 Month 3 (N=71)	5.89 (4.23 to 8.22)			
Anti-4 Month 6 (N=65)	2.23 (1.85 to 2.69)			
Anti-4 Month 7 (N=54)	8.22 (5.92 to 11.42)			
Anti-5 PRE (N=80)	0.05 (0.04 to 0.06)			
Anti-5 Month 3 (N=71)	2.81 (2.2 to 3.58)			
Anti-5 Month 6 (N=65)	1.39 (1.13 to 1.7)			
Anti-5 Month 7 (N=54)	5.32 (4.21 to 6.72)			
Anti-6B PRE (N=80)	0.03 (0.03 to 0.04)			
Anti-6B Month 3 (N=70)	0.71 (0.53 to 0.95)			

Anti-6B Month 6 (N=65)	0.61 (0.47 to 0.78)			
Anti-6B Month 7 (N=54)	1.4 (1.04 to 1.88)			
Anti-7F PRE (N=81)	0.06 (0.05 to 0.08)			
Anti-7F Month 3 (N=71)	4.63 (3.38 to 6.34)			
Anti-7F Month 6 (N=65)	2.72 (2.28 to 3.24)			
Anti-7F Month 7 (N=54)	7.41 (5.87 to 9.34)			
Anti-9V PRE (N=80)	0.04 (0.03 to 0.05)			
Anti-9V Month 3 (N=71)	2.09 (1.53 to 2.87)			
Anti-9V Month 6 (N=65)	1.74 (1.4 to 2.17)			
Anti-9V Month 7 (N=54)	4.88 (3.73 to 6.37)			
Anti-14 PRE (N=80)	0.06 (0.05 to 0.08)			
Anti-14 Month 3 (N=71)	5.01 (3.75 to 6.69)			
Anti-14 Month 6 (N=65)	2.84 (2.25 to 3.57)			
Anti-14 Month 7 (N=54)	7.59 (5.87 to 9.8)			
Anti-18C PRE (N=80)	0.04 (0.03 to 0.05)			
Anti-18C Month 3 (N=70)	29.1 (19.86 to 42.64)			
Anti-18C Month 6 (N=65)	12.44 (9.16 to 16.91)			
Anti-18C Month 7 (N=54)	75.19 (57.69 to 98.01)			
Anti-19F PRE (N=80)	0.07 (0.05 to 0.1)			
Anti-19F Month 3 (N=71)	16.39 (11.15 to 24.1)			
Anti-19F Month 6 (N=65)	7.74 (5.85 to 10.24)			
Anti-19F Month 7 (N=54)	30.71 (23.76 to 39.68)			
Anti-23F PRE (N=80)	0.04 (0.03 to 0.05)			
Anti-23F Month 3 (N=71)	1.13 (0.82 to 1.57)			
Anti-23F Month 6 (N=65)	0.85 (0.67 to 1.09)			
Anti-23F Month 7 (N=54)	2.15 (1.69 to 2.75)			

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against vaccine pneumococcal serotypes

(Persistence)

End point title	Concentrations of antibodies against vaccine pneumococcal serotypes (Persistence)

End point description:

Antibodies assessed for this outcome measure were those against the 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), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 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 booster vaccination (PRE) for the Synflorix 1 and Synflorix 2 Groups and prior to catch-up vaccination (PRE) for the Tritanrix-HepB+Hiberix Group

End point values	Synflorix 1 Group	Synflorix 2 Group	Tritanrix-HepB+Hiberix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	89	90	84	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-1 (N=88;87;84)	0.37 (0.29 to 0.48)	0.3 (0.24 to 0.39)	0.04 (0.03 to 0.04)	
Anti-4 (N=88;85;83)	0.76 (0.58 to 1)	0.57 (0.45 to 0.72)	0.04 (0.03 to 0.05)	
Anti-5 (N=88;87;83)	0.5 (0.4 to 0.63)	0.38 (0.31 to 0.47)	0.05 (0.04 to 0.06)	
Anti-6B (N=88;90;83)	0.65 (0.5 to 0.85)	0.51 (0.4 to 0.65)	0.03 (0.03 to 0.04)	
Anti-7F (N=88;89;84)	1.12 (0.92 to 1.38)	0.98 (0.79 to 1.23)	0.06 (0.04 to 0.08)	
Anti-9V (N=88;90;83)	1.2 (0.94 to 1.52)	0.98 (0.78 to 1.23)	0.04 (0.03 to 0.05)	
Anti-14 (N=89;89;83)	1.76 (1.22 to 2.53)	1.37 (1 to 1.87)	0.06 (0.05 to 0.08)	
Anti-18C (N=89;90;83)	2.51 (1.94 to 3.23)	1.61 (1.26 to 2.05)	0.04 (0.03 to 0.05)	
Anti-19F (N=89;88;83)	1.78 (1.34 to 2.36)	1.36 (1.1 to 1.68)	0.07 (0.05 to 0.09)	
Anti-23F (N=88;88;83)	0.73 (0.55 to 0.97)	0.64 (0.49 to 0.85)	0.04 (0.03 to 0.05)	

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic activity (OPA) titers against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (Persistence)

End point title	Opsonophagocytic activity (OPA) titers against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (Persistence)

End point description:

OPA titers against 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) were calculated, expressed as geometric mean titers (GMTs) and tabulated. 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 booster vaccination (PRE) for the Synflorix 1 and Synflorix 2 Groups and prior to catch-up vaccination (PRE) for the Tritanrix-HepB+Hiberix Group

End point values	Synflorix 1 Group	Synflorix 2 Group	Tritanrix-HepB+Hiberix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	87	84	78	
Units: Titer				
geometric mean (confidence interval 95%)				
Opsono-1 (N=87;84;77)	16.5 (11.2 to 24.3)	15.6 (10.5 to 23)	4.4 (3.9 to 5)	
Opsono-4 (N=85;81;67)	70.3 (43.9 to 112.5)	102.8 (66.4 to 159.1)	6.2 (4.2 to 9.3)	
Opsono-5 (N=87;81;78)	11.9 (8.9 to 15.9)	10.4 (7.8 to 13.7)	4.2 (3.8 to 4.7)	
Opsono-6B (N=87;82;71)	50.2 (30.7 to 82.1)	62 (36.5 to 105.5)	5.3 (3.9 to 7)	
Opsono-7F (N=87;84;65)	1162.5 (910 to 1485)	1551.1 (1269.4 to 1895.3)	1186.4 (588.8 to 2390.7)	
Opsono-9V (N=83;82;60)	430.4 (310.7 to 596.1)	617.6 (477.6 to 798.6)	192.6 (93.6 to 396.5)	
Opsono-14 (N=85;79;69)	206.4 (134.2 to 317.5)	166.3 (105.7 to 261.6)	13.5 (7.8 to 23.5)	
Opsono-18C (N=85;81;74)	30.4 (20.7 to 44.6)	23 (15.6 to 34)	4.8 (3.8 to 6)	
Opsono-19F (N=86;82;76)	43 (29.9 to 61.7)	42.4 (29.5 to 60.8)	4.2 (3.9 to 4.6)	
Opsono-23F (N=86;80;72)	157 (83.2 to 296.3)	531.1 (280.3 to 1006.4)	41.9 (18.8 to 93.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: OPA titers against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F

End point title	OPA titers against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F[4]

End point description:

OPA titers against 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) were calculated, expressed as geometric mean titers (GMTs) and tabulated. 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 booster vaccination (PRE), one month after booster vaccination (Month 1) and at approximately 24 months of age: at Month 15 for the Synflorix 1 Group and at Month 9 for Synflorix 2 Group (24 mths of age)

Notes:

[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 Synflorix 1 Group and the Synflorix 2 Group.

End point values	Synflorix 1 Group	Synflorix 2 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87	65		
Units: Titer				
geometric mean (confidence interval 95%)				
Opsono-1 PRE (N=87;65)	16.5 (11.2 to 24.3)	14.3 (9.3 to 22.1)		
Opsono-1 Month 1 (N=79;58)	1138.3 (828.6 to 1563.7)	2096.7 (1464.8 to 3001.1)		
Opsono-1 24 mths of age (N=57;54)	69.6 (40.1 to 121)	173.8 (105.5 to 286.5)		
Opsono-4 PRE (N=85;63)	70.3 (43.9 to 112.5)	101.6 (62.6 to 164.9)		
Opsono-4 Month 1 (N=79;58)	3368.8 (2618 to 4334.9)	7202.1 (5336.1 to 9720.6)		
Opsono-4 24 mths of age (N=57;54)	557.4 (284 to 1093.9)	2525.6 (1474.5 to 4325.9)		
Opsono-5 PRE (N=87;62)	11.9 (8.9 to 15.9)	9.7 (7.2 to 13.1)		
Opsono-5 Month 1 (N=79;58)	452.7 (353 to 580.6)	834.6 (610.9 to 1140.2)		
Opsono-5 24 mths of age (N=56;55)	45.7 (29.6 to 70.7)	90.6 (54.8 to 149.8)		
Opsono-6B PRE (N=87;63)	50.2 (30.7 to 82.1)	60 (32.9 to 109.3)		
Opsono-6B Month 1 (N=79;57)	1556.6 (1090 to 2223)	1781.2 (1042.5 to 3043.6)		
Opsono-6B 24 mths of age (N=51;52)	241.4 (127.7 to 456.4)	287.5 (149 to 555)		
Opsono-7F PRE (N=87;65)	1162.5 (910 to 1485)	1539.1 (1262.9 to 1875.6)		
Opsono-7F Month 1 (N=79;57)	7814.8 (5984.8 to 10204.3)	11064.4 (8182.9 to 14960.5)		
Opsono-7F 24 mths of age (N=55;52)	2891.2 (1954.4 to 4276.9)	5371.9 (3712.4 to 7773.4)		
Opsono-9V PRE (N=83;63)	430.4 (310.7 to 596.1)	704.9 (533.7 to 931.1)		
Opsono-9V Month 1 (N=79;58)	4440 (3305.4 to 5964.2)	7870.3 (5634.4 to 10993.4)		
Opsono-9V 24 mths of age (N=49;52)	1926.1 (1316.6 to 2817.9)	3504.5 (2501 to 4910.6)		

Opsono-14 PRE (N=85;62)	206.4 (134.2 to 317.5)	184 (109.8 to 308.2)		
Opsono-14 Month 1 (N=79;57)	2057.1 (1569.6 to 2696.1)	4407.5 (3193.2 to 6083.5)		
Opsono-14 24 mths of age (N=56;53)	668.5 (403.1 to 1108.6)	1641.2 (944.2 to 2852.9)		
Opsono-18C PRE (N=85;62)	30.4 (20.7 to 44.6)	22.2 (14.1 to 35)		
Opsono-18C Month 1 (N=79;58)	1889.7 (1429.4 to 2498.1)	3643.2 (2572.2 to 5160.2)		
Opsono-18C 24 mths of age (N=52;53)	233.6 (142.2 to 383.8)	1155 (662 to 2015)		
Opsono-19F PRE (N=86;63)	43 (29.9 to 61.7)	34.7 (23.4 to 51.6)		
Opsono-19F Month 1 (N=78;58)	1672.9 (1096.3 to 2552.7)	2404.4 (1583.1 to 3651.6)		
Opsono-19F 24 mths of age (N=51;53)	107.3 (61.4 to 187.6)	357.9 (218.9 to 585)		
Opsono-23F PRE (N=86;61)	157 (83.2 to 296.3)	498.2 (231.4 to 1072.9)		
Opsono-23F Month 1 (N=79;58)	3812.3 (2630.8 to 5524.5)	5937.2 (3587.6 to 9825.5)		
Opsono-23F 24 mths of age (N=54;55)	1994.1 (959.7 to 4143.4)	3018.5 (1389 to 6559.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic activity (OPA) titers against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F

End point title	Opsonophagocytic activity (OPA) titers against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F[5]

End point description:

OPA titers against 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) were calculated, expressed as geometric mean titers (GMTs) and tabulated. 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 vaccination (PRE), one month post-Dose 2 (Month 3), prior to (Month 6) and one month after the third (booster) vaccine dose (Month 7)

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+Hiberix Group.

End point values	Tritanrix-HepB+Hiberix Group			
Subject group type	Reporting group			
Number of subjects analysed	75			
Units: Titer				
geometric mean (confidence interval 95%)				
Opsono-1 PRE (N=74)	4.3 (3.9 to 4.8)			
Opsono-1 Month 3 (N=68)	76.1 (49 to 118.2)			
Opsono-1 Month 6 (N=64)	18.1 (11.5 to 28.4)			
Opsono-1 Month 7 (N=54)	309.8 (203 to 472.9)			
Opsono-4 PRE (N=64)	5.8 (4 to 8.6)			
Opsono-4 Month 3 (N=66)	2256.3 (1840 to 2766.8)			
Opsono-4 Month 6 (N=63)	959.7 (727.2 to 1266.6)			
Opsono-4 Month 7 (N=54)	2946.2 (2097.9 to 4137.4)			
Opsono-5 PRE (N=75)	4.2 (3.8 to 4.7)			
Opsono-5 Month 3 (N=64)	76.3 (53.3 to 109.3)			
Opsono-5 Month 6 (N=63)	24.6 (17 to 35.6)			
Opsono-5 Month 7 (N=54)	212 (148.9 to 301.7)			
Opsono-6B PRE (N=68)	5.3 (3.9 to 7.2)			
Opsono-6B Month 3 (N=63)	348.2 (165.7 to 731.6)			
Opsono-6B Month 6 (N=61)	201.5 (98.2 to 413.5)			
Opsono-6B Month 7 (N=53)	740.5 (419.6 to 1306.8)			
Opsono-7F PRE (N=63)	1106.8 (540.7 to 2265.9)			
Opsono-7F Month 3 (N=67)	7462.5 (5653.9 to 9849.6)			
Opsono-7F Month 6 (N=63)	6295.9 (4545 to 8721.4)			
Opsono-7F Month 7 (N=54)	10104 (7377.8 to 13837.4)			
Opsono-9V PRE (N=58)	205.9 (98.7 to 429.4)			
Opsono-9V Month 3 (N=61)	5792.5 (4586.3 to 7315.9)			
Opsono-9V Month 6 (N=62)	3463.4 (2716.3 to 4416.1)			
Opsono-9V Month 7 (N=53)	7000 (5265.1 to 9306.6)			
Opsono-14 PRE (N=67)	12.4 (7.1 to 21.6)			
Opsono-14 Month 3 (N=65)	2359.8 (1576.1 to 3533.2)			

Opsono-14 Month 6 (N=63)	1293.6 (886.8 to 1887.2)			
Opsono-14 Month 7 (N=54)	3709.4 (2463.5 to 5585.2)			
Opsono-18C PRE (N=71)	4.8 (3.8 to 6.1)			
Opsono-18C Month 3 (N=66)	2487.5 (1541.2 to 4014.8)			
Opsono-18C Month 6 (N=62)	2546.4 (1755 to 3694.7)			
Opsono-18C Month 7 (N=54)	8814.6 (6810.9 to 11407.7)			
Opsono-19F PRE (N=73)	4.2 (3.9 to 4.6)			
Opsono-19F Month 3 (N=65)	1768.6 (1120.3 to 2792)			
Opsono-19F Month 6 (N=62)	753.8 (497.3 to 1142.5)			
Opsono-19F Month 7 (N=51)	3808.8 (2689.5 to 5393.9)			
Opsono-23F PRE (N=69)	38.7 (17.1 to 87.5)			
Opsono-23F Month 3 (N=67)	3378.1 (2014.8 to 5664)			
Opsono-23F Month 6 (N=62)	1868.2 (956.9 to 3647.5)			
Opsono-23F Month 7 (N=53)	4357.3 (2246.9 to 8449.8)			

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Antibodies assessed for this outcome measure were those against cross-reactive pneumococcal serotypes 6A and 19A (ANTI-6A and -19A). Antibody concentrations were measured by 22F ELISA, expressed as geometric mean concentrations (GMCs), in µg/mL. The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 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 booster vaccination (PRE) for the Synflorix 1 and Synflorix 2 Groups and prior to catch-up vaccination (PRE) for the Tritanrix-HepB + Hiberix Group

End point values	Synflorix 1 Group	Synflorix 2 Group	Tritanrix-HepB+Hiberix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	89	89	84	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-6A (N=89;87;83)	0.19 (0.14 to 0.26)	0.22 (0.16 to 0.29)	0.03 (0.03 to 0.04)	
Anti-19A (N=88;89;84)	0.31 (0.21 to 0.45)	0.33 (0.25 to 0.45)	0.06 (0.04 to 0.08)	

Statistical analyses

No statistical analyses for this end point

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

End point title	Concentrations of antibodies against cross-reactive pneumococcal serotypes 6A and 19A[6]

End point description:

Antibodies assessed for this outcome measure were those against the cross-reactive pneumococcal serotypes 6A and 19A (ANTI-6A and -19A). Antibody concentrations were measured by 22F enzyme-linked immunosorbent assay (ELISA), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 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 booster vaccination (PRE), one month after booster vaccination (Month 1) and at approximately 24 months of age: at Month 15 for the Synflorix 1 Group and at Month 9 for Synflorix 2 Group (24 mths of age)

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 the Synflorix 1 Group and the Synflorix 2 Group.

End point values	Synflorix 1 Group	Synflorix 2 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	70		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-6A PRE (N=89;70)	0.19 (0.14 to 0.26)	0.19 (0.14 to 0.27)		
Anti-6A Month 1 (N=81;62)	0.82 (0.59 to 1.14)	0.95 (0.63 to 1.44)		
Anti-6A 24 mths of age (N=59;55)	0.32 (0.22 to 0.48)	0.36 (0.22 to 0.59)		
Anti-19A PRE (N=88;70)	0.31 (0.21 to 0.45)	0.3 (0.22 to 0.41)		
Anti-19A Month 1 (N=81;64)	2.54 (1.61 to 4.03)	2.87 (1.78 to 4.61)		

Anti-19A 24 mths of age (N=59;55)	0.71 (0.45 to 1.14)	1.33 (0.85 to 2.08)		

Statistical analyses

No statistical analyses for this end point

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

End point title	Concentrations of antibodies against cross-reactive pneumococcal serotypes 6A and 19A[7]

End point description:

Antibodies assessed for this outcome measure were those against cross-reactive pneumococcal serotypes 6A and 19A (ANTI-6A and -19A). Antibody concentrations were measured by 22F enzyme-linked immunosorbent assay (ELISA), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The seropositivity cut-off of the assay was an antibody concentration ≥ 0.05 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 vaccination (PRE), one month post-Dose 2 (Month 3), prior to (Month 6) and one month after the third (booster) vaccine dose (Month 7)

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 the Tritanrix-HepB+Hiberix Group.

End point values	Tritanrix-HepB+Hiberix Group			
Subject group type	Reporting group			
Number of subjects analysed	81			
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-6A PRE (N=80)	0.03 (0.03 to 0.04)			
Anti-6A Month 3 (N=70)	0.35 (0.25 to 0.5)			
Anti-6A Month 6 (N=65)	0.33 (0.24 to 0.45)			
Anti-6A Month 7 (N=54)	0.76 (0.53 to 1.09)			
Anti-19A PRE (N=81)	0.06 (0.04 to 0.08)			
Anti-19A Month 3 (N=71)	2.49 (1.77 to 3.51)			
Anti-19A Month 6 (N=65)	1.94 (1.44 to 2.61)			
Anti-19A Month 7 (N=54)	7.91 (5.62 to 11.13)			

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic activity (OPA) titers against cross-reactive pneumococcal serotypes 6A and 19A (Persistence)

End point title	Opsonophagocytic activity (OPA) titers against cross-reactive pneumococcal serotypes 6A and 19A (Persistence)

End point description:

OPA titers against cross-reactive pneumococcal serotypes 6A and 19A (Opsono-6A and -19A) were calculated, expressed as geometric mean titers (GMTs) and tabulated. 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 booster vaccination (PRE) for the Synflorix 1 and Synflorix 2 Groups and prior to catch-up vaccination (PRE) for the Tritanrix-HepB + Hiberix Group

End point values	Synflorix 1 Group	Synflorix 2 Group	Tritanrix-HepB+Hiberix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	86	82	78	
Units: Titer				
geometric mean (confidence interval 95%)				
Opsono-6A (N=86;82;72)	21.1 (13.2 to 33.6)	30.1 (18.4 to 49.3)	10.3 (6.3 to 17)	
Opsono-19A (N=86;82;78)	9.7 (6.8 to 13.7)	7.4 (5.7 to 9.7)	4.8 (4 to 5.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic activity (OPA) titers against cross-reactive pneumococcal serotypes 6A and 19A

End point title	Opsonophagocytic activity (OPA) titers against cross-reactive pneumococcal serotypes 6A and 19A[8]

End point description:

OPA titers against cross-reactive pneumococcal serotypes 6A and 19A (Opsono-6A and -19A) were calculated, expressed as geometric mean titers (GMTs) and tabulated. 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 booster vaccination (PRE), one month after booster vaccination (Month 1) and at approximately 24 months of age: at Month 15 for the Synflorix 1 Group and at Month 9 for Synflorix 2 Group (24 mths of age)

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 1 Group and the Synflorix 2 Group.

End point values	Synflorix 1 Group	Synflorix 2 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	86	63		
Units: Titer				
geometric mean (confidence interval 95%)				
Opsono-6A PRE (N=86;63)	21.1 (13.2 to 33.6)	27.1 (15.7 to 47)		
Opsono-6A Month 1 (N=79;57)	168.7 (96.3 to 295.5)	262.5 (135.4 to 509)		
Opsono-6A 24 mths of age (N=54;53)	62.2 (33.7 to 114.8)	96.6 (45.4 to 205.6)		
Opsono-19A PRE (N=86;63)	9.7 (6.8 to 13.7)	7 (5.3 to 9.3)		
Opsono-19A Month 1 (N=78;57)	161.6 (93.7 to 278.5)	385.6 (223.4 to 665.5)		
Opsono-19A 24 mths of age (N=53;51)	17.8 (9.8 to 32.1)	60 (33 to 109.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic activity (OPA) titers against cross-reactive pneumococcal serotypes 6A and 19A

End point title	Opsonophagocytic activity (OPA) titers against cross-reactive pneumococcal serotypes 6A and 19A[9]

End point description:

OPA titers against cross-reactive pneumococcal serotypes 6A and 19A (Opsono-6A and -19A) were calculated, expressed as geometric mean titers (GMTs) and tabulated. 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 vaccination (PRE), one month post-Dose 2 (Month 3), prior to (Month 6) and one month after the third (booster) vaccine dose (Month 7)

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 Tritanrix-HepB+Hiberix Group.

End point values	Tritanrix-HepB+Hiberix Group			
Subject group type	Reporting group			
Number of subjects analysed	75			
Units: Titer				
geometric mean (confidence interval 95%)				

Opsono-6A PRE (N=69)	10.2 (6.1 to 17.1)			
Opsono-6A Month 3 (N=65)	324.9 (176.1 to 599.5)			
Opsono-6A Month 6 (N=63)	329 (181 to 598.2)			
Opsono-6A Month 7 (N=52)	616.2 (369.2 to 1028.5)			
Opsono-19A PRE (N=75)	4.8 (4 to 5.8)			
Opsono-19A Month 3 (N=64)	506.6 (305.5 to 840.1)			
Opsono-19A Month 6 (N=61)	402.1 (248.9 to 649.5)			
Opsono-19A Month 7 (N=54)	1770.9 (1190.6 to 2634)			

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Anti-protein D (Anti-PD) antibody concentrations by Enzyme-Linked Immunosorbent Assay (ELISA) were calculated, expressed as geometric mean concentrations (GMCs) in ELISA unit per milliliter (EL.U/mL) and tabulated. The seropositivity cut-off for the assay was ≥ 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

End point timeframe:

Prior to booster vaccination (PRE) for the Synflorix 1 and Synflorix 2 Groups and prior to catch-up vaccination (PRE) for the Tritanrix-HepB + Hiberix Group

End point values	Synflorix 1 Group	Synflorix 2 Group	Tritanrix-HepB+Hiberix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	89	90	82	
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD	776.3 (629 to 958.2)	618.6 (488.2 to 783.9)	71.6 (62.3 to 82.2)	

Statistical analyses

No statistical analyses for this end point

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

End point title	Concentrations of antibodies against protein D (Anti-PD)[10]

End point description:

Anti-protein D (Anti-PD) antibody concentrations by Enzyme-Linked Immunosorbent Assay (ELISA) were calculated, expressed as geometric mean concentrations (GMCs) in ELISA unit per milliliter (EL.U/mL) and tabulated. The seropositivity cut-off for the assay was ≥ 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

End point timeframe:

Prior to booster vaccination (PRE), one month after booster vaccination (Month 1) and at approximately 24 months of age: at Month 15 for the Synflorix 1 Group and at Month 9 for Synflorix 2 Group (24 mths of age)

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 Synflorix 1 Group and the Synflorix 2 Group.

End point values	Synflorix 1 Group	Synflorix 2 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	71		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD PRE (N=89;71)	776.3 (629 to 958.2)	654.7 (497.9 to 860.9)		
Anti-PD Month 1 (N=81;61)	3704.2 (2825.6 to 4856)	5297.6 (3934 to 7133.8)		
Anti-PD 24 mths of age (N=59;54)	1337.3 (953.8 to 1875)	2191.9 (1582.5 to 3036)		

Statistical analyses

No statistical analyses for this end point

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

End point title	Concentrations of antibodies against protein D (Anti-PD)[11]

End point description:

Anti-protein D (Anti-PD) antibody concentrations by Enzyme-Linked Immunosorbent Assay (ELISA) were calculated, expressed as geometric mean concentrations (GMCs) in ELISA unit per milliliter (EL.U/mL) and tabulated. The seropositivity cut-off for the assay was ≥ 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

End point timeframe:

Prior to vaccination (PRE), one month post-Dose 2 (Month 3), prior to (Month 6) and one month after the third (booster) vaccine dose (Month 7)

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+Hiberix Group.

End point values	Tritanrix-HepB+Hiberix Group			
Subject group type	Reporting group			
Number of subjects analysed	79			
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD PRE (N=79)	72.5 (62.9 to 83.7)			
Anti-PD Month 3 (N=70)	527.7 (397.4 to 700.9)			
Anti-PD Month 6 (N=65)	443.2 (333.1 to 589.6)			
Anti-PD Month 7 (N=54)	1727.2 (1306.6 to 2283.3)			

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point type	Secondary

End point timeframe:

Within the 4-day follow-up period (Days 0-3) after the booster dose for the Synflorix 1 and Synflorix 2 Groups and across doses for the Tritanrix-HepB + Hiberix Group

End point values	Synflorix 1 Group	Synflorix 2 Group	Tritanrix-HepB+Hiberix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	93	85	82	
Units: Subjects				
Any Pain	31	25	26	
Grade 3 Pain	2	4	5	
Any Redness	16	12	11	
Grade 3 Redness	2	0	1	
Any Swelling	14	14	16	
Grade 3 Swelling	4	1	2	

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Assessed solicited general symptoms were Drowsiness, Irritability/Fussiness (Irr./Fuss.), Loss of appetite (Loss Appet.) and Fever (rectal temperature greater than or equal to [≥] 38.0 degrees Celsius [°C]). Any = Occurrence of the specified solicited general symptom, regardless of intensity or relationship to vaccination. Related = Occurrence of the specified symptom assessed by the investigators as causally related to vaccination. Grade 3 Drowsiness = Drowsiness that prevented normal everyday activities. Grade 3 Irr./Fuss. = Crying that could not be comforted/prevented normal everyday activities. Grade 3 Loss of appetite = Subject did not eat at all. Grade 3 Fever = Rectal temperature higher than (>) 40.0°C.

End point type	Secondary

End point timeframe:

Within the 4-day follow-up period (Days 0-3) after the booster dose for the Synflorix 1 and Synflorix 2 Groups and across doses for the Tritanrix-HepB + Hiberix Group

End point values	Synflorix 1 Group	Synflorix 2 Group	Tritanrix-HepB+Hiberix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	92	85	82	
Units: Subjects				
Any Drowsiness	5	4	5	
Grade 3 Drowsiness	0	0	2	
Related Drowsiness	4	4	3	
Any Fever	20	13	22	
Grade 3 Fever	0	1	0	
Related Fever	19	13	21	
Any Irr./Fuss	19	9	12	
Grade 3 Irr./Fuss.	1	1	1	
Related Irr./Fuss.	15	9	9	
Any Loss Appet.	14	9	10	
Grade 3 Loss Appet.	0	2	0	
Related Loss Appet.	9	8	9	

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

An AE is any untoward medical occurrence in a clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Unsolicited

AE covers any AE 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.

End point type	Secondary

End point timeframe:

Within 31-day follow-up period (Days 0-30) after vaccination

End point values	Synflorix 1 Group	Synflorix 2 Group	Tritanrix-HepB+Hiberix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	100	95	87	
Units: Subjects				
Any AE	7	1	5	

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point type	Secondary

End point timeframe:

After the first vaccination up to study end (from Month 0 to Month 15)

End point values	Synflorix 1 Group	Synflorix 2 Group	Tritanrix-HepB+Hiberix Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	100	95	87	
Units: Subjects				
Any SAE	2	0	1	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited AEs: during the 4 days post vaccination; Unsolicited AEs: during the 31 days post vaccination after booster dose in the Synflorix 1 and Synflorix 2 Groups and across doses in the Tritanrix-HepB+Hiberix Group; SAEs: from Month 0 to Month 15

Adverse event reporting additional description:

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

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.1

Reporting groups

Reporting group title	Synflorix 1 Group

Reporting group description:

Subjects who were previously primed with a 3-dose primary vaccination of Synflorix vaccine in the 10PN-PD-DIT-037 (111188) study, received a booster dose of Synflorix vaccine, administered intramuscularly in the right or left thigh, at 9-18 months of age.

Reporting group title	Tritanrix-HepB+Hiberix Group

Reporting group description:

Unprimed subjects who were previously vaccinated with Tritanrix-HepB and Hiberix vaccines in the Control Group of the 10PN-PD-DIT-037 (111188) study, received a catch-up vaccination with Synflorix vaccine (2 primary doses +1 booster dose), administered intramuscularly in the right or left thigh, during their second year of life: 2+1 catch-up vaccination starting at 12-18 months of age with an interval of at least 8 weeks (56-118 days) between primary doses; the booster dose was administered at 18-24 months of age.

Reporting group title	Synflorix 2 Group

Reporting group description:

Subjects who were previously primed with a 3-dose primary vaccination of Synflorix vaccine in the 10PN-PD-DIT-037 (111188) study, received a booster dose of Synflorix vaccine, administered intramuscularly in the right or left thigh, at 15-18 months of age.

Serious adverse events	Synflorix 1 Group	Tritanrix-HepB+Hiberix Group	Synflorix 2 Group
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 100 (2.00%)	1 / 87 (1.15%)	0 / 95 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	0 / 100 (0.00%)	1 / 87 (1.15%)	0 / 95 (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
Infections and infestations			
Skin infection			

subjects affected / exposed	1 / 100 (1.00%)	0 / 87 (0.00%)	0 / 95 (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			
subjects affected / exposed	1 / 100 (1.00%)	0 / 87 (0.00%)	0 / 95 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 100 (0.00%)	1 / 87 (1.15%)	0 / 95 (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

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

Non-serious adverse events	Synflorix 1 Group	Tritanrix-HepB+Hiberix Group	Synflorix 2 Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	48 / 100 (48.00%)	38 / 87 (43.68%)	29 / 95 (30.53%)
General disorders and administration site conditions			
Pain			
alternative assessment type: Systematic			
subjects affected / exposed[1]	31 / 93 (33.33%)	26 / 82 (31.71%)	25 / 85 (29.41%)
occurrences (all)	31	26	25
Redness			
alternative assessment type: Systematic			
subjects affected / exposed[2]	16 / 93 (17.20%)	11 / 82 (13.41%)	12 / 85 (14.12%)
occurrences (all)	16	11	12
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed[3]	14 / 93 (15.05%)	16 / 82 (19.51%)	14 / 85 (16.47%)
occurrences (all)	14	16	14
Drowsiness			
alternative assessment type: Systematic			

subjects affected / exposed[4]	5 / 92 (5.43%)	5 / 82 (6.10%)	4 / 85 (4.71%)
occurrences (all)	5	5	4
Fever (≥38°C)			
alternative assessment type: Systematic			
subjects affected / exposed[5]	20 / 92 (21.74%)	22 / 82 (26.83%)	13 / 85 (15.29%)
occurrences (all)	20	22	13
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed[6]	19 / 92 (20.65%)	12 / 82 (14.63%)	9 / 85 (10.59%)
occurrences (all)	19	12	9
Loss of appetite			
alternative assessment type: Systematic			
subjects affected / exposed[7]	14 / 92 (15.22%)	10 / 82 (12.20%)	9 / 85 (10.59%)
occurrences (all)	14	10	9

Notes:

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

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

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

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

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

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

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

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 April 2010	The inclusion criteria for enrolment in the Pn-Pn (booster dose) groups has been modified to 9-18 months of age at the time of randomisation instead of 9-12 months due to a delay in the study start. This amendment extended the age range at the time of randomization of subjects who were primed in the primary vaccination study 10PN-PD-DIT-037 and thereby optimized the number of primed subjects to be included in the booster dose groups in this study. This amendment also extended the age at the time of booster vaccination in the Pn-Pn9 Group (early booster group) to 9-18 months instead of 9-12 months in order to keep the study fully randomized; giving the opportunity to any primed subject to be randomly allocated to one of the two booster groups. For the purpose of analysis, this group was splited to 9-12 months and 13-18 months in order to have an analysis on the early booster subset for the primary objective.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported