Clinical trial results:
A phase II, randomized, controlled, observer-blind study to assess the safety, reactogenicity and immunogenicity of two formulations of GlaxoSmithKline (GSK) Biologicals' Streptococcus pneumoniae protein containing vaccine given as a 3-dose primary vaccination course co-administered with DTPa-HBV-IPV/Hib* vaccine during the first 6 months of life and as a booster dose at 12-15 months of age.
*DTPa-HBV-IPV/Hib = Infanrix hexa™

Summary

EudraCT number	2010-019730-27
Trial protocol	CZ PL SE DE
Global end of trial date	01 October 2012

Results information

Result version number	v1
This version publication date	01 March 2016
First version publication date	04 April 2015

Trial information

Trial identification

Sponsor protocol code	113994

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01204658
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium,
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)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	25 November 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 October 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1.Non-inferiority of the candidate pneumococcal vaccine (dPly-Low Dose [LD] and PhtD-LD)[10PP-LD] versus Synflorix™ vaccine when administered with Infanrix hexa™ (DTPa-HBV-IPV/Hib) as a 3-dose primary vaccination, in terms of post-primary immunization fever > 40.0°C (rectal temperature) with causal relationship to vaccination.
2.(sequential): Non-inferiority of the candidate pneumococcal vaccine (dPly-High Dose [HD] and PhtD-HD)[10PP-HD] versus Synflorix™ vaccine when administered with Infanrix hexa™ as a 3-dose primary vaccination, in terms of post-primary immunization fever > 40.0°C (rectal temperature) with causal relationship to vaccination.
Criteria = Non-inferiority supported if one can rule out an increase, in terms of percentage of subjects with fever >40.0°C with causal relationship to vaccination (10PP-LD or 10PP-HD group as compared to Synflorix™ group) above 5% + half the incidence in the control group (= null hypothesis) as shown by a one-sided P-value < 5%.

Protection of trial subjects:

GSK has monitored the study to verify that, amongst others, the:
- Data are authentic, accurate, and complete.
- Safety and rights of subjects are being protected.
- Study is conducted in accordance with the currently approved protocol and any amendments, any other study agreements, GCP and all applicable regulatory requirements.

All subjects were supervised after vaccination with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Only eligible subjects that had no contraindications to any components of the vaccines were vaccinated. Subjects were followed-up for 31 days after each/last vaccination.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 September 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	Poland: 110
Country: Number of subjects enrolled	Sweden: 22
Country: Number of subjects enrolled	Czech Republic: 434
Country: Number of subjects enrolled	Germany: 10
Worldwide total number of subjects	576
EEA total number of subjects	576

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)	576
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:

A total of 576 subjects were initially enrolled in the study. Of these, one subject was older than protocol defined age range for the first vaccination, and therefore did not receive any vaccination.

Pre-assignment

Screening details:

The study duration is approximately 10 to 14 months depending on age at recruitment and age at booster vaccination. 2 Phases in the study: Primary Phase when subjects received a 3-dose of pneumococcal vaccine co-administered with Infanrix hexa™ (Months 0, 1, 2), and Booster Phase when subjects received one dose of the same vaccines (Month 10).

Pre-assignment period milestones

Number of subjects started	576
Number of subjects completed	575

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Study vaccine dose not administrated: 1

Period 1

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

Blinding implementation details:

Data collected in an observer-blind manner, meaning that during the course of the study, the subject and those responsible for the evaluation of any study endpoint (e.g. safety, reactogenicity, and immunogenicity) will all be unaware of which vaccine was administered. To do so, vaccine preparation and administration will be done by authorised medical personnel who will not participate in any of the study clinical evaluation assays.
The laboratory will be blinded to the treatment.

Arms

Are arms mutually exclusive?	Yes
Arm title	10PP-LD/Infanrix hexa Group

Arm description:

This group consisted in infants aged 6-14 weeks at primary vaccination who received a 3-dose primary vaccination of the GSK 2189242A (or 10PP) vaccine combined with low doses (LD) of pneumococcal pneumolysin toxoid proteins (dPly) and pneumococcal histidine protein D (PhtD) co-administered with the Infanrix hexa™ vaccine at Study Months 0, 1 and 2. Subjects also received a booster dose of each of these vaccines, administered at Study Month 10.

Arm type	Experimental
Investigational medicinal product name	Pneumococcal vaccine GSK 2189242A (Low Dose formulation 1)
Investigational medicinal product code	GSK 2189242A LD
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

4 doses: 3 primary doses at Study Months 0, 1 and 2. Subjects also received a booster dose , administered at Study Month 10. The 3 primary doses of the 10PP vaccine were administered intramuscularly (IM) in the thigh, on the right side. Booster doses were administered IM into the deltoid or thigh if the deltoid muscle size was not adequate, on the left side for the 10PP vaccine.

Investigational medicinal product name	Infanrix hexa™
Investigational medicinal product code	DTPa-HBV-IPV/Hib
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

4 doses: 3 primary doses at Study Months 0, 1 and 2. Subjects also received a booster dose , administered at Study Month 10. The 3 primary doses of the Infanrix hexa™ vaccines were administered intramuscularly (IM) in the thigh, on the left side. Booster dose was administered IM into the deltoid or thigh if the deltoid muscle size was not adequate, on the right side.

Arm title	10PP-HD/Infanrix hexa Group

Arm description:

This group consisted in infants aged 6-14 weeks at primary vaccination who received a 3-dose primary vaccination of the GSK 2189242A (or 10PP) vaccine combined with high doses (HD) of pneumococcal pneumolysin toxoid proteins (dPly) and pneumococcal histidine protein D (PhtD), co-administered with the Infanrix hexa™ vaccine at Study Months 0, 1 and 2. Subjects also received a booster dose of each of these vaccines, administered at Study Month 10.

Arm type	Experimental
Investigational medicinal product name	Pneumococcal vaccine (High Dose formulation 2)
Investigational medicinal product code	GSK 2189242A HD
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

4 doses: 3-dose primary vaccination at Study Months 0, 1 and 2 and a booster dose administered at Study Month 10.The 3 primary doses of the 10PP vaccine were administered intramuscularly (IM) in the thigh, on the right side. Booster dose was administered IM into the deltoid or thigh if the deltoid muscle size was not adequate, on the left side.

Investigational medicinal product name	Infanrix hexa™
Investigational medicinal product code	DTPa-HBV-IPV/Hib
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

4 doses: 3 primary doses at Study Months 0, 1 and 2. Subjects also received a booster dose , administered at Study Month 10. The 3 primary doses of the Infanrix hexa™ vaccines were administered intramuscularly (IM) in the thigh, on the left side. Booster dose was administered IM into the deltoid or thigh if the deltoid muscle size was not adequate, on the right side.

Arm title	Synflorix/Infanrix hexa Group

Arm description:

This group consisted in infants aged 6-14 weeks at primary vaccination who received a 3-dose primary vaccination of Synflorix™ vaccine, co-administered with the Infanrix hexa™ vaccine at Study Months 0, 1 and 2. Subjects also received a booster dose of each of these vaccines, administered at Study Month 10.

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

Dosage and administration details:

4 doses: 3-dose primary vaccination at Study Months 0, 1 and 2 and a booster dose administered at Study Month 10. The 3 primary doses of Synflorix™ vaccine were administered intramuscularly (IM) in the thigh, on the right side. Booster dose was administered IM into the deltoid or thigh if the deltoid muscle size was not adequate, on the left side.

Investigational medicinal product name	Infanrix hexa™
Investigational medicinal product code	DTPa-HBV-IPV/Hib
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

4 doses: 3 primary doses at Study Months 0, 1 and 2. Subjects also received a booster dose , administered at Study Month 10. The 3 primary doses of the Infanrix hexa™ vaccines were administered intramuscularly (IM) in the thigh, on the left side. Booster dose was administered IM into the deltoid or thigh if the deltoid muscle size was not adequate, on the right side.

Arm title	Prevnar 13/Infanrix hexa Group

Arm description:

This group consisted in infants aged 6-14 weeks at primary vaccination who received a 3-dose primary vaccination of Prevnar 13™ vaccine, co-administered with the Infanrix hexa™ vaccine at Study Months 0, 1 and 2. Subjects also received a booster dose of each of these vaccines, administered at Study Month 10.

Arm type	Active comparator
Investigational medicinal product name	Prevenar 13™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

4 doses: 3-dose primary vaccination of Prevnar 13™ vaccine at Study Months 0, 1 and 2 and a booster dose , administered at Study Month 10. The 3 primary doses of Prevnar 13™ were administered intramuscularly (IM) in the thigh, on the right side. Booster dose was administered IM into the deltoid or thigh if the deltoid muscle size was not adequate, on the left side.

Investigational medicinal product name	Infanrix hexa™
Investigational medicinal product code	DTPa-HBV-IPV/Hib
Other name	
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

4 doses: 3 primary doses at Study Months 0, 1 and 2. Subjects also received a booster dose , administered at Study Month 10. The 3 primary doses of the Infanrix hexa™ vaccines were administered intramuscularly (IM) in the thigh, on the left side. Booster dose was administered IM into the deltoid or thigh if the deltoid muscle size was not adequate, on the right side.

Number of subjects in period 1[1]	10PP-LD/Infanrix hexa Group	10PP-HD/Infanrix hexa Group	Synflorix/Infanrix hexa Group
Started	146	142	145
Completed	144	140	140
Not completed	2	2	5
Consent withdrawn by subject	2	2	4
Adverse event, non-fatal	-	-	1

Number of subjects in period 1[1]	Prevnar 13/Infanrix hexa Group
Started	142
Completed	140
Not completed	2

Consent withdrawn by subject	2
Adverse event, non-fatal	-

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 576 subjects were initially enrolled in the study. Of these, one subject was older than protocol defined age range for the first vaccination, and therefore did not receive any vaccination.

Baseline characteristics

Reporting groups	
Reporting group title	10PP-LD/Infanrix hexa Group
Reporting group description:	
This group consisted in infants aged 6-14 weeks at primary vaccination who received a 3-dose primary vaccination of the GSK 2189242A (or 10PP) vaccine combined with low doses (LD) of pneumococcal pneumolysin toxoid proteins (dPly) and pneumococcal histidine protein D (PhtD) co-administered with the Infanrix hexa™ vaccine at Study Months 0, 1 and 2. Subjects also received a booster dose of each of these vaccines, administered at Study Month 10.	
Reporting group title	10PP-HD/Infanrix hexa Group
Reporting group description:	
This group consisted in infants aged 6-14 weeks at primary vaccination who received a 3-dose primary vaccination of the GSK 2189242A (or 10PP) vaccine combined with high doses (HD) of pneumococcal pneumolysin toxoid proteins (dPly) and pneumococcal histidine protein D (PhtD), co-administered with the Infanrix hexa™ vaccine at Study Months 0, 1 and 2. Subjects also received a booster dose of each of these vaccines, administered at Study Month 10.	
Reporting group title	Synflorix/Infanrix hexa Group
Reporting group description:	
This group consisted in infants aged 6-14 weeks at primary vaccination who received a 3-dose primary vaccination of Synflorix™ vaccine, co-administered with the Infanrix hexa™ vaccine at Study Months 0, 1 and 2. Subjects also received a booster dose of each of these vaccines, administered at Study Month 10.	
Reporting group title	Prevnar 13/Infanrix hexa Group
Reporting group description:	
This group consisted in infants aged 6-14 weeks at primary vaccination who received a 3-dose primary vaccination of Prevnar 13™ vaccine, co-administered with the Infanrix hexa™ vaccine at Study Months 0, 1 and 2. Subjects also received a booster dose of each of these vaccines, administered at Study Month 10.	

Reporting group values	10PP-LD/Infanrix hexa Group	10PP-HD/Infanrix hexa Group	Synflorix/Infanrix hexa Group
Number of subjects	146	142	145
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: weeks			
arithmetic mean	10.3	10.1	10.1
standard deviation	± 2.49	± 2.7	± 2.61
Gender categorical Units: Subjects			
Female	65	67	70
Male	81	75	75

Reporting group values	Prevnar 13/Infanrix hexa Group	Total	
Number of subjects	142	575	
Age categorical			
Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		0	
Newborns (0-27 days)		0	
Infants and toddlers (28 days-23 months)		0	
Children (2-11 years)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous			
Units: weeks			
arithmetic mean	10.2		
standard deviation	± 2.64	-	
Gender categorical			
Units: Subjects			
Female	66	268	
Male	76	307	

End points

End points reporting groups

Reporting group title	10PP-LD/Infanrix hexa Group

Reporting group description:

This group consisted in infants aged 6-14 weeks at primary vaccination who received a 3-dose primary vaccination of the GSK 2189242A (or 10PP) vaccine combined with low doses (LD) of pneumococcal pneumolysin toxoid proteins (dPly) and pneumococcal histidine protein D (PhtD) co-administered with the Infanrix hexa™ vaccine at Study Months 0, 1 and 2. Subjects also received a booster dose of each of these vaccines, administered at Study Month 10.

Reporting group title	10PP-HD/Infanrix hexa Group

Reporting group description:

This group consisted in infants aged 6-14 weeks at primary vaccination who received a 3-dose primary vaccination of the GSK 2189242A (or 10PP) vaccine combined with high doses (HD) of pneumococcal pneumolysin toxoid proteins (dPly) and pneumococcal histidine protein D (PhtD), co-administered with the Infanrix hexa™ vaccine at Study Months 0, 1 and 2. Subjects also received a booster dose of each of these vaccines, administered at Study Month 10.

Reporting group title	Synflorix/Infanrix hexa Group

Reporting group description:

This group consisted in infants aged 6-14 weeks at primary vaccination who received a 3-dose primary vaccination of Synflorix™ vaccine, co-administered with the Infanrix hexa™ vaccine at Study Months 0, 1 and 2. Subjects also received a booster dose of each of these vaccines, administered at Study Month 10.

Reporting group title	Prevnar 13/Infanrix hexa Group

Reporting group description:

This group consisted in infants aged 6-14 weeks at primary vaccination who received a 3-dose primary vaccination of Prevnar 13™ vaccine, co-administered with the Infanrix hexa™ vaccine at Study Months 0, 1 and 2. Subjects also received a booster dose of each of these vaccines, administered at Study Month 10.

Primary: Number of subjects with any and Grade 3 solicited general symptoms and with solicited general symptoms related to vaccination – Primary Phase of the study

End point title	Number of subjects with any and Grade 3 solicited general symptoms and with solicited general symptoms related to vaccination – Primary Phase of the study[1]

End point description:

Assessed solicited general symptoms were Drowsiness, Irritability, Loss of appetite (Loss Appet.) and Fever (rectal temperature higher than or equal to [>=] 38 degrees Celsius [°C]). Any = Occurrence of the specified solicited general symptom, regardless of intensity and relationship to vaccination. Related = Occurrence of the specified symptom assessed by the investigators as causally related to vaccination. Grade 3 (G3) Drowsiness = Drowsiness that prevented normal activity. G3 Irritability = Crying that could not be comforted/prevented normal activity. G3 Loss of appetite = Subject did not eat at all. G3 Fever = Rectal temperature higher than (>) 40.0°C. Primary results correspond to results for occurrences of G3 fever symptoms assessed by the investigators as related to vaccination (Related G3 fever).

End point type	Primary

End point timeframe:

Within the 7-day (Days 0-6) periods post vaccination, after each dose (D) of the 3-dose primary vaccination course

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 scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	10PP-LD/Infanrix hexa Group	10PP-HD/Infanrix hexa Group	Synflorix/Infanrix hexa Group	Prevnar 13/Infanrix hexa Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	146	142	144	142
Units: Subject				
Any Drowsiness, post D1 (N=146;142;144;142)	82	76	72	77
G3 Drowsiness, post D1 (N=146;142;144;142)	4	0	2	2
Related Drowsiness, post D1 (N=146;142;144;142)	63	58	52	58
Any Irritability, post D1 (N=146;142;144;142)	93	82	89	82
G3 Irritability, post D1 (N=146;142;144;142)	6	9	9	5
Related Irritability, post D1 (N=146;142;144;142)	70	62	66	57
Any Loss Appet., post D1 (N=146;142;144;142)	38	32	39	32
G3 Loss Appet., post D1 (N=146;142;144;142)	0	1	0	0
Related Loss Appet., post D1 (N=146;142;144;142)	28	26	29	21
Any Fever, post D1 (N=146;142;144;142)	45	32	53	28
G3 Fever, post D1 (N=146;142;144;142)	0	0	0	0
Related Fever, post D1 (N=146;142;144;142)	33	25	44	27
Related G3 Fever, post D1 (N=146;142;144;142)	0	0	0	0
Any Drowsiness, post D2 (N=146;142;144;142)	71	63	70	66
G3 Drowsiness, post D2 (N=146;142;144;142)	4	2	1	1
Related Drowsiness, post D2 (N=146;142;144;142)	53	49	56	55
Any Irritability, post D2 (N=146;142;144;142)	88	81	86	87
G3 Irritability, post D2 (N=146;142;144;142)	8	3	5	6
Related Irritability, post D2 (N=146;142;144;142)	69	66	66	67
Any Loss Appet., post D2 (N=146;142;144;142)	32	30	28	30
G3 Loss Appet., post D2 (N=146;142;144;142)	1	2	0	0
Related Loss Appet., post D2 (N=146;142;144;142)	23	21	18	25
Any Fever, post D2 (N=146;142;144;142)	40	50	38	38
G3 Fever, post D2 (N=146;142;144;142)	0	0	0	0
Related Fever, post D2 (N=146;142;144;142)	32	39	33	31
Related G3 Fever, post D2 (N=146;142;144;142)	0	0	0	0
Any Drowsiness, post D3 (N=146;141;143;142)	57	48	56	48
Grade 3 Drowsiness, post D3 (N=146;141;143;142)	2	0	1	1

Related Drowsiness, post D3 (N=146;141;143;142)	51	38	44	36
Any Irritability, post D3 (N=146;141;143;142)	62	73	62	72
G3 Irritability, post D3 (N=146;141;143;142)	7	1	3	2
Related Irritability, post D3 (N=146;141;143;142)	52	55	48	53
Any Loss Appet., post D3 (N=146,141,143,142)	28	25	24	21
G3 Loss Appet., post D3 (N=146,141,143,142)	0	0	2	2
Related Loss Appet., post D3 (N=146,141,143,142)	22	20	18	13
Any Fever, post D3 (N=146;141;143;142)	28	23	27	30
G3 Fever, post D3 (N=146;141;143;142)	0	0	0	0
Related Fever, post D3 (N=146;141;143;142)	23	19	20	22
Related G3 Fever, post D3 (N=146;141;143;142)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects reporting fever > 40.0°C with causal relationship to vaccination after each primary vaccination dose and across doses in 10PP-LD/Infanrix hexa group and in Synflorix/Infanrix hexa group

End point title	Number of subjects reporting fever > 40.0°C with causal relationship to vaccination after each primary vaccination dose and across doses in 10PP-LD/Infanrix hexa group and in Synflorix/Infanrix hexa group[2]

End point description:

Grade 3 fever was defined as fever by rectal measurement >40.0°C. Related was defined a causal relationship to vaccination. This endpoint was assessed after each primary vaccination dose and across doses and in subjects in the 10PP-LD/Infanrix hexa (or 10PP-LD) and Synflorix/Infanrix hexa (or 10PN) groups only.

End point type	Primary

End point timeframe:

during the 7-day (Days 0-6) post-vaccination period following each primary vaccination dose and across doses

Notes:

[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 related to the difference between 2 groups: the 10PP-LD/Infanrix hexa group and the Synflorix/Infanrix hexa group.

End point values	10PP-LD/Infanrix hexa Group	Synflorix/Infanrix hexa Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	146	144		
Units: percentage				
number (not applicable)				

Fever > 40.0°C & Related Dose 1 (N=146, 144)	0	0		
Fever> 40.0°C & Related Dose 2 (N=146, 144)	0	0		
Fever> 40.0°C & Related Dose 3 (N=146, 143)	0	0		
Fever> 40.0°C & Related across doses (N=146,144)	0	0		

Statistical analyses

Statistical analysis title	Non-inferiority: 10PP-LD versus Synflorix - dose 1

Statistical analysis description:

Non-inferiority of 10PP-LD vaccine vs Synflorix™ vaccine post dose 1 was assessed by computing the difference in percentages of subjects reporting Grade 3 fever causally related to dose 1 vaccination in the 10PP-LD Group minus 10PN Group. Non-inferiority was supported if one could rule out an increase in terms of percentage of subjects (10PP-LD Group minus 10PN Group) above 5% + half the incidence in the 10PN Group (= null hypothesis) as shown by a 1-sided P-value < 5%.

Comparison groups	Synflorix/Infanrix hexa Group v 10PP-LD/Infanrix hexa Group
Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.003 [3]
Method	Kem Phillip's statistical test
Parameter estimate	Difference in percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.61
upper limit	2.57

Notes:

[3] - 1-sided P-value computed using Kem Philips'approach for ruling out an increase in % subjects with fever > 40.0°C and causal relationship to vaccination > the boundary expressed as 5% + 0.5*rate in the 10PN group.

Statistical analysis title	Non-inferiority: 10PP-LD versus Synflorix - dose 2

Statistical analysis description:

Non-inferiority of 10PP-LD vaccine vs Synflorix™ vaccine post dose 2 was assessed by computing the difference in percentages of subjects reporting Grade 3 fever causally related to dose 2 vaccination in the 10PP-LD Group minus 10PN Group. Non-inferiority was supported if one could rule out an increase in terms of percentage of subjects (10PP-LD Group minus 10PN Group) above 5% + half the incidence in the 10PN Group (= null hypothesis) as shown by a 1-sided P-value < 5%

Comparison groups	Synflorix/Infanrix hexa Group v 10PP-LD/Infanrix hexa Group
Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.003 [4]
Method	Kem Phillip's statistical test
Parameter estimate	Difference in percentage
Point estimate	0

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.61
upper limit	2.57

Notes:

[4] - 1-sided P-value computed using Kem Philips'approach for ruling out an increase in % subjects with fever > 40.0°C and causal relationship to vaccination > the boundary expressed as 5% + 0.5*rate in the 10PN group.

Statistical analysis title	Non-inferiority: 10PP-LD versus Synflorix - dose 3

Statistical analysis description:

Non-inferiority of 10PP-LD vaccine vs Synflorix™ vaccine post dose 3 was assessed by computing the difference in percentages of subjects reporting Grade 3 fever causally related to dose 3 vaccination in the 10PP-LD Group minus 10PN Group. Non-inferiority was supported if one could rule out an increase in terms of percentage of subjects (10PP-LD Group minus 10PN Group) above 5% + half the incidence in the 10PN Group (= null hypothesis) as shown by a 1-sided P-value < 5%

Comparison groups	Synflorix/Infanrix hexa Group v 10PP-LD/Infanrix hexa Group
Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.003 [5]
Method	Kem Phillip's statistical test
Parameter estimate	Difference in percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.62
upper limit	2.57

Notes:

[5] - 1-sided P-value computed using Kem Philips'approach for ruling out an increase in % subjects with fever > 40.0°C and causal relationship to vaccination > the boundary expressed as 5% + 0.5*rate in the 10PN group.

Statistical analysis title	Non-inferiority:10PP-LD vs Synflorix - across dose

Statistical analysis description:

Non-inferiority of 10PP-LD vaccine vs Synflorix™ vaccine across doses was assessed by computing the difference in percentages of subjects reporting Grade 3 fever causally related to vaccination, across doses, in the 10PP-LD Group minus 10PN Group. Non-inferiority was supported if one could rule out an increase in terms of percentage of subjects (10PP-LD Group minus 10PN Group) above 5% + half the incidence in the 10PN Group (= null hypothesis) as shown by a 1-sided P-value < 5%

Comparison groups	Synflorix/Infanrix hexa Group v 10PP-LD/Infanrix hexa Group
Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.003 [6]
Method	Kem Phillip's statistical test
Parameter estimate	Difference in percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.61
upper limit	2.57

Notes:

[6] - 1-sided P-value computed using Kem Philips'approach for ruling out an increase in % subjects with fever > 40.0°C and causal relationship to vaccination > the boundary expressed as 5% + 0.5*rate in the 10PN group.

Primary: Number of subjects reporting fever > 40° C with causal relationship to vaccination after each primary vaccination dose and across doses in the 10PP-HD/Infanrix hexa group and in the Synflorix/Infanrix hexa group

End point title	Number of subjects reporting fever > 40° C with causal relationship to vaccination after each primary vaccination dose and across doses in the 10PP-HD/Infanrix hexa group and in the Synflorix/Infanrix hexa group[7]

End point description:

Grade 3 fever was defined as fever by rectal measurement >40.0°C. Related was defined a causal relationship to vaccination. This endpoint was assessed after each primary vaccination dose and across doses and in subjects in the 10PP-HD/Infanrix hexa (or 10PP-HD) and Synflorix/Infanrix hexa (or 10PN) groups only.

End point type	Primary

End point timeframe:

during the 7-day (Days 0-6) post-vaccination period following each primary vaccination dose and across doses

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 related to the difference between 2 groups: the 10PP-HD/Infanrix hexa group and the Synflorix/Infanrix hexa group.

End point values	10PP-HD/Infanrix hexa Group	Synflorix/Infanrix hexa Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	142	144		
Units: percentage				
number (not applicable)				
Fever > 40.0°C & Related Dose 1 (N= 142,144)	0	0		
Fever> 40.0°C & Related Dose 2 (N=142,144)	0	0		
Fever> 40.0°C & Related Dose 3 (N=141,143)	0	0		
Fever> 40.0°C & Related across doses (N=142,144)	0	0		

Statistical analyses

Statistical analysis title	Non-inferiority: 10PP-HD versus Synflorix- dose 1

Statistical analysis description:

Non-inferiority of 10PP-HD vaccine vs Synflorix™ vaccine post dose 1 was assessed by computing the difference in percentages of subjects reporting Grade 3 fever causally related to dose 1 vaccination in the 10PP-HD Group minus 10PN Group. Non-inferiority was supported if one could rule out an increase in terms of percentage of subjects (10PP-HD Group minus 10PN Group) above 5% + half the incidence in the 10PN Group (= null hypothesis) as shown by a 1-sided P-value < 5%.

Comparison groups	10PP-HD/Infanrix hexa Group v Synflorix/Infanrix hexa Group

Number of subjects included in analysis	286
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.003 [8]
Method	Kem Philips' statistical test
Parameter estimate	Difference in percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.61
upper limit	2.64

Notes:

[8] - 1-sided P-value computed using Kem Philips'approach for ruling out an increase in % of subjects with fever > 40.0°C and causal relationship to vaccination above the boundary expressed as 5% + 0.5 *rate in the 10PN group.

Statistical analysis title	Non-inferiority: 10PP-HD versus Synflorix- dose 2

Statistical analysis description:

Non-inferiority of 10PP-HD vaccine vs Synflorix™ vaccine post dose 2 was assessed by computing the difference in percentages of subjects reporting Grade 3 fever causally related to dose 2 vaccination in the 10PP-HD Group minus 10PN Group. Non-inferiority was supported if one could rule out an increase in terms of percentage of subjects (10PP-HD Group minus 10PN Group) above 5% + half the incidence in the 10PN Group (= null hypothesis) as shown by a 1-sided P-value < 5%.

Comparison groups	10PP-HD/Infanrix hexa Group v Synflorix/Infanrix hexa Group
Number of subjects included in analysis	286
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.003 [9]
Method	Kem Philips' statistical test
Parameter estimate	Difference in percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.61
upper limit	2.64

Notes:

[9] - 1-sided P-value computed using Kem Philips'approach for ruling out an increase in % of subjects with fever > 40.0°C and causal relationship to vaccination above the boundary expressed as 5% + 0.5 *rate in the 10PN group.

Statistical analysis title	Non-inferiority: 10PP-HD versus Synflorix - dose 3

Statistical analysis description:

Non-inferiority of 10PP-HD vaccine vs Synflorix™ vaccine post dose 3 was assessed by computing the difference in percentages of subjects reporting Grade 3 fever causally related to dose 3 vaccination in the 10PP-HD Group minus 10PN Group. Non-inferiority was supported if one could rule out an increase in terms of percentage of subjects (10PP-HD Group minus 10PN Group) above 5% + half the incidence in the 10PN Group (= null hypothesis) as shown by a 1-sided P-value < 5%.

Comparison groups	10PP-HD/Infanrix hexa Group v Synflorix/Infanrix hexa Group

Number of subjects included in analysis	286
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.003 [10]
Method	Kem Philips' statistical test
Parameter estimate	Difference in percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.63
upper limit	2.66

Notes:

[10] - 1-sided P-value computed using Kem Philips'approach for ruling out an increase in % of subjects with fever > 40.0°C and causal relationship to vaccination above the boundary expressed as 5% + 0.5 *rate in the 10PN group.

Statistical analysis title	Non-inferiority: 10PP-HD vs Synflorix-across doses

Statistical analysis description:

Non-inferiority of 10PP-HD vaccine vs Synflorix™ vaccine across doses was assessed by computing the difference in percentages of subjects reporting Grade 3 fever causally related to vaccination, across doses, in the 10PP-HD Group minus 10PN Group. Non-inferiority was supported if one could rule out an increase in terms of percentage of subjects (10PP-HD Group minus 10PN Group) above 5% + half the incidence in the 10PN Group (= null hypothesis) as shown by a 1-sided P-value < 5%.

Comparison groups	10PP-HD/Infanrix hexa Group v Synflorix/Infanrix hexa Group
Number of subjects included in analysis	286
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.003 [11]
Method	Kem Philips' statistical test
Parameter estimate	Difference in percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.61
upper limit	2.64

Notes:

[11] - 1-sided P-value computed using Kem Philips'approach for ruling out an increase in % of subjects with fever > 40.0°C and causal relationship to vaccination above the boundary expressed as 5% + 0.5 *rate in the 10PN group.

Secondary: Antibody concentrations against pneumococcal pneumolysin toxoid (dPly) and pneumococcal histidine triad protein D (PhtD) proteins – Primary Phase of the study.

End point title	Antibody concentrations against pneumococcal pneumolysin toxoid (dPly) and pneumococcal histidine triad protein D (PhtD) proteins – Primary Phase of the study.

End point description:

Antibody concentrations against dPly and PhtD (anti-dPly and anti-PhtD, respectively) were measured by enzyme-linked immunosorbent assay (ELISA), expressed as geometric mean concentrations (GMCs), in ELISA Units per milliliter (EL.U/mL). Cut-offs for seropositivity were concentrations higher than or equal to (≥)12 EL.U/mL for anti-dPly antibodies and ≥ 17 EL.U/mL for anti-PhtD antibodies. This outcome concerns results for the Primary Phase of the study.

End point type	Secondary

End point timeframe:

At Month 3, e. g. one month post-Dose 3 of pneumococcal vaccine (10PP, Synflorix™ or Prevnar 13™)

End point values	10PP-LD/Infanrix hexa Group	10PP-HD/Infanrix hexa Group	Synflorix/Infanrix hexa Group	Prevnar 13/Infanrix hexa Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	131	134	136	133
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-dPly – At Month 3	9501.35 (8260.68 to 10928.37)	12067.41 (10582.51 to 13760.66)	459.97 (398.31 to 531.18)	477.31 (409 to 557.03)
Anti-PhtD – At Month 3	1495.15 (1274.28 to 1754.29)	1986.96 (1726.88 to 2286.21)	523.61 (453.71 to 604.28)	555 (473.15 to 651.02)

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against protein D (anti-PD) – Primary Phase of the study.

End point title	Antibody concentrations against protein D (anti-PD) – Primary Phase of the study.

End point description:

Antibody concentrations were measured by enzyme-linked immunosorbent assay (ELISA), expressed as geometric mean concentrations (GMCs), in ELISA Units per milliliter (EL.U/mL). The seropositivity cut-off of the assay was a concentration of anti-PD antibodies ≥ 100 EL.U/mL. This outcome concerns results for the Primary Phase of the study.

End point type	Secondary

End point timeframe:

At Month 3, e. g. one month post-Dose 3 of pneumococcal vaccine (10PP, Synflorix™ or Prevnar 13™)

End point values	10PP-LD/Infanrix hexa Group	10PP-HD/Infanrix hexa Group	Synflorix/Infanrix hexa Group	Prevnar 13/Infanrix hexa Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	133	134	137	134
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD – At Month 3	1135.7 (929.3 to 1388)	1337.3 (1109.2 to 1612.2)	1539 (1258.4 to 1882.1)	149.6 (114.2 to 195.9)

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against pneumococcal serotypes – Primary Phase of the study.

End point title	Antibody concentrations against pneumococcal serotypes – Primary Phase of the study.

End point description:

Antibodies assessed for this outcome measure were those against the vaccine/cross-reactive pneumococcal serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F (ANTI-1, -3, -4, -5, -6A, -6B, -7F, -9V, -14, -18C, -19A, -19F and -23F). Antibody concentrations were measured by 22F 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. This outcome concerns results for the Primary Phase of the study.

End point type	Secondary

End point timeframe:

At Month 3, e. g. one month post-Dose 3 of pneumococcal vaccine (10PP, Synflorix™ or Prevnar 13™)

End point values	10PP-LD/Infanrix hexa Group	10PP-HD/Infanrix hexa Group	Synflorix/Infanrix hexa Group	Prevnar 13/Infanrix hexa Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	133	135	137	134
Units: µg/mL				
geometric mean (confidence interval 95%)				
ANTI-1 At Month 3 (N=132,131,134,134)	1.56 (1.36 to 1.79)	1.59 (1.37 to 1.84)	1.49 (1.28 to 1.74)	2.18 (1.84 to 2.57)
ANTI-4 At Month 3 (N=132,133,133,134)	2.04 (1.74 to 2.39)	2.12 (1.83 to 2.44)	1.82 (1.55 to 2.14)	2.41 (2.04 to 2.85)
ANTI-5 At Month 3 (N=133,134,134,134)	2.46 (2.13 to 2.85)	2.56 (2.24 to 2.94)	2.31 (2 to 2.67)	2.78 (2.29 to 3.39)
ANTI-6B At Month 3 (N=131,129,133,134)	0.37 (0.29 to 0.46)	0.37 (0.31 to 0.45)	0.4 (0.32 to 0.51)	0.45 (0.36 to 0.56)
ANTI-7F At Month 3 (N=131,131,134,134)	2.12 (1.86 to 2.41)	2.21 (1.97 to 2.48)	2.2 (1.92 to 2.5)	2.93 (2.5 to 3.43)
ANTI-9V At Month 3 (N=133,135,137,134)	1.83 (1.59 to 2.11)	1.95 (1.73 to 2.21)	1.99 (1.72 to 2.3)	2.32 (1.96 to 2.75)
ANTI-14 At Month 3 (N=133,133,135,134)	3.6 (3.11 to 4.17)	3.71 (3.3 to 4.18)	3.91 (3.41 to 4.48)	4.14 (3.38 to 5.06)
ANTI-18C At Month 3 (N=133,132,135,134)	2.27 (1.93 to 2.67)	2.21 (1.87 to 2.62)	2.45 (2.04 to 2.95)	2.56 (2.14 to 3.06)
ANTI-19F At Month 3 (N=133,132,135,134)	4.29 (3.64 to 5.07)	4.13 (3.52 to 4.84)	4.51 (3.79 to 5.36)	3.47 (2.92 to 4.13)
ANTI-23F At Month 3 N=132,133,135,134)	0.66 (0.54 to 0.81)	0.62 (0.5 to 0.78)	0.67 (0.54 to 0.82)	1.48 (1.17 to 1.87)
ANTI-3 (At Month 3 N=131,129,132,134)	0.05 (0.04 to 0.07)	0.06 (0.05 to 0.07)	0.05 (0.05 to 0.06)	2.43 (2.05 to 2.89)

ANTI-6A At Month 3 (N=130,132,133,134)	0.13 (0.1 to 0.16)	0.11 (0.09 to 0.14)	0.11 (0.09 to 0.14)	2.06 (1.7 to 2.5)
ANTI-19A At Month 3 (N=131,129,134,134)	0.18 (0.14 to 0.22)	0.17 (0.14 to 0.21)	0.16 (0.13 to 0.2)	2.75 (2.33 to 3.25)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and Grade 3 solicited local symptoms – Primary Phase of the study

End point title	Number of subjects with any and Grade 3 solicited local symptoms – Primary Phase of the study

End point description:

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

End point type	Secondary

End point timeframe:

Within the 7-day (Days 0-6) periods post vaccination, after each dose (D) of the 3-dose primary vaccination course

End point values	10PP-LD/Infanrix hexa Group	10PP-HD/Infanrix hexa Group	Synflorix/Infanrix hexa Group	Prevnar 13/Infanrix hexa Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	146	142	144	142
Units: Subject				
Any Pain, post D1 (N=146;142;144;142)	52	46	53	40
Grade 3 Pain, post D1 (N=146;142;144;142)	0	2	3	0
Any Redness, post D1 (N=146;142;144;142)	59	58	52	51
Grade 3 Redness, post D1 (N=146;142;144;142)	0	0	3	2
Any Swelling, post D1 (N=146;142;144;142)	47	46	34	37
Grade 3 Swelling, post D1 (N=146;142;144;142)	3	5	3	6
Any Pain, post D2 (N=146;142;144;142)	52	49	42	43
Grade 3 Pain, post D2 (N=146;142;144;142)	2	0	1	2
Any Redness, post D2 (N=146;142;144;142)	67	67	63	59
Grade 3 Redness, post D2 (N=146;142;144;142)	2	2	3	0
Any Swelling, post D2 (N=146;142;144;142)	49	56	43	38
Grade 3 Swelling, post D2 (N=146;142;144;142)	5	4	2	3

Any Pain, post D3 (N=146;141;143;142)	41	35	37	45
Grade 3 Pain, post D3 (N=146;141;143;142)	2	3	1	1
Any Redness, post D3 (N=146;141;143;142)	65	65	58	65
Grade 3 Redness, post D3 (N=146;141;143;142)	3	2	0	3
Any Swelling, post D3 (N=146;141;143;142)	52	52	43	43
Grade 3 Swelling, post D3 (N=146;141;143;142)	6	3	3	5

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and Grade 3 solicited local symptoms – Booster Phase of the study

End point title	Number of subjects with any and Grade 3 solicited local symptoms – Booster Phase of the study

End point description:

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

End point type	Secondary

End point timeframe:

Within the 7-day (Days 0-6) period after booster vaccination

End point values	10PP-LD/Infanrix hexa Group	10PP-HD/Infanrix hexa Group	Synflorix/Infanrix hexa Group	Prevnar 13/Infanrix hexa Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	144	140	139	140
Units: Subject				
Any Pain, (N=144;140;139;140)	77	73	61	68
Grade 3 Pain (N=144;140;139;140)	7	6	3	4
Any Redness (N=144;140;139;140)	83	81	68	66
Grade 3 Redness (N=144;140;139;140)	11	15	12	7
Any Swelling (N=144;140;139;140)	70	55	49	59
Grade 3 Swelling (N=144;140;139;140)	8	8	7	10

Statistical analyses

No statistical analyses for this end point

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

solicited general symptoms with relationship to vaccination – Booster Phase of the study

End point title	Number of subjects with any, Grade 3 solicited general symptoms and solicited general symptoms with relationship to vaccination – Booster Phase of the study

End point description:

Assessed solicited general symptoms were Drowsiness, Irritability, Loss of appetite (Loss Appet.) and Fever (rectal temperature higher than [≥] 38 degrees Celsius [°C]). Any = Occurrence of the specified solicited general symptom, regardless of intensity and relationship to vaccination. Related = Occurrence of the specified symptom assessed by the investigator as causally related to vaccination. Grade 3 (G3) Drowsiness = Drowsiness that prevented normal activity. Grade 3 Irritability = Crying that could not be comforted/prevented normal activity. Grade 3 Loss of appetite = Subject did not eat at all. Grade 3 Fever = Axillary temperature higher than (>) 40.0°C.

End point type	Secondary

End point timeframe:

Within the 7-day (Days 0-6) period post vaccination after booster vaccination

End point values	10PP-LD/Infanrix hexa Group	10PP-HD/Infanrix hexa Group	Synflorix/Infanrix hexa Group	Prevnar 13/Infanrix hexa Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	144	140	139	140
Units: Subject				
Any Drowsiness (N=144;140;139;140)	77	64	66	73
G3 Drowsiness (N=144;140;139;140)	1	5	1	1
Related Drowsiness (N=144;140;139;140)	68	61	59	69
Any Irritability (N=144;140;139;140)	95	84	82	90
G3 Irritability (N=144;140;139;140)	12	8	4	8
Related Irritability (N=144;140;139;140)	86	82	76	83
Any Loss Appet. (N=144;140;139;140)	49	38	36	57
G3 Loss Appet. (N=144;140;139;140)	3	4	2	2
Related Loss Appet. (N=144;140;139;140)	42	38	33	49
Any Fever (N=144;140;139;140)	50	55	51	53
G3 Fever (N=144;140;139;140)	1	0	1	3
Related Fever (N=144;140;139;140)	44	52	45	47

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited adverse events (AEs) – Primary Phase of the study

End point title	Number of subjects with unsolicited adverse events (AEs) – Primary Phase of the study

End point description:

An unsolicited AE was defined as any untoward medical occurrence in a clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An AE can therefore be any unfavourable and unintended sign (including an abnormal

laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. For the marketed products administered in the study, this also included failure to produce expected benefits (i.e. lack of efficacy), abuse or misuse of the product. Any = Occurrence of an unsolicited AE, regardless of intensity or relationship to vaccination.

End point type	Secondary

End point timeframe:

Within the 31-day (Days 0-30) period post primary vaccination, across doses

End point values	10PP-LD/Infanrix hexa Group	10PP-HD/Infanrix hexa Group	Synflorix/Infanrix hexa Group	Prevnar 13/Infanrix hexa Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	146	142	145	142
Units: Subject				
Any AE	55	68	64	61

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited adverse events (AEs) – Booster Phase of the study

End point title	Number of subjects with unsolicited adverse events (AEs) – Booster Phase of the study

End point description:

An unsolicited AE was defined as any untoward medical occurrence in a clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. For the marketed products administered in the study, this also included failure to produce expected benefits (i.e. lack of efficacy), abuse or misuse of the product. Any = Occurrence of an unsolicited AE, regardless of intensity or relationship to vaccination.

End point type	Secondary

End point timeframe:

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

End point values	10PP-LD/Infanrix hexa Group	10PP-HD/Infanrix hexa Group	Synflorix/Infanrix hexa Group	Prevnar 13/Infanrix hexa Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	144	140	140	140
Units: Subject				
Any AE	40	26	27	34

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms: during the 7 days post-primary vaccination and post-booster vaccination. Unsolicited AEs during 31 days post-primary vaccination and post booster vaccination. SAEs: during the entire study period (Months 0-11).

Adverse event reporting additional description:

Solicited symptoms results are presented only for subjects for whom results were available. SAEs are not presented (n affected = 0): Detailed data are blinded as the study is still ongoing. Note: the occurences (all) numbers were not calculated during the analysis: data entered are equal to the subject affected numbers.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17

Reporting groups

Reporting group title	10PP-LD/Infanrix hexa Group

Reporting group description:

This group consisted in infants aged 6-14 weeks at primary vaccination who received a 3-dose primary vaccination of the GSK 2189242A (or 10PP) vaccine combined with low doses (LD) of pneumococcal pneumolysin toxoid proteins (dPly) and pneumococcal histidine protein D (PhtD) co-administered with the Infanrix hexa™ vaccine at Study Months 0, 1 and 2. Subjects also received a booster dose of each of these vaccines, administered at Study Month 10.

Reporting group title	10PP-HD/Infanrix hexa Group

Reporting group description:

This group consisted in infants aged 6-14 weeks at primary vaccination who received a 3-dose primary vaccination of the GSK 2189242A (or 10PP) vaccine combined with high doses (HD) of pneumococcal pneumolysin toxoid proteins (dPly) and pneumococcal histidine protein D (PhtD), co-administered with the Infanrix hexa™ vaccine at Study Months 0, 1 and 2. Subjects also received a booster dose of each of these vaccines, administered at Study Month 10.

Reporting group title	Synflorix/Infanrix hexa Group

Reporting group description:

This group consisted in infants aged 6-14 weeks at primary vaccination who received a 3-dose primary vaccination of Synflorix™ vaccine, co-administered with the Infanrix hexa™ vaccine at Study Months 0, 1 and 2. Subjects also received a booster dose of each of these vaccines, administered at Study Month 10.

Reporting group title	Prevnar 13/Infanrix hexa Group

Reporting group description:

This group consisted in infants aged 6-14 weeks at primary vaccination who received a 3-dose primary vaccination of Prevnar 13™ vaccine, co-administered with the Infanrix hexa™ vaccine at Study Months 0, 1 and 2. Subjects also received a booster dose of each of these vaccines, administered at Study Month 10.

Serious adverse events	10PP-LD/Infanrix hexa Group	10PP-HD/Infanrix hexa Group	Synflorix/Infanrix hexa Group
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 146 (0.00%)	0 / 142 (0.00%)	0 / 145 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	Prevnar 13/Infanrix hexa Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 142 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

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

Non-serious adverse events	10PP-LD/Infanrix hexa Group	10PP-HD/Infanrix hexa Group	Synflorix/Infanrix hexa Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	118 / 146 (80.82%)	113 / 142 (79.58%)	110 / 145 (75.86%)
General disorders and administration site conditions			
Pain (primary vaccination)	Additional description: Symptom reported during the 7-day post-primary vaccination periods, across doses		
subjects affected / exposed[1]	75 / 146 (51.37%)	73 / 142 (51.41%)	72 / 144 (50.00%)
occurrences (all)	75	73	72
Redness (primary vaccination)	Additional description: Symptom reported during the 7-day post-primary vaccination periods, across doses		
subjects affected / exposed[2]	96 / 146 (65.75%)	97 / 142 (68.31%)	88 / 144 (61.11%)
occurrences (all)	96	97	88
Swelling (primary vaccination)	Additional description: Symptom reported during the 7-day post-primary vaccination periods, across doses		
subjects affected / exposed[3]	82 / 146 (56.16%)	74 / 142 (52.11%)	60 / 144 (41.67%)
occurrences (all)	82	74	60
Drowsiness (primary vaccination)	Additional description: Symptom reported during the 7-day post-primary vaccination periods, across doses		
subjects affected / exposed[4]	107 / 146 (73.29%)	96 / 142 (67.61%)	98 / 144 (68.06%)
occurrences (all)	107	96	98
Irritability (primary vaccination)	Additional description: Symptom reported during the 7-day post-primary vaccination periods, across doses		
alternative assessment type: Non-systematic			
subjects affected / exposed[5]	118 / 146 (80.82%)	113 / 142 (79.58%)	110 / 144 (76.39%)
occurrences (all)	118	113	110
Loss of appetite (primary vaccination)	Additional description: Symptom reported during the 7-day post-primary vaccination periods, across doses		
subjects affected / exposed[6]	65 / 146 (44.52%)	59 / 142 (41.55%)	59 / 144 (40.97%)
occurrences (all)	65	59	59
Fever (primary vaccination)	Additional description: (rectal temperature >= 38°C) Symptom reported during the 7-day post-primary vaccination periods, across doses		

subjects affected / exposed[7]	76 / 146 (52.05%)	71 / 142 (50.00%)	74 / 144 (51.39%)
occurrences (all)	76	71	74
Pain (booster vaccination)	Additional description: Symptom reported during the 7-day post-booster vaccination period		
subjects affected / exposed[8]	77 / 144 (53.47%)	73 / 140 (52.14%)	61 / 139 (43.88%)
occurrences (all)	77	73	61
Redness (booster vaccination)	Additional description: Symptom reported during the 7-day post-booster vaccination period		
subjects affected / exposed[9]	83 / 144 (57.64%)	81 / 140 (57.86%)	68 / 139 (48.92%)
occurrences (all)	83	81	68
Swelling (booster vaccination)	Additional description: Symptom reported during the 7-day post-booster vaccination period		
subjects affected / exposed[10]	70 / 144 (48.61%)	55 / 140 (39.29%)	49 / 139 (35.25%)
occurrences (all)	70	55	49
Drowsiness (booster vaccination)	Additional description: Symptom reported during the 7-day post-booster vaccination period		
subjects affected / exposed[11]	77 / 144 (53.47%)	64 / 140 (45.71%)	66 / 139 (47.48%)
occurrences (all)	77	64	66
Irritability (booster vaccination)	Additional description: Symptom reported during the 7-day post-booster vaccination period		
subjects affected / exposed[12]	95 / 144 (65.97%)	84 / 140 (60.00%)	82 / 139 (58.99%)
occurrences (all)	95	84	82
Loss of appetite (booster vaccination)	Additional description: Symptom reported during the 7-day post-booster vaccination period		
subjects affected / exposed[13]	49 / 144 (34.03%)	38 / 140 (27.14%)	36 / 139 (25.90%)
occurrences (all)	49	38	36
Fever (booster vaccination)	Additional description: (rectal temperature >= 38°C) Symptom reported during the 7-day post-booster vaccination period		
subjects affected / exposed[14]	50 / 144 (34.72%)	55 / 140 (39.29%)	51 / 139 (36.69%)
occurrences (all)	50	55	51
Eye disorders			
Conjunctivitis	Additional description: Unsolicited AE reported during the 31-day post-primary vaccination periods, across doses		
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 146 (2.05%)	9 / 142 (6.34%)	5 / 145 (3.45%)
occurrences (all)	3	9	5
Infections and infestations			
Bronchitis	Additional description: Unsolicited AE reported during the 31-day post-primary vaccination periods, across doses		
alternative assessment type: Non-systematic			
subjects affected / exposed	5 / 146 (3.42%)	11 / 142 (7.75%)	11 / 145 (7.59%)
occurrences (all)	5	11	11

Nasopharyngitis (primary vaccination)	Additional description: Unsolicited AE reported during the 31-day post-primary vaccination periods, across doses		
alternative assessment type: Non-systematic			
subjects affected / exposed	10 / 146 (6.85%)	7 / 142 (4.93%)	12 / 145 (8.28%)
occurrences (all)	10	7	12
Nasopharyngitis (booster vaccination)	Additional description: Unsolicited AE reported during the 31-day post-booster vaccination period		
alternative assessment type: Non-systematic			
subjects affected / exposed[15]	9 / 144 (6.25%)	4 / 140 (2.86%)	3 / 140 (2.14%)
occurrences (all)	9	4	3
Rhinitis	Additional description: Unsolicited AE reported during the 31-day post-primary vaccination periods, across doses		
alternative assessment type: Non-systematic			
subjects affected / exposed	11 / 146 (7.53%)	11 / 142 (7.75%)	12 / 145 (8.28%)
occurrences (all)	11	11	12
Viral infection	Additional description: Unsolicited AE reported during the 31-day post-primary vaccination periods, across doses		
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 146 (0.00%)	9 / 142 (6.34%)	5 / 145 (3.45%)
occurrences (all)	0	9	5

Non-serious adverse events	Prevnar 13/Infanrix hexa Group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	113 / 142 (79.58%)		
General disorders and administration site conditions			
Pain (primary vaccination)	Additional description: Symptom reported during the 7-day post-primary vaccination periods, across doses		
subjects affected / exposed[1]	64 / 142 (45.07%)		
occurrences (all)	64		
Redness (primary vaccination)	Additional description: Symptom reported during the 7-day post-primary vaccination periods, across doses		
subjects affected / exposed[2]	83 / 142 (58.45%)		
occurrences (all)	83		
Swelling (primary vaccination)	Additional description: Symptom reported during the 7-day post-primary vaccination periods, across doses		
subjects affected / exposed[3]	59 / 142 (41.55%)		
occurrences (all)	59		
Drowsiness (primary vaccination)	Additional description: Symptom reported during the 7-day post-primary vaccination periods, across doses		
subjects affected / exposed[4]	102 / 142 (71.83%)		
occurrences (all)	102		

Irritability (primary vaccination)	Additional description: Symptom reported during the 7-day post-primary vaccination periods, across doses		
alternative assessment type: Non-systematic			
subjects affected / exposed[5]	113 / 142 (79.58%)		
occurrences (all)	113		
Loss of appetite (primary vaccination)	Additional description: Symptom reported during the 7-day post-primary vaccination periods, across doses		
subjects affected / exposed[6]	57 / 142 (40.14%)		
occurrences (all)	57		
Fever (primary vaccination)	Additional description: (rectal temperature >= 38°C) Symptom reported during the 7-day post-primary vaccination periods, across doses		
subjects affected / exposed[7]	65 / 142 (45.77%)		
occurrences (all)	65		
Pain (booster vaccination)	Additional description: Symptom reported during the 7-day post-booster vaccination period		
subjects affected / exposed[8]	68 / 140 (48.57%)		
occurrences (all)	68		
Redness (booster vaccination)	Additional description: Symptom reported during the 7-day post-booster vaccination period		
subjects affected / exposed[9]	66 / 140 (47.14%)		
occurrences (all)	66		
Swelling (booster vaccination)	Additional description: Symptom reported during the 7-day post-booster vaccination period		
subjects affected / exposed[10]	59 / 140 (42.14%)		
occurrences (all)	59		
Drowsiness (booster vaccination)	Additional description: Symptom reported during the 7-day post-booster vaccination period		
subjects affected / exposed[11]	73 / 140 (52.14%)		
occurrences (all)	73		
Irritability (booster vaccination)	Additional description: Symptom reported during the 7-day post-booster vaccination period		
subjects affected / exposed[12]	90 / 140 (64.29%)		
occurrences (all)	90		
Loss of appetite (booster vaccination)	Additional description: Symptom reported during the 7-day post-booster vaccination period		
subjects affected / exposed[13]	57 / 140 (40.71%)		
occurrences (all)	57		
Fever (booster vaccination)	Additional description: (rectal temperature >= 38°C) Symptom reported during the 7-day post-booster vaccination period		
subjects affected / exposed[14]	53 / 140 (37.86%)		
occurrences (all)	53		
Eye disorders			

Conjunctivitis	Additional description: Unsolicited AE reported during the 31-day post-primary vaccination periods, across doses		
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 142 (2.11%)		
occurrences (all)	3		
Infections and infestations			
Bronchitis	Additional description: Unsolicited AE reported during the 31-day post-primary vaccination periods, across doses		
alternative assessment type: Non-systematic			
subjects affected / exposed	13 / 142 (9.15%)		
occurrences (all)	13		
Nasopharyngitis (primary vaccination)	Additional description: Unsolicited AE reported during the 31-day post-primary vaccination periods, across doses		
alternative assessment type: Non-systematic			
subjects affected / exposed	8 / 142 (5.63%)		
occurrences (all)	8		
Nasopharyngitis (booster vaccination)	Additional description: Unsolicited AE reported during the 31-day post-booster vaccination period		
alternative assessment type: Non-systematic			
subjects affected / exposed[15]	6 / 140 (4.29%)		
occurrences (all)	6		
Rhinitis	Additional description: Unsolicited AE reported during the 31-day post-primary vaccination periods, across doses		
alternative assessment type: Non-systematic			
subjects affected / exposed	14 / 142 (9.86%)		
occurrences (all)	14		
Viral infection	Additional description: Unsolicited AE reported during the 31-day post-primary vaccination periods, across doses		
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 142 (2.11%)		
occurrences (all)	3		

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Solicited symptoms results are presented only for subjects for whom results were available.
[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: Solicited symptoms results are presented only for subjects for whom results were available.
[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.
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[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: Solicited symptoms results are presented only for subjects for whom results were available.
[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.
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[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.
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[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: Solicited symptoms results are presented only for subjects for whom results were available.
[8] - 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: Solicited symptoms results are presented only for subjects for whom results were available.
[9] - 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: Solicited symptoms results are presented only for subjects for whom results were available.
[10] - 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: Solicited symptoms results are presented only for subjects for whom results were available.
[11] - 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: Solicited symptoms results are presented only for subjects for whom results were available.
[12] - 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: Solicited symptoms results are presented only for subjects for whom results were available.
[13] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Solicited symptoms results are presented only for subjects for whom results were available.
[14] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Solicited symptoms results are presented only for subjects for whom results were available.
[15] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Solicited symptoms results are presented only for subjects for whom results were available.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

The results of analysis of the anti-Ply haemolysis activity inhibition are not presented as assay was not validated.

Notes: