



Clinical trial results:

Prophylactic antipyretic treatment in children receiving booster dose of pneumococcal vaccine GSK1024850A and Infanrix hexa™ and assessment of impact of pneumococcal vaccination on nasopharyngeal carriage.

Summary

EudraCT number	2006-001481-17
Trial protocol	CZ
Global end of trial date	17 February 2009

Results information

Result version number	v1
This version publication date	13 June 2016
First version publication date	30 July 2015

Trial information

Trial identification

Sponsor protocol code	107137
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00496015
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, 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	24 July 2009
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 March 2008
Global end of trial reached?	Yes
Global end of trial date	17 February 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the percentage reduction in febrile reactions (rectal temperature $\geq 38.0^{\circ}\text{C}$ or oral/axillary/tympanic $\geq 37.5^{\circ}\text{C}$) when prophylactic antipyretic treatment is administered compared to no prophylactic antipyretic treatment, after booster vaccination with GSK Biologicals' 10-valent pneumococcal conjugate vaccine and routine DTPa-HBV-IPV/Hib (Infanrix hexa) vaccination in children at 12-15 months of age.

Protection of trial subjects:

The vaccines were observed closely for at least 30 minutes, with appropriate medical treatment readily available in case of a rare anaphylactic reaction following the administration of vaccine(s).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 July 2007
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	Czech Republic: 959
Worldwide total number of subjects	959
EEA total number of subjects	959

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)	959
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:

This was a multicenter study with the same centers as the primary vaccination study 10PN-PD-DIT-010 (107017) and all subjects enrolled in the primary vaccination study and having received 10Pn-PD-DIT vaccine were invited to participate in the study. In addition, an age-matched pneumococcal vaccine unprimed control group has been enrolled.

Pre-assignment

Screening details:

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

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	10Pn-PD-DiT/ Paracetamol Group

Arm description:

Subjects were vaccinated with three primary vaccination doses with prophylactic administration of paracetamol in study 10PN-PD-DIT-010 (107017), and received in this study at 12-15 months of age a booster dose of GSK Biologicals' 10Pn-PD-DiT vaccine, co-administered with Infanrix™ hexa (also referred to as DTPa-HBV-IPV/Hib) along with prophylactic antipyretic treatment (rectal paracetamol or acetaminophen) under the form of suppositories of CALPOL 80 or 125, depending on the subjects' body weight. (before the implementation of protocol amendment 3).

Arm type	Experimental
Investigational medicinal product name	10-valent Streptococcus pneumoniae conjugate vaccine
Investigational medicinal product code	
Other name	10Pn, 10Pn-PD-DiT, GlaxoSmithKline (GSK) Biologicals' 10-valent pneumococcal conjugate vaccine, Synflorix™, GlaxoSmithKline (GSK) Biologicals' 1024850A vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Three doses of the vaccine were administered intramuscularly, into the right thigh at 3, 4 and 5 months of age (Study Months 0, 1 and 2) and one booster dose at 12-15 months of age.

Investigational medicinal product name	Infanrix™ Hexa
Investigational medicinal product code	
Other name	DTPa-IPV-HBV/Hib, Infanrix Hexa GSK Biologicals' diphtheria-tetanus-acellular pertussis
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses of the vaccine were administered intramuscularly in the left thigh at 3, 4 and 5 months of age (Study Months 0, 1 and 2) and one booster dose at 12-15 months of age.

Investigational medicinal product name	CALPOL 80
Investigational medicinal product code	
Other name	Paracetamol 80 mg; Acetaminophen
Pharmaceutical forms	Suppository
Routes of administration	Rectal use

Dosage and administration details:

In subjects weighing 4.5 to < 7 kg: 3 doses administered rectally at 3, 4 and 5 months of age (Study Months 0, 1 and 2) and one booster dose at 12-15 months of age.

Arm title	10Pn-PD-DiT Group
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Arm description:

Subjects were vaccinated with three primary vaccination doses with prophylactic administration of paracetamol in study 10PN-PD-DIT-010 (107017), and who received in this study at 12-15 months of age a booster dose of GSK Biologicals' 10Pn-PD-DiT vaccine, co-administered with Infanrix™ hexa (also referred to as DTPa-HBV-IPV/Hib) without prophylactic antipyretic treatment (rectal paracetamol or acetaminophen) - (after the implementation of protocol amendment 3).

Arm type	Experimental
Investigational medicinal product name	10-valent Streptococcus pneumoniae conjugate vaccine
Investigational medicinal product code	
Other name	10Pn, 10Pn-PD-DiT, GlaxoSmithKline (GSK) Biologicals' 10-valent pneumococcal conjugate vaccine, Synflorix™, GlaxoSmithKline (GSK) Biologicals' 1024850A vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Three doses of the vaccine were administered intramuscularly, into the right thigh at 3, 4 and 5 months of age (Study Months 0, 1 and 2) and one booster dose at 12-15 months of age.

Investigational medicinal product name	Infanrix™ Hexa
Investigational medicinal product code	
Other name	DTPa-IPV-HBV/Hib, Infanrix Hexa GSK Biologicals' diphtheria-tetanus-acellular pertussis
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses of the vaccine were administered intramuscularly in the left thigh at 3, 4 and 5 months of age (Study Months 0, 1 and 2) and one booster dose at 12-15 months of age.

Arm title	10Pn-Pre Group
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Arm description:

Subjects were vaccinated with three primary vaccination doses without prophylactic administration of paracetamol in study 10PN-PD-DIT-010 (107017), and who received in this study at 12-15 months of age a booster dose of GSK Biologicals' 10Pn-PD-DiT vaccine, co-administered with Infanrix™ hexa (also referred to as DTPa-HBV-IPV/Hib) without prophylactic antipyretic treatment (rectal paracetamol or acetaminophen) - (before the implementation of protocol amendment 3).

Arm type	Active comparator
Investigational medicinal product name	10-valent Streptococcus pneumoniae conjugate vaccine
Investigational medicinal product code	
Other name	10Pn, 10Pn-PD-DiT, GlaxoSmithKline (GSK) Biologicals' 10-valent pneumococcal conjugate vaccine, Synflorix™, GlaxoSmithKline (GSK) Biologicals' 1024850A vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Three doses of the vaccine were administered intramuscularly, into the right thigh at 3, 4 and 5 months of age (Study Months 0, 1 and 2) and one booster dose at 12-15 months of age.

Investigational medicinal product name	Infanrix™ Hexa
Investigational medicinal product code	
Other name	DTPa-IPV-HBV/Hib, Infanrix Hexa GSK Biologicals' diphtheria-tetanus-acellular pertussis
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses of the vaccine were administered intramuscularly in the left thigh at 3, 4 and 5 months of age (Study Months 0, 1 and 2) and one booster dose at 12-15 months of age.

Arm title	10Pn-Post Group
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Arm description:

Subjects were vaccinated with three primary vaccination doses without prophylactic administration of paracetamol in study 10PN-PD-DIT-010 (107017), and who received in this study at 12-15 months of age a booster dose of GSK Biologicals' 10Pn-PD-DiT vaccine, co-administered with Infanrix™ hexa (also referred to as DTPa-HBV-IPV/Hib) without prophylactic antipyretic treatment (rectal paracetamol or acetaminophen) - (after the implementation of protocol amendment 3).

Arm type	Active comparator
Investigational medicinal product name	10-valent Streptococcus pneumoniae conjugate vaccine
Investigational medicinal product code	
Other name	10Pn, 10Pn-PD-DiT, GlaxoSmithKline (GSK) Biologicals' 10-valent pneumococcal conjugate vaccine, Synflorix™, GlaxoSmithKline (GSK) Biologicals' 1024850A vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Three doses of the vaccine were administered intramuscularly, into the right thigh at 3, 4 and 5 months of age (Study Months 0, 1 and 2) and one booster dose at 12-15 months of age.

Investigational medicinal product name	Infanrix™ Hexa
Investigational medicinal product code	
Other name	DTPa-IPV-HBV/Hib, Infanrix Hexa GSK Biologicals' diphtheria-tetanus-acellular pertussis
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses of the vaccine were administered intramuscularly in the left thigh at 3, 4 and 5 months of age (Study Months 0, 1 and 2) and one booster dose at 12-15 months of age.

Arm title	10Pn Group
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Arm description:

Subjects having received 3 primary vaccination doses without antipyretics and receiving a booster dose of pneumococcal conjugate vaccine GSK1024850A co-administered with DTPa-HBV-IPV/Hib (Infanrix hexa) without prophylactic antipyretics.

Arm type	Active comparator
Investigational medicinal product name	10-valent Streptococcus pneumoniae conjugate vaccine
Investigational medicinal product code	
Other name	10Pn, 10Pn-PD-DiT, GlaxoSmithKline (GSK) Biologicals' 10-valent pneumococcal conjugate vaccine, Synflorix™, GlaxoSmithKline (GSK) Biologicals' 1024850A vaccine
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Three doses of the vaccine were administered intramuscularly, into the right thigh at 3, 4 and 5 months of age (Study Months 0, 1 and 2) and one booster dose at 12-15 months of age.

Investigational medicinal product name	Infanrix™ hexa
Investigational medicinal product code	
Other name	DTPa-IPV-HBV/Hib, Infanrix Hexa GSK Biologicals' diphtheria-tetanus-acellular pertussis
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses of the vaccine were administered intramuscularly in the left thigh at 3, 4 and 5 months of age (Study Months 0, 1 and 2) and one booster dose at 12-15 months of age.

Arm title	Unprimed Group
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Arm description:

Age-matched pneumococcal vaccine unprimed group receiving a single dose of meningococcal conjugate vaccine GSK134612 co-administered with DTPa-HBV-IPV/Hib (Infanrix hexa).

Arm type	Active comparator
Investigational medicinal product name	Meningococcal vaccine GSK134612
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose, intramuscularly injection in the right thigh at 12-15 months of age.

Investigational medicinal product name	Infanrix™ hexa
Investigational medicinal product code	
Other name	DTPa-IPV-HBV/Hib, Infanrix Hexa GSK Biologicals' diphtheria-tetanus-acellular pertussis
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose, intramuscularly injection in the left thigh at 12-15 months of age.

Number of subjects in period 1	10Pn-PD-DiT/ Paracetamol Group	10Pn-PD-DiT Group	10Pn-Pre Group
Started	178	27	172
Completed	177	27	172
Not completed	1	0	0
Unspecified	1	-	-

Number of subjects in period 1	10Pn-Post Group	10Pn Group	Unprimed Group
Started	37	209	336
Completed	36	208	336
Not completed	1	1	0
Unspecified	1	1	-

Baseline characteristics

Reporting groups

Reporting group title	10Pn-PD-DiT/ Paracetamol Group
Reporting group description:	
Subjects were vaccinated with three primary vaccination doses with prophylactic administration of paracetamol in study 10PN-PD-DIT-010 (107017), and received in this study at 12-15 months of age a booster dose of GSK Biologicals' 10Pn-PD-DiT vaccine, co-administered with Infanrix™ hexa (also referred to as DTPa-HBV-IPV/Hib) along with prophylactic antipyretic treatment (rectal paracetamol or acetaminophen) under the form of suppositories of CALPOL 80 or 125, depending on the subjects' body weight. (before the implementation of protocol amendment 3).	
Reporting group title	10Pn-PD-DiT Group
Reporting group description:	
Subjects were vaccinated with three primary vaccination doses with prophylactic administration of paracetamol in study 10PN-PD-DIT-010 (107017), and who received in this study at 12-15 months of age a booster dose of GSK Biologicals' 10Pn-PD-DiT vaccine, co-administered with Infanrix™ hexa (also referred to as DTPa-HBV-IPV/Hib) without prophylactic antipyretic treatment (rectal paracetamol or acetaminophen) - (after the implementation of protocol amendment 3).	
Reporting group title	10Pn-Pre Group
Reporting group description:	
Subjects were vaccinated with three primary vaccination doses without prophylactic administration of paracetamol in study 10PN-PD-DIT-010 (107017), and who received in this study at 12-15 months of age a booster dose of GSK Biologicals' 10Pn-PD-DiT vaccine, co-administered with Infanrix™ hexa (also referred to as DTPa-HBV-IPV/Hib) without prophylactic antipyretic treatment (rectal paracetamol or acetaminophen) - (before the implementation of protocol amendment 3).	
Reporting group title	10Pn-Post Group
Reporting group description:	
Subjects were vaccinated with three primary vaccination doses without prophylactic administration of paracetamol in study 10PN-PD-DIT-010 (107017), and who received in this study at 12-15 months of age a booster dose of GSK Biologicals' 10Pn-PD-DiT vaccine, co-administered with Infanrix™ hexa (also referred to as DTPa-HBV-IPV/Hib) without prophylactic antipyretic treatment (rectal paracetamol or acetaminophen) - (after the implementation of protocol amendment 3).	
Reporting group title	10Pn Group
Reporting group description:	
Subjects having received 3 primary vaccination doses without antipyretics and receiving a booster dose of pneumococcal conjugate vaccine GSK1024850A co-administered with DTPa-HBV-IPV/Hib (Infanrix hexa) without prophylactic antipyretics.	
Reporting group title	Unprimed Group
Reporting group description:	
Age-matched pneumococcal vaccine unprimed group receiving a single dose of meningococcal conjugate vaccine GSK134612 co-administered with DTPa-HBV-IPV/Hib (Infanrix hexa).	

Reporting group values	10Pn-PD-DiT/ Paracetamol Group	10Pn-PD-DiT Group	10Pn-Pre Group
Number of subjects	178	27	172
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			
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Age continuous Units: months arithmetic mean standard deviation	12.6 ± 0.77	13.2 ± 0.74	12.7 ± 0.77
Gender categorical Units: Subjects			
Female	90	11	79
Male	88	16	93

Reporting group values	10Pn-Post Group	10Pn Group	Unprimed Group
Number of subjects	37	209	336
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: months arithmetic mean standard deviation	13.1 ± 1.15	12.8 ± 0.86	13.1 ± 1.1
Gender categorical Units: Subjects			
Female	18	97	155
Male	19	112	181

Reporting group values	Total		
Number of subjects	959		
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: months arithmetic mean standard deviation	-		
Gender categorical Units: Subjects			
Female	450		
Male	509		

Subject analysis sets

Subject analysis set title	Poled primed Group
Subject analysis set type	Safety analysis

Subject analysis set description:

For carriage analyses the 10Pn-AP, 10Pn-AP-NAP, 10Pn-NAP-pre and 10Pn-NAP-post groups were pooled (pooled primed groups).

Reporting group values	Poled primed Group		
Number of subjects	414		
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: months arithmetic mean standard deviation	12.73 ± 0.83		
Gender categorical Units: Subjects			
Female	198		
Male	216		

End points

End points reporting groups

Reporting group title	10Pn-PD-DiT/ Paracetamol Group
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Reporting group description:

Subjects were vaccinated with three primary vaccination doses with prophylactic administration of paracetamol in study 10PN-PD-DIT-010 (107017), and received in this study at 12-15 months of age a booster dose of GSK Biologicals' 10Pn-PD-DiT vaccine, co-administered with Infanrix™ hexa (also referred to as DTPa-HBV-IPV/Hib) along with prophylactic antipyretic treatment (rectal paracetamol or acetaminophen) under the form of suppositories of CALPOL 80 or 125, depending on the subjects' body weight. (before the implementation of protocol amendment 3).

Reporting group title	10Pn-PD-DiT Group
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Reporting group description:

Subjects were vaccinated with three primary vaccination doses with prophylactic administration of paracetamol in study 10PN-PD-DIT-010 (107017), and who received in this study at 12-15 months of age a booster dose of GSK Biologicals' 10Pn-PD-DiT vaccine, co-administered with Infanrix™ hexa (also referred to as DTPa-HBV-IPV/Hib) without prophylactic antipyretic treatment (rectal paracetamol or acetaminophen) - (after the implementation of protocol amendment 3).

Reporting group title	10Pn-Pre Group
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Reporting group description:

Subjects were vaccinated with three primary vaccination doses without prophylactic administration of paracetamol in study 10PN-PD-DIT-010 (107017), and who received in this study at 12-15 months of age a booster dose of GSK Biologicals' 10Pn-PD-DiT vaccine, co-administered with Infanrix™ hexa (also referred to as DTPa-HBV-IPV/Hib) without prophylactic antipyretic treatment (rectal paracetamol or acetaminophen) - (before the implementation of protocol amendment 3).

Reporting group title	10Pn-Post Group
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Reporting group description:

Subjects were vaccinated with three primary vaccination doses without prophylactic administration of paracetamol in study 10PN-PD-DIT-010 (107017), and who received in this study at 12-15 months of age a booster dose of GSK Biologicals' 10Pn-PD-DiT vaccine, co-administered with Infanrix™ hexa (also referred to as DTPa-HBV-IPV/Hib) without prophylactic antipyretic treatment (rectal paracetamol or acetaminophen) - (after the implementation of protocol amendment 3).

Reporting group title	10Pn Group
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Reporting group description:

Subjects having received 3 primary vaccination doses without antipyretics and receiving a booster dose of pneumococcal conjugate vaccine GSK1024850A co-administered with DTPa-HBV-IPV/Hib (Infanrix hexa) without prophylactic antipyretics.

Reporting group title	Unprimed Group
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Reporting group description:

Age-matched pneumococcal vaccine unprimed group receiving a single dose of meningococcal conjugate vaccine GSK134612 co-administered with DTPa-HBV-IPV/Hib (Infanrix hexa).

Subject analysis set title	Pooled primed Group
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Subject analysis set type	Safety analysis
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Subject analysis set description:

For carriage analyses the 10Pn-AP, 10Pn-AP-NAP, 10Pn-NAP-pre and 10Pn-NAP-post groups were pooled (pooled primed groups).

Primary: Number of subjects reported with core fever (rectal temperature) ≥ 38.0 degrees Celsius ($^{\circ}\text{C}$).

End point title	Number of subjects reported with core fever (rectal temperature) ≥ 38.0 degrees Celsius ($^{\circ}\text{C}$).
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End point description:

End point type	Primary
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End point timeframe:

Within 4 days (Day 0-3) after primary vaccine dose.

End point values	10Pn-PD-DiT/ Paracetamol Group	10Pn-PD-DiT Group	10Pn-Pre Group	10Pn-Post Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	178	27	172	37
Units: Subjects				
Fever $\geq 38.0^{\circ}\text{C}$	64	14	100	16

End point values	10Pn Group	Unprimed Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	336		
Units: Subjects				
Fever $\geq 38.0^{\circ}\text{C}$	116	146		

Statistical analyses

Statistical analysis title	Difference between groups (core fever $\geq 38.0^{\circ}\text{C}$)
Statistical analysis description:	
Analysis aimed at demonstrating the superiority in terms of post-immunization core fever $\geq 38.0^{\circ}\text{C}$ of 10Pn-PD-DiT vaccine when co-administered with paracetamol compared to the 10Pn-PD-DiT vaccine when administered without such co-administration. Towards this analysis, standardized asymptotic 95% confidence interval (CI) for the groups difference [10Pn-pre Group minus 10Pn-PD-DiT/Paracetamol Group] in percentages of subjects reported with core fever $\geq 38.0^{\circ}\text{C}$ was computed.	
Comparison groups	10Pn-Pre Group v 10Pn-PD-DiT/ Paracetamol Group
Number of subjects included in analysis	350
Analysis specification	Pre-specified
Analysis type	superiority ^[1]
Parameter estimate	Difference in percentages
Point estimate	22.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.78
upper limit	32.11

Notes:

[1] - Superiority was demonstrated if the lower limit (LL) computed standardized asymptotic 95% CI was above 0%.

Secondary: Number of subjects reported with core fever (rectal temperature) $> 39.0^{\circ}\text{C}$.

End point title	Number of subjects reported with core fever (rectal temperature) $> 39.0^{\circ}\text{C}$.
End point description:	
End point type	Secondary

End point timeframe:

Within 4 days (Day 0-3) after primary vaccination dose.

End point values	10Pn-PD-DiT/ Paracetamol Group	10Pn-PD-DiT Group	10Pn-Pre Group	10Pn-Post Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	178	27	172	37
Units: Subjects				
Fever (rectal temperature) > 39.0°C	4	0	14	1

End point values	10Pn Group	Unprimed Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	336		
Units: Subjects				
Fever (rectal temperature) > 39.0°C	15	16		

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects reported with any and Grade 3 solicited local symptoms.
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End point description:

Solicited local symptoms assessed were pain, redness and swelling. Any was defined as any occurrence of the specified symptom regardless of intensity. Grade 3 pain was defined as cried when limb was moved/spontaneously painful. Grade 3 redness/swelling was defined as redness/swelling > 30 millimeters from injection site.

End point type	Secondary
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End point timeframe:

Within 4 days after primary vaccination.

End point values	10Pn-PD-DiT/ Paracetamol Group	10Pn-PD-DiT Group	10Pn-Pre Group	10Pn-Post Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	178	27	172	37
Units: Subjects				
Any pain	54	10	79	19
Grade 3 pain	2	2	10	3
Any redness	89	9	74	12

Grade 3 redness	7	1	14	1
Any swelling	52	8	50	13
Grade 3 swelling	2	1	9	3

End point values	10Pn Group	Unprimed Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	336		
Units: Subjects				
Any pain	98	114		
Grade 3 pain	13	4		
Any redness	86	146		
Grade 3 redness	15	16		
Any swelling	63	71		
Grade 3 swelling	12	12		

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects reported with any and Grade 3 solicited general symptoms.
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End point description:

Solicited general symptoms assessed were drowsiness, fever (rectal temperature $\geq 38.5^{\circ}\text{C}$), irritability and loss of appetite. Any was defined as any occurrence of the specified symptom regardless of intensity and relation to vaccination. Grade 3 drowsiness was defined as drowsiness that prevented normal activity. Grade 3 fever was defined as rectal temperature $>40.0^{\circ}\text{C}$. Grade 3 irritability was defined as crying that could not be comforted/ prevented normal activity. Grade 3 loss of appetite was defined as not eating at all.

End point type	Secondary
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End point timeframe:

Within 4 days after primary vaccination.

End point values	10Pn-PD-DiT/ Paracetamol Group	10Pn-PD-DiT Group	10Pn-Pre Group	10Pn-Post Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	178	27	172	37
Units: Subjects				
Any drowsiness	91	11	84	18
Grade 3 drowsiness	0	0	1	1
Any fever (rectal temperature $\geq 38.0^{\circ}\text{C}$)	64	14	100	16
Grade 3 fever (rectal temperature $> 40.0^{\circ}\text{C}$)	4	0	14	1

Any irritability	86	17	105	19
Grade 3 irritability	1	0	2	2
Any loss of appetite	47	8	46	10
Grade 3 loss of appetite	0	0	4	1

End point values	10Pn Group	Unprimed Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	336		
Units: Subjects				
Any drowsiness	102	146		
Grade 3 drowsiness	2	2		
Any fever (rectal temperature $\geq 38.0^{\circ}\text{C}$)	116	146		
Grade 3 fever (rectal temperature $> 40.0^{\circ}\text{C}$)	15	16		
Any irritability	124	147		
Grade 3 irritability	4	2		
Any loss of appetite	56	88		
Grade 3 loss of appetite	5	3		

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects reported with unsolicited adverse events (AEs). ^[2]
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End point description:

End point type	Secondary
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End point timeframe:

Within 31 days (Day 0-30) after primary vaccine dose.

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: Results were only tabulated for subjects who received a vaccine including the respective antigens.

End point values	10Pn-PD-DiT/ Paracetamol Group	10Pn-PD-DiT Group	10Pn Group	Unprimed Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	178	27	209	336
Units: Subjects				
Subject(s) with any AE(s)	22	3	30	64

Statistical analyses

No statistical analyses for this end point

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

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

End point type	Secondary
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End point timeframe:

Throughout the entire study period (Month 0-Month 12).

End point values	10Pn-PD-DiT/ Paracetamol Group	10Pn-PD-DiT Group	10Pn-Pre Group	10Pn-Post Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	178	27	172	37
Units: Subjects				
Subject(s) with any SAE(s)	13	5	13	4

End point values	10Pn Group	Unprimed Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	209	336		
Units: Subjects				
Subject(s) with any SAE(s)	17	30		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reported with AEs resulting in rash, new onset of chronic illness (NOCI), emergency room (ER) visits and non-routine physician office visits.

End point title	Number of subjects reported with AEs resulting in rash, new onset of chronic illness (NOCI), emergency room (ER) visits and non-routine physician office visits. ^[3]
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End point description:

End point type	Secondary
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End point timeframe:

Up to 6 months after vaccination with GSK Biologicals' meningococcal serogroups A, C, W-135, Y tetanus toxoid conjugate vaccine.

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Results were only tabulated for subjects who received a vaccine including the respective antigens.

End point values	Unprimed Group			
Subject group type	Reporting group			
Number of subjects analysed	336			
Units: Subjects				
Subject(s) with any rash(es)	7			
Subject(s) with any NOCI(s)	1			
Subject(s) with any ER visit(s)	0			
Subject(s) with any visit(s) at physician office	53			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with antibody concentrations against 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) ≥ 0.2 µg/mL.

End point title	Number of subjects with antibody concentrations against 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) ≥ 0.2 µg/mL. ^[4]
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End point description:

Anti-1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antibody concentrations were measured by 22F-inhibition Enzyme-Linked ImmunoSorbent Assay (ELISA). Seroprotection and seropositivity cut-offs for the assay were ≥ 0.20 and 0.05 µg/mL, respectively.

End point type	Secondary
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End point timeframe:

Prior to vaccination, 1 month and 12 months post-vaccination.

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Results were only tabulated for subjects who received a vaccine including the respective antigens.

End point values	10Pn-PD-DiT/ Paracetamol Group	10Pn Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	165	206		
Units: Subjects				
Anti-1 ≥ 0.2 µg/mL, M3 (N=164; 205)	159	203		
Anti-1 ≥ 0.2 µg/mL, PRE (N=157; 202)	88	144		
Anti-4 ≥ 0.2 µg/mL, M3 (N=165; 205)	164	204		
Anti-4 ≥ 0.2 µg/mL, PRE (N=164; 197)	138	180		
Anti-5 ≥ 0.2 µg/mL, M3 (N=164; 206)	163	205		
Anti-5 ≥ 0.2 µg/mL, PRE (N=156; 195)	117	174		
Anti-6B ≥ 0.2 µg/mL, M3 (N=165; 204)	100	154		

Anti-6B \geq 0.2 $\mu\text{g/mL}$, PRE (N=164; 203)	123	177		
Anti-7F \geq 0.2 $\mu\text{g/mL}$, M3 (N=165; 206)	163	205		
Anti-7F \geq 0.2 $\mu\text{g/mL}$, PRE (N=160; 196)	151	192		
Anti-9V \geq 0.2 $\mu\text{g/mL}$, M3 (N=164; 204)	161	201		
Anti-9V \geq 0.2 $\mu\text{g/mL}$, PRE (N=151; 191)	137	188		
Anti-14 \geq 0.2 $\mu\text{g/mL}$, M3 (N=164; 204)	163	203		
Anti-14 \geq 0.2 $\mu\text{g/mL}$, PRE (N=161; 203)	153	196		
Anti-18C \geq 0.2 $\mu\text{g/mL}$, M3 (N=165; 206)	157	205		
Anti-18C \geq 0.2 $\mu\text{g/mL}$, PRE (N=160; 200)	132	185		
Anti-19F \geq 0.2 $\mu\text{g/mL}$, M3 (N=165; 206)	160	206		
Anti-19F \geq 0.2 $\mu\text{g/mL}$, PRE (N=162; 204)	149	201		
Anti-23F \geq 0.2 $\mu\text{g/mL}$, M3 (N=163; 205)	128	179		
Anti-23F \geq 0.2 $\mu\text{g/mL}$, PRE (N=161; 192)	117	164		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against 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).

End point title	Antibody concentrations against 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). ^[5]
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End point description:

Anti-1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antibody concentrations were measured by 22F-inhibition Enzyme-Linked ImmunoSorbent Assay (ELISA). Seropositivity cut-off for the assay was $\geq 0.05 \mu\text{g/mL}$.

End point type	Secondary
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End point timeframe:

Prior to vaccination, 1 month and 12 months post-vaccination.

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Results were only tabulated for subjects who received a vaccine including the respective antigens.

End point values	10Pn-PD-DiT/ Paracetamol Group	10Pn Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	165	206		
Units: $\mu\text{g/mL}$				
geometric mean (confidence interval 95%)				
Anti-1, M3 (N=164; 205)	0.96 (0.84 to 1.09)	1.43 (1.28 to 1.6)		
Anti-1, PRE (N=157; 202)	0.21 (0.19 to 0.24)	0.3 (0.27 to 0.34)		

Anti-4, M3 (N=165; 205)	1.3 (1.13 to 1.5)	2.14 (1.91 to 2.4)		
Anti-4 , PRE (N=164; 197)	0.37 (0.33 to 0.41)	0.58 (0.51 to 0.66)		
Anti-5, M3 (N=164; 206)	1.44 (1.28 to 1.62)	1.97 (1.77 to 2.19)		
Anti-5, PRE (N=156; 195)	0.35 (0.31 to 0.41)	0.59 (0.51 to 0.67)		
Anti-6B, M3 (N=165; 204)	0.25 (0.21 to 0.31)	0.45 (0.38 to 0.54)		
Anti-6B, PRE (N=164; 203)	0.32 (0.27 to 0.38)	0.54 (0.48 to 0.62)		
Anti-7F, M3 (N=165; 206)	1.57 (1.41 to 1.74)	2.07 (1.87 to 2.3)		
Anti-7F, PRE (N=160; 196)	0.71 (0.63 to 0.8)	1.02 (0.91 to 1.14)		
Anti-9V, M3 (N=164; 204)	1.03 (0.91 to 1.17)	1.48 (1.33 to 1.66)		
Anti-9V, PRE (N=151; 191)	0.61 (0.52 to 0.7)	1 (0.89 to 1.11)		
Anti-14, M3 (N=164; 204)	2.33 (2.05 to 2.66)	3.62 (3.21 to 4.08)		
Anti-14, PRE (N=161; 203)	0.76 (0.66 to 0.88)	1.51 (1.3 to 1.76)		
Anti-18C, M3 (N=165; 206)	1.17 (0.99 to 1.38)	2.67 (2.37 to 3.01)		
Anti-18C, PRE (N=160; 200)	0.44 (0.38 to 0.5)	0.73 (0.65 to 0.83)		
Anti-19F, M3 (N=165; 206)	3.27 (2.78 to 3.84)	5.71 (5.06 to 6.44)		
Anti-19F, PRE (N=162; 204)	0.92 (0.77 to 1.1)	1.48 (1.29 to 1.7)		
Anti-23F, M3 (N=163; 205)	0.49 (0.4 to 0.59)	0.76 (0.64 to 0.9)		
Anti-23F, PRE (N=161; 192)	0.37 (0.3 to 0.44)	0.52 (0.45 to 0.61)		

Statistical analyses

No statistical analyses for this end point

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

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

OPA titers against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (Opsono-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F) were calculated, expressed as geometric mean titers (GMTs) and tabulated. The seropositivity cut-off for the assay was ≥ 8 .

End point type	Secondary
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End point timeframe:

Prior to vaccination, 1 month and 12 months post-vaccination.

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Results were only tabulated for subjects who received a vaccine including the respective antigens.

End point values	10Pn-PD-DiT/ Paracetamol Group	10Pn Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	150	187		
Units: Titers				
geometric mean (confidence interval 95%)				
OPSONO-1, M3 (N=128; 158)	9.7 (7.6 to 12.5)	23.5 (17.7 to 31.2)		
OPSONO-1, PRE (N=150; 185)	6 (5.1 to 7.1)	7.7 (6.4 to 9.2)		
OPSONO-4, M3 (N=129; 157)	736.1 (634.1 to 854.5)	794.6 (688.8 to 916.7)		
OPSONO-4 , PRE (N=143; 180)	20.4 (14.8 to 28.2)	42.7 (32.3 to 56.4)		
OPSONO-5, M3 (N=125; 156)	31.1 (24.1 to 40)	70.7 (57.5 to 86.9)		
OPSONO-5, PRE (N=145; 178)	8.8 (7.3 to 10.6)	16.4 (13.3 to 20.3)		
OPSONO-6B, M3 (N=124; 146)	337.6 (223.4 to 510.1)	730 (553 to 963.7)		
OPSONO-6B, PRE (N=148; 187)	29.2 (20.1 to 42.5)	45.6 (34.1 to 61)		
OPSONO-7F, M3 (N=125; 152)	2417.8 (2005.3 to 2915.1)	2475.6 (2071.4 to 2958.7)		
OPSONO-7F, PRE (N=137; 182)	374.1 (247.4 to 565.7)	505.9 (377.4 to 678.1)		
OPSONO-9V, M3 (N=121; 151)	1461.8 (1248.8 to 1711.1)	1277.7 (1061.1 to 1538.5)		
OPSONO-9V, PRE (N=140; 180)	428.2 (352.6 to 519.8)	406.5 (345 to 479)		
OPSONO-14, M3 (N=126; 157)	803.5 (658.1 to 981)	1190.6 (996.6 to 1422.5)		
OPSONO-14, PRE (N=139; 183)	183.1 (141 to 238)	284.2 (230.3 to 350.7)		
OPSONO-18C, M3 (N=125; 151)	123.5 (95.3 to 160)	213.6 (179.5 to 254.1)		
OPSONO-18C, PRE (N=147; 173)	6.1 (5.2 to 7.1)	11.3 (9 to 14.3)		
OPSONO-19F, M3 (N=121; 147)	206.6 (151.4 to 282.1)	390.1 (309 to 492.7)		
OPSONO-19F, PRE (N=145; 183)	20.5 (16.1 to 26.2)	35.8 (29.2 to 43.8)		
OPSONO-23F, M3 (N=123; 154)	1004.4 (723 to 1395.4)	291.7 (198 to 429.6)		
OPSONO-23F, PRE (N=142; 182)	1664.3 (1352.1 to 2048.7)	396.8 (289.7 to 543.7)		

Statistical analyses

No statistical analyses for this end point

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

End point title	Concentrations of antibodies against protein D (Anti-PD). ^[7]
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End point description:

The seropositivity cut-off for the assay was ≥ 100 Enzyme-Linked ImmunoSorbent Assay (ELISA) units per milliliter.

End point type	Secondary
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End point timeframe:

Prior to vaccination, 1 month and 12 months post-vaccination.

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Results were only tabulated for subjects who received a vaccine including the respective antigens.

End point values	10Pn-PD-DiT/ Paracetamol Group	10Pn Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	164	201		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
ANTI-PD, M3 (N=164; 201)	949.7 (825 to 1093.2)	1561.5 (1393.8 to 1749.4)		
ANTI-PD, PRE (N=160; 197)	363.7 (307.4 to 430.4)	662.3 (572.5 to 766.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against pneumococcal serotypes 6A and 19A (anti-6A and 19A).

End point title	Antibody concentrations against pneumococcal serotypes 6A and 19A (anti-6A and 19A). ^[8]
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End point description:

Anti-6A and 19A antibody concentrations were measured by 22F-inhibition Enzyme-Linked ImmunoSorbent Assay (ELISA).

End point type	Secondary
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End point timeframe:

Prior to vaccination, 1 month and 12 months post-vaccination.

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Results were only tabulated for subjects who received a vaccine including the respective antigens.

End point values	10Pn-PD-DiT/ Paracetamol Group	10Pn Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	203		
Units: µg/mL				
geometric mean (confidence interval 95%)				

ANTI-6A, M3 (N=162; 203)	0.07 (0.06 to 0.09)	0.12 (0.1 to 0.14)		
ANTI-6A, PRE (N=161; 200)	0.11 (0.09 to 0.14)	0.21 (0.18 to 0.25)		
ANTI-19A, M3 (N=163; 202)	0.11 (0.1 to 0.14)	0.21 (0.17 to 0.24)		
ANTI-19A, PRE (N=163; 203)	0.15 (0.12 to 0.17)	0.22 (0.19 to 0.26)		

Statistical analyses

No statistical analyses for this end point

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

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

OPA titers against pneumococcal serotypes 6A and 19A (Opsono-6A and 19A) were calculated, expressed as geometric mean titers (GMTs) and tabulated. The seropositivity cut-off for the assay was ≥ 8 .

End point type	Secondary
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End point timeframe:

Prior to vaccination, 1 month and 12 months post-vaccination.

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Results were only tabulated for subjects who received a vaccine including the respective antigens.

End point values	10Pn-PD-DiT/ Paracetamol Group	10Pn Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	139	170		
Units: Titers				
geometric mean (confidence interval 95%)				
OPSONO-6A, M3 (N=122; 147)	45.9 (30.9 to 68)	60 (41.8 to 86)		
OPSONO-6A, PRE (N=135; 160)	65.5 (45 to 95.3)	66 (47.5 to 91.9)		
OPSONO-19A, M3 (N=125; 153)	6.1 (4.9 to 7.6)	8.4 (6.5 to 10.8)		
OPSONO-19A, PRE (N=139; 170)	5 (4.4 to 5.6)	4.9 (4.4 to 5.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with titers $\geq 1:8$ and $1:128$ for meningococcal polysaccharides A , C, W-135 and Y serum bactericidal antibodies, using baby rabbit

complement for assay (rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY).

End point title	Number of subjects with titers $\geq 1:8$ and $1:128$ for meningococcal polysaccharides A , C, W-135 and Y serum bactericidal antibodies, using baby rabbit complement for assay (rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY). ^[10]
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End point description:

End point type	Secondary
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End point timeframe:

Prior to vaccination(PRE), 1 month (M1) and 12 months (M12) post-vaccination.

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Results were only tabulated for subjects who received a vaccine including the respective antigens.

End point values	Unprimed Group			
Subject group type	Reporting group			
Number of subjects analysed	301			
Units: Subjects				
rSBA-MenA,Pre, $\geq 1:8$ [N=244]	69			
rSBA-MenA, Pre, $\geq 1:128$ [N=244]	44			
rSBA-MenA, M1, $\geq 1:8$ [N=299]	298			
rSBA-MenA, M1, $\geq 1:128$ [N=299]	298			
rSBA-MenA, M12, $\geq 1:8$ [N=136]	136			
rSBA-MenA, M12, $\geq 1:128$ [N=136]	134			
rSBA-MenC,Pre, $\geq 1:8$ [N=295]	50			
rSBA-MenC, Pre, $\geq 1:128$ [N=295]	17			
rSBA-MenC, M1, $\geq 1:8$ [N=301]	300			
rSBA-MenC, M1, $\geq 1:128$ [N=301]	294			
rSBA-MenC, M12, $\geq 1:8$ [N=161]	154			
rSBA-MenC, M12, $\geq 1:128$ [N=161]	105			
rSBA-MenW-135,Pre, $\geq 1:8$ [N=287]	114			
rSBA-MenW-135, Pre, $\geq 1:128$ [N=287]	59			
rSBA-MenW-135, M1, $\geq 1:8$ [N=301]	301			
rSBA-MenW-135, M1, $\geq 1:128$ [N=301]	301			
rSBA-MenW-135, M12, $\geq 1:8$ [N=139]	138			
rSBA-MenW-135, M12, $\geq 1:128$ [N=139]	129			
rSBA-MenY,Pre, $\geq 1:8$ [N=297]	167			
rSBA-MenY, Pre, $\geq 1:128$ [N=297]	93			
rSBA-MenY, M1, $\geq 1:8$ [N=301]	300			
rSBA-MenY, M1, $\geq 1:128$ [N=301]	300			
rSBA-MenY, M12, $\geq 1:8$ [N=138]	137			
rSBA-MenY, M12, $\geq 1:128$ [N=138]	127			

Statistical analyses

No statistical analyses for this end point

Secondary: rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY titers.

End point title	rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY titers. ^[11]
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End point description:

End point type	Secondary
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End point timeframe:

Prior to vaccination, 1 month and 12 months post-vaccination.

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Results were only tabulated for subjects who received a vaccine including the respective antigens.

End point values	Unprimed Group			
Subject group type	Reporting group			
Number of subjects analysed	301			
Units: Titers				
geometric mean (confidence interval 95%)				
rSBA-MenA,Pre [N=244]	11.5 (9.2 to 14.3)			
rSBA-MenA, M1 [N=299]	2151.3 (1927.4 to 2401.2)			
rSBA-MenA, M12 [N=136]	677.6 (579.9 to 791.8)			
rSBA-MenC,Pre [N=295]	6.9 (6 to 8)			
rSBA-MenC, M1 [N=301]	811.2 (728 to 904)			
rSBA-MenC, M12 [N=161]	191.1 (153.5 to 238)			
rSBA-MenW-135,Pre [N=287]	16.3 (13.2 to 20.1)			
rSBA-MenW-135, M1 [N=301]	5393.6 (4888.2 to 5951.1)			
rSBA-MenW-135, M12 [N=139]	573.1 (479.3 to 685.3)			
rSBA-MenY,Pre [N=297]	30.2 (24.2 to 37.7)			
rSBA-MenY, M1 [N=301]	2863.7 (2537.8 to 3231.4)			
rSBA-MenY, M12 [N=138]	665.2 (547.9 to 807.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-polysaccharide N. meningitidis serogroup A (anti-PSA), C (anti-PSC), W (anti-PSW-135) and Y (anti-PSY) ≥ 0.3 $\mu\text{g/mL}$ and 2.0 $\mu\text{g/mL}$.

End point title	Number of subjects with anti-polysaccharide N. meningitidis serogroup A (anti-PSA), C (anti-PSC), W (anti-PSW-135) and Y (anti-PSY) $\geq 0.3 \mu\text{g/mL}$ and $2.0 \mu\text{g/mL}$. ^[12]
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End point description:

End point type	Secondary
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End point timeframe:

Prior to vaccination, 1 month and 12 months post-vaccination.

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Results were only tabulated for subjects who received a vaccine including the respective antigens.

End point values	Unprimed Group			
Subject group type	Reporting group			
Number of subjects analysed	278			
Units: Subjects				
Anti-PSA, M1, $\geq 0.3 \mu\text{g/mL}$	271			
Anti-PSA, M1, $\geq 2.0 \mu\text{g/mL}$	271			
Anti-PSA, M12, $\geq 0.3 \mu\text{g/mL}$	133			
Anti-PSA, M12, $\geq 2.0 \mu\text{g/mL}$	47			
Anti-PSC, M1, $\geq 0.3 \mu\text{g/mL}$	278			
Anti-PSC, M1, $\geq 2.0 \mu\text{g/mL}$	277			
Anti-PSC, M12, $\geq 0.3 \mu\text{g/mL}$	157			
Anti-PSC, M12, $\geq 2.0 \mu\text{g/mL}$	9			
Anti-PSW-135, M1, $\geq 0.3 \mu\text{g/mL}$	258			
Anti-PSW-135, M1, $\geq 2.0 \mu\text{g/mL}$	234			
Anti-PSW-135, M12, $\geq 0.3 \mu\text{g/mL}$	117			
Anti-PSW-135, M12, $\geq 2.0 \mu\text{g/mL}$	45			
Anti-PSY, M1, $\geq 0.3 \mu\text{g/mL}$	261			
Anti-PSY, M1, $\geq 2.0 \mu\text{g/mL}$	249			
Anti-PSY, M12, $\geq 0.3 \mu\text{g/mL}$	131			
Anti-PSY, M12, $\geq 2.0 \mu\text{g/mL}$	59			

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PSA, anti-PSC, anti-PSW-135 and anti-PSY antibody concentrations.

End point title	Anti-PSA, anti-PSC, anti-PSW-135 and anti-PSY antibody concentrations. ^[13]
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End point description:

End point type	Secondary
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End point timeframe:

Prior to vaccination, 1 month and 12 months post-vaccination.

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: Results were only tabulated for subjects who received a vaccine including the respective antigens.

End point values	Unprimed Group			
Subject group type	Reporting group			
Number of subjects analysed	278			
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PSA, Pre [N=246]	0.16 (0.15 to 0.17)			
Anti-PSA, M1 [N=272]	36.28 (32.8 to 40.15)			
Anti-PSA, M12 [N=153]	0.99 (0.82 to 1.19)			
Anti-PSC, Pre [N=269]	0.15 (0.15 to 0.16)			
Anti-PSC, M1 [N=278]	14.12 (13 to 15.32)			
Anti-PSC, M12 [N=157]	0.42 (0.36 to 0.49)			
Anti-PSW-135, Pre [N=236]	0.15 (0.15 to 0.15)			
Anti-PSW-135, M1 [N=259]	6.11 (5.45 to 6.86)			
Anti-PSW-135, M12 [N=132]	1.21 (0.98 to 1.48)			
Anti-PSY, Pre [N=261]	0.15 (0.15 to 0.16)			
Anti-PSY, M1 [N=263]	8.03 (7.17 to 8.99)			
Anti-PSY, M12 [N=135]	1.81 (1.5 to 2.19)			

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-tetanus toxoids (anti-T) antibody concentrations.

End point title	Anti-tetanus toxoids (anti-T) antibody concentrations. ^[14]
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End point description:

The seroprotection cut-off for the assay was ≥ 0.1 IU/mL.

End point type	Secondary
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End point timeframe:

Prior to vaccination (Pre).

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Results were only tabulated for subjects who received a vaccine including the respective antigens.

End point values	Unprimed Group			
Subject group type	Reporting group			
Number of subjects analysed	266			
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-T, Pre [266]	0.512 (0.456 to 0.575)			

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-hepatitis B surface antigen (anti-HBs) antibody concentrations.

End point title	Anti-hepatitis B surface antigen (anti-HBs) antibody concentrations. ^[15]
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End point description:

The seroprotection cut-off for the assay was ≥ 10 mIU/mL.

End point type	Secondary
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End point timeframe:

Prior to vaccination (Pre).

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Results were only tabulated for subjects who received a vaccine including the respective antigens.

End point values	Unprimed Group			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs, Pre [2]	1336.1 (52.3 to 34160.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations of antibodies against diphtheria and tetanus toxoids (anti-D and T).

End point title	Concentrations of antibodies against diphtheria and tetanus toxoids (anti-D and T).
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End point description:

The seroprotection cut-off for the assay was ≥ 0.1 IU/mL.

End point type	Secondary
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End point timeframe:
1 month post-vaccination.

End point values	10Pn-PD-DiT/ Paracetamol Group	10Pn-PD-DiT Group	10Pn-Pre Group	10Pn-Post Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	140	24	167	37
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-D, M1 [N=140; 24; 166; 37; 203; 245]	10.112 (9.042 to 11.309)	9.839 (7.475 to 12.95)	12.285 (11.18 to 13.5)	11 (8.786 to 13.77)
Anti-T, M1 [N=139; 24; 167; 37; 204; 245]	7.382 (6.639 to 8.208)	8.684 (6.37 to 11.839)	9.583 (8.927 to 10.287)	8.196 (6.829 to 9.837)

End point values	10Pn Group	Unprimed Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	204	266		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-D, M1 [N=140; 24; 166; 37; 203; 245]	12.04 (11.041 to 13.13)	7.291 (6.592 to 8.064)		
Anti-T, M1 [N=139; 24; 167; 37; 204; 245]	9.315 (8.715 to 9.957)	11.79 (10.684 to 13.011)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) antibody concentrations.

End point title	Anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) antibody concentrations.
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End point description:

The seropositivity cut-off for the assay was ≥ 5 Enzyme-Linked ImmunoSorbent Assay (ELISA) units per milliliter (EL.U/mL).

End point type	Secondary
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End point timeframe:

1 month post-vaccination.

End point values	10Pn-PD-DiT/ Paracetamol Group	10Pn-PD-DiT Group	10Pn-Pre Group	10Pn-Post Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	140	24	167	37
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PT, M1 [N=138; 24; 166; 36; 202; 248]	83.3 (73.8 to 94)	81.6 (62.2 to 106.9)	82 (73.4 to 91.7)	76.7 (62.2 to 94.4)
Anti-FHA, M1 [N=140; 24; 167; 37; 204; 251]	467.9 (422.4 to 518.3)	431.1 (318.8 to 582.9)	453.8 (412.6 to 499.1)	400.4 (321.8 to 498.2)
Anti-PRN, M1 [N=140; 24; 167; 36; 203; 246]	222.8 (193.9 to 256)	153.4 (97.5 to 241.2)	254.9 (225.8 to 287.8)	220.4 (168.7 to 288)

End point values	10Pn Group	Unprimed Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	37		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PT, M1 [N=138; 24; 166; 36; 202; 248]	81.1 (73.5 to 89.4)	163.1 (143 to 185.9)		
Anti-FHA, M1 [N=140; 24; 167; 37; 204; 251]	443.6 (406.7 to 483.9)	580.8 (532.2 to 633.8)		
Anti-PRN, M1 [N=140; 24; 167; 36; 203; 246]	248.4 (222.6 to 277.2)	350.7 (316.8 to 388.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-hepatitis B surface antigen (anti-HBs) antibody concentrations.

End point title	Anti-hepatitis B surface antigen (anti-HBs) antibody concentrations.
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End point description:

The seroprotection cut-off for the assay was ≥ 10 mIU/mL.

End point type	Secondary
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End point timeframe:

1 month post-vaccination.

End point values	10Pn-PD-DiT/ Paracetamol Group	10Pn-PD-DiT Group	10Pn-Pre Group	10Pn-Post Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	107	16	133	26
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs, M1 [N=105; 16; 130; 26; 156; 1]	1883.9 (1332.9 to 2662.7)	1460.6 (816.4 to 2613.2)	2133 (1615 to 2817.1)	1818.5 (1142.8 to 2893.6)

End point values	10Pn Group	Unprimed Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	19 ^[16]		
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs, M1 [N=105; 16; 130; 26; 156; 1]	2077 (1629.3 to 2647.7)	20610 (0 to 99999)		

Notes:

[16] - Only one subject was analyzed. As a result the LL and UL values are 0 and 99999.

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-polyribosyl-ribitol phosphate (anti-PRP) antibody concentrations.

End point title	Anti-polyribosyl-ribitol phosphate (anti-PRP) antibody concentrations.
End point description:	The seroprotection cut-off for the assay was $\geq 0.15 \mu\text{g/mL}$.
End point type	Secondary
End point timeframe:	1 month post-vaccination.

End point values	10Pn-PD-DiT/ Paracetamol Group	10Pn-PD-DiT Group	10Pn-Pre Group	10Pn-Post Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	141	24	167	36
Units: $\mu\text{g/mL}$				
geometric mean (confidence interval 95%)				
Anti-PRP, M1 [N=141; 24; 167; 36; 203; 269]	23.066 (18.806 to 28.291)	26.006 (15.56 to 43.463)	27.373 (22.915 to 32.697)	22.011 (16.288 to 29.745)

End point values	10Pn Group	Unprimed Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	203	269		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PRP, M1 [N=141; 24; 167; 36; 203; 269]	26.335 (22.55 to 30.754)	20.985 (17.966 to 24.511)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-polio types 1, 2 and 3 titers.

End point title	Anti-polio types 1, 2 and 3 titers.
End point description:	The seroprotection cut-off for the assay was ≥ 8 .
End point type	Secondary
End point timeframe:	1 month post-vaccination.

End point values	10Pn-PD-DiT/ Paracetamol Group	10Pn-PD-DiT Group	10Pn-Pre Group	10Pn-Post Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	97	13	122	23
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-P1, M1 [N=93; 12; 114; 23; 137; 1]	1193 (993.8 to 1432.2)	1534.2 (952 to 2472.5)	1058.7 (870.2 to 1288)	1208.6 (764.2 to 1911.2)
Anti-P2, M1 [N=93; 12; 113; 22; 135; 1]	1354.1 (1115.8 to 1643.3)	2047.9 (1246 to 3365.9)	1413.2 (1174.3 to 1700.7)	2215.8 (1544.4 to 3178.9)
Anti-P3, M1 [N=92; 12; 114; 23; 137; 1]	2354.2 (1946.1 to 2847.9)	2233.3 (1300.9 to 3834)	2647.5 (2221.5 to 3155.3)	3576.5 (2617.3 to 4887.2)

End point values	10Pn Group	Unprimed Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	137	9 ^[17]		

Units: Titers				
geometric mean (confidence interval 95%)				
Anti-P1, M1 [N=93; 12; 114; 23; 137; 1]	1082.5 (905.9 to 1293.6)	4096 (0 to 99999)		
Anti-P2, M1 [N=93; 12; 113; 22; 135; 1]	1520.7 (1287.4 to 1796.1)	8192 (0 to 99999)		
Anti-P3, M1 [N=92; 12; 114; 23; 137; 1]	2784.6 (2385.2 to 3251)	8192 (0 to 99999)		

Notes:

[17] - Only one subject was analyzed. As a result the LL and UL values are 0 and 99999.

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HBs antibody concentrations.

End point title	Anti-HBs antibody concentrations.
End point description:	
End point type	Secondary
End point timeframe:	
12 month post-vaccination.	

End point values	10Pn-PD-DiT/ Paracetamol Group	10Pn-PD-DiT Group	10Pn-Pre Group	10Pn-Post Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	107	16	133	26
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs, M12 [N=107; 16; 133; 20; 153; 19]	219.3 (164.8 to 291.7)	147.3 (62.6 to 346.9)	231.2 (179.7 to 297.6)	139.2 (74.3 to 260.9)

End point values	10Pn Group	Unprimed Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	156	19		
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs, M12 [N=107; 16; 133; 20; 153; 19]	216.4 (171.4 to 273.2)	535.1 (277.8 to 1030.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-Polio type 1, 2 and 3 titres.

End point title Anti-Polio type 1, 2 and 3 titres.

End point description:

End point type Secondary

End point timeframe:

12 month post-vaccination.

End point values	10Pn-PD-DiT/ Paracetamol Group	10Pn-PD-DiT Group	10Pn-Pre Group	10Pn-Post Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	97	13	122	23
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-POLIO1, M12 [N=97; 13; 122; 14; 136; 9]	208.2 (164.7 to 263.2)	150.4 (87.2 to 259.3)	234.5 (189.5 to 290.3)	220.8 (92.3 to 528.2)
Anti-POLIO2, M12 [N=96; 13; 122; 14; 136; 9]	311.2 (241.5 to 401)	212.4 (100.5 to 449)	310.6 (256 to 376.9)	400 (218.6 to 732.1)
Anti-POLIO3, M12 [N=97; 13; 122; 14; 136; 9]	431.3 (332.4 to 559.5)	301 (125.8 to 720.4)	506.3 (406.3 to 630.7)	672.2 (330 to 1369.4)

End point values	10Pn Group	Unprimed Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	137	9		
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-POLIO1, M12 [N=97; 13; 122; 14; 136; 9]	233.1 (189.5 to 286.7)	335.4 (146.4 to 768.2)		
Anti-POLIO2, M12 [N=96; 13; 122; 14; 136; 9]	318.8 (265.7 to 382.6)	322.7 (172.9 to 602.3)		
Anti-POLIO3, M12 [N=97; 13; 122; 14; 136; 9]	521.3 (423.4 to 641.7)	203.3 (63.7 to 649.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with S.pneumoniae (vaccine serotypes) in nasopharyngeal swabs.

End point title Number of subjects with S.pneumoniae (vaccine serotypes) in

End point description:

End point type	Secondary
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End point timeframe:

Prior to vaccination(Pre), 1 month post-vaccination [PIV(M1)], at 15-18 months of age[PIV(M3)], at 19-22 months of age [PIV(M7)]and at 24-27 months of age [PIV(M12)] and overall.

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Results were only tabulated for subjects who received a vaccine including the respective antigens.

End point values	Unprimed Group	Poled primed Group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	336	414		
Units: Subjects				
PRE (N=407; 330)	53	43		
PIV(M1) (N=408; 332)	47	45		
PIV(M3) (N=408; 332)	55	49		
PIV(M7) (N=406; 334)	50	42		
PIV(M12) (N=409; 334)	43	34		
Overall (N=414; 336)	115	111		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with S.pneumoniae (cross-reactive serotypes) in nasopharyngeal swabs.

End point title	Number of subjects with S.pneumoniae (cross-reactive serotypes) in nasopharyngeal swabs. ^[19]
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End point description:

End point type	Secondary
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End point timeframe:

Prior to vaccination(Pre), 1 month post-vaccination [PIV(M1)], at 15-18 months of age[PIV(M3)], at 19-22 months of age [PIV(M7)]and at 24-27 months of age [PIV(M12)] and overall.

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Results were only tabulated for subjects who received a vaccine including the respective antigens.

End point values	Unprimed Group	Poled primed Group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	336	414		
Units: Subjects				
PRE (N=407; 330)	13	15		
PIV(M1) (N=408; 332)	19	22		
PIV(M3) (N=408; 332)	21	27		
PIV(M7) (N=406; 334)	19	21		
PIV(M12) (N=409; 334)	19	18		
Overall (N=414; 336)	55	59		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with S.pneumoniae (non-vaccine and non-cross-reactive serotypes) in nasopharyngeal.

End point title	Number of subjects with S.pneumoniae (non-vaccine and non-cross-reactive serotypes) in nasopharyngeal. ^[20]
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End point description:

End point type	Secondary
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End point timeframe:

Prior to vaccination(Pre), 1 month post-vaccination [PIV(M1)], at 15-18 months of age[PIV(M3)], at 19-22 months of age [PIV(M7)]and at 24-27 months of age [PIV(M12)] and overall.

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Results were only tabulated for subjects who received a vaccine including the respective antigens.

End point values	Unprimed Group	Poled primed Group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	336	414		
Units: Subjects				
PRE (N=407; 330)	26	27		
PIV(M1) (N=408; 332)	30	42		
PIV(M3) (N=408; 332)	32	45		
PIV(M7) (N=406; 334)	29	42		
PIV(M12) (N=409; 334)	22	39		
Overall (N=414; 336)	82	111		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with H. influenzae in nasopharyngeal swabs.

End point title	Number of subjects with H. influenzae in nasopharyngeal swabs. ^[21]
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End point description:

End point type	Secondary
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End point timeframe:

Prior to vaccination(Pre), 1 month post-vaccination [PIV(M1)], at 15-18 months of age[PIV(M3)], at 19-22 months of age [PIV(M7)]and at 24-27 months of age [PIV(M12)] and overall.

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Results were only tabulated for subjects who received a vaccine including the respective antigens.

End point values	Unprimed Group	Poled primed Group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	336	414		
Units: Subjects				
PRE (N=397; 312)	41	48		
PIV(M1) (N=402; 318)	39	56		
PIV(M3) (N=403; 328)	34	62		
PIV(M7) (N=403; 332)	49	64		
PIV(M12) (N=406; 333)	57	46		
Overall (N=414; 336)	124	160		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with S. pneumoniae and H. influenzae in nasopharyngeal swabs.

End point title	Number of subjects with S. pneumoniae and H. influenzae in nasopharyngeal swabs. ^[22]
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End point description:

End point type	Secondary
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End point timeframe:

Prior to vaccination(Pre), 1 month post-vaccination [PIV(M1)], at 15-18 months of age[PIV(M3)], at 19-22 months of age [PIV(M7)]and at 24-27 months of age [PIV(M12)] and overall.

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Results were only tabulated for subjects who received a vaccine including the respective antigens.

End point values	Unprimed Group	Poled primed Group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	336	414		
Units: Subjects				
PRE (N=397; 312)	19	21		
PIV(M1) (N=402; 318)	20	30		
PIV(M3) (N=403; 328)	17	31		
PIV(M7) (N=403; 332)	22	28		
PIV(M12) (N=406; 333)	22	19		
Overall (N=414; 336)	61	86		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with S. pneumoniae detected in nasopharyngeal swabs.

End point title	Number of subjects with S. pneumoniae detected in nasopharyngeal swabs. ^[23]
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End point description:

End point type	Secondary
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End point timeframe:

1 month post-vaccination [PIV(M1)], at 15-18 months of age[PIV(M3)], at 19-22 months of age [PIV(M7)]and at 24-27 months of age [PIV(M12)] and overall.

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Results were only tabulated for subjects who received a vaccine including the respective antigens.

End point values	Unprimed Group	Poled primed Group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	336	414		
Units: Subjects				
PIV(M1) (N=408; 332)	43	56		
PIV(M3) (N=408; 332)	63	76		
PIV(M7) (N=406; 334)	70	73		
PIV(M12) (N=409; 334)	65	70		
Overall (N=414; 336)	161	195		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with H. influenzae detected in nasopharyngeal

swabs.

End point title	Number of subjects with H. influenzae detected in nasopharyngeal swabs. ^[24]
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End point description:

End point type	Secondary
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End point timeframe:

1 month post-vaccination [PIV(M1)], at 15-18 months of age[PIV(M3)], at 19-22 months of age [PIV(M7)]and at 24-27 months of age [PIV(M12)] and overall.

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: Results were only tabulated for subjects who received a vaccine including the respective antigens.

End point values	Unprimed Group	Poled primed Group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	336	414		
Units: Subjects				
PIV(M1) (N=402; 318)	21	32		
PIV(M3) (N=403; 328)	22	40		
PIV(M7) (N=403; 332)	37	42		
PIV(M12) (N=406; 333)	39	35		
Overall (N=414; 336)	104	129		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms: 4-day (Days 0- 3) follow-up periods after vaccination;

Unsolicited AEs: 31-day (Days 0-30) follow-up periods after vaccination;

SAEs: Entire study period (Months 0-12).

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	12.0
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Reporting groups

Reporting group title	10Pn-PD-DiT/ Paracetamol Group
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Reporting group description:

Subjects were vaccinated with three primary vaccination doses with prophylactic administration of paracetamol in study 10PN-PD-DIT-010 (107017), and who received in this study at 12-15 months of age a booster dose of GSK Biologicals' 10Pn-PD-DiT vaccine, co-administered with Infanrix™ hexa (also referred to as DTPa-HBV-IPV/Hib) and with prophylactic antipyretic treatment (rectal paracetamol or acetaminophen) under the form of suppositories of CALPOL 80 or 125, depending on the subjects' body weight. (before the implementation of protocol amendment 3).

Reporting group title	10Pn-PD-DiT Group
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Reporting group description:

Subjects were vaccinated with three primary vaccination doses with prophylactic administration of paracetamol in study 10PN-PD-DIT-010 (107017), and who received in this study at 12-15 months of age a booster dose of GSK Biologicals' 10Pn-PD-DiT vaccine, co-administered with Infanrix™ hexa (also referred to as DTPa-HBV-IPV/Hib) without prophylactic antipyretic treatment (rectal paracetamol or acetaminophen) - (after the implementation of protocol amendment 3).

Reporting group title	10Pn-pre Group
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Reporting group description:

Subjects were vaccinated with three primary vaccination doses without prophylactic administration of paracetamol in study 10PN-PD-DIT-010 (107017), and who received in this study at 12-15 months of age a booster dose of GSK Biologicals' 10Pn-PD-DiT vaccine, co-administered with Infanrix™ hexa (also referred to as DTPa-HBV-IPV/Hib) without prophylactic antipyretic treatment (rectal paracetamol or acetaminophen) - (before the implementation of protocol amendment 3).

Reporting group title	10Pn-post Group
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Reporting group description:

Subjects were vaccinated with three primary vaccination doses without prophylactic administration of paracetamol in study 10PN-PD-DIT-010 (107017), and who received in this study at 12-15 months of age a booster dose of GSK Biologicals' 10Pn-PD-DiT vaccine, co-administered with Infanrix™ hexa (also referred to as DTPa-HBV-IPV/Hib) without prophylactic antipyretic treatment (rectal paracetamol or acetaminophen) - (after the implementation of protocol amendment 3).

Reporting group title	10Pn Group
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Reporting group description:

Subjects having received 3 primary vaccination doses without antipyretics and receiving a booster dose of pneumococcal conjugate vaccine GSK1024850A co-administered with DTPa-HBV-IPV/Hib (Infanrix hexa) without prophylactic antipyretics.

Reporting group title	Unprimed Group
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Reporting group description:

Age-matched pneumococcal vaccine unprimed group receiving a single dose of meningococcal conjugate vaccine GSK134612 co-administered with DTPa-HBV-IPV/Hib (Infanrix hexa).

Serious adverse events	10Pn-PD-DiT/ Paracetamol Group	10Pn-PD-DiT Group	10Pn-pre Group
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 178 (7.30%)	5 / 27 (18.52%)	13 / 172 (7.56%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	1 / 178 (0.56%)	0 / 27 (0.00%)	2 / 172 (1.16%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	2 / 178 (1.12%)	0 / 27 (0.00%)	0 / 172 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foreign body trauma			
subjects affected / exposed	1 / 178 (0.56%)	1 / 27 (3.70%)	1 / 172 (0.58%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Accidental exposure			
subjects affected / exposed	0 / 178 (0.00%)	0 / 27 (0.00%)	0 / 172 (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
Head injury			
subjects affected / exposed	0 / 178 (0.00%)	0 / 27 (0.00%)	1 / 172 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thermal burn			
subjects affected / exposed	0 / 178 (0.00%)	0 / 27 (0.00%)	1 / 172 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Caustic injury			
subjects affected / exposed	0 / 178 (0.00%)	0 / 27 (0.00%)	1 / 172 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pharyngeal injury			
subjects affected / exposed	0 / 178 (0.00%)	1 / 27 (3.70%)	0 / 172 (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
Poisoning			
subjects affected / exposed	0 / 178 (0.00%)	0 / 27 (0.00%)	0 / 172 (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
Skull fracture			
subjects affected / exposed	0 / 178 (0.00%)	0 / 27 (0.00%)	0 / 172 (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
Congenital, familial and genetic disorders			
Arteriovenous malformation			
subjects affected / exposed	0 / 178 (0.00%)	0 / 27 (0.00%)	0 / 172 (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
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	1 / 178 (0.56%)	0 / 27 (0.00%)	0 / 172 (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
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 178 (0.56%)	0 / 27 (0.00%)	0 / 172 (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
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 178 (0.00%)	0 / 27 (0.00%)	0 / 172 (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
Reproductive system and breast disorders			

Testicular retraction			
subjects affected / exposed	0 / 178 (0.00%)	0 / 27 (0.00%)	1 / 172 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Dyspepsia			
subjects affected / exposed	1 / 178 (0.56%)	0 / 27 (0.00%)	0 / 172 (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			
Adenoidal hypertrophy			
subjects affected / exposed	1 / 178 (0.56%)	1 / 27 (3.70%)	0 / 172 (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
Tonsillar disorder			
subjects affected / exposed	0 / 178 (0.00%)	1 / 27 (3.70%)	0 / 172 (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			
Dermal cyst			
subjects affected / exposed	0 / 178 (0.00%)	0 / 27 (0.00%)	0 / 172 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 178 (0.56%)	1 / 27 (3.70%)	2 / 172 (1.16%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngitis			
subjects affected / exposed	2 / 178 (1.12%)	1 / 27 (3.70%)	1 / 172 (0.58%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			

subjects affected / exposed	0 / 178 (0.00%)	0 / 27 (0.00%)	2 / 172 (1.16%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis rotavirus			
subjects affected / exposed	1 / 178 (0.56%)	0 / 27 (0.00%)	0 / 172 (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
Viral infection			
subjects affected / exposed	0 / 178 (0.00%)	1 / 27 (3.70%)	0 / 172 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 178 (0.00%)	0 / 27 (0.00%)	0 / 172 (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
Tonsillitis			
subjects affected / exposed	0 / 178 (0.00%)	0 / 27 (0.00%)	0 / 172 (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
Nasopharyngitis			
subjects affected / exposed	1 / 178 (0.56%)	0 / 27 (0.00%)	0 / 172 (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
Pyelonephritis			
subjects affected / exposed	0 / 178 (0.00%)	0 / 27 (0.00%)	0 / 172 (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
Otitis media			
subjects affected / exposed	1 / 178 (0.56%)	0 / 27 (0.00%)	0 / 172 (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
Pharyngitis			

subjects affected / exposed	0 / 178 (0.00%)	0 / 27 (0.00%)	0 / 172 (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
Pyelonephritis acute			
subjects affected / exposed	0 / 178 (0.00%)	0 / 27 (0.00%)	0 / 172 (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
Salmonellosis			
subjects affected / exposed	0 / 178 (0.00%)	1 / 27 (3.70%)	0 / 172 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 178 (0.00%)	0 / 27 (0.00%)	0 / 172 (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
Vulvitis			
subjects affected / exposed	0 / 178 (0.00%)	0 / 27 (0.00%)	0 / 172 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 178 (0.00%)	0 / 27 (0.00%)	1 / 172 (0.58%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	10Pn-post Group	10Pn Group	Unprimed Group
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 37 (10.81%)	17 / 209 (8.13%)	30 / 336 (8.93%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Concussion			

subjects affected / exposed	0 / 37 (0.00%)	2 / 209 (0.96%)	3 / 336 (0.89%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 37 (0.00%)	0 / 209 (0.00%)	2 / 336 (0.60%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foreign body trauma			
subjects affected / exposed	0 / 37 (0.00%)	1 / 209 (0.48%)	0 / 336 (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
Accidental exposure			
subjects affected / exposed	1 / 37 (2.70%)	1 / 209 (0.48%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			
subjects affected / exposed	0 / 37 (0.00%)	1 / 209 (0.48%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thermal burn			
subjects affected / exposed	0 / 37 (0.00%)	1 / 209 (0.48%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Caustic injury			
subjects affected / exposed	0 / 37 (0.00%)	1 / 209 (0.48%)	0 / 336 (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
Pharyngeal injury			
subjects affected / exposed	0 / 37 (0.00%)	0 / 209 (0.00%)	0 / 336 (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
Poisoning			

subjects affected / exposed	0 / 37 (0.00%)	0 / 209 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skull fracture			
subjects affected / exposed	0 / 37 (0.00%)	0 / 209 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Arteriovenous malformation			
subjects affected / exposed	0 / 37 (0.00%)	0 / 209 (0.00%)	1 / 336 (0.30%)
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			
Febrile convulsion			
subjects affected / exposed	0 / 37 (0.00%)	0 / 209 (0.00%)	2 / 336 (0.60%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 209 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 37 (0.00%)	0 / 209 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Testicular retraction			
subjects affected / exposed	0 / 37 (0.00%)	1 / 209 (0.48%)	0 / 336 (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
Gastrointestinal disorders			

Dyspepsia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 209 (0.00%)	0 / 336 (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
Respiratory, thoracic and mediastinal disorders			
Adenoidal hypertrophy			
subjects affected / exposed	0 / 37 (0.00%)	0 / 209 (0.00%)	0 / 336 (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
Tonsillar disorder			
subjects affected / exposed	0 / 37 (0.00%)	0 / 209 (0.00%)	0 / 336 (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
Skin and subcutaneous tissue disorders			
Dermal cyst			
subjects affected / exposed	0 / 37 (0.00%)	0 / 209 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 37 (2.70%)	3 / 209 (1.44%)	4 / 336 (1.19%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngitis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 209 (0.48%)	4 / 336 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			
subjects affected / exposed	0 / 37 (0.00%)	2 / 209 (0.96%)	2 / 336 (0.60%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis rotavirus			

subjects affected / exposed	1 / 37 (2.70%)	1 / 209 (0.48%)	3 / 336 (0.89%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	0 / 37 (0.00%)	0 / 209 (0.00%)	4 / 336 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 209 (0.00%)	4 / 336 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	1 / 37 (2.70%)	1 / 209 (0.48%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasopharyngitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 209 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 209 (0.00%)	2 / 336 (0.60%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			
subjects affected / exposed	0 / 37 (0.00%)	0 / 209 (0.00%)	0 / 336 (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
Pharyngitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 209 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			

subjects affected / exposed	0 / 37 (0.00%)	0 / 209 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salmonellosis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 209 (0.00%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 37 (0.00%)	0 / 209 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vulvitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 209 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 37 (0.00%)	1 / 209 (0.48%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	10Pn-PD-DiT/ Paracetamol Group	10Pn-PD-DiT Group	10Pn-pre Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	91 / 178 (51.12%)	17 / 27 (62.96%)	105 / 172 (61.05%)
General disorders and administration site conditions			
Pain			
alternative assessment type: Systematic			
subjects affected / exposed	54 / 178 (30.34%)	10 / 27 (37.04%)	79 / 172 (45.93%)
occurrences (all)	54	10	79
Redness			
alternative assessment type: Systematic			

subjects affected / exposed	89 / 178 (50.00%)	9 / 27 (33.33%)	74 / 172 (43.02%)
occurrences (all)	89	9	74
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed	52 / 178 (29.21%)	8 / 27 (29.63%)	50 / 172 (29.07%)
occurrences (all)	52	8	50
Drowsiness			
subjects affected / exposed	91 / 178 (51.12%)	11 / 27 (40.74%)	84 / 172 (48.84%)
occurrences (all)	91	11	84
Fever/(rectal temperature $\geq 38.0^{\circ}\text{C}$)			
alternative assessment type: Systematic			
subjects affected / exposed	64 / 178 (35.96%)	14 / 27 (51.85%)	100 / 172 (58.14%)
occurrences (all)	64	14	100
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed	86 / 178 (48.31%)	17 / 27 (62.96%)	105 / 172 (61.05%)
occurrences (all)	86	17	105
Loss of appetite			
subjects affected / exposed	47 / 178 (26.40%)	8 / 27 (29.63%)	46 / 172 (26.74%)
occurrences (all)	47	8	46
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 178 (1.12%)	3 / 27 (11.11%)	0 / 172 (0.00%)
occurrences (all)	2	3	0

Non-serious adverse events	10Pn-post Group	10Pn Group	Unprimed Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 37 (51.35%)	124 / 209 (59.33%)	147 / 336 (43.75%)
General disorders and administration site conditions			
Pain			
alternative assessment type: Systematic			
subjects affected / exposed	19 / 37 (51.35%)	98 / 209 (46.89%)	114 / 336 (33.93%)
occurrences (all)	19	98	114
Redness			
alternative assessment type: Systematic			

subjects affected / exposed	12 / 37 (32.43%)	86 / 209 (41.15%)	146 / 336 (43.45%)
occurrences (all)	12	86	146
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed	13 / 37 (35.14%)	63 / 209 (30.14%)	71 / 336 (21.13%)
occurrences (all)	13	63	71
Drowsiness			
subjects affected / exposed	18 / 37 (48.65%)	102 / 209 (48.80%)	146 / 336 (43.45%)
occurrences (all)	18	102	146
Fever/(rectal temperature $\geq 38.0^{\circ}\text{C}$)			
alternative assessment type: Systematic			
subjects affected / exposed	16 / 37 (43.24%)	116 / 209 (55.50%)	146 / 336 (43.45%)
occurrences (all)	16	116	146
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed	19 / 37 (51.35%)	124 / 209 (59.33%)	147 / 336 (43.75%)
occurrences (all)	19	124	147
Loss of appetite			
subjects affected / exposed	10 / 37 (27.03%)	56 / 209 (26.79%)	88 / 336 (26.19%)
occurrences (all)	10	56	88
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 37 (0.00%)	5 / 209 (2.39%)	0 / 336 (0.00%)
occurrences (all)	0	5	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 April 2007	<p>The amendment is written in response to comments given by the Czech Republic Authorities.</p> <p>In addition the following changes have been included :</p> <ul style="list-style-type: none">• Change in Central Study Coordinator.• The microbiological procedures to assess the occurrence of other bacteriological pathogens have been described in more detail.• To avoid confusion regarding the administration of DTPa-HBV-IPV/Hib vaccine, this section has been rewritten.• Clarification of attribution of subject and treatment numbers to the subjects in the unprimed group.• Estimation of sample size of unprimed group has been clarified.• Analysis of carriage has been updated in accordance with the microbiological procedures used to assess the occurrence of other bacteriological pathogens.• Update of literature references.
19 July 2007	<p>As groups were defined as primed and unprimed with regard to pneumococcal vaccination it seemed obvious that the unprimed group was supposed not to have been vaccinated with any pneumococcal vaccine before enrolment. To ensure that the subjects that had previously received a pneumococcal vaccine would not be enrolled or that subjects that received a pneumococcal vaccine during the study would be eliminated, this criterium was added.</p> <ul style="list-style-type: none">• Serology testing with regard to pneumococcal antibodies for the unprimed group was considered scientifically relevant to set a baseline for the interpretation of the carriage results of the primed group. In addition serology testing with regard to antibodies against the co-administered vaccine was added for both groups.• As GSK Biologicals is considering an extension study, the possibility to participate in a long-term follow-up study should be addressed at the concluding visit of this study.• For the unprimed group the power to detect group difference in carriage of <i>S. pneumoniae</i> and <i>H. influenzae</i> was adjusted to better reflect what was already observed in POET (study Undeca-Pn-010 [347414/010])• Update of literature references.

24 September 2007	<p>The results of the primary vaccination study 10PN-PD-DIT-010 have shown that paracetamol (acetaminophen) given as a prophylactic treatment at the time of vaccination significantly reduced the incidence of febrile reactions following vaccination with GSK Biologicals. 10-valent pneumococcal conjugate vaccine coadministered with DTPa-HBV-IPV/Hib (Infanrix hexa) vaccine at 3, 4 and 5 months of age and GSK Biologicals. oral live attenuated HRV (Rotarix) vaccine at 3 and 4 months of age [41.6% of subjects experienced fever $\geq 38^{\circ}\text{C}$ (rectal temperature) in the antipyretic group versus 66.1% of subjects in the non-antipyretic group].</p> <p>In addition, the study also showed that the use of prophylactic paracetamol seemed to interfere with the primary immune response. The reason for a decrease in the immune response may relate to a reduction of the inflammatory signals that attract the dendritic cells to the injection sites, such that fewer and/or less activated dendritic cells reach the draining lymph nodes, resulting in a reduced B cell stimulation and lower antibody concentrations.</p> <p>In addition, it cannot be excluded that the induction of memory cells (T cells and B cells) is also affected by the prophylactic administration of paracetamol, which may prevent children from developing an adequate booster immune response. Therefore, the prophylactic administration of paracetamol during the booster phase will be stopped.</p> <p>Approximately 50% of the subjects were already enrolled and vaccinated according to the protocol (with or without prophylactic administration of paracetamol). The immune responses of all vaccinated children will be carefully monitored and the need for additional doses will be evaluated after the booster dose. Additional doses of vaccines will be made available, when necessary.</p>
18 January 2008	<ul style="list-style-type: none"> • Details about the planned interim analysis. • Planning of a second interim analysis. • Correction in the EudraCT number. <p>In addition, strikethrough text related to previous amendments has been removed. Furthermore, all bold italic text related to previous amendments has been changed into normal text. Those additional changes are documented below following the changes for which this fourth amendment has been developed.</p>
03 February 2009	<p>The study protocol has been amended for the following reason:</p> <ul style="list-style-type: none"> - The availability of the results of the microbiological assessments on nasopharyngeal carriage up to Visit 3 has been delayed. Therefore there is a need to cancel second interim analysis on carriage based on the time point V3 and to involve additional other laboratories designated by GSK Biologicals to speed up the microbiological work. • The fact that microbial assessments can be performed not only at the regional laboratory in the Czech Republic, but also at a laboratory designated by GSK Biologicals, was added. • The planned second interim analysis will not be performed anymore.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported