Clinical trial results:
A phase II, randomized, controlled, partially-blind study to demonstrate immunogenicity and assess safety of GlaxoSmithKline (GSK) Biologicals' pneumococcal vaccines (2830929A and 2830930A) administered as a 3-dose primary vaccination course during the first 6 months of life and as a booster dose at 12-15 months of age.

Summary

EudraCT number	2011-005743-27
Trial protocol	CZ ES DE PL
Global end of trial date	22 January 2014

Results information

Result version number	v2
This version publication date	02 July 2016
First version publication date	27 May 2015
Version creation reason	• New data added to full data set Data for primary/secondary endpoints have been added.

Trial information

Trial identification

Sponsor protocol code	116485

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01616459
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, 1330
Public contact	Clinical Disclosure Advisor, GlaxoSmithKline Biologicals, +44 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Disclosure Advisor, GlaxoSmithKline Biologicals, +44 2089904466, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	17 May 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 January 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that 2830929A vaccine co-administered with DTPa-HBV-IPV/Hib as a three-dose primary vaccination course at approximately 2, 3, 4 months of age is non-inferior to Prevnar 13 or Synflorix in terms of percentage of subjects with antibody concentrations greater or equal to the seropositivity threshold and in terms of ELISA Geometric Mean Concentrations (GMCs).

To demonstrate that 2830930A vaccine co-administered with DTPa-HBV-IPV/Hib at approximately 2, 3, 4 months of age is non-inferior to Prevnar 13 or Synflorix in terms of percentage of subjects with antibody concentrations greater or equal to the seropositivity threshold and in terms of ELISA GMCs.

Protection of trial subjects:

All subjects were supervised for 30 min 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 30 days after each/last vaccination.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 July 2012
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: 150
Country: Number of subjects enrolled	Spain: 398
Country: Number of subjects enrolled	Czech Republic: 253
Country: Number of subjects enrolled	Germany: 152
Worldwide total number of subjects	953
EEA total number of subjects	953

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)	953
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:

953 subjects were enrolled in the study, among whom 951 received at least one dose of study vaccine, while 2 were allocated a subject number but did not receive any study vaccine dose.

Pre-assignment

Screening details:

Study vaccines were administered as a 3-dose primary vaccination in healthy infants between 6-12 weeks (42-90 days) of age at the time of the first vaccination (Primary Phase), and then as an additional booster dose when subjects reached 12-15 months of age (Booster Phase).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	11Pn Group

Arm description:

Healthy male or female subjects between, and including 6 to 12 weeks (42-90 days) of age at the time of first vaccination, received a 3-dose primary vaccination course of GSK2830929A, or 11Pn, vaccine at 2, 3 and 4 months of age, followed by a booster dose of the same vaccine at 12-15 months of age, each dose being co-administered with one dose of Infanrix hexa™. The first 3 doses of 11Pn vaccine were administered intramuscularly into the right anterolateral thigh and Infanrix hexa™ was administered intramuscularly into the left anterolateral thigh. The booster dose of 11Pn vaccine was administered intramuscularly into the right deltoid (or thigh if the deltoid muscle size was not adequate) and that of Infanrix hexa™ was administered intramuscularly into the left deltoid (or thigh if the deltoid muscle size was not adequate).

Arm type	Experimental
Investigational medicinal product name	Pneumococcal conjugate vaccine GSK2830929A
Investigational medicinal product code	
Other name	11Pn
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received a 3-dose primary vaccination course of GSK2830929A, or 11Pn, vaccine at 2, 3 and 4 months of age, followed by a booster dose of the same vaccine at 12-15 months of age, each dose being co-administered with one dose of Infanrix hexa™. The first 3 doses of 11Pn vaccine were administered intramuscularly into the right anterolateral thigh and Infanrix hexa™ was administered intramuscularly into the left anterolateral thigh. The booster dose of 11Pn vaccine was administered intramuscularly into the right deltoid (or thigh if the deltoid muscle size was not adequate) and that of Infanrix hexa™ was administered intramuscularly into the left deltoid (or thigh if the deltoid muscle size was not adequate).

Investigational medicinal product name	Infanrix hexa™
Investigational medicinal product code	
Other name	DTPA-HBV-IPV/Hib
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received a 3-dose primary vaccination course of GSK2830929A, or 11Pn, vaccine at 2, 3 and 4 months of age, followed by a booster dose of the same vaccine at 12-15 months of age, each dose being co-administered with one dose of Infanrix hexa™. The first 3 doses of 11Pn vaccine were administered intramuscularly into the right anterolateral thigh and Infanrix hexa™ was administered

intramuscularly into the left anterolateral thigh. The booster dose of 11Pn vaccine was administered intramuscularly into the right deltoid (or thigh if the deltoid muscle size was not adequate) and that of Infanrix hexa™ was administered intramuscularly into the left deltoid (or thigh if the deltoid muscle size was not adequate).

Arm title	12Pn Group

Arm description:

Healthy male or female subjects between, and including 6 to 12 weeks (42-90 days) of age at the time of first vaccination, received a 3-dose primary vaccination course of GSK2830930A, or 12Pn, vaccine at 2, 3 and 4 months of age, followed by a booster dose of the same vaccine at 12-15 months of age, each dose being co-administered with one dose of Infanrix hexa™. The first 3 doses of 12Pn vaccine were administered intramuscularly into the right anterolateral thigh and Infanrix hexa™ was administered intramuscularly into the left anterolateral thigh. The booster dose of 12Pn vaccine was administered intramuscularly into the right deltoid (or thigh if the deltoid muscle size was not adequate) and that of Infanrix hexa™ was administered intramuscularly into the left deltoid (or thigh if the deltoid muscle size was not adequate).

Arm type	Experimental
Investigational medicinal product name	Pneumococcal conjugate vaccine GSK2830930A
Investigational medicinal product code	
Other name	12Pn
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received a 3-dose primary vaccination course of GSK2830930A, or 12Pn, vaccine at 2, 3 and 4 months of age, followed by a booster dose of the same vaccine at 12-15 months of age, each dose being co-administered with one dose of Infanrix hexa™. The first 3 doses of 12Pn vaccine were administered intramuscularly into the right anterolateral thigh and Infanrix hexa™ was administered intramuscularly into the left anterolateral thigh. The booster dose of 12Pn vaccine was administered intramuscularly into the right deltoid (or thigh if the deltoid muscle size was not adequate) and that of Infanrix hexa™ was administered intramuscularly into the left deltoid (or thigh if the deltoid muscle size was not adequate).

Investigational medicinal product name	Infanrix hexa™
Investigational medicinal product code	
Other name	DTPA-HBV-IPV/Hib
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received a 3-dose primary vaccination course of GSK2830930A, or 12Pn, vaccine at 2, 3 and 4 months of age, followed by a booster dose of the same vaccine at 12-15 months of age, each dose being co-administered with one dose of Infanrix hexa™. The first 3 doses of 12Pn vaccine were administered intramuscularly into the right anterolateral thigh and Infanrix hexa™ was administered intramuscularly into the left anterolateral thigh. The booster dose of 12Pn vaccine was administered intramuscularly into the right deltoid (or thigh if the deltoid muscle size was not adequate) and that of Infanrix hexa™ was administered intramuscularly into the left deltoid (or thigh if the deltoid muscle size was not adequate).

Arm title	Synflorix Group

Arm description:

Healthy male or female subjects between, and including 6 to 12 weeks (42-90 days) of age at the time of first vaccination, received a 3-dose primary vaccination course of Synflorix™ at 2, 3 and 4 months of age, followed by a booster dose of the same vaccine at 12-15 months of age, each dose being co-administered with one dose of Infanrix hexa™. The first 3 doses of Synflorix™ were administered intramuscularly into the right anterolateral thigh and Infanrix hexa™ was administered intramuscularly into the left anterolateral thigh. The booster dose of Synflorix™ was administered intramuscularly into the right deltoid (or thigh if the deltoid muscle size was not adequate) and that of Infanrix hexa™ was administered intramuscularly into the left deltoid (or thigh if the deltoid muscle size was not adequate).

Arm type	Active comparator

Investigational medicinal product name	Synflorix™
Investigational medicinal product code	
Other name	10Pn
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received a 3-dose primary vaccination course of Synflorix™ at 2, 3 and 4 months of age, followed by a booster dose of the same vaccine at 12-15 months of age, each dose being co-administered with one dose of Infanrix hexa™. The first 3 doses of Synflorix™ were administered intramuscularly into the right anterolateral thigh and Infanrix hexa™ was administered intramuscularly into the left anterolateral thigh. The booster dose of Synflorix™ was administered intramuscularly into the right deltoid (or thigh if the deltoid muscle size was not adequate) and that of Infanrix hexa™ was administered intramuscularly into the left deltoid (or thigh if the deltoid muscle size was not adequate).

Investigational medicinal product name	Infanrix hexa™
Investigational medicinal product code	
Other name	DTPA-HBV-IPV/Hib
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received a 3-dose primary vaccination course of Synflorix™ at 2, 3 and 4 months of age, followed by a booster dose of the same vaccine at 12-15 months of age, each dose being co-administered with one dose of Infanrix hexa™. The first 3 doses of Synflorix™ were administered intramuscularly into the right anterolateral thigh and Infanrix hexa™ was administered intramuscularly into the left anterolateral thigh. The booster dose of Synflorix™ was administered intramuscularly into the right deltoid (or thigh if the deltoid muscle size was not adequate) and that of Infanrix hexa™ was administered intramuscularly into the left deltoid (or thigh if the deltoid muscle size was not adequate).

Arm title	Prevnar13 Group

Arm description:

Healthy male or female subjects between, and including 6 to 12 weeks (42-90 days) of age at the time of first vaccination, received a 3-dose primary vaccination course of Prevnar13™ vaccine at 2, 3 and 4 months of age, followed by a booster dose of the same vaccine at 12-15 months of age, each dose being co-administered with one dose of Infanrix hexa™. The first 3 doses of Prevnar13™ were administered intramuscularly into the right anterolateral thigh and Infanrix hexa™ was administered intramuscularly into the left anterolateral thigh. The booster dose of Prevnar13™ was administered intramuscularly into the right deltoid (or thigh if the deltoid muscle size was not adequate) and that of Infanrix hexa™ was administered intramuscularly into the left deltoid (or thigh if the deltoid muscle size was not adequate).

Arm type	Active comparator
Investigational medicinal product name	Prevnar 13™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received a 3-dose primary vaccination course of Prevnar13™ vaccine at 2, 3 and 4 months of age, followed by a booster dose of the same vaccine at 12-15 months of age, each dose being co-administered with one dose of Infanrix hexa™. The first 3 doses of Prevnar13™ were administered intramuscularly into the right anterolateral thigh and Infanrix hexa™ was administered intramuscularly into the left anterolateral thigh. The booster dose of Prevnar13™ was administered intramuscularly into the right deltoid (or thigh if the deltoid muscle size was not adequate) and that of Infanrix hexa™ was administered intramuscularly into the left deltoid (or thigh if the deltoid muscle size was not adequate).

Investigational medicinal product name	Infanrix hexa™
Investigational medicinal product code	
Other name	DTPA-HBV-IPV/Hib
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received a 3-dose primary vaccination course of Prevnar13™ vaccine at 2, 3 and 4 months of age, followed by a booster dose of the same vaccine at 12-15 months of age, each dose being co-

administered with one dose of Infanrix hexa™. The first 3 doses of Prevnar13™ were administered intramuscularly into the right anterolateral thigh and Infanrix hexa™ was administered intramuscularly into the left anterolateral thigh. The booster dose of Prevnar13™ was administered intramuscularly into the right deltoid (or thigh if the deltoid muscle size was not adequate) and that of Infanrix hexa™ was administered intramuscularly into the left deltoid (or thigh if the deltoid muscle size was not adequate).

Number of subjects in period 1[1]	11Pn Group	12Pn Group	Synflorix Group
Started	240	240	230
Completed	236	223	220
Not completed	4	17	10
Consent withdrawn by subject	2	4	4
Adverse event, non-fatal	1	1	2
Consent withdrawal/not willing to participate not	-	1	1
Lost to follow-up	1	11	3
Protocol deviation	-	-	-

Number of subjects in period 1[1]	Prevnar13 Group
Started	241
Completed	233
Not completed	8
Consent withdrawn by subject	4
Adverse event, non-fatal	-
Consent withdrawal/not willing to participate not	-
Lost to follow-up	2
Protocol deviation	2

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: Although 953 subjects were enrolled, only 951 subjects started the study and were vaccinated.

Baseline characteristics

Reporting groups

Reporting group title	11Pn Group

Reporting group description:

Healthy male or female subjects between, and including 6 to 12 weeks (42-90 days) of age at the time of first vaccination, received a 3-dose primary vaccination course of GSK2830929A, or 11Pn, vaccine at 2, 3 and 4 months of age, followed by a booster dose of the same vaccine at 12-15 months of age, each dose being co-administered with one dose of Infanrix hexa™. The first 3 doses of 11Pn vaccine were administered intramuscularly into the right anterolateral thigh and Infanrix hexa™ was administered intramuscularly into the left anterolateral thigh. The booster dose of 11Pn vaccine was administered intramuscularly into the right deltoid (or thigh if the deltoid muscle size was not adequate) and that of Infanrix hexa™ was administered intramuscularly into the left deltoid (or thigh if the deltoid muscle size was not adequate).

Reporting group title	12Pn Group

Reporting group description:

Healthy male or female subjects between, and including 6 to 12 weeks (42-90 days) of age at the time of first vaccination, received a 3-dose primary vaccination course of GSK2830930A, or 12Pn, vaccine at 2, 3 and 4 months of age, followed by a booster dose of the same vaccine at 12-15 months of age, each dose being co-administered with one dose of Infanrix hexa™. The first 3 doses of 12Pn vaccine were administered intramuscularly into the right anterolateral thigh and Infanrix hexa™ was administered intramuscularly into the left anterolateral thigh. The booster dose of 12Pn vaccine was administered intramuscularly into the right deltoid (or thigh if the deltoid muscle size was not adequate) and that of Infanrix hexa™ was administered intramuscularly into the left deltoid (or thigh if the deltoid muscle size was not adequate).

Reporting group title	Synflorix Group

Reporting group description:

Healthy male or female subjects between, and including 6 to 12 weeks (42-90 days) of age at the time of first vaccination, received a 3-dose primary vaccination course of Synflorix™ at 2, 3 and 4 months of age, followed by a booster dose of the same vaccine at 12-15 months of age, each dose being co-administered with one dose of Infanrix hexa™. The first 3 doses of Synflorix™ were administered intramuscularly into the right anterolateral thigh and Infanrix hexa™ was administered intramuscularly into the left anterolateral thigh. The booster dose of Synflorix™ was administered intramuscularly into the right deltoid (or thigh if the deltoid muscle size was not adequate) and that of Infanrix hexa™ was administered intramuscularly into the left deltoid (or thigh if the deltoid muscle size was not adequate).

Reporting group title	Prevnar13 Group

Reporting group description:

Healthy male or female subjects between, and including 6 to 12 weeks (42-90 days) of age at the time of first vaccination, received a 3-dose primary vaccination course of Prevnar13™ vaccine at 2, 3 and 4 months of age, followed by a booster dose of the same vaccine at 12-15 months of age, each dose being co-administered with one dose of Infanrix hexa™. The first 3 doses of Prevnar13™ were administered intramuscularly into the right anterolateral thigh and Infanrix hexa™ was administered intramuscularly into the left anterolateral thigh. The booster dose of Prevnar13™ was administered intramuscularly into the right deltoid (or thigh if the deltoid muscle size was not adequate) and that of Infanrix hexa™ was administered intramuscularly into the left deltoid (or thigh if the deltoid muscle size was not adequate).

Reporting group values	11Pn Group	12Pn Group	Synflorix Group
Number of subjects	240	240	230
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	8.6	8.7	8.7
standard deviation	± 1.49	± 1.61	± 1.62
Gender categorical			
Units: Subjects			
Female	113	120	113
Male	127	120	117

Reporting group values	Prevnar13 Group	Total	
Number of subjects	241	951	
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	8.6		
standard deviation	± 1.54	-	
Gender categorical			
Units: Subjects			
Female	121	467	
Male	120	484	

End points

End points reporting groups

Reporting group title	11Pn Group

Reporting group description:

Healthy male or female subjects between, and including 6 to 12 weeks (42-90 days) of age at the time of first vaccination, received a 3-dose primary vaccination course of GSK2830929A, or 11Pn, vaccine at 2, 3 and 4 months of age, followed by a booster dose of the same vaccine at 12-15 months of age, each dose being co-administered with one dose of Infanrix hexa™. The first 3 doses of 11Pn vaccine were administered intramuscularly into the right anterolateral thigh and Infanrix hexa™ was administered intramuscularly into the left anterolateral thigh. The booster dose of 11Pn vaccine was administered intramuscularly into the right deltoid (or thigh if the deltoid muscle size was not adequate) and that of Infanrix hexa™ was administered intramuscularly into the left deltoid (or thigh if the deltoid muscle size was not adequate).

Reporting group title	12Pn Group

Reporting group description:

Healthy male or female subjects between, and including 6 to 12 weeks (42-90 days) of age at the time of first vaccination, received a 3-dose primary vaccination course of GSK2830930A, or 12Pn, vaccine at 2, 3 and 4 months of age, followed by a booster dose of the same vaccine at 12-15 months of age, each dose being co-administered with one dose of Infanrix hexa™. The first 3 doses of 12Pn vaccine were administered intramuscularly into the right anterolateral thigh and Infanrix hexa™ was administered intramuscularly into the left anterolateral thigh. The booster dose of 12Pn vaccine was administered intramuscularly into the right deltoid (or thigh if the deltoid muscle size was not adequate) and that of Infanrix hexa™ was administered intramuscularly into the left deltoid (or thigh if the deltoid muscle size was not adequate).

Reporting group title	Synflorix Group

Reporting group description:

Healthy male or female subjects between, and including 6 to 12 weeks (42-90 days) of age at the time of first vaccination, received a 3-dose primary vaccination course of Synflorix™ at 2, 3 and 4 months of age, followed by a booster dose of the same vaccine at 12-15 months of age, each dose being co-administered with one dose of Infanrix hexa™. The first 3 doses of Synflorix™ were administered intramuscularly into the right anterolateral thigh and Infanrix hexa™ was administered intramuscularly into the left anterolateral thigh. The booster dose of Synflorix™ was administered intramuscularly into the right deltoid (or thigh if the deltoid muscle size was not adequate) and that of Infanrix hexa™ was administered intramuscularly into the left deltoid (or thigh if the deltoid muscle size was not adequate).

Reporting group title	Prevnar13 Group

Reporting group description:

Healthy male or female subjects between, and including 6 to 12 weeks (42-90 days) of age at the time of first vaccination, received a 3-dose primary vaccination course of Prevnar13™ vaccine at 2, 3 and 4 months of age, followed by a booster dose of the same vaccine at 12-15 months of age, each dose being co-administered with one dose of Infanrix hexa™. The first 3 doses of Prevnar13™ were administered intramuscularly into the right anterolateral thigh and Infanrix hexa™ was administered intramuscularly into the left anterolateral thigh. The booster dose of Prevnar13™ was administered intramuscularly into the right deltoid (or thigh if the deltoid muscle size was not adequate) and that of Infanrix hexa™ was administered intramuscularly into the left deltoid (or thigh if the deltoid muscle size was not adequate).

Primary: Antibody concentrations against pneumococcal serotypes during the Primary Phase of the study

End point title	Antibody concentrations against pneumococcal serotypes during the Primary Phase of the study[1]

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-Inhibition enzyme-linked immunosorbent assay (ELISA), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The cut-off of the assay was an antibody concentration higher than or equal to (≥) 0.05 µg/mL. Primary outcome results correspond to antibody concentrations for all serotypes presented at the exception of those for the antibodies against the cross-reactive

pneumococcal serotype 3 (ANTI-3). Analysis of concentrations of antibodies against the cross-reactive pneumococcal serotype 6C (ANTI-6C) was not performed due to unavailability of a specific qualified assay.

End point type	Primary

End point timeframe:

At study Month 3, e. g. at one month post-Dose 3 of pneumococcal vaccine

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The scope of this primary end point was descriptive, no statistical hypothesis test was performed.

End point values	11Pn Group	12Pn Group	Synflorix Group	Prevnar13 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	223	214	210	219
Units: µg/mL				
geometric mean (confidence interval 95%)				
ANTI-1 (N=222,214,210,218)	1.54 (1.37 to 1.74)	1.59 (1.41 to 1.79)	1.37 (1.21 to 1.54)	2.18 (1.97 to 2.42)
ANTI-3 (N=221,214,209,218)	0.06 (0.05 to 0.06)	0.06 (0.05 to 0.07)	0.05 (0.05 to 0.06)	2.27 (2.06 to 2.49)
ANTI-4 (N=222,214,210,218)	1.78 (1.56 to 2.02)	1.99 (1.73 to 2.28)	1.68 (1.47 to 1.93)	2.83 (2.6 to 3.09)
ANTI-5 (N=222,214,209,218)	2.48 (2.24 to 2.74)	2.37 (2.13 to 2.64)	2.19 (1.97 to 2.44)	2.81 (2.52 to 3.13)
ANTI-6A (N=222,214,208,218)	0.14 (0.12 to 0.17)	1.12 (0.93 to 1.34)	0.12 (0.1 to 0.14)	2.05 (1.81 to 2.32)
ANTI-6B (N=222,214,210,218)	0.51 (0.42 to 0.61)	0.58 (0.48 to 0.69)	0.48 (0.4 to 0.58)	0.49 (0.42 to 0.58)
ANTI-7F (N=223,214,210,219)	2.3 (2.1 to 2.52)	2.44 (2.18 to 2.72)	2.2 (1.97 to 2.47)	3.16 (2.91 to 3.43)
ANTI-9V (N=222,214,210,218)	1.57 (1.4 to 1.76)	1.77 (1.58 to 1.97)	1.42 (1.27 to 1.59)	2.27 (2.05 to 2.51)
ANTI-14 (N=222,214,210,218)	4.19 (3.72 to 4.71)	4.45 (3.95 to 5)	4.21 (3.72 to 4.77)	4.2 (3.68 to 4.8)
ANTI-18C (N=222,214,210,219)	2.84 (2.45 to 3.28)	2.56 (2.21 to 2.96)	2.56 (2.19 to 2.98)	3.17 (2.87 to 3.51)
ANTI-19A (N=222,214,209,219)	1.63 (1.43 to 1.86)	1.18 (1.03 to 1.36)	0.18 (0.15 to 0.22)	2.67 (2.39 to 3)
ANTI-19F (N=223,214,210,218)	3.65 (3.2 to 4.16)	3.31 (2.91 to 3.76)	3.68 (3.15 to 4.3)	3.07 (2.83 to 3.34)
ANTI-23F (N=222,214,210,218)	0.62 (0.52 to 0.73)	0.69 (0.57 to 0.83)	0.72 (0.61 to 0.86)	1.59 (1.38 to 1.84)

Statistical analyses

No statistical analyses for this end point

Primary: Percentage (%) of subjects (Synflorix and 11Pn groups) with antibody concentration ≥ 0.2 µg/mL for pneumococcal serotypes

End point title	Percentage (%) of subjects (Synflorix and 11Pn groups) with antibody concentration ≥ 0.2 µg/mL for pneumococcal serotypes[2]

End point description:

N = number of subjects with post primary vaccination results available
% = percentage of subjects with ELISA pneumococcal antibody concentrations ≥ 0.2 µg/mL
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-Inhibition enzyme-linked immunosorbent assay (ELISA).

End point type	Primary

End point timeframe:

1 month post-dose 3 (primary phase)

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 analysis of the difference in terms of percentage of subjects between the 2 following groups: 11Pn group and Synflorix group.

End point values	11Pn Group	Synflorix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	223	210		
Units: percent				
number (not applicable)				
ANTI-1 (N=222,210)	99.5	98.6		
ANTI-4 (N=222,210)	97.7	96.7		
ANTI-5 (N=222,209)	100	99.5		
ANTI-6B (N=222,210)	77.5	75.2		
ANTI-7F (N=223,210)	99.6	99.5		
ANTI-9V (N=222,210)	98.6	99		
ANTI-14 (N=222,210)	99.5	100		
ANTI-18C (N=222,210)	99.1	98.1		
ANTI-19F (N=223,210)	100	97.6		
ANTI-23F (N=222,210)	81.1	83.8		

Statistical analyses

Statistical analysis title	(Synflorix - 11Pn) % subjects with ANTI-1≥0.2µg/mL

Statistical analysis description:

To demonstrate that 11Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 9 out of 11 serotypes to Prevnar13 vaccine (for 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of % of subjects with antibody concentrations ≥ 0.2 µg/mL.
Criteria: UL of the 2-sided 95.9% CI of the difference between (Prevnar13 minus 11Pn) and (Synflorix minus 11Pn) groups <10% for at least 9 out of 11 vaccine pneumococcal serotypes.

Comparison groups	11Pn Group v Synflorix Group
Number of subjects included in analysis	433
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	Difference in percentage
Point estimate	-0.98
Confidence interval	
level	95.9 %
sides	2-sided
lower limit	-3.89
upper limit	1.36

Notes:

[3] - 2-sided 95.9% Confidence Interval (CI) adjusted 1-sided alpha =2.05%) of the difference between groups in terms of percentage of subjects.
Confidence Interval (CI) for difference in proportion:
Proc StatXact was used to derive the standardized asymptotic CI for the group difference in proportions [Newcombe, 1998]. The standardized asymptotic method used within GSK Biologicals is method 6.

Statistical analysis title	(Synflorix - 11Pn) % subjects with ANTI-4≥0.2µg/mL

Statistical analysis description:

To demonstrate that 11Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 9 out of 11 serotypes to Prevnar13 vaccine (for 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of % of subjects with antibody concentrations ≥ 0.2 µg/mL.
Criteria: UL of the 2-sided 95.9% CI of the difference between (Prevnar13 minus 11Pn) and (Synflorix minus 11Pn) groups <10% for at least 9 out of 11 vaccine pneumococcal serotypes.

Comparison groups	11Pn Group v Synflorix Group
Number of subjects included in analysis	433
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Parameter estimate	Difference in percentage
Point estimate	-1.08
Confidence interval	
level	95.9 %
sides	2-sided
lower limit	-4.94
upper limit	2.45

Notes:

[4] - 2-sided 95.9% Confidence Interval (CI) adjusted 1-sided alpha =2.05%) of the difference between groups in terms of percentage of subjects.
Confidence Interval (CI) for difference in proportion:
Proc StatXact was used to derive the standardized asymptotic CI for the group difference in proportions [Newcombe, 1998]. The standardized asymptotic method used within GSK Biologicals is method 6.

Statistical analysis title	(Synflorix - 11Pn) % subjects with ANTI-5≥0.2µg/mL

Statistical analysis description:

To demonstrate that 11Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 9 out of 11 serotypes to Prevnar13 vaccine (for 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of % of subjects with antibody concentrations ≥ 0.2 µg/mL.
Criteria: UL of the 2-sided 95.9% CI of the difference between (Prevnar13 minus 11Pn) and (Synflorix minus 11Pn) groups <10% for at least 9 out of 11 vaccine pneumococcal serotypes.

Comparison groups	11Pn Group v Synflorix Group
Number of subjects included in analysis	433
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
Parameter estimate	Difference in percentage
Point estimate	-0.48
Confidence interval	
level	95.9 %
sides	2-sided
lower limit	-2.82
upper limit	1.38

Notes:

[5] - 2-sided 95.9% Confidence Interval (CI) adjusted 1-sided alpha =2.05%) of the difference between groups in terms of percentage of subjects.
Confidence Interval (CI) for difference in proportion:
Proc StatXact was used to derive the standardized asymptotic CI for the group difference in proportions [Newcombe, 1998]. The standardized asymptotic method used within GSK Biologicals is method 6.

Statistical analysis title	(Synflorix-11Pn) % subjects with ANTI-6B≥0.2µg/mL

Statistical analysis description:

To demonstrate that 11Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 9 out of 11 serotypes to Prevnar13 vaccine (for 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of % of subjects with antibody concentrations ≥ 0.2 µg/mL.
Criteria: UL of the 2-sided 95.9% CI of the difference between (Prevnar13 minus 11Pn) and (Synflorix minus 11Pn) groups <10% for at least 9 out of 11 vaccine pneumococcal serotypes.

Comparison groups	11Pn Group v Synflorix Group
Number of subjects included in analysis	433
Analysis specification	Pre-specified
Analysis type	non-inferiority[6]
Parameter estimate	Difference in percentage
Point estimate	-2.24
Confidence interval	
level	95.9 %
sides	2-sided
lower limit	-10.65
upper limit	6.13

Notes:

[6] - 2-sided 95.9% Confidence Interval (CI) adjusted 1-sided alpha =2.05%) of the difference between groups in terms of percentage of subjects.
Confidence Interval (CI) for difference in proportion:
Proc StatXact was used to derive the standardized asymptotic CI for the group difference in proportions [Newcombe, 1998]. The standardized asymptotic method used within GSK Biologicals is method 6.

Statistical analysis title	(Synflorix-11Pn) % subjects with ANTI-7F≥0.2µg/mL

Statistical analysis description:

To demonstrate that 11Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 9 out of 11 serotypes to Prevnar13 vaccine (for 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of % of subjects with antibody concentrations ≥ 0.2 µg/mL.
Criteria: UL of the 2-sided 95.9% CI of the difference between (Prevnar13 minus 11Pn) and (Synflorix minus 11Pn) groups <10% for at least 9 out of 11 vaccine pneumococcal serotypes.

Comparison groups	11Pn Group v Synflorix Group
Number of subjects included in analysis	433
Analysis specification	Pre-specified
Analysis type	non-inferiority[7]
Parameter estimate	Difference in percentage
Point estimate	-0.03
Confidence interval	
level	95.9 %
sides	2-sided
lower limit	-2.39
upper limit	2.21

Notes:

[7] - 2-sided 95.9% Confidence Interval (CI) adjusted 1-sided alpha =2.05%) of the difference between groups in terms of percentage of subjects.
Confidence Interval (CI) for difference in proportion:
Proc StatXact was used to derive the standardized asymptotic CI for the group difference in proportions [Newcombe, 1998]. The standardized asymptotic method used within GSK Biologicals is method 6.

Statistical analysis title	(Synflorix-11Pn) % subjects with ANTI-9V≥0.2µg/mL

Statistical analysis description:

To demonstrate that 11Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 9 out of 11 serotypes to Prevnar13 vaccine (for 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of % of subjects with antibody concentrations ≥ 0.2 µg/mL.
Criteria: UL of the 2-sided 95.9% CI of the difference between (Prevnar13 minus 11Pn) and (Synflorix minus 11Pn) groups <10% for at least 9 out of 11 vaccine pneumococcal serotypes.

Comparison groups	11Pn Group v Synflorix Group
Number of subjects included in analysis	433
Analysis specification	Pre-specified
Analysis type	non-inferiority[8]
Parameter estimate	Difference in percentage
Point estimate	0.4
Confidence interval	
level	95.9 %
sides	2-sided
lower limit	-2.36
upper limit	3.22

Notes:

[8] - 2-sided 95.9% Confidence Interval (CI) adjusted 1-sided alpha =2.05%) of the difference between groups in terms of percentage of subjects.
Confidence Interval (CI) for difference in proportion:
Proc StatXact was used to derive the standardized asymptotic CI for the group difference in proportions [Newcombe, 1998]. The standardized asymptotic method used within GSK Biologicals is method 6.

Statistical analysis title	(Synflorix-11Pn) % subjects with ANTI-14≥0.2µg/mL

Statistical analysis description:

To demonstrate that 11Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 9 out of 11 serotypes to Prevnar13 vaccine (for 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of % of subjects with antibody concentrations ≥ 0.2 µg/mL.
Criteria: UL of the 2-sided 95.9% CI of the difference between (Prevnar13 minus 11Pn) and (Synflorix minus 11Pn) groups <10% for at least 9 out of 11 vaccine pneumococcal serotypes.

Comparison groups	11Pn Group v Synflorix Group
Number of subjects included in analysis	433
Analysis specification	Pre-specified
Analysis type	non-inferiority[9]
Parameter estimate	Difference in percentage
Point estimate	0.45
Confidence interval	
level	95.9 %
sides	2-sided
lower limit	-1.51
upper limit	2.66

Notes:

[9] - 2-sided 95.9% Confidence Interval (CI) adjusted 1-sided alpha =2.05%) of the difference between groups in terms of percentage of subjects.
Confidence Interval (CI) for difference in proportion:
Proc StatXact was used to derive the standardized asymptotic CI for the group difference in proportions [Newcombe, 1998]. The standardized asymptotic method used within GSK Biologicals is method 6.

Statistical analysis title	(Synflorix-11Pn) % subjects with ANTI-18C≥0.2µg/mL

Statistical analysis description:

To demonstrate that 11Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 9 out of 11 serotypes to Prevnar13 vaccine (for 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of % of subjects with antibody concentrations ≥ 0.2 µg/mL.
Criteria: UL of the 2-sided 95.9% CI of the difference between (Prevnar13 minus 11Pn) and (Synflorix

minus 11Pn) groups <10% for at least 9 out of 11 vaccine pneumococcal serotypes.

Comparison groups	11Pn Group v Synflorix Group
Number of subjects included in analysis	433
Analysis specification	Pre-specified
Analysis type	non-inferiority[10]
Parameter estimate	Difference in percentage
Point estimate	-1
Confidence interval	
level	95.9 %
sides	2-sided
lower limit	-4.18
upper limit	1.7

Notes:

[10] - 2-sided 95.9% Confidence Interval (CI) adjusted 1-sided alpha =2.05%) of the difference between groups in terms of percentage of subjects.
Confidence Interval (CI) for difference in proportion:
Proc StatXact was used to derive the standardized asymptotic CI for the group difference in proportions [Newcombe, 1998]. The standardized asymptotic method used within GSK Biologicals is method 6.

Statistical analysis title	(Synflorix-11Pn) % subjects with ANTI-19F≥0.2µg/mL

Statistical analysis description:

To demonstrate that 11Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 9 out of 11 serotypes to Prevnar13 vaccine (for 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of % of subjects with antibody concentrations ≥ 0.2 µg/mL.
Criteria: UL of the 2-sided 95.9% CI of the difference between (Prevnar13 minus 11Pn) and (Synflorix minus 11Pn) groups <10% for at least 9 out of 11 vaccine pneumococcal serotypes.

Comparison groups	11Pn Group v Synflorix Group
Number of subjects included in analysis	433
Analysis specification	Pre-specified
Analysis type	non-inferiority[11]
Parameter estimate	Difference in percentage
Point estimate	-2.38
Confidence interval	
level	95.9 %
sides	2-sided
lower limit	-5.64
upper limit	-0.52

Notes:

[11] - 2-sided 95.9% Confidence Interval (CI) adjusted 1-sided alpha =2.05%) of the difference between groups in terms of percentage of subjects.
Confidence Interval (CI) for difference in proportion:
Proc StatXact was used to derive the standardized asymptotic CI for the group difference in proportions [Newcombe, 1998]. The standardized asymptotic method used within GSK Biologicals is method 6.

Statistical analysis title	(Synflorix-11Pn) % subjects with ANTI-23F≥0.2µg/mL

Statistical analysis description:

To demonstrate that 11Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 9 out of 11 serotypes to Prevnar13 vaccine (for 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of % of subjects with antibody concentrations ≥ 0.2 µg/mL.
Criteria: UL of the 2-sided 95.9% CI of the difference between (Prevnar13 minus 11Pn) and (Synflorix minus 11Pn) groups <10% for at least 9 out of 11 vaccine pneumococcal serotypes.

Comparison groups	11Pn Group v Synflorix Group

Number of subjects included in analysis	433
Analysis specification	Pre-specified
Analysis type	non-inferiority[12]
Parameter estimate	Difference in percentage
Point estimate	2.73
Confidence interval	
level	95.9 %
sides	2-sided
lower limit	-4.84
upper limit	10.25

Notes:

[12] - 2-sided 95.9% Confidence Interval (CI) adjusted 1-sided alpha =2.05%) of the difference between groups in terms of percentage of subjects.
Confidence Interval (CI) for difference in proportion:
Proc StatXact was used to derive the standardized asymptotic CI for the group difference in proportions [Newcombe, 1998]. The standardized asymptotic method used within GSK Biologicals is method 6.

Primary: Adjusted Geometric Mean Concentrations (GMC) (Synflorix and 11Pn Groups) for pneumococcal serotypes

End point title	Adjusted Geometric Mean Concentrations (GMC) (Synflorix and 11Pn Groups) for pneumococcal serotypes[13]

End point description:

Adjusted GMC = geometric mean antibody concentration adjusted for baseline concentration
N = number of subjects with both pre- and post-vaccination results available
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-Inhibition enzyme-linked immunosorbent assay (ELISA).

End point type	Primary

End point timeframe:

1 month post-dose 3 (primary phase)

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is related to the analysis of the GMCs ratio between the 2 following groups: 11Pn group and Synflorix group.

End point values	11Pn Group	Synflorix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	219	203		
Units: µg/mL				
number (not applicable)				
ANTI-1 (N=218, 203)	1.51	1.36		
ANTI-4 (N=218,203)	1.77	1.66		
ANTI-5 (N=218,201)	2.46	2.16		
ANTI-6B (N=218,200)	0.51	0.47		
ANTI-7F (N=219,202)	2.3	2.17		
ANTI-9V (N=218,200)	1.56	1.4		
ANTI-14 (N=218,201)	4.22	4.06		
ANTI-18C (N=218,201)	2.81	2.57		
ANTI-19F (N=218,202)	3.7	3.68		
ANTI-23F (N=218,199)	0.62	0.71		

Statistical analyses

Statistical analysis title	(Synflorix/11Pn) GMCs ratio for ANTI-1 serotype

Statistical analysis description:

To demonstrate that 11Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 9 out of 11 vaccine serotypes to Prevnar13 vaccine (for 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of Enzyme-linked immunosorbent assay (ELISA) GMCs.
Criteria: UL of the 2-sided 95.9% CI of the ELISA GMC ratios (Prevnar13/11Pn) and (Synflorix/11Pn) groups < a limit of 2-fold for at least 9 out of 11 vaccine pneumococcal serotypes.

Comparison groups	11Pn Group v Synflorix Group
Number of subjects included in analysis	422
Analysis specification	Pre-specified
Analysis type	non-inferiority[14]
Parameter estimate	Adjusted GMCs ratio
Point estimate	0.9
Confidence interval	
level	95.9 %
sides	2-sided
lower limit	0.75
upper limit	1.07

Notes:

[14] - -2-sided 95.9% Confidence Interval (CI) adjusted 1-sided alpha = 2.05%) around the ELISA GMCs ratio between groups
-GMCs ratio and its CI were obtained using an ANCOVA model on the logarithm-transformed concentrations/titres, including the vaccine group as fixed effect and the pre-vaccination concentration as regressor.

Statistical analysis title	(Synflorix/11Pn) GMCs ratio for ANTI-4 serotype

Statistical analysis description:

To demonstrate that 11Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 9 out of 11 vaccine serotypes to Prevnar13 vaccine (for 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of Enzyme-linked immunosorbent assay (ELISA) GMCs.
Criteria: UL of the 2-sided 95.9% CI of the ELISA GMC ratios (Prevnar13/11Pn) and (Synflorix/11Pn) groups < a limit of 2-fold for at least 9 out of 11 vaccine pneumococcal serotypes.

Comparison groups	11Pn Group v Synflorix Group
Number of subjects included in analysis	422
Analysis specification	Pre-specified
Analysis type	non-inferiority[15]
Parameter estimate	Adjusted GMCs ratio
Point estimate	0.94
Confidence interval	
level	95.9 %
sides	2-sided
lower limit	0.77
upper limit	1.14

Notes:

[15] - -2-sided 95.9% Confidence Interval (CI) adjusted 1-sided alpha =2.05%) around the ELISA GMCs ratio between groups
-GMCs ratio and its CI were obtained using an ANCOVA model on the logarithm-transformed concentrations/titres, including the vaccine group as fixed effect and the pre-vaccination concentration as regressor.

Statistical analysis title	(Synflorix/11Pn) GMCs ratio for ANTI-6B serotype

Statistical analysis description:

To demonstrate that 11Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 9 out of 11 vaccine serotypes to Prevnar13 vaccine (for 19A) or Synflorix™ vaccine

(for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of Enzyme-linked immunosorbent assay (ELISA) GMCs.
Criteria: UL of the 2-sided 95.9% CI of the ELISA GMC ratios (Prevnar13/11Pn) and (Synflorix/11Pn) groups < a limit of 2-fold for at least 9 out of 11 vaccine pneumococcal serotypes.

Comparison groups	11Pn Group v Synflorix Group
Number of subjects included in analysis	422
Analysis specification	Pre-specified
Analysis type	non-inferiority[16]
Parameter estimate	Adjusted GMCs ratio
Point estimate	0.93
Confidence interval	
level	95.9 %
sides	2-sided
lower limit	0.71
upper limit	1.23

Notes:

[16] - -2-sided 95.9% Confidence Interval (CI) adjusted 1-sided alpha =2.05%) around the ELISA GMCs ratio between groups
-GMCs ratio and its CI were obtained using an ANCOVA model on the logarithm-transformed concentrations/titres, including the vaccine group as fixed effect and the pre-vaccination concentration as regressor.

Statistical analysis title	(Synflorix/11Pn) GMCs ratio for ANTI-7F serotype

Statistical analysis description:

To demonstrate that 11Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 9 out of 11 vaccine serotypes to Prevnar13 vaccine (for 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of Enzyme-linked immunosorbent assay (ELISA) GMCs.
Criteria: UL of the 2-sided 95.9% CI of the ELISA GMC ratios (Prevnar13/11Pn) and (Synflorix/11Pn) groups < a limit of 2-fold for at least 9 out of 11 vaccine pneumococcal serotypes.

Comparison groups	11Pn Group v Synflorix Group
Number of subjects included in analysis	422
Analysis specification	Pre-specified
Analysis type	non-inferiority[17]
Parameter estimate	Adjusted GMCs ratio
Point estimate	0.94
Confidence interval	
level	95.9 %
sides	2-sided
lower limit	0.81
upper limit	1.1

Notes:

[17] - -2-sided 95.9% Confidence Interval (CI) adjusted 1-sided alpha =2.05%) around the ELISA GMCs ratio between groups
-GMCs ratio and its CI were obtained using an ANCOVA model on the logarithm-transformed concentrations/titres, including the vaccine group as fixed effect and the pre-vaccination concentration as regressor.

Statistical analysis title	(Synflorix/11Pn) GMCs ratio for ANTI-9V serotype

Statistical analysis description:

To demonstrate that 11Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 9 out of 11 vaccine serotypes to Prevnar13 vaccine (for 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of Enzyme-linked immunosorbent assay (ELISA) GMCs.
Criteria: UL of the 2-sided 95.9% CI of the ELISA GMC ratios (Prevnar13/11Pn) and (Synflorix/11Pn) groups < a limit of 2-fold for at least 9 out of 11 vaccine pneumococcal serotypes.

Comparison groups	11Pn Group v Synflorix Group

Number of subjects included in analysis	422
Analysis specification	Pre-specified
Analysis type	non-inferiority[18]
Parameter estimate	Adjusted GMCs ratio
Point estimate	0.89
Confidence interval	
level	95.9 %
sides	2-sided
lower limit	0.76
upper limit	1.06

Notes:

[18] - -2-sided 95.9% Confidence Interval (CI) adjusted 1-sided alpha =2.05%) around the ELISA GMCs ratio between groups
-GMCs ratio and its CI were obtained using an ANCOVA model on the logarithm-transformed concentrations/titres, including the vaccine group as fixed effect and the pre-vaccination concentration as regressor.

Statistical analysis title	(Synflorix/11Pn) GMCs ratio for ANTI-14 serotype

Statistical analysis description:

To demonstrate that 11Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 9 out of 11 vaccine serotypes to Prevnar13 vaccine (for 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of Enzyme-linked immunosorbent assay (ELISA) GMCs.
Criteria: UL of the 2-sided 95.9% CI of the ELISA GMC ratios (Prevnar13/11Pn) and (Synflorix/11Pn) groups < a limit of 2-fold for at least 9 out of 11 vaccine pneumococcal serotypes.

Comparison groups	11Pn Group v Synflorix Group
Number of subjects included in analysis	422
Analysis specification	Pre-specified
Analysis type	non-inferiority[19]
Parameter estimate	Adjusted GMCs ratio
Point estimate	0.96
Confidence interval	
level	95.9 %
sides	2-sided
lower limit	0.81
upper limit	1.15

Notes:

[19] - -2-sided 95.9% Confidence Interval (CI) adjusted 1-sided alpha =2.05%) around the ELISA GMCs ratio between groups
-GMCs ratio and its CI were obtained using an ANCOVA model on the logarithm-transformed concentrations/titres, including the vaccine group as fixed effect and the pre-vaccination concentration as regressor.

Statistical analysis title	(Synflorix/11Pn) GMCs ratio for ANTI-18C serotype

Statistical analysis description:

To demonstrate that 11Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 9 out of 11 vaccine serotypes to Prevnar13 vaccine (for 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of Enzyme-linked immunosorbent assay (ELISA) GMCs.
Criteria: UL of the 2-sided 95.9% CI of the ELISA GMC ratios (Prevnar13/11Pn) and (Synflorix/11Pn) groups < a limit of 2-fold for at least 9 out of 11 vaccine pneumococcal serotypes.

Comparison groups	11Pn Group v Synflorix Group

Number of subjects included in analysis	422
Analysis specification	Pre-specified
Analysis type	non-inferiority[20]
Parameter estimate	Adjusted GMCs ratio
Point estimate	0.92
Confidence interval	
level	95.9 %
sides	2-sided
lower limit	0.74
upper limit	1.14

Notes:

[20] - -2-sided 95.9% Confidence Interval (CI) adjusted 1-sided alpha =2.05%) around the ELISA GMCs ratio between groups
-GMCs ratio and its CI were obtained using an ANCOVA model on the logarithm-transformed concentrations/titres, including the vaccine group as fixed effect and the pre-vaccination concentration as regressor.

Statistical analysis title	(Synflorix/11Pn) GMCs ratio for ANTI-19F serotype

Statistical analysis description:

To demonstrate that 11Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 9 out of 11 vaccine serotypes to Prevnar13 vaccine (for 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of Enzyme-linked immunosorbent assay (ELISA) GMCs.
Criteria: UL of the 2-sided 95.9% CI of the ELISA GMC ratios (Prevnar13/11Pn) and (Synflorix/11Pn) groups < a limit of 2-fold for at least 9 out of 11 vaccine pneumococcal serotypes.

Comparison groups	11Pn Group v Synflorix Group
Number of subjects included in analysis	422
Analysis specification	Pre-specified
Analysis type	non-inferiority[21]
Parameter estimate	Adjusted GMCs ratio
Point estimate	1
Confidence interval	
level	95.9 %
sides	2-sided
lower limit	0.81
upper limit	1.23

Notes:

[21] - -2-sided 95.9% Confidence Interval (CI) adjusted 1-sided alpha =2.05%) around the ELISA GMCs ratio between groups
-GMCs ratio and its CI were obtained using an ANCOVA model on the logarithm-transformed concentrations/titres, including the vaccine group as fixed effect and the pre-vaccination concentration as regressor.

Statistical analysis title	(Synflorix/11Pn) GMCs ratio for ANTI-23F serotype

Statistical analysis description:

To demonstrate that 11Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 9 out of 11 vaccine serotypes to Prevnar13 vaccine (for 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of Enzyme-linked immunosorbent assay (ELISA) GMCs.
Criteria: UL of the 2-sided 95.9% CI of the ELISA GMC ratios (Prevnar13/11Pn) and (Synflorix/11Pn) groups < a limit of 2-fold for at least 9 out of 11 vaccine pneumococcal serotypes.

Comparison groups	11Pn Group v Synflorix Group

Number of subjects included in analysis	422
Analysis specification	Pre-specified
Analysis type	non-inferiority[22]
Parameter estimate	Adjusted GMCs ratio
Point estimate	1.15
Confidence interval	
level	95.9 %
sides	2-sided
lower limit	0.89
upper limit	1.48

Notes:

[22] - -2-sided 95.9% Confidence Interval (CI) adjusted 1-sided alpha =2.05%) around the ELISA GMCs ratio between groups
-GMCs ratio and its CI were obtained using an ANCOVA model on the logarithm-transformed concentrations/titres, including the vaccine group as fixed effect and the pre-vaccination concentration as regressor.

Statistical analysis title	(Synflorix/11Pn) GMCs ratio for ANTI-5 serotype

Statistical analysis description:

To demonstrate that 11Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 9 out of 11 vaccine serotypes to Prevnar13 vaccine (for 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of Enzyme-linked immunosorbent assay (ELISA) GMCs.
Criteria: UL of the 2-sided 95.9% CI of the ELISA GMC ratios (Prevnar13/11Pn) and (Synflorix/11Pn) groups < a limit of 2-fold for at least 9 out of 11 vaccine pneumococcal serotypes.

Comparison groups	11Pn Group v Synflorix Group
Number of subjects included in analysis	422
Analysis specification	Pre-specified
Analysis type	non-inferiority[23]
Parameter estimate	Adjusted GMCs ratio
Point estimate	0.88
Confidence interval	
level	95.9 %
sides	2-sided
lower limit	0.75
upper limit	1.03

Notes:

[23] - -2-sided 95.9% Confidence Interval (CI) adjusted 1-sided alpha =2.05%) around the ELISA GMCs ratio between groups
-GMCs ratio and its CI were obtained using an ANCOVA model on the logarithm-transformed concentrations/titres, including the vaccine group as fixed effect and the pre-vaccination concentration as regressor.

Primary: Percentage (%) of subjects (Prevnar13 and 11Pn groups) with antibody concentration ≥ 0.2 µg/mL for ANTI-19A pneumococcal serotype

End point title	Percentage (%) of subjects (Prevnar13 and 11Pn groups) with antibody concentration ≥ 0.2 µg/mL for ANTI-19A pneumococcal serotype[24]

End point description:

N = number of subjects with post primary vaccination results available
% = percentage of subjects with ELISA pneumococcal antibody concentrations ≥ 0.2 µg/mL
Antibodies assessed for this outcome measure were those against the vaccine pneumococcal serotypes 19A (ANTI-19A).
Antibody concentrations were measured by 22F-Inhibition enzyme-linked immunosorbent assay (ELISA).

End point type	Primary

End point timeframe:

1 month post-dose 3 (primary phase)

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is related to the analysis of the difference in terms of percentage of subjects between the 2 following groups: 11Pn group and Prevnar group.

End point values	11Pn Group	Prevnar13 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	222	219		
Units: percent				
number (not applicable)				
ANTI-19A (N=222,219)	98.6	99.5		

Statistical analyses

Statistical analysis title	(Prevnar13-11Pn) % subjects with ANTI-19A≥0.2µg/mL

Statistical analysis description:

To demonstrate that 11Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 9 out of 11 serotypes to Prevnar13 vaccine (for 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of % of subjects with antibody concentrations ≥ 0.2 µg/mL.
Criteria: UL of the 2-sided 95.9% CI of the difference between (Prevnar13 minus 11Pn) and (Synflorix minus 11Pn) groups <10% for at least 9 out of 11 vaccine pneumococcal serotypes.

Comparison groups	11Pn Group v Prevnar13 Group
Number of subjects included in analysis	441
Analysis specification	Pre-specified
Analysis type	non-inferiority[25]
Parameter estimate	Difference in percentage
Point estimate	0.89
Confidence interval	
level	95.9 %
sides	2-sided
lower limit	-1.46
upper limit	3.66

Notes:

[25] - 2-sided 95.9% Confidence Interval (CI) adjusted 1-sided alpha =2.05%) of the difference between groups in terms of percentage of subjects.
Confidence Interval (CI) for difference in proportion: Proc StatXact was used to derive the standardized asymptotic CI for the group difference in proportions [Newcombe, 1998]. The standardized asymptotic method used within GSK Biologicals is method 6.

Primary: Adjusted Geometric Mean Concentrations (GMC) (Prevnar13 and 11Pn Groups) for ANTI-19A pneumococcal serotype

End point title	Adjusted Geometric Mean Concentrations (GMC) (Prevnar13 and 11Pn Groups) for ANTI-19A pneumococcal serotype[26]

End point description:

Adjusted GMC = geometric mean antibody concentration adjusted for baseline concentration
N = number of subjects with both pre- and post-vaccination results available
Antibodies assessed for this outcome measure were those against the vaccine pneumococcal serotype 19A (ANTI -19A).
Antibody concentrations were measured by 22F-Inhibition enzyme-linked immunosorbent assay (ELISA).

End point type	Primary

End point timeframe:

1 month post-dose 3 (primary phase)

Notes:

[26] - 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 analysis of the GMCs ratio between the 2 following groups: 11Pn group and Prevnar group.

End point values	11Pn Group	Prevnar13 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	217	206		
Units: µg/mL				
number (not applicable)				
ANTI-19A (N=217,206)	1.61	2.75		

Statistical analyses

Statistical analysis title	(Prevnar13/11Pn) GMCs ratio for ANTI-19A serotype

Statistical analysis description:

To demonstrate that 11Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 9 out of 11 vaccine serotypes to Prevnar13 vaccine (for 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of Enzyme-linked immunosorbent assay (ELISA) GMCs.
Criteria: UL of the 2-sided 95.9% CI of the ELISA GMC ratios (Prevnar13/11Pn) and (Synflorix/11Pn) groups < a limit of 2-fold for at least 9 out of 11 vaccine pneumococcal serotypes.

Comparison groups	11Pn Group v Prevnar13 Group
Number of subjects included in analysis	423
Analysis specification	Pre-specified
Analysis type	non-inferiority[27]
Parameter estimate	Adjusted GMCs ratio
Point estimate	1.71
Confidence interval	
level	95.9 %
sides	2-sided
lower limit	1.44
upper limit	2.03

Notes:

[27] - 2-sided 95.9% Confidence Interval (CI) adjusted 1-sided alpha = 2.05%) around the ELISA GMCs ratio between groups
GMCs ratio and its CI were obtained using an ANCOVA model on the logarithm-transformed concentrations/titres,including the vaccine group as fixed effect and the pre-vaccination concentration as regressor.

Primary: Percentage (%) of subjects (Synflorix and 12Pn groups) with antibody concentration ≥ 0.2 µg/mL for pneumococcal serotypes

End point title	Percentage (%) of subjects (Synflorix and 12Pn groups) with antibody concentration ≥ 0.2 µg/mL for pneumococcal serotypes[28]

End point description:

N = number of subjects with post primary vaccination results available
% = percentage of subjects with ELISA pneumococcal antibody concentrations ≥ 0.2 µg/mL
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-Inhibition enzyme-linked immunosorbent assay (ELISA).

End point type	Primary

End point timeframe:

1 month post-dose 3 (primary phase)

Notes:

[28] - 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 analysis of the difference in terms of percentage of subjects between the 2 following groups: 12Pn group and Synflorix group.

End point values	12Pn Group	Synflorix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	214	210		
Units: percent				
number (not applicable)				
ANTI-1 (N=214,210)	99.1	98.6		
ANTI-4 (N=214,210)	96.7	96.7		
ANTI-5 (N=214,209)	99.5	99.5		
ANTI-6B (N=214,210)	79.9	75.2		
ANTI-7F (N=214,210)	99.1	99.5		
ANTI-9V (N=214,210)	99.1	99		
ANTI-14 (N=214,210)	100	100		
ANTI-18C (N=214,210)	98.6	98.1		
ANTI-19F (N=214,210)	98.6	97.6		
ANTI-23F (N=214,210)	81.3	83.8		

Statistical analyses

Statistical analysis title	(Synflorix-12Pn) % subjects with ANTI-1≥0.2µg/mL

Statistical analysis description:

To demonstrate that 12Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 10 out of 12 serotypes to Prevnar13 vaccine (for 6A and 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of % of subjects with antibody concentrations ≥ 0.2 µg/mL.
Criteria: UL of the 2-sided 95.8%CI of the difference between (Prevnar13 minus 12Pn) and (Synflorix minus 12Pn) groups <10% for at least 10 out of 12 vaccine pneumococcal serotypes.

Comparison groups	12Pn Group v Synflorix Group
Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	non-inferiority[29]
Parameter estimate	Difference in percentage
Point estimate	-0.49
Confidence interval	
level	95.8 %
sides	2-sided
lower limit	-3.44
upper limit	2.22

Notes:

[29] - Objectives for 12-valent formulation were to be assessed sequentially after demonstration of objectives for 11-valent formulation.
2-sided 95.8% Confidence Interval (CI) adjusted 1-sided alpha = 2.08%) of the difference between

groups in terms of % of subjects.
Confidence Interval (CI) for difference in proportion: Proc StatXact was used to derive the standardized asymptotic CI for the group difference in proportions [Newcombe, 1998]. The standardized asymptotic method used is method 6.

Statistical analysis title	(Synflorix-12Pn) % subjects with ANTI-4≥0.2µg/mL

Statistical analysis description:

To demonstrate that 12Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 10 out of 12 serotypes to Prevnar13 vaccine (for 6A and 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of % of subjects with antibody concentrations ≥ 0.2 µg/mL.
Criteria: UL of the 2-sided 95.8%CI of the difference between (Prevnar13 minus 12Pn) and (Synflorix minus 12Pn) groups <10% for at least 10 out of 12 vaccine pneumococcal serotypes.

Comparison groups	12Pn Group v Synflorix Group
Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	non-inferiority[30]
Parameter estimate	Difference in percentage
Point estimate	-0.06
Confidence interval	
level	95.8 %
sides	2-sided
lower limit	-4.03
upper limit	3.86

Notes:

[30] - Objectives for 12-valent formulation were to be assessed sequentially after demonstration of objectives for 11-valent formulation.
2-sided 95.8% Confidence Interval (CI) adjusted 1-sided alpha = 2.08%) of the difference between groups in terms of % of subjects.
Confidence Interval (CI) for difference in proportion: Proc StatXact was used to derive the standardized asymptotic CI for the group difference in proportions [Newcombe, 1998]. The standardized asymptotic method used is method 6.

Statistical analysis title	(Synflorix-12Pn) % subjects with ANTI-5≥0.2µg/mL

Statistical analysis description:

To demonstrate that 12Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 10 out of 12 serotypes to Prevnar13 vaccine (for 6A and 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of % of subjects with antibody concentrations ≥ 0.2 µg/mL.
Criteria: UL of the 2-sided 95.8%CI of the difference between (Prevnar13 minus 12Pn) and (Synflorix minus 12Pn) groups <10% for at least 10 out of 12 vaccine pneumococcal serotypes.

Comparison groups	12Pn Group v Synflorix Group
Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	non-inferiority[31]
Parameter estimate	Difference in percentage
Point estimate	-0.01
Confidence interval	
level	95.8 %
sides	2-sided
lower limit	-2.37
upper limit	2.3

Notes:

[31] - Objectives for 12-valent formulation were to be assessed sequentially after demonstration of objectives for 11-valent formulation.
2-sided 95.8% Confidence Interval (CI) adjusted 1-sided alpha = 2.08%) of the difference between groups in terms of % of subjects.
Confidence Interval (CI) for difference in proportion: Proc StatXact was used to derive the standardized asymptotic CI for the group difference in proportions [Newcombe, 1998]. The standardized asymptotic

method used is method 6.

Statistical analysis title	(Synflorix-12Pn) % subjects with ANTI-6B≥0.2µg/mL

Statistical analysis description:

To demonstrate that 12Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 10 out of 12 serotypes to Prevnar13 vaccine (for 6A and 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of % of subjects with antibody concentrations ≥ 0.2 µg/mL.
Criteria: UL of the 2-sided 95.8%CI of the difference between (Prevnar13 minus 12Pn) and (Synflorix minus 12Pn) groups <10% for at least 10 out of 12 vaccine pneumococcal serotypes.

Comparison groups	12Pn Group v Synflorix Group
Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	non-inferiority[32]
Parameter estimate	Difference in percentage
Point estimate	-4.67
Confidence interval	
level	95.8 %
sides	2-sided
lower limit	-12.94
upper limit	3.6

Notes:

[32] - Objectives for 12-valent formulation were to be assessed sequentially after demonstration of objectives for 11-valent formulation.
2-sided 95.8% Confidence Interval (CI) adjusted 1-sided alpha = 2.08%) of the difference between groups in terms of % of subjects.
Confidence Interval (CI) for difference in proportion: Proc StatXact was used to derive the standardized asymptotic CI for the group difference in proportions [Newcombe, 1998]. The standardized asymptotic method used is method 6.

Statistical analysis title	(Synflorix-12Pn) % subjects with ANTI-7F≥0.2µg/mL

Statistical analysis description:

To demonstrate that 12Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 10 out of 12 serotypes to Prevnar13 vaccine (for 6A and 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of % of subjects with antibody concentrations ≥ 0.2 µg/mL.
Criteria: UL of the 2-sided 95.8%CI of the difference between (Prevnar13 minus 12Pn) and (Synflorix minus 12Pn) groups <10% for at least 10 out of 12 vaccine pneumococcal serotypes.

Comparison groups	12Pn Group v Synflorix Group
Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	non-inferiority[33]
Parameter estimate	Difference in percentage
Point estimate	0.46
Confidence interval	
level	95.8 %
sides	2-sided
lower limit	-1.93
upper limit	3.06

Notes:

[33] - Objectives for 12-valent formulation were to be assessed sequentially after demonstration of objectives for 11-valent formulation.
2-sided 95.8% Confidence Interval (CI) adjusted 1-sided alpha = 2.08%) of the difference between groups in terms of % of subjects.
Confidence Interval (CI) for difference in proportion: Proc StatXact was used to derive the standardized asymptotic CI for the group difference in proportions [Newcombe, 1998]. The standardized asymptotic

method used is method 6.

Statistical analysis title	(Synflorix-12Pn) % subjects with ANTI-9V≥0.2µg/mL

Statistical analysis description:

To demonstrate that 12Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 10 out of 12 serotypes to Prevnar13 vaccine (for 6A and 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of % of subjects with antibody concentrations ≥ 0.2 µg/mL.
Criteria: UL of the 2-sided 95.8%CI of the difference between (Prevnar13 minus 12Pn) and (Synflorix minus 12Pn) groups <10% for at least 10 out of 12 vaccine pneumococcal serotypes.

Comparison groups	12Pn Group v Synflorix Group
Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	non-inferiority[34]
Parameter estimate	Difference in percentage
Point estimate	-0.02
Confidence interval	
level	95.8 %
sides	2-sided
lower limit	-2.72
upper limit	2.64

Notes:

[34] - Objectives for 12-valent formulation were to be assessed sequentially after demonstration of objectives for 11-valent formulation.
2-sided 95.8% Confidence Interval (CI) adjusted 1-sided alpha = 2.08%) of the difference between groups in terms of % of subjects.
Confidence Interval (CI) for difference in proportion: Proc StatXact was used to derive the standardized asymptotic CI for the group difference in proportions [Newcombe, 1998]. The standardized asymptotic method used is method 6.

Statistical analysis title	(Synflorix-12Pn) % subjects with ANTI-14≥0.2µg/mL

Statistical analysis description:

To demonstrate that 12Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 10 out of 12 serotypes to Prevnar13 vaccine (for 6A and 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of % of subjects with antibody concentrations ≥ 0.2 µg/mL.
Criteria: UL of the 2-sided 95.8%CI of the difference between (Prevnar13 minus 12Pn) and (Synflorix minus 12Pn) groups <10% for at least 10 out of 12 vaccine pneumococcal serotypes.

Comparison groups	12Pn Group v Synflorix Group
Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	non-inferiority[35]
Parameter estimate	Difference in percentage
Point estimate	0
Confidence interval	
level	95.8 %
sides	2-sided
lower limit	-1.94
upper limit	1.9

Notes:

[35] - Objectives for 12-valent formulation were to be assessed sequentially after demonstration of objectives for 11-valent formulation.
2-sided 95.8% Confidence Interval (CI) adjusted 1-sided alpha = 2.08%) of the difference between groups in terms of % of subjects.
Confidence Interval (CI) for difference in proportion: Proc StatXact was used to derive the standardized asymptotic CI for the group difference in proportions [Newcombe, 1998]. The standardized asymptotic

method used is method 6.

Statistical analysis title	(Synflorix-12Pn) % subjects with ANTI-18C≥0.2µg/mL

Statistical analysis description:

To demonstrate that 12Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 10 out of 12 serotypes to Prevnar13 vaccine (for 6A and 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of % of subjects with antibody concentrations ≥ 0.2 µg/mL.
Criteria: UL of the 2-sided 95.8%CI of the difference between (Prevnar13 minus 12Pn) and (Synflorix minus 12Pn) groups <10% for at least 10 out of 12 vaccine pneumococcal serotypes.

Comparison groups	12Pn Group v Synflorix Group
Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	non-inferiority[36]
Parameter estimate	Difference in percentage
Point estimate	-0.5
Confidence interval	
level	95.8 %
sides	2-sided
lower limit	-3.72
upper limit	2.52

Notes:

[36] - Objectives for 12-valent formulation were to be assessed sequentially after demonstration of objectives for 11-valent formulation.
2-sided 95.8% Confidence Interval (CI) adjusted 1-sided alpha = 2.08%) of the difference between groups in terms of % of subjects.
Confidence Interval (CI) for difference in proportion: Proc StatXact was used to derive the standardized asymptotic CI for the group difference in proportions [Newcombe, 1998]. The standardized asymptotic method used is method 6.

Statistical analysis title	(Synflorix-12Pn) % subjects with ANTI-19F≥0.2µg/mL

Statistical analysis description:

To demonstrate that 12Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 10 out of 12 serotypes to Prevnar13 vaccine (for 6A and 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of % of subjects with antibody concentrations ≥ 0.2 µg/mL.
Criteria: UL of the 2-sided 95.8%CI of the difference between (Prevnar13 minus 12Pn) and (Synflorix minus 12Pn) groups <10% for at least 10 out of 12 vaccine pneumococcal serotypes.

Comparison groups	12Pn Group v Synflorix Group
Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	non-inferiority[37]
Parameter estimate	Difference in percentage
Point estimate	-0.98
Confidence interval	
level	95.8 %
sides	2-sided
lower limit	-4.38
upper limit	2.1

Notes:

[37] - Objectives for 12-valent formulation were to be assessed sequentially after demonstration of objectives for 11-valent formulation.
2-sided 95.8% Confidence Interval (CI) adjusted 1-sided alpha = 2.08%) of the difference between groups in terms of % of subjects.
Confidence Interval (CI) for difference in proportion: Proc StatXact was used to derive the standardized asymptotic CI for the group difference in proportions [Newcombe, 1998]. The standardized asymptotic

method used is method 6.

Statistical analysis title	(Synflorix-12Pn) % subjects with ANTI-23F≥0.2µg/mL

Statistical analysis description:

To demonstrate that 12Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 10 out of 12 serotypes to Prevnar13 vaccine (for 6A and 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of % of subjects with antibody concentrations ≥ 0.2 µg/mL.
Criteria: UL of the 2-sided 95.8%CI of the difference between (Prevnar13 minus 12Pn) and (Synflorix minus 12Pn) groups <10% for at least 10 out of 12 vaccine pneumococcal serotypes.

Comparison groups	12Pn Group v Synflorix Group
Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	non-inferiority[38]
Parameter estimate	Difference in percentage
Point estimate	2.5
Confidence interval	
level	95.8 %
sides	2-sided
lower limit	-5.07
upper limit	10.06

Notes:

[38] - Objectives for 12-valent formulation were to be assessed sequentially after demonstration of objectives for 11-valent formulation.
2-sided 95.8% Confidence Interval (CI) adjusted 1-sided alpha = 2.08%) of the difference between groups in terms of % of subjects.
Confidence Interval (CI) for difference in proportion: Proc StatXact was used to derive the standardized asymptotic CI for the group difference in proportions [Newcombe, 1998]. The standardized asymptotic method used is method 6.

Primary: Adjusted Geometric Mean Concentrations (GMC) (Synflorix and 12Pn Groups) for pneumococcal serotypes

End point title	Adjusted Geometric Mean Concentrations (GMC) (Synflorix and 12Pn Groups) for pneumococcal serotypes[39]

End point description:

Adjusted GMC = geometric mean antibody concentration adjusted for baseline concentration
N = number of subjects with both pre- and post-vaccination results available
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-Inhibition enzyme-linked immunosorbent assay (ELISA).

End point type	Primary

End point timeframe:

1 month post-dose 3 (primary phase)

Notes:

[39] - 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 analysis of the GMCs ratio between the 2 following groups: 12Pn group and Synflorix group.

End point values	12Pn Group	Synflorix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	211	203		
Units: µg/mL				
number (not applicable)				
ANTI-1 (N=207,203)	1.58	1.35		
ANTI-4 (N=208,203)	1.94	1.66		
ANTI-5 (N=208,201)	2.37	2.16		
ANTI-6B (N=208,200)	0.56	0.47		
ANTI-7F (N=211,202)	2.42	2.17		
ANTI-9V (N=208,200)	1.78	1.4		
ANTI-14 (N=209,201)	4.48	4.1		
ANTI-18C (N=209,201)	2.55	2.57		
ANTI-19F (N=211,202)	3.29	3.67		
ANTI-23F (N=208,199)	0.68	0.71		

Statistical analyses

Statistical analysis title	(Synflorix/12Pn) GMCs ratio for ANTI-1 serotype

Statistical analysis description:

To demonstrate that 12Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 10 out of 12 vaccine serotypes to Prevnar13 vaccine (for 6A & 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of Enzyme-linked immunosorbent assay (ELISA) GMCs.
Criteria: UL of the 2-sided 95.8% CI of the ELISA GMC ratios (Prevnar13/12Pn) and (Synflorix/12Pn) groups < a limit of 2-fold for at least 10 out of 12 vaccine pneumococcal serotypes.

Comparison groups	12Pn Group v Synflorix Group
Number of subjects included in analysis	414
Analysis specification	Pre-specified
Analysis type	non-inferiority[40]
Parameter estimate	Adjusted GMCs ratio
Point estimate	0.86
Confidence interval	
level	95.8 %
sides	2-sided
lower limit	0.72
upper limit	1.02

Notes:

[40] - Objectives for 12-valent formulation were to be assessed sequentially after demonstration of objectives for 11-valent formulation.
2-sided 95.8% Confidence Interval (CI) adjusted 1-sided alpha = 2.08%) around the ELISA GMCs ratio between groups.
GMCs ratio and CI were obtained using ANCOVA model on the logarithm-transformed concentrations/titres, including the vaccine group as fixed effect and the pre-vaccination concentration as regressor.

Statistical analysis title	(Synflorix/12Pn) GMCs ratio for ANTI-4 serotype

Statistical analysis description:

To demonstrate that 12Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 10 out of 12 vaccine serotypes to Prevnar13 vaccine (for 6A & 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of Enzyme-linked immunosorbent assay (ELISA) GMCs.
Criteria: UL of the 2-sided 95.8% CI of the ELISA GMC ratios (Prevnar13/12Pn) and (Synflorix/12Pn) groups < a limit of 2-fold for at least 10 out of 12 vaccine pneumococcal serotypes.

Comparison groups	12Pn Group v Synflorix Group
Number of subjects included in analysis	414
Analysis specification	Pre-specified
Analysis type	non-inferiority[41]
Parameter estimate	Adjusted GMCs ratio
Point estimate	0.86
Confidence interval	
level	95.8 %
sides	2-sided
lower limit	0.7
upper limit	1.05

Notes:

[41] - Objectives for 12-valent formulation were to be assessed sequentially after demonstration of objectives for 11-valent formulation.
2-sided 95.8% Confidence Interval (CI) adjusted 1-sided alpha = 2.08%) around the ELISA GMCs ratio between groups.
GMCs ratio and CI were obtained using ANCOVA model on the logarithm-transformed concentrations/titres, including the vaccine group as fixed effect and the pre-vaccination concentration as regressor.

Statistical analysis title	(Synflorix/12Pn) GMCs ratio for ANTI-5 serotype

Statistical analysis description:

To demonstrate that 12Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 10 out of 12 vaccine serotypes to Prevnar13 vaccine (for 6A & 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of Enzyme-linked immunosorbent assay (ELISA) GMCs.
Criteria: UL of the 2-sided 95.8% CI of the ELISA GMC ratios (Prevnar13/12Pn) and (Synflorix/12Pn) groups < a limit of 2-fold for at least 10 out of 12 vaccine pneumococcal serotypes.

Comparison groups	Synflorix Group v 12Pn Group
Number of subjects included in analysis	414
Analysis specification	Pre-specified
Analysis type	non-inferiority[42]
Parameter estimate	Adjusted GMCs ratio
Point estimate	0.91
Confidence interval	
level	95.8 %
sides	2-sided
lower limit	0.78
upper limit	1.07

Notes:

[42] - Objectives for 12-valent formulation were to be assessed sequentially after demonstration of objectives for 11-valent formulation.
2-sided 95.8% Confidence Interval (CI) adjusted 1-sided alpha = 2.08%) around the ELISA GMCs ratio between groups.
GMCs ratio and CI were obtained using ANCOVA model on the logarithm-transformed concentrations/titres, including the vaccine group as fixed effect and the pre-vaccination concentration as regressor.

Statistical analysis title	(Synflorix/12Pn) GMCs ratio for ANTI-6B serotype

Statistical analysis description:

To demonstrate that 12Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 10 out of 12 vaccine serotypes to Prevnar13 vaccine (for 6A & 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of Enzyme-linked immunosorbent assay (ELISA) GMCs.
Criteria: UL of the 2-sided 95.8% CI of the ELISA GMC ratios (Prevnar13/12Pn) and (Synflorix/12Pn) groups < a limit of 2-fold for at least 10 out of 12 vaccine pneumococcal serotypes.

Comparison groups	12Pn Group v Synflorix Group

Number of subjects included in analysis	414
Analysis specification	Pre-specified
Analysis type	non-inferiority[43]
Parameter estimate	Adjusted GMCs ratio
Point estimate	0.84
Confidence interval	
level	95.8 %
sides	2-sided
lower limit	0.64
upper limit	1.11

Notes:

[43] - Objectives for 12-valent formulation were to be assessed sequentially after demonstration of objectives for 11-valent formulation.
2-sided 95.8% Confidence Interval (CI) adjusted 1-sided alpha = 2.08%) around the ELISA GMCs ratio between groups.
GMCs ratio and CI were obtained using ANCOVA model on the logarithm-transformed concentrations/titres, including the vaccine group as fixed effect and the pre-vaccination concentration as regressor.

Statistical analysis title	(Synflorix/12Pn) GMCs ratio for ANTI-7F serotype

Statistical analysis description:

To demonstrate that 12Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 10 out of 12 vaccine serotypes to Prevnar13 vaccine (for 6A & 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of Enzyme-linked immunosorbent assay (ELISA) GMCs.
Criteria: UL of the 2-sided 95.8% CI of the ELISA GMC ratios (Prevnar13/12Pn) and (Synflorix/12Pn) groups < a limit of 2-fold for at least 10 out of 12 vaccine pneumococcal serotypes.

Comparison groups	12Pn Group v Synflorix Group
Number of subjects included in analysis	414
Analysis specification	Pre-specified
Analysis type	non-inferiority[44]
Parameter estimate	Adjusted GMCs ratio
Point estimate	0.9
Confidence interval	
level	95.8 %
sides	2-sided
lower limit	0.76
upper limit	1.06

Notes:

[44] - Objectives for 12-valent formulation were to be assessed sequentially after demonstration of objectives for 11-valent formulation.
2-sided 95.8% Confidence Interval (CI) adjusted 1-sided alpha = 2.08%) around the ELISA GMCs ratio between groups.
GMCs ratio and CI were obtained using ANCOVA model on the logarithm-transformed concentrations/titres, including the vaccine group as fixed effect and the pre-vaccination concentration as regressor.

Statistical analysis title	(Synflorix/12Pn) GMCs ratio for ANTI-9V serotype

Statistical analysis description:

To demonstrate that 12Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 10 out of 12 vaccine serotypes to Prevnar13 vaccine (for 6A & 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of Enzyme-linked immunosorbent assay (ELISA) GMCs.
Criteria: UL of the 2-sided 95.8% CI of the ELISA GMC ratios (Prevnar13/12Pn) and (Synflorix/12Pn) groups < a limit of 2-fold for at least 10 out of 12 vaccine pneumococcal serotypes.

Comparison groups	12Pn Group v Synflorix Group

Number of subjects included in analysis	414
Analysis specification	Pre-specified
Analysis type	non-inferiority[45]
Parameter estimate	Adjusted GMCs ratio
Point estimate	0.79
Confidence interval	
level	95.8 %
sides	2-sided
lower limit	0.67
upper limit	0.93

Notes:

[45] - Objectives for 12-valent formulation were to be assessed sequentially after demonstration of objectives for 11-valent formulation.
2-sided 95.8% Confidence Interval (CI) adjusted 1-sided alpha = 2.08%) around the ELISA GMCs ratio between groups.
GMCs ratio and CI were obtained using ANCOVA model on the logarithm-transformed concentrations/titres, including the vaccine group as fixed effect and the pre-vaccination concentration as regressor.

Statistical analysis title	(Synflorix/12Pn) GMCs ratio for ANTI-14 serotype

Statistical analysis description:

To demonstrate that 12Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 10 out of 12 vaccine serotypes to Prevnar13 vaccine (for 6A & 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of Enzyme-linked immunosorbent assay (ELISA) GMCs.
Criteria: UL of the 2-sided 95.8% CI of the ELISA GMC ratios (Prevnar13/12Pn) and (Synflorix/12Pn) groups < a limit of 2-fold for at least 10 out of 12 vaccine pneumococcal serotypes.

Comparison groups	12Pn Group v Synflorix Group
Number of subjects included in analysis	414
Analysis specification	Pre-specified
Analysis type	non-inferiority[46]
Parameter estimate	Adjusted GMCs ratio
Point estimate	0.91
Confidence interval	
level	95.8 %
sides	2-sided
lower limit	0.77
upper limit	1.09

Notes:

[46] - Objectives for 12-valent formulation were to be assessed sequentially after demonstration of objectives for 11-valent formulation.
2-sided 95.8% Confidence Interval (CI) adjusted 1-sided alpha = 2.08%) around the ELISA GMCs ratio between groups.
GMCs ratio and CI were obtained using ANCOVA model on the logarithm-transformed concentrations/titres, including the vaccine group as fixed effect and the pre-vaccination concentration as regressor.

Statistical analysis title	(Synflorix/12Pn) GMCs ratio for ANTI-18C serotype

Statistical analysis description:

To demonstrate that 12Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 10 out of 12 vaccine serotypes to Prevnar13 vaccine (for 6A & 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of Enzyme-linked immunosorbent assay (ELISA) GMCs.
Criteria: UL of the 2-sided 95.8% CI of the ELISA GMC ratios (Prevnar13/12Pn) and (Synflorix/12Pn) groups < a limit of 2-fold for at least 10 out of 12 vaccine pneumococcal serotypes.

Comparison groups	12Pn Group v Synflorix Group

Number of subjects included in analysis	414
Analysis specification	Pre-specified
Analysis type	non-inferiority[47]
Parameter estimate	Adjusted GMCs ratio
Point estimate	1.01
Confidence interval	
level	95.8 %
sides	2-sided
lower limit	0.81
upper limit	1.26

Notes:

[47] - Objectives for 12-valent formulation were to be assessed sequentially after demonstration ofobjectives for 11-valent formulation.
2-sided 95.8% Confidence Interval (CI) adjusted 1-sided alpha = 2.08%) around the ELISA GMCs ratio between groups.
GMCs ratio and CI were obtained using ANCOVA model on the logarithm-transformed concentrations/titres, including the vaccine group as fixed effect and the pre-vaccination concentration as regressor.

Statistical analysis title	(Synflorix/12Pn) GMCs ratio for ANTI-19F serotype

Statistical analysis description:

To demonstrate that 12Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 10 out of 12 vaccine serotypes to Prevnar13 vaccine (for 6A & 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of Enzyme-linked immunosorbent assay (ELISA) GMCs.
Criteria: UL of the 2-sided 95.8% CI of the ELISA GMC ratios (Prevnar13/12Pn) and (Synflorix/12Pn) groups < a limit of 2-fold for at least 10 out of 12 vaccine pneumococcal serotypes.

Comparison groups	12Pn Group v Synflorix Group
Number of subjects included in analysis	414
Analysis specification	Pre-specified
Analysis type	non-inferiority[48]
Parameter estimate	Adjusted GMCs ratio
Point estimate	1.12
Confidence interval	
level	95.8 %
sides	2-sided
lower limit	0.9
upper limit	1.38

Notes:

[48] - Objectives for 12-valent formulation were to be assessed sequentially after demonstration of objectives for 11-valent formulation.
2-sided 95.8% Confidence Interval (CI) adjusted 1-sided alpha = 2.08%) around the ELISA GMCs ratio between groups.
GMCs ratio and CI were obtained using ANCOVA model on the logarithm-transformed concentrations/titres, including the vaccine group as fixed effect and the pre-vaccination concentration as regressor.

Statistical analysis title	(Synflorix/12Pn) GMCs ratio for ANTI-23F serotype

Statistical analysis description:

To demonstrate that 12Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 10 out of 12 vaccine serotypes to Prevnar13 vaccine (for 6A & 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of Enzyme-linked immunosorbent assay (ELISA) GMCs.
Criteria: UL of the 2-sided 95.8% CI of the ELISA GMC ratios (Prevnar13/12Pn) and (Synflorix/12Pn) groups < a limit of 2-fold for at least 10 out of 12 vaccine pneumococcal serotypes.

Comparison groups	12Pn Group v Synflorix Group

Number of subjects included in analysis	414
Analysis specification	Pre-specified
Analysis type	non-inferiority[49]
Parameter estimate	Adjusted GMCs ratio
Point estimate	1.05
Confidence interval	
level	95.8 %
sides	2-sided
lower limit	0.81
upper limit	1.37

Notes:

[49] - Objectives for 12-valent formulation were to be assessed sequentially after demonstration of objectives for 11-valent formulation.
2-sided 95.8% Confidence Interval (CI) adjusted 1-sided alpha = 2.08%) around the ELISA GMCs ratio between groups.
GMCs ratio and CI were obtained using ANCOVA model on the logarithm-transformed concentrations/titres, including the vaccine group as fixed effect and the pre-vaccination concentration as regressor.

Primary: Percentage (%) of subjects (Prevnar13 and 12Pn groups) with antibody concentration ≥ 0.2 µg/mL for anti-6A and anti-19A pneumococcal serotypes

End point title	Percentage (%) of subjects (Prevnar13 and 12Pn groups) with antibody concentration ≥ 0.2 µg/mL for anti-6A and anti-19A pneumococcal serotypes[50]

End point description:

N = number of subjects with post primary vaccination results available
% = percentage of subjects with ELISA pneumococcal antibody concentrations ≥ 0.2 µg/mL
Antibodies assessed for this outcome measure were those against the vaccine pneumococcal serotypes 6A and 19A (ANTI-6A and ANTI-19A).
Antibody concentrations were measured by 22F-Inhibition enzyme-linked immunosorbent assay (ELISA).

End point type	Primary

End point timeframe:

1 month post-dose 3 (primary phase)

Notes:

[50] - 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 analysis of the difference in terms of percentage of subjects between the 2 following groups: 12Pn group and Prevnar group.

End point values	12Pn Group	Prevnar13 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	214	219		
Units: percent				
number (not applicable)				
ANTI-6A (N=214,218)	88.3	99.5		
ANTI-19A (N=214,219)	95.8	99.5		

Statistical analyses

Statistical analysis title	(Prevnar13-12Pn) % subjects with ANTI-6A≥ 0.2µg/mL

Statistical analysis description:

To demonstrate that 12Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 10 out of 12 serotypes to Prevnar13 vaccine (for 6A and 19A) or Synflorix™ vaccine

(for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of % of subjects with antibody concentrations ≥ 0.2 µg/mL.
Criteria: UL of the 2-sided 95.8%CI of the difference between (Prevnar13 minus 12Pn) and (Synflorix minus 12Pn) groups <10% for at least 10 out of 12 vaccine pneumococcal serotypes.

Comparison groups	12Pn Group v Prevnar13 Group
Number of subjects included in analysis	433
Analysis specification	Pre-specified
Analysis type	non-inferiority[51]
Parameter estimate	Difference in percentage
Point estimate	11.22
Confidence interval	
level	95.8 %
sides	2-sided
lower limit	7.22
upper limit	16.49

Notes:

[51] - Objectives for 12-valent formulation were to be assessed sequentially after demonstration of objectives for 11-valent formulation.
2-sided 95.8% Confidence Interval (CI) adjusted 1-sided alpha = 2.08%) of the difference between groups in terms of % of subjects.
Confidence Interval (CI) for difference in proportion: Proc StatXact was used to derive the standardized asymptotic CI for the group difference in proportions [Newcombe, 1998]. The standardized asymptotic method used is method 6.

Statistical analysis title	(Prevnar13-12Pn) % subjects with ANTI-19A≥0.2µg/mL

Statistical analysis description:

To demonstrate that 12Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 10 out of 12 serotypes to Prevnar13 vaccine (for 6A and 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of % of subjects with antibody concentrations ≥ 0.2 µg/mL.
Criteria: UL of the 2-sided 95.8%CI of the difference between (Prevnar13 minus 12Pn) and (Synflorix minus 12Pn) groups <10% for at least 10 out of 12 vaccine pneumococcal serotypes.

Comparison groups	12Pn Group v Prevnar13 Group
Number of subjects included in analysis	433
Analysis specification	Pre-specified
Analysis type	non-inferiority[52]
Parameter estimate	Difference in percentage
Point estimate	3.75
Confidence interval	
level	95.8 %
sides	2-sided
lower limit	1.03
upper limit	7.57

Notes:

[52] - Objectives for 12-valent formulation were to be assessed sequentially after demonstration of objectives for 11-valent formulation.
2-sided 95.8% Confidence Interval (CI) adjusted 1-sided alpha = 2.08%) of the difference between groups in terms of % of subjects.
Confidence Interval (CI) for difference in proportion: Proc StatXact was used to derive the standardized asymptotic CI for the group difference in proportions [Newcombe, 1998]. The standardized asymptotic method used is method 6.

Primary: Adjusted Geometric Mean Concentrations (GMC) (Prevnar13 and 12Pn Groups) for anti-6A and anti-19A pneumococcal serotypes

End point title	Adjusted Geometric Mean Concentrations (GMC) (Prevnar13 and 12Pn Groups) for anti-6A and anti-19A pneumococcal serotypes[53]

End point description:

Adjusted GMC = geometric mean antibody concentration adjusted for baseline concentration
N = number of subjects with both pre- and post-vaccination results available
Antibodies assessed for this outcome measure were those against the vaccine pneumococcal serotypes 6A and 19A (ANTI -6A and ANTI-19A).
Antibody concentrations were measured by 22F-Inhibition enzyme-linked immunosorbent assay (ELISA).

End point type	Primary

End point timeframe:

1 month post-dose 3 (primary phase)

Notes:

[53] - 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 analysis of the GMCs ratio between the 2 following groups: 12Pn group and Prevnar group.

End point values	12Pn Group	Prevnar13 Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	210	214		
Units: µg/mL				
number (not applicable)				
ANTI-6A (N=210,214)	1.09	2.07		
ANTI-19A (N=208,206)	1.19	2.76		

Statistical analyses

Statistical analysis title	(Prevnar13/12Pn) GMCs ratio for ANTI-6A serotype

Statistical analysis description:

To demonstrate that 12Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 10 out of 12 vaccine serotypes to Prevnar13 vaccine (for 6A & 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of Enzyme-linked immunosorbent assay (ELISA) GMCs.
Criteria: UL of the 2-sided 95.8% CI of the ELISA GMC ratios (Prevnar13/12Pn) and (Synflorix/12Pn) groups < a limit of 2-fold for at least 10 out of 12 vaccine pneumococcal serotypes.

Comparison groups	12Pn Group v Prevnar13 Group
Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	non-inferiority[54]
Parameter estimate	Adjusted GMCs ratio
Point estimate	1.9
Confidence interval	
level	95.8 %
sides	2-sided
lower limit	1.51
upper limit	2.39

Notes:

[54] - Objectives for 12-valent formulation were to be assessed sequentially after demonstration of objectives for 11-valent formulation.
2-sided 95.8% Confidence Interval (CI) adjusted 1-sided alpha = 2.08%) around the ELISA GMCs ratio between groups.
GMCs ratio and CI were obtained using ANCOVA model on the logarithm-transformed concentrations/titres, including the vaccine group as fixed effect and the pre-vaccination concentration as regressor.

Statistical analysis title	(Prevnar13/12Pn) GMCs ratio for ANTI-19A serotype

Statistical analysis description:

To demonstrate that 12Pn co-administered with Infanrix hexa™ vaccine 1 month post-dose 3 was non-inferior for at least 10 out of 12 vaccine serotypes to Prevnar13 vaccine (for 6A & 19A) or Synflorix™ vaccine (for 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F) in terms of Enzyme-linked immunosorbent assay (ELISA) GMCs.
Criteria: UL of the 2-sided 95.8% CI of the ELISA GMC ratios (Prevnar13/12Pn) and (Synflorix/12Pn) groups < a limit of 2-fold for at least 10 out of 12 vaccine pneumococcal serotypes.

Comparison groups	12Pn Group v Prevnar13 Group
Number of subjects included in analysis	424
Analysis specification	Pre-specified
Analysis type	non-inferiority[55]
Parameter estimate	Adjusted GMCs ratio
Point estimate	2.32
Confidence interval	
level	95.8 %
sides	2-sided
lower limit	1.94
upper limit	2.77

Notes:

[55] - Objectives for 12-valent formulation were to be assessed sequentially after demonstration of objectives for 11-valent formulation.
2-sided 95.8% Confidence Interval (CI) adjusted 1-sided alpha = 2.08%) around the ELISA GMCs ratio between groups.
GMCs ratio and CI were obtained using ANCOVA model on the logarithm-transformed concentrations/titres, including the vaccine group as fixed effect and the pre-vaccination concentration as regressor.

Secondary: Concentrations of antibodies against protein D (Anti-PD) during the Primary Phase of the study

End point title	Concentrations of antibodies against protein D (Anti-PD) during the Primary Phase of the study

End point description:

Anti-PD 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 cut-off of the assay was an anti-PD antibody concentration higher than or equal to (≥) 100 EL.U/mL.

End point type	Secondary

End point timeframe:

At study Month 3, e. g. at one month post-Dose 3 of pneumococcal vaccine

End point values	11Pn Group	12Pn Group	Synflorix Group	Prevnar13 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	112	106	103	106
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD	1430.1 (1194.2 to 1712.7)	1194.2 (1017.7 to 1401.3)	1344.8 (1116.4 to 1619.9)	64.4 (57.7 to 71.9)

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point type	Secondary

End point timeframe:

Within the 4-day (Days 0-3) post-vaccination period following each primary dose (D).

End point values	11Pn Group	12Pn Group	Synflorix Group	Prevnar13 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	240	236	228	238
Units: Subjects				
Any Pain, post D1 (N=240;236;228;238)	104	105	94	85
Grade 3 Pain, post D1 (N=240;236;228;238)	16	5	12	6
Any Redness, post D1 (N=240;236;228;238)	82	90	72	75
Grade 3 Redness, post D1 (N=240;236;228;238)	0	0	1	0
Any Swelling, post D1 (N=240;236;228;238)	51	57	46	47
Grade 3 Swelling, post D1 (N=240;236;228;238)	1	4	7	1
Any Pain, post D2 (N=239;232;227;234)	89	100	88	90
Grade 3 Pain, post D2 (N=239;232;227;234)	12	12	10	6
Any Redness, post D2 (N=239;232;227;234)	86	95	78	79
Grade 3 Redness, post D2 (N=239;232;227;234)	2	1	1	1
Any Swelling, post D2 (N=239;232;227;234)	61	72	54	49
Grade 3 Swelling, post D2 (N=239;232;227;234)	2	3	5	2
Any Pain, post D3 (N=238;229;226;234)	76	75	76	75
Grade 3 Pain, post D3 (N=238;229;226;234)	4	4	6	3
Any Redness, post D3 (N=238;229;226;234)	93	85	91	85
Grade 3 Redness, post D3 (N=238;229;226;234)	3	2	2	1
Any Swelling, post D3 (N=238;229;226;234)	72	76	58	61

Grade 3 Swelling, post D3 (N=238;229;226;234)	2	5	2	3

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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

End point type	Secondary

End point timeframe:

Within the 4-day (Days 0-3) period after booster vaccination

End point values	11Pn Group	12Pn Group	Synflorix Group	Prevnar13 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	235	224	219	231
Units: Subjects				
Any Pain	112	123	119	110
Grade 3 Pain	13	16	18	8
Any Redness	109	117	108	107
Grade 3 Redness	5	10	7	5
Any Swelling	84	88	89	85
Grade 3 Swelling	8	7	5	7

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and Grade 3 solicited general symptoms and with solicited general symptoms with relationship to vaccination, during the Primary Phase of the study

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

End point description:

Assessed solicited general symptoms were Drowsiness, Irritability/Fussiness (Irr./Fuss.), Loss of appetite (Loss Appet.) and Fever (rectal temperature higher than [≥] 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 activity. Grade 3 Irr./Fuss. = Crying that could not be comforted/prevented normal activity. 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 (Days 0-3) post-vaccination period following each primary dose (D).

End point values	11Pn Group	12Pn Group	Synflorix Group	Prevnar13 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	240	236	227	238
Units: Subjects				
Any Drowsiness, post D1 (N=240;236;227;238)	148	144	129	129
Grade 3 Drowsiness, post D1 (N=240;236;227;238)	7	6	10	10
Related Drowsiness, post D1 (N=240;236;227;238)	124	104	95	103
Any Irr./Fuss., post D1 (N=240;236;227;238)	151	156	134	138
Grade 3 Irr./Fuss., post D1 (N=240;236;227;238)	16	15	17	10
Related Irr./Fuss., post D1 (N=240;236;227;238)	119	122	98	103
Any Loss Appet., post D1 (N=240;236;227;238)	85	89	81	73
Grade 3 Loss Appet., post D1 (N=240;236;227;238)	2	2	3	2
Related Loss Appet., post D1 (N=240;236;227;238)	59	65	56	57
Any Fever, post D1 (N=240;236;227;238)	108	104	107	87
Grade 3 Fever, post D1 (N=240;236;227;238)	0	0	0	0
Related Fever, post D1 (N=240;236;227;238)	94	91	92	76
Any Drowsiness, post D2 (N=239;232;227;234)	125	115	105	111
Grade 3 Drowsiness, post D2 (N=239;232;227;234)	6	7	6	8
Related Drowsiness, post D2 (N=239;232;227;234)	96	89	81	97
Any Irr./Fuss., post D2 (N=239;232;227;234)	151	151	141	128
Grade 3 Irr./Fuss., post D2 (N=239;232;227;234)	18	12	17	10
Related Irr./Fuss., post D2 (N=239;232;227;234)	123	113	114	106
Any Loss Appet., post D2 (N=239;232;227;234)	69	78	71	72
Grade 3 Loss Appet., post D2 (N=239;232;227;234)	2	3	1	3
Related Loss Appet., post D2 (N=239;232;227;234)	52	58	48	56
Any Fever, post D2 (N=239;232;227;234)	97	84	90	90

Grade 3 Fever, post D2 (N=239;232;227;234)	0	0	0	0
Related Fever, post D2 (N=239;232;227;234)	87	75	82	82
Any Drowsiness, post D3 (N=238;229;227;234)	99	92	88	87
Grade 3 Drowsiness, post D3 (N=238;229;227;234)	4	2	3	5
Related Drowsiness, post D3 (N=238;229;227;234)	80	67	70	71
Any Irr./Fuss., post D3 (N=238;229;227;234)	117	123	118	112
Grade 3 Irr./Fuss., post D3 (N=238;229;227;234)	6	7	8	7
Related Irr./Fuss., post D3 (N=238;229;227;234)	95	92	96	87
Any Loss Appet., post D3 (N=238;229;227;234)	63	62	67	54
Grade 3 Loss Appet., post D3 (N=238;229;227;234)	0	3	3	5
Related Loss Appet., post D3 (N=238;229;227;234)	49	42	54	41
Any Fever, post D3 (N=238;229;227;234)	51	53	61	58
Grade 3 Fever, post D3 (N=238;229;227;234)	0	0	0	0
Related Fever, post D3 (N=238;229;227;234)	50	51	56	49

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and Grade 3 solicited general symptoms and with solicited general symptoms with relationship to vaccination, during the Booster Phase of the study

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

End point description:

Assessed solicited general symptoms were Drowsiness, Irritability/Fussiness (Irr./Fuss.), Loss of appetite (Loss Appet.) and Fever (rectal temperature higher than [≥] 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 activity. Grade 3 Irr./Fuss. = Crying that could not be comforted/prevented normal activity. 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 (Days 0-3) period after booster vaccination

End point values	11Pn Group	12Pn Group	Synflorix Group	Prevnar13 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	235	224	219	231
Units: Subjects				
Any Drowsiness	109	100	84	96
Grade 3 Drowsiness	9	6	4	2
Related Drowsiness	93	79	68	81
Any Irr./Fuss.	140	136	137	129
Grade 3 Irr./Fuss.	14	14	12	9
Related Irr./Fuss.	107	117	109	107
Any Loss Appet.	80	85	83	61
Grade 3 Loss Appet.	6	3	9	7
Related Loss Appet.	66	64	65	45
Any Fever	80	72	68	75
Grade 3 Fever	2	0	1	0
Related Fever	72	66	60	67

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects with any unsolicited adverse events (AEs) during the 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	11Pn Group	12Pn Group	Synflorix Group	Prevnar13 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	240	240	230	241
Units: Subjects				
Any AE(s)	110	108	123	124

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects with any unsolicited adverse events (AEs) during the 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	11Pn Group	12Pn Group	Synflorix Group	Prevnar13 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	237	226	222	234
Units: Subjects				
Any AE(s)	69	68	74	53

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any serious adverse events (SAEs) during the Primary Phase of the study

End point title	Number of subjects with any serious adverse events (SAEs) during the Primary Phase of the study

End point description:

A SAE was defined as any medical occurrence that resulted in death, was life-threatening, required hospitalization or prolongation of hospitalization, resulted in disability/incapacity in a subject. AE(s) considered as SAE(s) also included invasive or malignant cancers, intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that did not result in hospitalization, as per the medical or scientific judgement of the physician. Any = Occurrence of a SAE, regardless of relationship to vaccination.

End point type	Secondary

End point timeframe:

From Month 0 to Month 3

End point values	11Pn Group	12Pn Group	Synflorix Group	Prevnar13 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	240	240	230	241
Units: Subjects				
Any SAE(s)	12	11	17	12

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any serious adverse events (SAEs) during the entire duration of the study

End point title	Number of subjects with any serious adverse events (SAEs) during the entire duration of the study

End point description:

A SAE was defined as any medical occurrence that resulted in death, was life-threatening, required hospitalization or prolongation of hospitalization, resulted in disability/incapacity in a subject. AE(s) considered as SAE(s) also included invasive or malignant cancers, intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that did not result in hospitalization, as per the medical or scientific judgement of the the physician. Any = Occurrence of a SAE, regardless of relationship to vaccination.

End point type	Secondary

End point timeframe:

From Day 0 to Month 11

End point values	11Pn Group	12Pn Group	Synflorix Group	Prevnar13 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	240	240	230	241
Units: Subjects				
Any SAE(s)	29	26	38	24

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against pneumococcal serotypes during the Booster Phase of the study

End point title	Antibody concentrations against pneumococcal serotypes during the Booster 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, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F (ANTI-1, -3, -4, -5, -6B, -7F, -9V, -14, -18C, -19A, -19F and -23F). Antibody concentrations were measured by 22F-Inhibition enzyme-linked immunosorbent assay (ELISA), expressed as geometric mean concentrations (GMCs), in micrograms per milliliter (µg/mL). The cut-off of the assay was an antibody concentration higher than or equal to (≥) 0.05 µg/mL. Analysis of concentrations of antibodies against the cross-reactive

pneumococcal serotype 6C (ANTI-6C) was not performed due to unavailability of a specific qualified assay.

End point type	Secondary

End point timeframe:

At study Month 10 (M10) and Month 11 (M11), e.g.: prior to and at one month post booster vaccination with pneumococcal vaccine

End point values	11Pn Group	12Pn Group	Synflorix Group	Prevnar13 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	216	206	203	210
Units: µg/mL				
geometric mean (confidence interval 95%)				
ANTI-1 (M10) (N=216,206,202,210)	0.26 (0.24 to 0.3)	0.26 (0.24 to 0.3)	0.26 (0.23 to 0.29)	0.44 (0.4 to 0.48)
ANTI-1 (M11) (N=214,203,201,209)	2.49 (2.21 to 2.82)	2.18 (1.94 to 2.46)	2.25 (2.01 to 2.53)	3.84 (3.5 to 4.22)
ANTI-3 (M10) (N=214,204,199,208)	0.06 (0.05 to 0.07)	0.06 (0.05 to 0.06)	0.06 (0.05 to 0.07)	0.25 (0.22 to 0.29)
ANTI-3 (M11) (N=210,202,197,209)	0.07 (0.06 to 0.08)	0.07 (0.06 to 0.08)	0.07 (0.06 to 0.09)	1.68 (1.53 to 1.85)
ANTI-4 (M10) (N=213,203,203,210)	0.49 (0.44 to 0.54)	0.48 (0.43 to 0.54)	0.5 (0.45 to 0.56)	0.41 (0.37 to 0.46)
ANTI-4 (M11) (N=214,203,202,209)	3.89 (3.49 to 4.34)	4.18 (3.77 to 4.63)	4.06 (3.7 to 4.45)	3.86 (3.43 to 4.35)
ANTI-5 (M10) (N=213,202,199,208)	0.51 (0.46 to 0.57)	0.51 (0.45 to 0.57)	0.48 (0.43 to 0.53)	0.77 (0.69 to 0.85)
ANTI-5 (M11) (N=215,203,202,209)	3.23 (2.88 to 3.64)	3.31 (2.98 to 3.68)	3.05 (2.75 to 3.38)	6.84 (6.12 to 7.66)
ANTI-6B (M10) (N=213,202,199,209)	0.57 (0.49 to 0.65)	0.64 (0.56 to 0.74)	0.59 (0.51 to 0.69)	0.22 (0.19 to 0.25)
ANTI-6B (M11) (N=214,205,203,209)	2.66 (2.34 to 3.03)	4.09 (3.6 to 4.66)	2.53 (2.24 to 2.86)	3.8 (3.34 to 4.33)
ANTI-7F (M10) (N=213,203,200,207)	1.04 (0.94 to 1.16)	0.99 (0.89 to 1.1)	0.94 (0.84 to 1.05)	1.21 (1.11 to 1.32)
ANTI-7F (M11) (N=214,203,201,209)	4.88 (4.4 to 5.4)	4.57 (4.14 to 5.04)	4.31 (3.91 to 4.75)	6.34 (5.8 to 6.95)
ANTI-9V (M10) (N=213,202,198,207)	0.76 (0.68 to 0.85)	0.77 (0.69 to 0.87)	0.7 (0.63 to 0.77)	0.53 (0.48 to 0.58)
ANTI-9V (M11) (N=214,203,202,209)	4.14 (3.7 to 4.62)	4.36 (3.93 to 4.84)	3.68 (3.32 to 4.09)	5.83 (5.26 to 6.46)
ANTI-14 (M10) (N=214,204,201,209)	1.3 (1.11 to 1.53)	1.45 (1.28 to 1.64)	1.12 (0.97 to 1.3)	1.66 (1.44 to 1.93)
ANTI-14 (M11) (N=213,203,201,209)	6.17 (5.45 to 6.98)	6.52 (5.8 to 7.33)	5.75 (5.07 to 6.51)	10.05 (8.97 to 11.25)
ANTI-18C (M10) (N=212,200,195,207)	0.76 (0.67 to 0.86)	0.68 (0.6 to 0.77)	0.74 (0.65 to 0.84)	0.59 (0.54 to 0.65)
ANTI-18C (M11) (N=213,203,201,209)	7.65 (6.79 to 8.61)	7.2 (6.39 to 8.11)	8 (7.06 to 9.06)	6.01 (5.45 to 6.63)
ANTI-19A (M10) (N=212,199,197,208)	0.46 (0.39 to 0.54)	0.36 (0.31 to 0.42)	0.18 (0.15 to 0.21)	0.42 (0.35 to 0.49)
ANTI-19A (M11) (N=214,203,201,209)	5.35 (4.67 to 6.13)	4.46 (3.83 to 5.2)	1.11 (0.91 to 1.35)	7.06 (6.25 to 7.98)
ANTI-19F (M10) (N=212,199,196,207)	1.11 (0.97 to 1.28)	1.11 (0.96 to 1.29)	1.1 (0.95 to 1.29)	0.5 (0.44 to 0.57)

ANTI-19F (M11) (N=213,203,203,209)	8.67 (7.72 to 9.73)	8.5 (7.55 to 9.59)	8.22 (7.4 to 9.13)	6.4 (5.77 to 7.11)
ANTI-23F (M10) (N=214,205,198,208)	0.51 (0.44 to 0.58)	0.54 (0.47 to 0.62)	0.49 (0.43 to 0.56)	0.34 (0.29 to 0.39)
ANTI-23F (M11) (N=214,203,201,209)	3.09 (2.73 to 3.49)	3.31 (2.93 to 3.73)	2.98 (2.65 to 3.35)	6.49 (5.69 to 7.39)

Statistical analyses

No statistical analyses for this end point

Secondary: Titers for opsonophagocytic activity against pneumococcal serotypes during the Primary Phase of the study

End point title	Titers for opsonophagocytic activity against pneumococcal serotypes during the Primary Phase of the study

End point description:

Titers for opsonophagocytic activity assessed for this outcome measure were those for opsonophagocytic activity against the vaccine/cross-reactive pneumococcal serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19F and 23F (OPA -1, -3, -4, -5, -6A, -6B, -7F, -9V, -14, -18C, -19F and -23F). The cut-off of the assay was a titer for opsonophagocytic activity higher than or equal to (≥) 8. Testing for opsonophagocytic activity against the cross reactive pneumococcal serotype 6C will not be performed due to unavailability of a specific qualified assay.

End point type	Secondary

End point timeframe:

At study Month 3, e. g. at one month post-Dose 3 of pneumococcal vaccine

End point values	11Pn Group	12Pn Group	Synflorix Group	Prevnar13 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	105	105	99	105
Units: Titers				
geometric mean (confidence interval 95%)				
OPA-1 (N=105,105,98,105)	13.2 (9.6 to 18.2)	15.6 (11.4 to 21.1)	13.6 (9.9 to 18.6)	26.4 (19.3 to 36)
OPA-3 (N=101,100,94,100)	4.8 (4.2 to 5.5)	5.2 (4.4 to 6)	5 (4.3 to 5.7)	97.2 (81.6 to 116)
OPA-4 (N=103,105,99,104)	527.3 (401.5 to 692.4)	609 (492.8 to 752.5)	616.7 (503.2 to 756)	540.1 (444.7 to 656.1)
OPA-5 (N=102,104,98,105)	43 (32.6 to 56.9)	46.7 (36.8 to 59.3)	40.5 (30.4 to 54)	57.2 (44.3 to 74)
OPA-6A (N=100,103,94,103)	37.4 (22.9 to 60.9)	1292.6 (940.3 to 1777)	36.5 (22.6 to 59)	2832 (2212.8 to 3624.4)
OPA-6B (N=101,104,96,103)	478.3 (345.2 to 662.7)	603.2 (436.9 to 832.8)	622.6 (444.2 to 872.7)	742.3 (533.9 to 1031.8)
OPA-7F (N=104,103,98,104)	3515 (2787.1 to 4433)	4472.3 (3463.6 to 5774.9)	3424.1 (2631.9 to 4454.8)	9737.9 (7540.5 to 12575.8)
OPA-9V (N=105,105,98,104)	1212.9 (953.6 to 1542.6)	1629 (1293 to 2052.4)	1469.9 (1178.3 to 1833.6)	1614.5 (1283.9 to 2030.2)
OPA-14 (N=105,104,97,103)	1000.8 (743.1 to 1347.9)	1699.1 (1313.8 to 2197.3)	1417.4 (1059.6 to 1896)	2034.4 (1513.4 to 2734.8)

OPA-18C (N=105,102,98,102)	100.9 (67.7 to 150.4)	131.5 (86.9 to 198.8)	72 (47 to 110.4)	145.7 (102.6 to 206.8)
OPA-19F (N=102,102,96,103)	144.2 (101.8 to 204.3)	201.4 (147.2 to 275.4)	210.4 (143.6 to 308.2)	66 (49.8 to 87.5)
OPA-23F (N=104,104,98,104)	989.6 (652.9 to 1499.8)	1377.9 (951.5 to 1995.3)	1097.3 (742.1 to 1622.4)	5136.4 (3829.2 to 6889.8)

Statistical analyses

No statistical analyses for this end point

Secondary: Titers for opsonophagocytic activity against pneumococcal serotypes during the Booster Phase of the study

End point title	Titers for opsonophagocytic activity against pneumococcal serotypes during the Booster Phase of the study

End point description:

Titers for opsonophagocytic activity assessed for this outcome measure were those for opsonophagocytic activity against the vaccine/cross-reactive pneumococcal serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F (OPA -1, -3, -4, -5, -6A, -6B, -7F, -9V, -14, -18C, -19A, -19F and -23F). The cut-off of the assay was a titer for opsonophagocytic activity higher than or equal to (≥) 8. Testing for opsonophagocytic activity against the cross-reactive pneumococcal serotype 6C will not be performed due to unavailability of a specific qualified assay.

End point type	Secondary

End point timeframe:

At study Month 11 , e.g.: at one month post booster vaccination with pneumococcal vaccine

End point values	11Pn Group	12Pn Group	Synflorix Group	Prevnar13 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	99	97	96	101
Units: Titers				
geometric mean (confidence interval 95%)				
OPA-1 (N=99,97,96,101)	192.4 (129 to 287.1)	192.4 (133.3 to 277.5)	216.8 (148.3 to 316.9)	207.6 (145.8 to 295.6)
OPA-3 (N=93,89,85,96)	9.7 (7.5 to 12.7)	10.5 (8 to 13.7)	10.9 (7.6 to 15.5)	317.2 (275.4 to 365.4)
OPA-4 (N=96,96,95,100)	1455.3 (1208.9 to 1751.9)	1650.5 (1360.9 to 2001.9)	1550.5 (1230.2 to 1954.1)	1972.2 (1586.3 to 2451.9)
OPA-5 (N=99,96,96,100)	134.5 (100.3 to 180.4)	133.3 (105.2 to 168.8)	133.4 (100.5 to 177.1)	269.9 (216.2 to 337)
OPA-6A (N=95,93,92,98)	116.8 (67.9 to 201)	3436.7 (2716 to 4348.5)	146.4 (87.6 to 244.6)	5200.7 (4134.9 to 6541.3)
OPA-6B (N=98,96,95,100)	681.4 (520.3 to 892.5)	1246.4 (963.1 to 1613)	694.6 (546.5 to 882.6)	1727.9 (1406.2 to 2123.4)
OPA-7F (N=96,96,96,97)	8362.9 (6977.1 to 10023.9)	7516.4 (6223 to 9078.7)	7880.8 (6408.6 to 9691.3)	16592.6 (13909.7 to 19792.9)

OPA-9V (N=99,97,93,98)	3406.9 (2758.2 to 4208.1)	3616.1 (2838.1 to 4607.5)	3260.6 (2620.1 to 4057.6)	8470.4 (6692.4 to 10720.8)
OPA-14 (N=99,96,94,100)	2038.4 (1594.3 to 2606.2)	2519.9 (1960.2 to 3239.6)	2285.1 (1845.9 to 2828.9)	2772.6 (2218.6 to 3464.9)
OPA-18C (N=97,95,93,97)	914.8 (621.8 to 1345.9)	781.2 (536.3 to 1137.8)	912 (605.4 to 1374.1)	610.7 (421.3 to 885.1)
OPA-19F (N=95,96,96,98)	523.9 (382.9 to 716.8)	565.3 (406.4 to 786.6)	759.6 (554.3 to 1040.8)	438 (312.7 to 613.7)
OPA-23F (N=97,96,95,97)	2562.9 (2016.3 to 3257.6)	2923.6 (2248.9 to 3800.9)	2600 (1896.8 to 3563.9)	24350.4 (18303.2 to 32395.5)

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against protein D (Anti-PD) during the Booster Phase of the study

End point title	Concentrations of antibodies against protein D (Anti-PD) during the Booster Phase of the study

End point description:

Anti-PD 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 cut-off of the assay was an anti-PD antibody concentration higher than or equal to (≥) 100 EL.U/mL.

End point type	Secondary

End point timeframe:

At study Month 10 (M10) and Month 11 (M11), e.g.: prior to and at one month post booster vaccination with pneumococcal vaccine

End point values	11Pn Group	12Pn Group	Synflorix Group	Prevnar13 Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	108	102	101	106
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD (M10) (N=108,102,101,106)	445.87 (364.98 to 544.68)	447.55 (363.39 to 551.22)	459.99 (376.24 to 562.38)	70.87 (61.76 to 81.33)
Anti-PD (M11) (N=108,100,101,104)	1866.01 (1535.69 to 2267.38)	1835.49 (1511.45 to 2229.01)	2128.41 (1777.07 to 2549.21)	77.75 (67.1 to 90.09)

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms: during the 4 days post-primary and post-booster vaccination. Unsolicited AEs: during 31 days post-primary and post-booster vaccination. SAEs: during the whole study period (from Day 0 to Month 11).

Adverse event reporting additional description:

Analysis of AEs & SAEs performed on subjects who received at least one primary dose or at least the booster vaccination. Analysis of solicited symptoms performed on the same subjects and for whom results were available. Occurrences (all and "related to the treatment") not calculated during the analysis are filled in with "subjects affected" info.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	12Pn Group

Reporting group description:

Healthy male or female subjects between, and including 6 to 12 weeks (42-90 days) of age at the time of first vaccination, received a 3-dose primary vaccination course of GSK2830930A, or 12Pn, vaccine at 2, 3 and 4 months of age, followed by a booster dose of the same vaccine at 12-15 months of age, each dose being co-administered with one dose of Infanrix hexa™. The first 3 doses of 12Pn vaccine were administered intramuscularly into the right anterolateral thigh and Infanrix hexa™ was administered intramuscularly into the left anterolateral thigh. The booster dose of 12Pn vaccine was administered intramuscularly into the right deltoid (or thigh if the deltoid muscle size was not adequate) and that of Infanrix hexa™ was administered intramuscularly into the left deltoid (or thigh if the deltoid muscle size was not adequate).

Reporting group title	Synflorix Group

Reporting group description:

Healthy male or female subjects between, and including 6 to 12 weeks (42-90 days) of age at the time of first vaccination, received a 3-dose primary vaccination course of Synflorix™ at 2, 3 and 4 months of age, followed by a booster dose of the same vaccine at 12-15 months of age, each dose being co-administered with one dose of Infanrix hexa™. The first 3 doses of Synflorix™ were administered intramuscularly into the right anterolateral thigh and Infanrix hexa™ was administered intramuscularly into the left anterolateral thigh. The booster dose of Synflorix™ was administered intramuscularly into the right deltoid (or thigh if the deltoid muscle size was not adequate) and that of Infanrix hexa™ was administered intramuscularly into the left deltoid (or thigh if the deltoid muscle size was not adequate).

Reporting group title	Prevnar13 Group

Reporting group description:

Healthy male or female subjects between, and including 6 to 12 weeks (42-90 days) of age at the time of first vaccination, received a 3-dose primary vaccination course of Prevnar13™ vaccine at 2, 3 and 4 months of age, followed by a booster dose of the same vaccine at 12-15 months of age, each dose being co-administered with one dose of Infanrix hexa™. The first 3 doses of Prevnar13™ were administered intramuscularly into the right anterolateral thigh and Infanrix hexa™ was administered intramuscularly into the left anterolateral thigh. The booster dose of Prevnar13™ was administered intramuscularly into the right deltoid (or thigh if the deltoid muscle size was not adequate) and that of Infanrix hexa™ was administered intramuscularly into the left deltoid (or thigh if the deltoid muscle size was not adequate).

Reporting group title	11Pn Group

Reporting group description:

Healthy male or female subjects between, and including 6 to 12 weeks (42-90 days) of age at the time of first vaccination, received a 3-dose primary vaccination course of GSK2830929A, or 11Pn, vaccine at 2, 3 and 4 months of age, followed by a booster dose of the same vaccine at 12-15 months of age, each dose being co-administered with one dose of Infanrix hexa™. The first 3 doses of 11Pn vaccine were administered intramuscularly into the right anterolateral thigh and Infanrix hexa™ was administered intramuscularly into the left anterolateral thigh. The booster dose of 11Pn vaccine was administered intramuscularly into the right deltoid (or thigh if the deltoid muscle size was not adequate) and that of Infanrix hexa™ was administered intramuscularly into the left deltoid (or thigh if the deltoid muscle size was not adequate).

Serious adverse events	12Pn Group	Synflorix Group	Prevnar13 Group
Total subjects affected by serious adverse events			
subjects affected / exposed	26 / 240 (10.83%)	38 / 230 (16.52%)	24 / 241 (9.96%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Retinoblastoma	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	0 / 230 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Concussion	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	1 / 240 (0.42%)	1 / 230 (0.43%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxicity to various agents	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	1 / 240 (0.42%)	0 / 230 (0.00%)	0 / 241 (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
Head injury	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	1 / 240 (0.42%)	1 / 230 (0.43%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contusion	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	0 / 230 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Exposure to toxic agent	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	1 / 240 (0.42%)	0 / 230 (0.00%)	0 / 241 (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
Fall	Additional description: SAE reported between Day 0 and Month 11		

subjects affected / exposed	0 / 240 (0.00%)	1 / 230 (0.43%)	0 / 241 (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
Foreign body	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	1 / 240 (0.42%)	0 / 230 (0.00%)	0 / 241 (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
Thermal burn	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	1 / 230 (0.43%)	0 / 241 (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
Congenital, familial and genetic disorders			
Dacryostenosis congenital	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	0 / 230 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Hypotonic-hyporesponsive episode	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	0 / 230 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myoclonus	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	0 / 230 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile convulsion	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	1 / 240 (0.42%)	2 / 230 (0.87%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Burning sensation	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	1 / 230 (0.43%)	0 / 241 (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

Hypotonia	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	1 / 230 (0.43%)	0 / 241 (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
General disorders and administration site conditions			
Pyrexia	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	4 / 240 (1.67%)	1 / 230 (0.43%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	2 / 4	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	0 / 230 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Milk allergy	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	0 / 230 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Inguinal hernia	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	0 / 230 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	1 / 240 (0.42%)	0 / 230 (0.00%)	0 / 241 (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
Constipation			
subjects affected / exposed	1 / 240 (0.42%)	0 / 230 (0.00%)	0 / 241 (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
Respiratory, thoracic and mediastinal disorders			
Bronchitis chronic	Additional description: SAE reported between Day 0 and Month 11		

subjects affected / exposed	1 / 240 (0.42%)	0 / 230 (0.00%)	0 / 241 (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
Bronchospasm	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	0 / 230 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atelectasis	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	1 / 230 (0.43%)	0 / 241 (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
Bronchiectasis	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	1 / 240 (0.42%)	0 / 230 (0.00%)	0 / 241 (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
Pneumonitis	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	1 / 230 (0.43%)	0 / 241 (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
Skin and subcutaneous tissue disorders			
Dermatitis allergic	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	1 / 240 (0.42%)	0 / 230 (0.00%)	0 / 241 (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
Ingrowing nail	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	1 / 240 (0.42%)	0 / 230 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Conjunctivitis	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	1 / 230 (0.43%)	0 / 241 (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
Bacteraemia	Additional description: SAE reported between Day 0 and Month 11		

subjects affected / exposed	1 / 240 (0.42%)	1 / 230 (0.43%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial pyelonephritis	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	0 / 230 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast abscess	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	1 / 230 (0.43%)	0 / 241 (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
Bronchiolitis	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	1 / 240 (0.42%)	2 / 230 (0.87%)	3 / 241 (1.24%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	1 / 240 (0.42%)	7 / 230 (3.04%)	4 / 241 (1.66%)
occurrences causally related to treatment / all	0 / 1	0 / 7	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis viral	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	0 / 230 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	1 / 230 (0.43%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia urinary tract infection	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	1 / 230 (0.43%)	0 / 241 (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
Gastroenteritis	Additional description: SAE reported between Day 0 and Month 11		

subjects affected / exposed	2 / 240 (0.83%)	1 / 230 (0.43%)	2 / 241 (0.83%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	0 / 230 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngitis	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	1 / 230 (0.43%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasopharyngitis	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	1 / 240 (0.42%)	1 / 230 (0.43%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pertussis	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	0 / 230 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	2 / 240 (0.83%)	3 / 230 (1.30%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia respiratory syncytial viral	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	2 / 240 (0.83%)	0 / 230 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	4 / 230 (1.74%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchiolitis	Additional description: SAE reported between Day 0 and Month 11		

subjects affected / exposed	1 / 240 (0.42%)	5 / 230 (2.17%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 1	0 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheitis	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	1 / 230 (0.43%)	0 / 241 (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
Upper respiratory tract infection	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	3 / 230 (1.30%)	2 / 241 (0.83%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	1 / 230 (0.43%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection bacterial	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	1 / 230 (0.43%)	0 / 241 (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
Gastroenteritis rotavirus	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	2 / 230 (0.87%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impetigo	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	1 / 230 (0.43%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	2 / 230 (0.87%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchitis	Additional description: SAE reported between Day 0 and Month 11		

subjects affected / exposed	0 / 240 (0.00%)	2 / 230 (0.87%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenoiditis	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	1 / 240 (0.42%)	0 / 230 (0.00%)	0 / 241 (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
Escherichia pyelonephritis	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	0 / 230 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis adenovirus	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	0 / 230 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral discitis	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	1 / 240 (0.42%)	0 / 230 (0.00%)	0 / 241 (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
Otitis media acute	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	1 / 230 (0.43%)	0 / 241 (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
Paronychia	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	0 / 230 (0.00%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngotonsillitis	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	1 / 230 (0.43%)	0 / 241 (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
Pyomyositis	Additional description: SAE reported between Day 0 and Month 11		

subjects affected / exposed	1 / 240 (0.42%)	0 / 230 (0.00%)	0 / 241 (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
Respiratory tract infection viral	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	0 / 230 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicella	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	1 / 230 (0.43%)	0 / 241 (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
Viral infection	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	0 / 230 (0.00%)	0 / 241 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral tonsillitis	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	1 / 240 (0.42%)	0 / 230 (0.00%)	0 / 241 (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
Metabolism and nutrition disorders			
Dehydration	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)	1 / 230 (0.43%)	1 / 241 (0.41%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	11Pn Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	29 / 240 (12.08%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Retinoblastoma	Additional description: SAE reported between Day 0 and Month 11		

subjects affected / exposed	1 / 240 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Concussion	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	1 / 240 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Toxicity to various agents	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Head injury	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	1 / 240 (0.42%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Contusion	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	1 / 240 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Exposure to toxic agent	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fall	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Foreign body	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thermal burn	Additional description: SAE reported between Day 0 and Month 11		

subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Congenital, familial and genetic disorders			
Dacryostenosis congenital	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Hypotonic-hyporesponsive episode	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myoclonus	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Febrile convulsion	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Burning sensation	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypotonia	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia	Additional description: SAE reported between Day 0 and Month 11		

subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Milk allergy	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	1 / 240 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Inguinal hernia	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	1 / 240 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Constipation			
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Bronchitis chronic	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchospasm	Additional description: SAE reported between Day 0 and Month 11		

subjects affected / exposed	2 / 240 (0.83%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Atelectasis	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchiectasis	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonitis	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Dermatitis allergic	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ingrowing nail	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Conjunctivitis	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	1 / 240 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bacteraemia	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bacterial pyelonephritis	Additional description: SAE reported between Day 0 and Month 11		

subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Breast abscess	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchiolitis	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	5 / 240 (2.08%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Bronchitis	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	5 / 240 (2.08%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Bronchitis viral	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	1 / 240 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchopneumonia	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Escherichia urinary tract infection	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	2 / 240 (0.83%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Influenza	Additional description: SAE reported between Day 0 and Month 11		

subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Laryngitis	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nasopharyngitis	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pertussis	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	3 / 240 (1.25%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Pneumonia respiratory syncytial viral	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory syncytial virus bronchiolitis	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	1 / 240 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tracheitis	Additional description: SAE reported between Day 0 and Month 11		

subjects affected / exposed	1 / 240 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Upper respiratory tract infection	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection bacterial	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis rotavirus	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	1 / 240 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Impetigo	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Otitis media	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory syncytial virus bronchitis	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Adenoiditis	Additional description: SAE reported between Day 0 and Month 11		

subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Escherichia pyelonephritis	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	1 / 240 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis adenovirus	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	1 / 240 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intervertebral discitis	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Otitis media acute	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Paronychia	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pharyngotonsillitis	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyomyositis	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection viral	Additional description: SAE reported between Day 0 and Month 11		

subjects affected / exposed	1 / 240 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Varicella	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Viral infection	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	1 / 240 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Viral tonsillitis	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration	Additional description: SAE reported between Day 0 and Month 11		
subjects affected / exposed	0 / 240 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	12Pn Group	Synflorix Group	Prevnar13 Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	203 / 240 (84.58%)	185 / 230 (80.43%)	186 / 241 (77.18%)
General disorders and administration site conditions			
Pain (primary phase)			
alternative assessment type: Systematic			
subjects affected / exposed[1]	141 / 236 (59.75%)	134 / 228 (58.77%)	126 / 238 (52.94%)
occurrences (all)	141	134	126
Redness (primary phase)			
alternative assessment type: Systematic			

subjects affected / exposed[2]	144 / 236 (61.02%)	130 / 228 (57.02%)	134 / 238 (56.30%)
occurrences (all)	144	130	134
Swelling (primary phase)			
alternative assessment type: Systematic			
subjects affected / exposed[3]	117 / 236 (49.58%)	91 / 228 (39.91%)	93 / 238 (39.08%)
occurrences (all)	117	91	93
Drowsiness (primary phase)			
alternative assessment type: Systematic			
subjects affected / exposed[4]	178 / 236 (75.42%)	162 / 228 (71.05%)	168 / 238 (70.59%)
occurrences (all)	178	162	168
Irritability/Fussiness (primary phase)			
alternative assessment type: Systematic			
subjects affected / exposed[5]	203 / 236 (86.02%)	185 / 228 (81.14%)	186 / 238 (78.15%)
occurrences (all)	203	185	186
Loss of appetite (primary phase)			
alternative assessment type: Systematic			
subjects affected / exposed[6]	132 / 236 (55.93%)	125 / 228 (54.82%)	125 / 238 (52.52%)
occurrences (all)	132	125	125
Fever (rectal temperature ≥ 38°C) (primary phase)			
alternative assessment type: Systematic			
subjects affected / exposed[7]	144 / 236 (61.02%)	148 / 228 (64.91%)	143 / 238 (60.08%)
occurrences (all)	144	148	143
Pain (booster phase)	Additional description: Symptom reported during the 4-day post-booster vaccination period		
alternative assessment type: Systematic			
subjects affected / exposed[8]	123 / 224 (54.91%)	119 / 219 (54.34%)	110 / 231 (47.62%)
occurrences (all)	123	119	110
Redness (booster phase)	Additional description: Symptom reported during the 4-day post-booster vaccination period		
alternative assessment type: Systematic			
subjects affected / exposed[9]	117 / 224 (52.23%)	108 / 219 (49.32%)	107 / 231 (46.32%)
occurrences (all)	117	108	107
Swelling (booster phase)	Additional description: Symptom reported during the 4-day post-booster vaccination period		
alternative assessment type: Systematic			

subjects affected / exposed[10]	88 / 224 (39.29%)	89 / 219 (40.64%)	85 / 231 (36.80%)
occurrences (all)	88	89	85
Drowsiness (booster phase)	Additional description: Symptom reported during the 4-day post-booster vaccination period		
alternative assessment type: Systematic			
subjects affected / exposed[11]	100 / 224 (44.64%)	84 / 219 (38.36%)	96 / 231 (41.56%)
occurrences (all)	100	84	96
Irritability/Fusiness (booster phase)	Additional description: Symptom reported during the 4-day post-booster vaccination period		
alternative assessment type: Systematic			
subjects affected / exposed[12]	136 / 224 (60.71%)	137 / 219 (62.56%)	129 / 231 (55.84%)
occurrences (all)	136	137	129
Loss of appetite (booster phase)	Additional description: Symptom reported during the 4-day post-booster vaccination period		
alternative assessment type: Systematic			
subjects affected / exposed[13]	85 / 224 (37.95%)	83 / 219 (37.90%)	61 / 231 (26.41%)
occurrences (all)	85	83	61
Fever (rectal temperature ≥ 38°C) (booster phase)	Additional description: Symptom reported during the 4-day post-booster vaccination period		
alternative assessment type: Systematic			
subjects affected / exposed[14]	72 / 224 (32.14%)	68 / 219 (31.05%)	75 / 231 (32.47%)
occurrences (all)	72	68	75
Infections and infestations			
Upper respiratory tract infection (primary phase)			
subjects affected / exposed	39 / 240 (16.25%)	49 / 230 (21.30%)	28 / 241 (11.62%)
occurrences (all)	39	49	28
Rhinitis			
subjects affected / exposed	15 / 240 (6.25%)	12 / 230 (5.22%)	16 / 241 (6.64%)
occurrences (all)	15	12	16
Bronchiolitis			
subjects affected / exposed	10 / 240 (4.17%)	13 / 230 (5.65%)	11 / 241 (4.56%)
occurrences (all)	10	13	11
Bronchitis			
subjects affected / exposed	7 / 240 (2.92%)	18 / 230 (7.83%)	16 / 241 (6.64%)
occurrences (all)	7	18	16
Nasopharyngitis			

subjects affected / exposed	14 / 240 (5.83%)	8 / 230 (3.48%)	11 / 241 (4.56%)
occurrences (all)	14	8	11
Upper respiratory tract infection (booster phase)	Additional description: Unsolicited AE reported during the 31-day post-booster vaccination period		
subjects affected / exposed[15]	16 / 226 (7.08%)	20 / 222 (9.01%)	13 / 234 (5.56%)
occurrences (all)	16	20	13

Non-serious adverse events	11Pn Group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	202 / 240 (84.17%)		
General disorders and administration site conditions			
Pain (primary phase)			
alternative assessment type: Systematic			
subjects affected / exposed[1]	140 / 240 (58.33%)		
occurrences (all)	140		
Redness (primary phase)			
alternative assessment type: Systematic			
subjects affected / exposed[2]	132 / 240 (55.00%)		
occurrences (all)	132		
Swelling (primary phase)			
alternative assessment type: Systematic			
subjects affected / exposed[3]	108 / 240 (45.00%)		
occurrences (all)	108		
Drowsiness (primary phase)			
alternative assessment type: Systematic			
subjects affected / exposed[4]	185 / 240 (77.08%)		
occurrences (all)	185		
Irritability/Fussiness (primary phase)			
alternative assessment type: Systematic			
subjects affected / exposed[5]	202 / 240 (84.17%)		
occurrences (all)	202		
Loss of appetite (primary phase)			
alternative assessment type: Systematic			
subjects affected / exposed[6]	124 / 240 (51.67%)		
occurrences (all)	124		

Fever (rectal temperature ≥ 38°C) (primary phase)			
alternative assessment type: Systematic			
subjects affected / exposed[7]	153 / 240 (63.75%)		
occurrences (all)	153		
Pain (booster phase)	Additional description: Symptom reported during the 4-day post-booster vaccination period		
alternative assessment type: Systematic			
subjects affected / exposed[8]	112 / 235 (47.66%)		
occurrences (all)	112		
Redness (booster phase)	Additional description: Symptom reported during the 4-day post-booster vaccination period		
alternative assessment type: Systematic			
subjects affected / exposed[9]	109 / 235 (46.38%)		
occurrences (all)	109		
Swelling (booster phase)	Additional description: Symptom reported during the 4-day post-booster vaccination period		
alternative assessment type: Systematic			
subjects affected / exposed[10]	84 / 235 (35.74%)		
occurrences (all)	84		
Drowsiness (booster phase)	Additional description: Symptom reported during the 4-day post-booster vaccination period		
alternative assessment type: Systematic			
subjects affected / exposed[11]	109 / 235 (46.38%)		
occurrences (all)	109		
Irritability/Fusiness (booster phase)	Additional description: Symptom reported during the 4-day post-booster vaccination period		
alternative assessment type: Systematic			
subjects affected / exposed[12]	140 / 235 (59.57%)		
occurrences (all)	140		
Loss of appetite (booster phase)	Additional description: Symptom reported during the 4-day post-booster vaccination period		
alternative assessment type: Systematic			
subjects affected / exposed[13]	80 / 235 (34.04%)		
occurrences (all)	80		
Fever (rectal temperature ≥ 38°C) (booster phase)	Additional description: Symptom reported during the 4-day post-booster vaccination period		
alternative assessment type: Systematic			
subjects affected / exposed[14]	80 / 235 (34.04%)		
occurrences (all)	80		

Infections and infestations			
Upper respiratory tract infection (primary phase)			
subjects affected / exposed	38 / 240 (15.83%)		
occurrences (all)	38		
Rhinitis			
subjects affected / exposed	18 / 240 (7.50%)		
occurrences (all)	18		
Bronchiolitis			
subjects affected / exposed	12 / 240 (5.00%)		
occurrences (all)	12		
Bronchitis			
subjects affected / exposed	10 / 240 (4.17%)		
occurrences (all)	10		
Nasopharyngitis			
subjects affected / exposed	10 / 240 (4.17%)		
occurrences (all)	10		
Upper respiratory tract infection (booster phase)	Additional description: Unsolicited AE reported during the 31-day post-booster vaccination period		
subjects affected / exposed[15]	11 / 237 (4.64%)		
occurrences (all)	11		

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.
Justification: Solicited symptoms results are presented only for subjects for whom results were available.

[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.
Justification: Solicited symptoms results are presented only for subjects for whom results were available.

[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: Solicited symptoms results are presented only for subjects for whom results were available.

[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: Unolicited 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? Yes

Date	Amendment
13 February 2013	Amendment 2 The protocol has been amended to include the opsonophagocytic activity (OPA) testing for pneumococcal serotypes 1, 3, 4, 5, 6B, 6C, 7F, 9V, 14, 18C, 19F and 23F, in addition to the previously planned OPA testing for serotypes 6A and 19A. This testing was added to gather further evidence, early in the clinical development, of any potential impact of addition of 6A and/or 19A-CRM197 conjugates on the immune response to the 10 pneumococcal polysaccharide conjugates common with Synflorix. The following exploratory analyses were added: • comparison of serotype-specific immune response elicited by the 11-valent and 12-valent pneumococcal conjugate vaccines versus the immune response elicited by Synflorix for the common serotypes, based on OPA GMT ratios for post-primary and post-booster timepoints and percentages of subjects with OPA titre >8 for post-primary timepoint. • comparison of serotype-specific immune response elicited by the 11-valent and 12-valent pneumococcal conjugate vaccines versus the immune response elicited by Synflorix for the common serotypes and by Prevenar 13 for the additional serotypes 6A and 19A, based on antibody GMC ratios and OPA GMT ratios for post-booster timepoint. • comparison of the immune response to serotypes 6A and 19A elicited by the 11-valent and 12-valent pneumococcal conjugate vaccines versus the lowest response elicited by Synflorix for any of the 10 vaccine serotypes, based on percentages of subjects reaching antibody concentrations/OPA titres above defined threshold for post-primary timepoint and antibody GMC/OPA GMT ratios for post-primary and post-booster timepoints.

Notes:

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.

Opsonophagocytic Activity results against pneumococcal serotype-19A and booster ELISA 6A results were not available at the time of writing this summary. The summary will be updated when they become available.

Notes: