Clinical trial results:
A phase III long-term follow-up study to assess antibody persistence and immunological memory in children previously vaccinated with four doses of pneumococcal conjugate vaccine in primary vaccination study 10PN-PD-DIT-001 and booster vaccination study 10PN-PD-DIT-007 and assessment of immune responses following a 2-dose catch-up immunization with GlaxoSmithKline (GSK) Biologicals' 10-valent pneumococcal vaccine in the 6th year of life.

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

Summary

EudraCT number	2007-005392-34
Trial protocol	PL
Global end of trial date	21 November 2011

Results information

Result version number	v2
This version publication date	21 April 2016
First version publication date	30 July 2015
Version creation reason	• Correction of full data set Data correction due to a system error in EudraCT – Results + Some typo errors

Trial information

Trial identification

Sponsor protocol code	111345, 111346, 111347

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00624819
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)	Yes
EMA paediatric investigation plan number(s)	EMEA-000673-PIP01-09

Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 October 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 November 2011
Global end of trial reached?	Yes
Global end of trial date	21 November 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

•To assess the antibody persistence 1 year post booster (12 to 14 months), 2 years post booster (24 to 26 months) and 4 years post booster (48 to 50 months) following a four dose vaccination course with a pneumococcal conjugate vaccines.

Protection of trial subjects:

The study corresponds to 3 studies by GSK Biologicals, 1st, study 111345 (Year [Y] 1 persistence follow-up), 2nd, study 111346, and 3rd, study 111347, taking place, respectively, at 1, 2 & 4 years post Dose 1 in Study 10PN-PD-DIT-001. Studies 111345 and 111346 were persistence and safety follow-ups starting at the end of study 10PN-PD-DIT-007 (EudraCT: 2006-001628-38), respectively taking place at approximately one and 2 years post Dose 1 of 10Pn vaccine in study 10PN-PD-DIT-001 (105553). Study 111347 included 2 phases, a persistence phase taking place at approximately 4 years post Dose 1 of 10Pn vaccine in study 10PN-PD-DIT-001 (105553) followed by an immunological memory phase of up 3 months duration. In the persistence phases of the study, during subjects were followed up for serious adverse events (SAEs) related to study procedures, previous study vaccination or non-participation at a defined visit. This SAE follow-up started at the last follow-up contact in study 10PN-PD-DIT-007 and ended at the Y4 persistence follow-up in study 111347.
In the immunological memory phase of the study, subjects were supervised for solicited local and general symptoms and unsolicited adverse events (AEs) after vaccination/product administration with appropriate medical treatment readily available. The 10Pn vaccine was administered by qualified and trained personnel and only to eligible subjects that had no contraindications to any components of the vaccine. Reports of SAEs were collected throughout this phase and assessed as regards severity, outcome and relation to vaccination.

Background therapy: -
Evidence for comparator: -

Actual start date of recruitment	03 March 2008
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 524

Worldwide total number of subjects	524
EEA total number of subjects	524

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)	0
Children (2-11 years)	524
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:

Primed groups included 10Pn-vaccinated subjects in study 10PN-PD-DIT-007. The Unprimed Group included subjects unprimed with any pneumococcal vaccine age-matched with primed groups. The study included 3 sub-studies, 111345, 111346 & 111347, corresponding to Year 1, 2 & 4 time points post Dose 1 in Study 10PN-PD-DIT-001.

Pre-assignment

Screening details:

At screening, subjects with previous participation in 10PN-PD-DIT-007 (2006-001628-38) study were invited to join this study. Informed consent was obtained and signed from subjects' parents/guardians, check for inclusion/exclusion criteria and contraindications/precautions was performed, and medical history of subjects was collected.

Period 1

Period 1 title	Y1 Persistence - Study 111345
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Primed 10Pn-10Pn Group

Arm description:

This group consisted of subjects primed with 10Pn-PD-DiT vaccine in the 10PN-PD-DIT-001 (1105553) and 007 (107046) studies (EudraCT: 2005-003300-11 & 2006-001628-38). In 105553 study, subjects had been primed with 3 doses of 10Pn vaccine at 2, 3 and 4 months of age co-administered with DTPa-related vaccines. In 107046 study, subjects had received a booster dose of 10Pn vaccine at 12-18 months of age co-administered with DTPa-HBV-IPV/Hib vaccine. In this study, in the Year 4 111347 study, subjects received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of 10Pn-PD-DiT vaccine intramuscularly in the right of left deltoid muscle. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix™) and/or against varicella (a single dose of Varilrix™). These vaccines were to be given after the blood sampling procedure.

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

Dosage and administration details:

One dose administered in the left thigh or deltoid at 64-68 months of age (= Day 0 in the 111347 study = Year 4 in study 10PN-PD-DIT-001 [105553])

Investigational medicinal product name	Varilrix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

One dose was proposed post blood sampling procedure to subjects in the Primed 10Pn-10Pn, Primed 7Pn-7Pn, and Primed 7Pn-10Pn groups.

Investigational medicinal product name	Havrix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection

Routes of administration	Intramuscular use

Dosage and administration details:

Two doses were proposed post blood sampling procedure to subjects in the Primed 10Pn-10Pn, Primed 7Pn-7Pn, and Primed 7Pn-10Pn groups.

Arm title	Primed 7Pn-7Pn Group

Arm description:

This group consisted of subjects vaccinated with 7Pn (Prevenar™) vaccine in the 10PN-PD-DIT-001 (105553) and 007 (107046) studies (EudraCT: 2005-003300-11 & 2006-001628-38). In 105553 study, subjects had been primed with 3 doses of 7Pn vaccine at 2, 3 and 4 months of age co-administered with DTPa-related vaccines. In 107046 study, subjects had received a booster dose at 12-18 months of age of 7Pn vaccine co-administered with DTPa-HBV-IPV/Hib vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one dose of 10Pn-PD-DiT vaccine intramuscularly in the right of left deltoid muscle. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix™ and/or against varicella (a single dose of Varilrix™). These vaccines were to be given after the blood sampling procedure.

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

Dosage and administration details:

One dose administered in the left thigh or deltoid at 64-68 months of age (= Day 0 in the 111347 study = Year 4 in study 10PN-PD-DIT-001 [105553])

Investigational medicinal product name	Varilrix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

One dose was proposed post blood sampling procedure to subjects in the Primed 10Pn-10Pn, Primed 7Pn-7Pn, and Primed 7Pn-10Pn groups.

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

Dosage and administration details:

Two doses were proposed post blood sampling procedure to subjects in the Primed 10Pn-10Pn, Primed 7Pn-7Pn, and Primed 7Pn-10Pn groups.

Arm title	Primed 7Pn-10Pn Group

Arm description:

This group consisted of subjects vaccinated with 7Pn (Prevenar™) and 10Pn-PD-DiT vaccines in the 10PN-PD-DIT-001 (105553) and 10PN-PD-DIT-007 (107046) studies (EudraCT: 2005-003300-11 and 2006-001628-38). In 105553 study, subjects had been primed with 3 doses 7Pn vaccine at 2, 3 and 4 months of age co-administered with DTPa-related vaccines. In the 107046 study, subjects had received at 12-18 months of age a booster dose of 10Pn-PD-DiT vaccine co-administered with DTPa-HBV-IPV/Hib vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of 10Pn-PD-DiT vaccine intramuscularly in the right of left deltoid muscle. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix™ and/or against varicella (a single dose of Varilrix™). These vaccines were to be given after the blood sampling procedure.

Arm type	Experimental

Investigational medicinal product name	10 valent streptococcus pneumoniae conjugate vaccine
Investigational medicinal product code	
Other name	10Pn-PD-DiT, Synflorix™ (by GSK Biologicals)
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose administered in the left thigh or deltoid at 64-68 months of age (= Day 0 in the 111347 study = Year 4 in study 10PN-PD-DIT-001 [105553])

Investigational medicinal product name	Varilrix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

One dose was proposed post blood sampling procedure to subjects in the Primed 10Pn-10Pn, Primed 7Pn-7Pn, and Primed 7Pn-10Pn groups.

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

Dosage and administration details:

Two doses were proposed post blood sampling procedure to subjects in the Primed 10Pn-10Pn, Primed 7Pn-7Pn, and Primed 7Pn-10Pn groups.

Number of subjects in period 1	Primed 10Pn-10Pn Group	Primed 7Pn-7Pn Group	Primed 7Pn-10Pn Group
Started	391	31	102
Completed	391	31	102

Period 2

Period 2 title	Y2 Persistence - Study 111346
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Primed 10Pn-10Pn Group

Arm description:

This group consisted of subjects primed with 10Pn-PD-DiT vaccine in the 10PN-PD-DIT-001 (1105553) and 007 (107046) studies (EudraCT: 2005-003300-11 & 2006-001628-38). In 105553 study, subjects had been primed with 3 doses of 10Pn vaccine at 2, 3 and 4 months of age co-administered with DTPa-related vaccines. In 107046 study, subjects had received a booster dose of 10Pn vaccine at 12-18 months of age co-administered with DTPa-HBV-IPV/Hib vaccine. In this study, in the Year 4 111347

study, subjects received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of 10Pn-PD-DiT vaccine intramuscularly in the right of left deltoid muscle. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix™) and/or against varicella (a single dose of Varilrix™). These vaccines were to be given after the blood sampling procedure.

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

Dosage and administration details:

One dose administered in the left thigh or deltoid at 64-68 months of age (= Day 0 in the 111347 study = Year 4 in study 10PN-PD-DIT-001 [105553])

Investigational medicinal product name	Varilrix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

One dose was proposed post blood sampling procedure to subjects in the Primed 10Pn-10Pn, Primed 7Pn-7Pn, and Primed 7Pn-10Pn groups.

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

Dosage and administration details:

Two doses were proposed post blood sampling procedure to subjects in the Primed 10Pn-10Pn, Primed 7Pn-7Pn, and Primed 7Pn-10Pn groups.

Arm title	Primed 7Pn-7Pn Group

Arm description:

This group consisted of subjects vaccinated with 7Pn (Prevenar™) vaccine in the 10PN-PD-DIT-001 (105553) and 007 (107046) studies (EudraCT: 2005-003300-11 & 2006-001628-38). In 105553 study, subjects had been primed with 3 doses of 7Pn vaccine at 2, 3 and 4 months of age co-administered with DTPa-related vaccines. In 107046 study, subjects had received a booster dose at 12-18 months of age of 7Pn vaccine co-administered with DTPa-HBV-IPV/Hib vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one dose of 10Pn-PD-DiT vaccine intramuscularly in the right of left deltoid muscle. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix™ and/or against varicella (a single dose of Varilrix™). These vaccines were to be given after the blood sampling procedure.

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

Dosage and administration details:

One dose administered in the left thigh or deltoid at 64-68 months of age (= Day 0 in the 111347 study = Year 4 in study 10PN-PD-DIT-001 [105553])

Investigational medicinal product name	Varilrix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

One dose was proposed post blood sampling procedure to subjects in the Primed 10Pn-10Pn, Primed

7Pn-7Pn, and Primed 7Pn-10Pn groups.

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

Dosage and administration details:

Two doses were proposed post blood sampling procedure to subjects in the Primed 10Pn-10Pn, Primed 7Pn-7Pn, and Primed 7Pn-10Pn groups.

Arm title	Primed 7Pn-10Pn Group

Arm description:

This group consisted of subjects vaccinated with 7Pn (Prevenar™) and 10Pn-PD-DiT vaccines in the 10PN-PD-DIT-001 (105553) and 10PN-PD-DIT-007 (107046) studies (EudraCT: 2005-003300-11 and 2006-001628-38). In 105553 study, subjects had been primed with 3 doses 7Pn vaccine at 2, 3 and 4 months of age co-administered with DTPa-related vaccines. In the 107046 study, subjects had received at 12-18 months of age a booster dose of 10Pn-PD-DiT vaccine co-administered with DTPa-HBV-IPV/Hib vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of 10Pn-PD-DiT vaccine intramuscularly in the right of left deltoid muscle. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix™ and/or against varicella (a single dose of Varilrix™). These vaccines were to be given after the blood sampling procedure.

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

Dosage and administration details:

One dose administered in the left thigh or deltoid at 64-68 months of age (= Day 0 in the 111347 study = Year 4 in study 10PN-PD-DIT-001 [105553])

Investigational medicinal product name	Varilrix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

One dose was proposed post blood sampling procedure to subjects in the Primed 10Pn-10Pn, Primed 7Pn-7Pn, and Primed 7Pn-10Pn groups.

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

Dosage and administration details:

Two doses were proposed post blood sampling procedure to subjects in the Primed 10Pn-10Pn, Primed 7Pn-7Pn, and Primed 7Pn-10Pn groups.

Number of subjects in period 2[1]	Primed 10Pn-10Pn Group	Primed 7Pn-7Pn Group	Primed 7Pn-10Pn Group
Started	370	31	96
Completed	370	31	96

Notes:

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

Justification: Out of the 524 subjects who participated to the year 1 persistence analysis in study 111345, 497 returned participating to the year 2 persistence analysis in study 111346 and 27 were lost to follow up.

Period 3

Period 3 title	Y4 Persistence - Pt 1 Study 111347
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Primed 10Pn-10Pn Group

Arm description:

This group consisted of subjects primed with 10Pn-PD-DiT vaccine in the 10PN-PD-DIT-001 (1105553) and 007 (107046) studies (EudraCT: 2005-003300-11 & 2006-001628-38). In 105553 study, subjects had been primed with 3 doses of 10Pn vaccine at 2, 3 and 4 months of age co-administered with DTPa-related vaccines. In 107046 study, subjects had received a booster dose of 10Pn vaccine at 12-18 months of age co-administered with DTPa-HBV-IPV/Hib vaccine. In this study, in the Year 4 111347 study, subjects received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of 10Pn-PD-DiT vaccine intramuscularly in the right of left deltoid muscle. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix™) and/or against varicella (a single dose of Varilrix™). These vaccines were to be given after the blood sampling procedure.

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

Dosage and administration details:

One dose administered in the left thigh or deltoid at 64-68 months of age (= Day 0 in the 111347 study = Year 4 in study 10PN-PD-DIT-001 [105553])

Investigational medicinal product name	Varilrix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

One dose was proposed post blood sampling procedure to subjects in the Primed 10Pn-10Pn, Primed 7Pn-7Pn, and Primed 7Pn-10Pn groups.

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

Dosage and administration details:

Two doses were proposed post blood sampling procedure to subjects in the Primed 10Pn-10Pn, Primed 7Pn-7Pn, and Primed 7Pn-10Pn groups.

Arm title	Primed 7Pn-7Pn Group

Arm description:

This group consisted of subjects vaccinated with 7Pn (Prevenar™) vaccine in the 10PN-PD-DIT-001 (105553) and 007 (107046) studies (EudraCT: 2005-003300-11 & 2006-001628-38). In 105553 study, subjects had been primed with 3 doses of 7Pn vaccine at 2, 3 and 4 months of age co-administered with DTPa-related vaccines. In 107046 study, subjects had received a booster dose at 12-18 months of age of 7Pn vaccine co-administered with DTPa-HBV-IPV/Hib vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one dose of 10Pn-PD-DiT vaccine intramuscularly in the right of left deltoid muscle. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix™ and/or against varicella (a single dose of Varilrix™). These vaccines were to be given after the blood sampling procedure.

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

Dosage and administration details:

One dose administered in the left thigh or deltoid at 64-68 months of age (= Day 0 in the 111347 study = Year 4 in study 10PN-PD-DIT-001 [105553])

Investigational medicinal product name	Varilrix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

One dose was proposed post blood sampling procedure to subjects in the Primed 10Pn-10Pn, Primed 7Pn-7Pn, and Primed 7Pn-10Pn groups.

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

Dosage and administration details:

Two doses were proposed post blood sampling procedure to subjects in the Primed 10Pn-10Pn, Primed 7Pn-7Pn, and Primed 7Pn-10Pn groups.

Arm title	Primed 7Pn-10Pn Group

Arm description:

This group consisted of subjects vaccinated with 7Pn (Prevenar™) and 10Pn-PD-DiT vaccines in the 10PN-PD-DIT-001 (105553) and 10PN-PD-DIT-007 (107046) studies (EudraCT: 2005-003300-11 and 2006-001628-38). In 105553 study, subjects had been primed with 3 doses 7Pn vaccine at 2, 3 and 4 months of age co-administered with DTPa-related vaccines. In the 107046 study, subjects had received at 12-18 months of age a booster dose of 10Pn-PD-DiT vaccine co-administered with DTPa-HBV-IPV/Hib vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of 10Pn-PD-DiT vaccine intramuscularly in the right of left deltoid muscle. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix™ and/or against varicella (a single dose of Varilrix™). These vaccines were to be given after the blood sampling procedure.

Arm type	Experimental

Investigational medicinal product name	10 valent streptococcus pneumoniae conjugate vaccine
Investigational medicinal product code	
Other name	10Pn-PD-DiT, Synflorix™ (by GSK Biologicals)
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose administered in the left thigh or deltoid at 64-68 months of age (= Day 0 in the 111347 study = Year 4 in study 10PN-PD-DIT-001 [105553])

Investigational medicinal product name	Varilrix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

One dose was proposed post blood sampling procedure to subjects in the Primed 10Pn-10Pn, Primed 7Pn-7Pn, and Primed 7Pn-10Pn groups.

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

Dosage and administration details:

Two doses were proposed post blood sampling procedure to subjects in the Primed 10Pn-10Pn, Primed 7Pn-7Pn, and Primed 7Pn-10Pn groups.

Number of subjects in period 3[2]	Primed 10Pn-10Pn Group	Primed 7Pn-7Pn Group	Primed 7Pn-10Pn Group
Started	316	25	85
Completed	316	25	85

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Out of the 497 subjects who participated to the year 2 persistence analysis in study 111346, 426 returned participating to the year 4 persistence analysis in study 111347 and 71 were lost to follow up.

Period 4

Period 4 title	Immunological Memory – Pt 2 Study 111347
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes

Arm title	Primed 10Pn-10Pn Group

Arm description:

This group consisted of subjects primed with 10Pn-PD-DiT vaccine in the 10PN-PD-DIT-001 (1105553) and 007 (107046) studies (EudraCT: 2005-003300-11 & 2006-001628-38). In 105553 study, subjects had been primed with 3 doses of 10Pn vaccine at 2, 3 and 4 months of age co-administered with DTPa-related vaccines. In 107046 study, subjects had received a booster dose of 10Pn vaccine at 12-18 months of age co-administered with DTPa-HBV-IPV/Hib vaccine. In this study, in the Year 4 111347 study, subjects received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of 10Pn-PD-DiT vaccine intramuscularly in the right of left deltoid muscle. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix™) and/or against varicella (a single dose of Varilrix™). These vaccines were to be given after the blood sampling procedure.

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

Dosage and administration details:

One dose administered in the left thigh or deltoid at 64-68 months of age (= Day 0 in the 111347 study = Year 4 in study 10PN-PD-DIT-001 [105553])

Investigational medicinal product name	Varilrix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

One dose was proposed post blood sampling procedure to subjects in the Primed 10Pn-10Pn, Primed 7Pn-7Pn, and Primed 7Pn-10Pn groups.

Investigational medicinal product name	Havrix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Two doses were proposed post blood sampling procedure to subjects in the Primed 10Pn-10Pn, Primed 7Pn-7Pn, and Primed 7Pn-10Pn groups.

Arm title	Primed 7Pn-7Pn Group

Arm description:

This group consisted of subjects vaccinated with 7Pn (Prevenar™) vaccine in the 10PN-PD-DIT-001 (105553) and 007 (107046) studies (EudraCT: 2005-003300-11 & 2006-001628-38). In 105553 study, subjects had been primed with 3 doses of 7Pn vaccine at 2, 3 and 4 months of age co-administered with DTPa-related vaccines. In 107046 study, subjects had received a booster dose at 12-18 months of age of 7Pn vaccine co-administered with DTPa-HBV-IPV/Hib vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one dose of 10Pn-PD-DiT vaccine intramuscularly in the right of left deltoid muscle. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix™ and/or against varicella (a single dose of Varilrix™). These vaccines were to be given after the blood sampling procedure.

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

Dosage and administration details:

One dose administered in the left thigh or deltoid at 64-68 months of age (= Day 0 in the 111347 study = Year 4 in study 10PN-PD-DIT-001 [105553])

Investigational medicinal product name	Varilrix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

One dose was proposed post blood sampling procedure to subjects in the Primed 10Pn-10Pn, Primed 7Pn-7Pn, and Primed 7Pn-10Pn groups.

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

Dosage and administration details:

Two doses were proposed post blood sampling procedure to subjects in the Primed 10Pn-10Pn, Primed 7Pn-7Pn, and Primed 7Pn-10Pn groups.

Arm title	Primed 7Pn-10Pn Group

Arm description:

This group consisted of subjects vaccinated with 7Pn (Prevenar™) and 10Pn-PD-DiT vaccines in the 10PN-PD-DIT-001 (105553) and 10PN-PD-DIT-007 (107046) studies (EudraCT: 2005-003300-11 and 2006-001628-38). In 105553 study, subjects had been primed with 3 doses 7Pn vaccine at 2, 3 and 4 months of age co-administered with DTPa-related vaccines. In the 107046 study, subjects had received at 12-18 months of age a booster dose of 10Pn-PD-DiT vaccine co-administered with DTPa-HBV-IPV/Hib vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of 10Pn-PD-DiT vaccine intramuscularly in the right of left deltoid muscle. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix™ and/or against varicella (a single dose of Varilrix™). These vaccines were to be given after the blood sampling procedure.

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

Dosage and administration details:

One dose administered in the left thigh or deltoid at 64-68 months of age (= Day 0 in the 111347 study = Year 4 in study 10PN-PD-DIT-001 [105553])

Investigational medicinal product name	Varilrix™
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

One dose was proposed post blood sampling procedure to subjects in the Primed 10Pn-10Pn, Primed 7Pn-7Pn, and Primed 7Pn-10Pn groups.

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

Dosage and administration details:

Two doses were proposed post blood sampling procedure to subjects in the Primed 10Pn-10Pn, Primed 7Pn-7Pn, and Primed 7Pn-10Pn groups.

Number of subjects in period 4[3]	Primed 10Pn-10Pn Group	Primed 7Pn-7Pn Group	Primed 7Pn-10Pn Group
Started	264	20	65
Completed	263	19	64
Not completed	1	1	1
Parents' Decision	-	-	1
Lost to follow-up	1	1	-

Notes:

[3] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Out of the 426 subjects who participated to the year 4 persistence analysis in study 111347, 349 participated to the Immunological Memory phase in this study 111347 and 77 were lost to follow up/did not participate to this 2nd phase. Kindly note that to these 349 subjects, 100 additional subjects were added, who constituted an Unprimed Group. No withdrawal was reported for this group, which included 53 females and 47 males and in which mean age was 65.4 months (SD: 1.31 months).

Baseline characteristics

Reporting groups	
Reporting group title	Primed 10Pn-10Pn Group

Reporting group description:

This group consisted of subjects primed with 10Pn-PD-DiT vaccine in the 10PN-PD-DIT-001 (1105553) and 007 (107046) studies (EudraCT: 2005-003300-11 & 2006-001628-38). In 105553 study, subjects had been primed with 3 doses of 10Pn vaccine at 2, 3 and 4 months of age co-administered with DTPa-related vaccines. In 107046 study, subjects had received a booster dose of 10Pn vaccine at 12-18 months of age co-administered with DTPa-HBV-IPV/Hib vaccine. In this study, in the Year 4 111347 study, subjects received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of 10Pn-PD-DiT vaccine intramuscularly in the right of left deltoid muscle. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix™) and/or against varicella (a single dose of Varilrix™). These vaccines were to be given after the blood sampling procedure.

Reporting group title	Primed 7Pn-7Pn Group

Reporting group description:

This group consisted of subjects vaccinated with 7Pn (Prevenar™) vaccine in the 10PN-PD-DIT-001 (105553) and 007 (107046) studies (EudraCT: 2005-003300-11 & 2006-001628-38). In 105553 study, subjects had been primed with 3 doses of 7Pn vaccine at 2, 3 and 4 months of age co-administered with DTPa-related vaccines. In 107046 study, subjects had received a booster dose at 12-18 months of age of 7Pn vaccine co-administered with DTPa-HBV-IPV/Hib vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one dose of 10Pn-PD-DiT vaccine intramuscularly in the right of left deltoid muscle. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix™ and/or against varicella (a single dose of Varilrix™). These vaccines were to be given after the blood sampling procedure.

Reporting group title	Primed 7Pn-10Pn Group

Reporting group description:

This group consisted of subjects vaccinated with 7Pn (Prevenar™) and 10Pn-PD-DiT vaccines in the 10PN-PD-DIT-001 (105553) and 10PN-PD-DIT-007 (107046) studies (EudraCT: 2005-003300-11 and 2006-001628-38). In 105553 study, subjects had been primed with 3 doses 7Pn vaccine at 2, 3 and 4 months of age co-administered with DTPa-related vaccines. In the 107046 study, subjects had received at 12-18 months of age a booster dose of 10Pn-PD-DiT vaccine co-administered with DTPa-HBV-IPV/Hib vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of 10Pn-PD-DiT vaccine intramuscularly in the right of left deltoid muscle. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix™ and/or against varicella (a single dose of Varilrix™). These vaccines were to be given after the blood sampling procedure.

Reporting group values	Primed 10Pn-10Pn Group	Primed 7Pn-7Pn Group	Primed 7Pn-10Pn Group
Number of subjects	391	31	102
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	29.1	29	29.1

standard deviation	± 0.88	± 0.75	± 0.81

Gender categorical Units: Subjects			
Female	203	14	52
Male	188	17	50

Reporting group values	Total		
Number of subjects	524		
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	269		
Male	255		

End points reporting groups

Reporting group title	Primed 10Pn-10Pn Group

Reporting group description:

This group consisted of subjects primed with 10Pn-PD-DiT vaccine in the 10PN-PD-DIT-001 (1105553) and 007 (107046) studies (EudraCT: 2005-003300-11 & 2006-001628-38). In 105553 study, subjects had been primed with 3 doses of 10Pn vaccine at 2, 3 and 4 months of age co-administered with DTPa-related vaccines. In 107046 study, subjects had received a booster dose of 10Pn vaccine at 12-18 months of age co-administered with DTPa-HBV-IPV/Hib vaccine. In this study, in the Year 4 111347 study, subjects received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of 10Pn-PD-DiT vaccine intramuscularly in the right of left deltoid muscle. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix™) and/or against varicella (a single dose of Varilrix™). These vaccines were to be given after the blood sampling procedure.

Reporting group title	Primed 7Pn-7Pn Group

Reporting group description:

This group consisted of subjects vaccinated with 7Pn (Prevenar™) vaccine in the 10PN-PD-DIT-001 (105553) and 007 (107046) studies (EudraCT: 2005-003300-11 & 2006-001628-38). In 105553 study, subjects had been primed with 3 doses of 7Pn vaccine at 2, 3 and 4 months of age co-administered with DTPa-related vaccines. In 107046 study, subjects had received a booster dose at 12-18 months of age of 7Pn vaccine co-administered with DTPa-HBV-IPV/Hib vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one dose of 10Pn-PD-DiT vaccine intramuscularly in the right of left deltoid muscle. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix™ and/or against varicella (a single dose of Varilrix™). These vaccines were to be given after the blood sampling procedure.

Reporting group title	Primed 7Pn-10Pn Group

Reporting group description:

This group consisted of subjects vaccinated with 7Pn (Prevenar™) and 10Pn-PD-DiT vaccines in the 10PN-PD-DIT-001 (105553) and 10PN-PD-DIT-007 (107046) studies (EudraCT: 2005-003300-11 and 2006-001628-38). In 105553 study, subjects had been primed with 3 doses 7Pn vaccine at 2, 3 and 4 months of age co-administered with DTPa-related vaccines. In the 107046 study, subjects had received at 12-18 months of age a booster dose of 10Pn-PD-DiT vaccine co-administered with DTPa-HBV-IPV/Hib vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of 10Pn-PD-DiT vaccine intramuscularly in the right of left deltoid muscle. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix™ and/or against varicella (a single dose of Varilrix™). These vaccines were to be given after the blood sampling procedure.

Reporting group title	Primed 10Pn-10Pn Group

Reporting group description:

This group consisted of subjects primed with 10Pn-PD-DiT vaccine in the 10PN-PD-DIT-001 (1105553) and 007 (107046) studies (EudraCT: 2005-003300-11 & 2006-001628-38). In 105553 study, subjects had been primed with 3 doses of 10Pn vaccine at 2, 3 and 4 months of age co-administered with DTPa-related vaccines. In 107046 study, subjects had received a booster dose of 10Pn vaccine at 12-18 months of age co-administered with DTPa-HBV-IPV/Hib vaccine. In this study, in the Year 4 111347 study, subjects received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of 10Pn-PD-DiT vaccine intramuscularly in the right of left deltoid muscle. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix™) and/or against varicella (a single dose of Varilrix™). These vaccines were to be given after the blood sampling procedure.

Reporting group title	Primed 7Pn-7Pn Group

Reporting group description:

This group consisted of subjects vaccinated with 7Pn (Prevenar™) vaccine in the 10PN-PD-DIT-001 (105553) and 007 (107046) studies (EudraCT: 2005-003300-11 & 2006-001628-38). In 105553 study, subjects had been primed with 3 doses of 7Pn vaccine at 2, 3 and 4 months of age co-administered with DTPa-related vaccines. In 107046 study, subjects had received a booster dose at 12-18 months of age of 7Pn vaccine co-administered with DTPa-HBV-IPV/Hib vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one dose of 10Pn-PD-DiT vaccine intramuscularly in the right of left deltoid muscle. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix™ and/or against varicella (a single dose of Varilrix™). These vaccines were to be given after the blood sampling procedure.

Reporting group title	Primed 7Pn-10Pn Group

Reporting group description:

This group consisted of subjects vaccinated with 7Pn (Prevenar™) and 10Pn-PD-DiT vaccines in the

10PN-PD-DIT-001 (105553) and 10PN-PD-DIT-007 (107046) studies (EudraCT: 2005-003300-11 and 2006-001628-38). In 105553 study, subjects had been primed with 3 doses 7Pn vaccine at 2, 3 and 4 months of age co-administered with DTPa-related vaccines. In the 107046 study, subjects had received at 12-18 months of age a booster dose of 10Pn-PD-DiT vaccine co-administered with DTPa-HBV-IPV/Hib vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of 10Pn-PD-DiT vaccine intramuscularly in the right of left deltoid muscle. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix™ and/or against varicella (a single dose of Varilrix™). These vaccines were to be given after the blood sampling procedure.

Reporting group title	Primed 10Pn-10Pn Group

Reporting group description:

This group consisted of subjects primed with 10Pn-PD-DiT vaccine in the 10PN-PD-DIT-001 (1105553) and 007 (107046) studies (EudraCT: 2005-003300-11 & 2006-001628-38). In 105553 study, subjects had been primed with 3 doses of 10Pn vaccine at 2, 3 and 4 months of age co-administered with DTPa-related vaccines. In 107046 study, subjects had received a booster dose of 10Pn vaccine at 12-18 months of age co-administered with DTPa-HBV-IPV/Hib vaccine. In this study, in the Year 4 111347 study, subjects received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of 10Pn-PD-DiT vaccine intramuscularly in the right of left deltoid muscle. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix™) and/or against varicella (a single dose of Varilrix™). These vaccines were to be given after the blood sampling procedure.

Reporting group title	Primed 7Pn-7Pn Group

Reporting group description:

This group consisted of subjects vaccinated with 7Pn (Prevenar™) vaccine in the 10PN-PD-DIT-001 (105553) and 007 (107046) studies (EudraCT: 2005-003300-11 & 2006-001628-38). In 105553 study, subjects had been primed with 3 doses of 7Pn vaccine at 2, 3 and 4 months of age co-administered with DTPa-related vaccines. In 107046 study, subjects had received a booster dose at 12-18 months of age of 7Pn vaccine co-administered with DTPa-HBV-IPV/Hib vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one dose of 10Pn-PD-DiT vaccine intramuscularly in the right of left deltoid muscle. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix™ and/or against varicella (a single dose of Varilrix™). These vaccines were to be given after the blood sampling procedure.

Reporting group title	Primed 7Pn-10Pn Group

Reporting group description:

This group consisted of subjects vaccinated with 7Pn (Prevenar™) and 10Pn-PD-DiT vaccines in the 10PN-PD-DIT-001 (105553) and 10PN-PD-DIT-007 (107046) studies (EudraCT: 2005-003300-11 and 2006-001628-38). In 105553 study, subjects had been primed with 3 doses 7Pn vaccine at 2, 3 and 4 months of age co-administered with DTPa-related vaccines. In the 107046 study, subjects had received at 12-18 months of age a booster dose of 10Pn-PD-DiT vaccine co-administered with DTPa-HBV-IPV/Hib vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of 10Pn-PD-DiT vaccine intramuscularly in the right of left deltoid muscle. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix™ and/or against varicella (a single dose of Varilrix™). These vaccines were to be given after the blood sampling procedure.

Reporting group title	Primed 10Pn-10Pn Group

Reporting group description:

This group consisted of subjects primed with 10Pn-PD-DiT vaccine in the 10PN-PD-DIT-001 (1105553) and 007 (107046) studies (EudraCT: 2005-003300-11 & 2006-001628-38). In 105553 study, subjects had been primed with 3 doses of 10Pn vaccine at 2, 3 and 4 months of age co-administered with DTPa-related vaccines. In 107046 study, subjects had received a booster dose of 10Pn vaccine at 12-18 months of age co-administered with DTPa-HBV-IPV/Hib vaccine. In this study, in the Year 4 111347 study, subjects received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of 10Pn-PD-DiT vaccine intramuscularly in the right of left deltoid muscle. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix™) and/or against varicella (a single dose of Varilrix™). These vaccines were to be given after the blood sampling procedure.

Reporting group title	Primed 7Pn-7Pn Group

Reporting group description:

This group consisted of subjects vaccinated with 7Pn (Prevenar™) vaccine in the 10PN-PD-DIT-001 (105553) and 007 (107046) studies (EudraCT: 2005-003300-11 & 2006-001628-38). In 105553 study, subjects had been primed with 3 doses of 7Pn vaccine at 2, 3 and 4 months of age co-administered with DTPa-related vaccines. In 107046 study, subjects had received a booster dose at 12-18 months of age of 7Pn vaccine co-administered with DTPa-HBV-IPV/Hib vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one dose of 10Pn-PD-DiT vaccine intramuscularly in the right of left deltoid muscle. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix™ and/or against varicella (a single dose of Varilrix™). These vaccines were to be given after the blood sampling procedure.

Reporting group title	Primed 7Pn-10Pn Group

Reporting group description:

This group consisted of subjects vaccinated with 7Pn (Prevenar™) and 10Pn-PD-DiT vaccines in the 10PN-PD-DIT-001 (105553) and 10PN-PD-DIT-007 (107046) studies (EudraCT: 2005-003300-11 and 2006-001628-38). In 105553 study, subjects had been primed with 3 doses 7Pn vaccine at 2, 3 and 4 months of age co-administered with DTPa-related vaccines. In the 107046 study, subjects had received at 12-18 months of age a booster dose of 10Pn-PD-DiT vaccine co-administered with DTPa-HBV-IPV/Hib vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of 10Pn-PD-DiT vaccine intramuscularly in the right of left deltoid muscle. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix™ and/or against varicella (a single dose of Varilrix™). These vaccines were to be given after the blood sampling procedure.

Subject analysis set title	Unprimed Group
Subject analysis set type	Per protocol

Subject analysis set description:

This group consisted of age-matched subjects enrolled at the time of and in the Year 4 111347 study alone aged between 64 and 68 months previously unprimed with any pneumococcal vaccine who received 2 doses of the 10Pn-PD-DiT vaccine in their 6th year of life at Months 48 and 50 (timing by reference to Month 0 as Dose 1 of vaccine in study 10PN-PD-DIT-001 (105553) by GSK Biologicals (EudraCT: 2005-003300-11). The 10Pn-PD-DiT vaccine was injected intramuscularly in the right of left deltoid muscle. Age-matching to Primed Subjects was met by first vaccination of unprimed subjects at 64-68 months of age, time when primed subjects received an additional dose of 10Pn-PD-DiT vaccine. Two doses of 10Pn vaccine by intramuscular use were administered in the left thigh or deltoid at 64-68 (= Day 0 in the 111347 study) and 65-69 months of age (= Month 1 in the 111347 study).

Primary: Number of subjects with anti-vaccine pneumococcal serotypes antibody concentrations >= 0.05 microgram per millilitre (µg/mL) – Persistence Analysis in 111345 Year 1 Follow-up study.

End point title	Number of subjects with anti-vaccine pneumococcal serotypes antibody concentrations >= 0.05 microgram per millilitre (µg/mL) – Persistence Analysis in 111345 Year 1 Follow-up study.[1]

End point description:

Analysis was performed using the 22F-inhibition Enzyme-linked immunosorbent assay (ELISA), using >= 0.05 µg/mL as seropositivity cut off. For this endpoint, the analysis was a persistence analysis performed for the time point specified, on the evaluable subjects for this persistence analysis at the specified time point, that is, subjects enrolled in the applicable 111345 Year 1 Follow-Up Study, evaluated as evaluable and for whom for whom assay results were available for the antibodies against at least one vaccine antigen component for the blood sampling taken at Month 1 and/or Year 1.

End point type	Primary

End point timeframe:

At Month 1 (M1) and Year 1 (Y1) time points, e.g. one month and one year (12 to 14 months) post booster vaccination in study 10PN-PD-DIT-007.

Notes:

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

End point values	Primed 10Pn-10Pn Group	Primed 7Pn-7Pn Group	Primed 7Pn-10Pn Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	389	31	102	
Units: Subjects				
Anti-1 >= 0.05 µg/mL, M1 (N=195;29;47)	195	11	45	
Anti-1 >= 0.05 µg/mL, Y1 (N=387;29;102)	372	7	99	
Anti-4 >= 0.05 µg/mL, M1 (N=196;30;47)	196	30	47	

Anti-4 >= 0.05 µg/mL, Y1 (N=387;31;102)	384	31	102	
Anti-5 >= 0.05 µg/mL, M1 (N=195;30;47)	195	17	45	
Anti-5 >= 0.05 µg/mL, Y1 (N=387 ;30;101)	386	19	101	
Anti-6B >= 0.05 µg/mL, M1 (N=193;30;47)	191	30	47	
Anti-6B >= 0.05 µg/mL, Y1 (N=389;31;102)	384	31	100	
Anti-7F >= 0.05 µg/mL, M1 (N=194;29;47)	194	12	46	
Anti-7F >= 0.05 µg/mL, Y1 (N=387;31;102)	387	17	102	
Anti-9V >= 0.05 µg/mL, M1 (N=193;31;47)	193	31	47	
Anti-9V >= 0.05 µg/mL, Y1 (N=388;31;102)	388	31	102	
Anti-14 >= 0.05 µg/mL, M1 (N=192;30;47)	192	30	47	
Anti-14 >= 0.05 µg/mL, Y1 (N=388;31;102)	387	31	102	
Anti-18C >= 0.05 µg/mL, M1 (N=195;30;48)	195	30	48	
Anti-18C >= 0.05 µg/mL, Y1 (N=384;31;102)	384	31	102	
Anti-19F >= 0.05 µg/mL, M1 (N=196;30;48)	196	30	48	
Anti-19F >= 0.05 µg/mL, Y1 (N=387;30;102)	387	30	102	
Anti-23F >= 0.05 µg/mL, M1 (N=194;30;46)	193	30	46	
Anti-23F >= 0.05 µg/mL, Y1 (N=388;31;102)	386	31	102	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with anti-vaccine pneumococcal serotypes antibody concentrations >= 0.05 microgram per millilitre (µg/mL) – Persistence Analysis in 111346 Year 2 Follow-Up Study.

End point title	Number of subjects with anti-vaccine pneumococcal serotypes antibody concentrations >= 0.05 microgram per millilitre (µg/mL) – Persistence Analysis in 111346 Year 2 Follow-Up Study.[2]

End point description:

Analysis was performed using the 22F-inhibition Enzyme-linked immunosorbent assay (ELISA), using >= 0.05 µg/mL as seropositivity cut off. For this endpoint, the analysis was a persistence analysis performed for the time point specified, on the evaluable subjects for this persistence analysis at the specified time point, that is, subjects enrolled in the applicable 111346 Year 2 Follow-Up Study, evaluated as evaluable and for whom for whom assay results were available for the antibodies against at least one vaccine antigen component for the blood sampling taken at Year 1 and/or Year 2 time points.

End point type	Primary

End point timeframe:

At Year 1 (Y1) and Year 2 (Y2) time points, e. g. one year (12 to 14 months) and two years (24 to 26 months) post booster vaccination in study 10PN-PD-DIT-007.

Notes:

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

End point values	Primed 10Pn-10Pn Group	Primed 7Pn-7Pn Group	Primed 7Pn-10Pn Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	368	30	96	
Units: Subjects				
Anti-1 >= 0.05 µg/mL, Y1 (N=365;28;96)	351	7	93	
Anti-1 >= 0.05 µg/mL, Y2 (N=367;29;96)	354	18	90	
Anti-4 >= 0.05 µg/mL, Y1 (N=365;30;96)	362	30	96	
Anti-4 >= 0.05 µg/mL, Y2 (N=368;30;96)	356	30	96	
Anti-5 >= 0.05 µg/mL, Y1 (N=365;29;95)	364	18	95	
Anti-5 >= 0.05 µg/mL, Y2 (N=368;29;95)	362	21	95	
Anti-6B >= 0.05 µg/mL, Y1 (N=367;30;96)	362	30	94	
Anti-6B >= 0.05 µg/mL, Y2 (N=368;30;96)	355	30	95	
Anti-7F >= 0.05 µg/mL, Y1 (N=365;30;96)	365	16	96	
Anti-7F >= 0.05 µg/mL, Y2 (N=368;30;96)	367	19	95	
Anti-9V >= 0.05 µg/mL, Y1 (N=366;30;96)	366	30	96	
Anti-9V >= 0.05 µg/mL, Y2 (N=368;30;96)	362	30	96	
Anti-14 >= 0.05 µg/mL, Y1 (N=366;30;96)	365	30	96	
Anti-14 >= 0.05 µg/mL, Y2 (N=368;30;96)	367	30	96	
Anti-18C >= 0.05 µg/mL, Y1 (N=362;30;96)	362	30	96	
Anti-18C >= 0.05 µg/mL, Y2 (N=368;30;96)	365	30	96	
Anti-19F >= 0.05 µg/mL, Y1 (N=365;29;96)	365	29	96	
Anti-19F >= 0.05 µg/mL, Y2 (N=368;30;95)	368	30	95	
Anti-23F >= 0.05 µg/mL, Y1 (N=366;30;96)	364	30	96	
Anti-23F >= 0.05 µg/mL, Y2 (N=368;30;96)	357	30	95	

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects with anti-vaccine pneumococcal serotypes antibody

concentrations >= 0.05 microgram per millilitre (µg/mL) – Persistence Analysis in Year 4 Persistence and Immunological Memory 111347 Study.

End point title	Number of subjects with anti-vaccine pneumococcal serotypes antibody concentrations >= 0.05 microgram per millilitre (µg/mL) – Persistence Analysis in Year 4 Persistence and Immunological Memory 111347 Study.[3]

End point description:

Analysis was performed using the 22F-inhibition Enzyme-linked immunosorbent assay (ELISA), using >= 0.05 µg/mL as seropositivity cut off. For this endpoint, the analysis was a persistence analysis performed for the time point specified, on the evaluable subjects for this persistence analysis at the specified time points, that is, subjects enrolled in the applicable Year 4 Persistence and Immunological Memory 111347 Study, evaluated as evaluable and for whom for whom assay results were available for the antibodies against at least one vaccine antigen component for the blood sampling taken at Year 2 and/or Year 4 time points.

End point type	Primary

End point timeframe:

At Years 2 and 4 (Y2 and Y4) time points, e.g. two years (24 to 26 months) and four years (48 to 50 months) post booster vaccination in study 10PN-PD-DIT-007.

Notes:

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

End point values	Primed 10Pn-10Pn Group	Primed 7Pn-7Pn Group	Primed 7Pn-10Pn Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	264	19	75	
Units: Subjects				
Anti-1 >= 0.05 µg/mL, Y2 (N=263;18;75)	250	11	70	
Anti-1 >= 0.05 µg/mL, Y4 (N=263;19;75)	238	14	71	
Anti-4 >= 0.05 µg/mL, Y2 (N=264;19;75)	254	19	75	
Anti-4 >= 0.05 µg/mL, Y4 (N=263;18;74)	238	18	72	
Anti-5 >= 0.05 µg/mL, Y2 (N=264;18;75)	260	10	75	
Anti-5 >= 0.05 µg/mL, Y4 (N=263;19;74)	257	19	73	
Anti-6B >= 0.05 µg/mL, Y2 (N=264;19;75)	255	19	74	
Anti-6B >= 0.05 µg/mL, Y4 (N=263;19;75)	258	19	74	
Anti-7F >= 0.05 µg/mL, Y2 (N=264;19;75)	263	15	75	
Anti-7F >= 0.05 µg/mL, Y4 (N=263;19;75)	260	13	73	
Anti-9V >= 0.05 µg/mL, Y2 (N=264;19;75)	259	19	75	
Anti-9V >= 0.05 µg/mL, Y4 (N=263;19;75)	255	19	72	
Anti-14 >= 0.05 µg/mL, Y2 (N=264;19;75)	263	19	75	
Anti-14 >= 0.05 µg/mL, Y4 (N=263;19;75)	263	19	75	
Anti-18C >= 0.05 µg/mL, Y2 (N=264;18;75)	262	19	75	
Anti-18C >= 0.05 µg/mL, Y4 (N=263;18;74)	256	19	73	

Anti-19F >= 0.05 µg/mL, Y2 (N=264;19;74)	264	19	74	
Anti-19F >= 0.05 µg/mL, Y4 (N=263;19;75)	260	19	75	
Anti-23F >= 0.05 µg/mL, Y2 (N=264;19;75)	259	19	74	
Anti-23F >= 0.05 µg/mL, Y4 (N=262;19;75)	254	19	74	

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) – Persistence Analysis in 111345 Year 1 Follow-Up Study.

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) – Persistence Analysis in 111345 Year 1 Follow-Up Study.

End point description:

Anti-pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antibody concentrations (Anti-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F) were calculated, expressed as geometric mean concentrations (GMCs), in microgram per milliliter (µg/mL). The seropositivity cut-off for the assay was ≥ 0.05 µg/mL. For this endpoint, the analysis was a persistence analysis performed for the time point specified, on the evaluable subjects for this persistence analysis at the specified time point, that is, subjects enrolled in the applicable 111345 Year 1 Follow-Up Study, evaluated as evaluable and for whom for whom assay results were available for the antibodies against at least one vaccine antigen component for the blood sampling taken at Month 1 and/or Year 1.

End point type	Secondary

End point timeframe:

At Month 1 (M1) and Year 1 (Y1) time points, e.g. one month and one year (12 to 14 months) post booster vaccination in study 10PN-PD-DIT-007.

End point values	Primed 10Pn-10Pn Group	Primed 7Pn-7Pn Group	Primed 7Pn-10Pn Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	389	31	102	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-1 antibodies, M1 (N=195;29;47)	1.62 (1.44 to 1.82)	0.07 (0.04 to 0.12)	1.07 (0.79 to 1.47)	
Anti-1 antibodies, Y1 (N=387;29;102)	0.29 (0.27 to 0.32)	0.04 (0.03 to 0.06)	0.26 (0.21 to 0.31)	
Anti-4 antibodies, M1 (N=196;30;47)	4 (3.58 to 4.47)	5.54 (4.41 to 6.95)	6.14 (5.02 to 7.5)	
Anti-4 antibodies, Y1 (N=387;31;102)	0.5 (0.45 to 0.55)	0.59 (0.46 to 0.75)	1.01 (0.84 to 1.21)	
Anti-5 antibodies, M1 (N=195;30;47)	2.35 (2.05 to 2.69)	0.08 (0.04 to 0.14)	0.94 (0.64 to 1.38)	
Anti-5 antibodies, Y1 (N=387 ;30;101)	0.59 (0.54 to 0.65)	0.07 (0.05 to 0.11)	0.42 (0.35 to 0.52)	

Anti-6B antibodies, M1 (N=193;30;47)	2.15 (1.88 to 2.46)	4.33 (3.43 to 5.47)	2.52 (2 to 3.19)	
Anti-6B antibodies, Y1 (N=389;31;102)	0.52 (0.45 to 0.6)	0.98 (0.63 to 1.53)	0.54 (0.42 to 0.69)	
Anti-7F antibodies, M1 (N=194;29;47)	3.67 (3.32 to 4.05)	0.08 (0.04 to 0.15)	2.44 (1.7 to 3.5)	
Anti-7F antibodies, Y1 (N=387;31;102)	0.71 (0.66 to 0.77)	0.08 (0.05 to 0.13)	0.83 (0.7 to 0.99)	
Anti-9V antibodies, M1 (N=193;31;47)	3.41 (3.04 to 3.83)	7.28 (5.4 to 9.81)	2.39 (2.02 to 2.83)	
Anti-9V antibodies, Y1 (N=388;31;102)	0.79 (0.71 to 0.89)	0.93 (0.7 to 1.22)	0.58 (0.49 to 0.68)	
Anti-14 antibodies, M1 (N=192;30;47)	6.04 (5.23 to 6.98)	11.26 (8.57 to 14.8)	5.62 (4.15 to 7.61)	
Anti-14 antibodies, Y1 (N=388;31;102)	1.27 (1.12 to 1.44)	1.79 (1.29 to 2.48)	1.47 (1.17 to 1.85)	
Anti-18C antibodies, M1 (N=195;30;48)	5.2 (4.64 to 5.82)	5.89 (4.48 to 7.74)	6.32 (4.99 to 8.01)	
Anti-18C antibodies, Y1 (N=384;31;102)	0.88 (0.81 to 0.96)	0.91 (0.71 to 1.16)	0.82 (0.69 to 0.98)	
Anti-19F antibodies, M1 (N=196;30;48)	7.4 (6.48 to 8.46)	4.9 (4.12 to 5.84)	6.52 (4.64 to 9.16)	
Anti-19F antibodies, Y1 (N=387;30;102)	1.43 (1.27 to 1.6)	0.83 (0.47 to 1.45)	1.51 (1.19 to 1.92)	
Anti-23F antibodies, M1 (N=194;30;46)	2.74 (2.38 to 3.15)	6.94 (5.16 to 9.35)	3.75 (2.8 to 5.03)	
Anti-23F antibodies, Y1 (N=388;31;102)	0.61 (0.54 to 0.69)	1.18 (0.84 to 1.68)	0.7 (0.56 to 0.88)	

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) – Persistence Analysis in 111346 Year 2 Follow-Up Study.

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) – Persistence Analysis in 111346 Year 2 Follow-Up Study.

End point description:

Anti-pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antibody concentrations (Anti-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F) were calculated, expressed as geometric mean concentrations (GMCs), in microgram per milliliter (µg/mL). The seropositivity cut-off for the assay was ≥ 0.05 µg/mL. For this endpoint, the analysis was a persistence analysis performed for the time point specified, on the evaluable subjects for this persistence analysis at the specified time point, that is, subjects enrolled in the applicable 111346 Year 2 Follow-Up Study, evaluated as evaluable and for whom for whom assay results were available for the antibodies against at least one vaccine antigen component for the blood sampling taken at Year 1 and/or Year 2 time points.

End point type	Secondary

End point timeframe:

At Year 1 (Y1) and Year 2 (Y2) time points, e. g. one year (12 to 14 months) and two years (24 to 26 months) post booster vaccination in study 10PN-PD-DIT-007.

End point values	Primed 10Pn-10Pn Group	Primed 7Pn-7Pn Group	Primed 7Pn-10Pn Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	368	30	96	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-1 antibodies, Y1 (N=365;28;96)	0.29 (0.26 to 0.32)	0.04 (0.03 to 0.06)	0.25 (0.21 to 0.3)	
Anti-1 antibodies, Y2 (N=367;29;96)	0.19 (0.17 to 0.21)	0.07 (0.05 to 0.1)	0.17 (0.14 to 0.2)	
Anti-4 antibodies, Y1 (N=365;30;96)	0.49 (0.44 to 0.55)	0.6 (0.47 to 0.78)	0.98 (0.82 to 1.17)	
Anti-4 antibodies, Y2 (N=368;30;96)	0.27 (0.24 to 0.3)	0.3 (0.24 to 0.38)	0.52 (0.43 to 0.64)	
Anti-5 antibodies, Y1 (N=365;29;95)	0.58 (0.52 to 0.63)	0.07 (0.05 to 0.11)	0.43 (0.35 to 0.53)	
Anti-5 antibodies, Y2 (N=368;29;95)	0.41 (0.37 to 0.45)	0.09 (0.06 to 0.13)	0.33 (0.27 to 0.41)	
Anti-6B antibodies, Y1 (N=367;30;96)	0.51 (0.44 to 0.59)	1.04 (0.67 to 1.62)	0.54 (0.42 to 0.7)	
Anti-6B antibodies, Y2 (N=368;30;96)	0.7 (0.58 to 0.83)	0.99 (0.57 to 1.71)	0.9 (0.63 to 1.29)	
Anti-7F antibodies, Y1 (N=365;30;96)	0.7 (0.65 to 0.76)	0.08 (0.05 to 0.13)	0.86 (0.72 to 1.02)	
Anti-7F antibodies, Y2 (N=368;30;96)	0.53 (0.48 to 0.58)	0.1 (0.06 to 0.16)	0.59 (0.49 to 0.71)	
Anti-9V antibodies, Y1 (N=366;30;96)	0.79 (0.7 to 0.88)	0.93 (0.7 to 1.24)	0.58 (0.49 to 0.7)	
Anti-9V antibodies, Y2 (N=368;30;96)	0.64 (0.54 to 0.75)	0.61 (0.37 to 1)	0.5 (0.37 to 0.68)	
Anti-14 antibodies, Y1 (N=366;30;96)	1.23 (1.09 to 1.4)	1.79 (1.27 to 2.51)	1.48 (1.16 to 1.88)	
Anti-14 antibodies, Y2 (N=368;30;96)	1.73 (1.48 to 2.02)	1.94 (1.12 to 3.36)	1.7 (1.25 to 2.31)	
Anti-18C antibodies, Y1 (N=362;30;96)	0.86 (0.79 to 0.94)	0.92 (0.72 to 1.19)	0.82 (0.68 to 0.98)	
Anti-18C antibodies, Y2 (N=368;30;96)	0.54 (0.48 to 0.62)	0.59 (0.39 to 0.88)	0.48 (0.38 to 0.59)	
Anti-19F antibodies, Y1 (N=365;29;96)	1.39 (1.24 to 1.57)	0.87 (0.49 to 1.54)	1.52 (1.19 to 1.95)	
Anti-19F antibodies, Y2 (N=368;30;95)	2.16 (1.77 to 2.65)	0.99 (0.51 to 1.91)	2.41 (1.67 to 3.46)	
Anti-23F antibodies, Y1 (N=366;30;96)	0.59 (0.52 to 0.68)	1.25 (0.89 to 1.76)	0.7 (0.56 to 0.87)	
Anti-23F antibodies, Y2 (N=368;30;96)	0.68 (0.56 to 0.82)	1.24 (0.83 to 1.85)	0.64 (0.48 to 0.86)	

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A and -19A) – Persistence Analysis in 111345 Year 1 Follow-Up Study.

End point title	Antibody concentrations against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A and -19A) – Persistence

	Analysis in 111345 Year 1 Follow-Up Study.

End point description:

Anti-pneumococcal serotypes 6A and 19A antibody concentrations (Anti-6A and -19A) were calculated, expressed as geometric mean concentrations (GMCs), in microgram per milliliter (µg/mL). The seropositivity cut-off for the assay was ≥ 0.05 µg/mL. For this endpoint, the analysis was a persistence analysis performed for the time point specified, on the evaluable subjects for this persistence analysis at the specified time point, that is, subjects enrolled in the applicable 111345 Year 1 Follow-Up Study, evaluated as evaluable and for whom for whom assay results were available for the antibodies against at least one vaccine antigen component for the blood sampling taken at Month 1 and/or Year 1.

End point type	Secondary

End point timeframe:

At Month 1 (M1) and Year 1 (Y1) time points, e.g. one month and one year (12 to 14 months) post booster vaccination in study 10PN-PD-DIT-007.

End point values	Primed 10Pn-10Pn Group	Primed 7Pn-7Pn Group	Primed 7Pn-10Pn Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	390	31	102	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-6A antibodies, M1 (N=194;30;48)	0.81 (0.68 to 0.98)	2.05 (1.32 to 3.18)	0.88 (0.59 to 1.32)	
Anti-6A antibodies, Y1 (N=390;31;102)	0.28 (0.24 to 0.32)	0.44 (0.28 to 0.7)	0.27 (0.21 to 0.36)	
Anti-19A antibodies, M1 (N=188;28;48)	1.11 (0.9 to 1.37)	0.6 (0.39 to 0.95)	0.69 (0.46 to 1.03)	
Anti-19A antibodies, Y1 (N=190;31;102)	0.28 (0.25 to 0.32)	0.21 (0.13 to 0.33)	0.23 (0.17 to 0.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A and -19A) – Persistence Analysis in 111346 Year 2 Follow-Up Study.

End point title	Antibody concentrations against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A and -19A) – Persistence Analysis in 111346 Year 2 Follow-Up Study.

End point description:

Anti-pneumococcal serotypes 6A and 19A antibody concentrations (Anti-6A and -19A) were calculated, expressed as geometric mean concentrations (GMCs), in microgram per milliliter (µg/mL). The seropositivity cut-off for the assay was ≥ 0.05 µg/mL. For this endpoint, the analysis was a persistence analysis performed for the time point specified, on the evaluable subjects for this persistence analysis at the specified time point, that is, subjects enrolled in the applicable 111346 Year 2 Follow-Up Study, evaluated as evaluable and for whom for whom assay results were available for the antibodies against at least one vaccine antigen component for the blood sampling taken at Year 1 and/or Year 2 time points.

End point type	Secondary

End point timeframe:

At Year 1 (Y1) and Year 2 (Y2) time points, e. g. one year (12 to 14 months) and two years (24 to 26 months) post booster vaccination in study 10PN-PD-DIT-007.

End point values	Primed 10Pn-10Pn Group	Primed 7Pn-7Pn Group	Primed 7Pn-10Pn Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	368	30	96	
Units: µg/mL				
geometric mean (confidence interval 9%)				
Anti-6A antibodies, Y1	0.27 (0.24 to 0.32)	0.44 (0.27 to 0.71)	0.28 (0.21 to 0.37)	
Anti-6A antibodies, Y2	0.33 (0.28 to 0.4)	0.57 (0.3 to 1.11)	0.4 (0.27 to 0.58)	
Anti-19A antibodies, Y1	0.27 (0.24 to 0.31)	0.22 (0.14 to 0.35)	0.22 (0.17 to 0.29)	
Anti-19A antibodies, Y2	0.37 (0.31 to 0.44)	0.25 (0.14 to 0.44)	0.35 (0.25 to 0.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic activity (OPA) titers against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F – Persistence Analysis in 111345 Year 1 Follow-Up Study.

End point title	Opsonophagocytic activity (OPA) titers against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F – Persistence Analysis in 111345 Year 1 Follow-Up Study.

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. For this endpoint, the analysis was a persistence analysis performed for the time point specified, on the evaluable subjects for this persistence analysis at the specified time point, that is, subjects enrolled in the applicable 111345 Year 1 Follow-Up Study, evaluated as evaluable and for whom for whom assay results were available for the antibodies against at least one vaccine antigen component for the blood sampling taken at Month 1 and/or Year 1.

End point type	Secondary

End point timeframe:

At Month 1 (M1) and Year 1 (Y1) time points, e.g. one month and one year (12 to 14 months) post booster vaccination in study 10PN-PD-DIT-007.

End point values	Primed 10Pn-10Pn Group	Primed 7Pn-7Pn Group	Primed 7Pn-10Pn Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	359	27	93	
Units: Titer				
geometric mean (confidence interval 95%)				
Anti-1 OPA Titers, M1 (N=165;25;38)	236 (184 to 302.7)	4.8 (3.7 to 6.3)	15.7 (9.5 to 25.7)	

Anti-1 OPA Titers, Y1 (N=354;27;92)	16.2 (13.8 to 19)	4.8 (3.6 to 6.4)	7.3 (5.9 to 9)	
Anti-4 OPA Titers, M1 (N=164;24;40)	2256.8 (1955.8 to 2604.3)	3403.1 (2334.9 to 4960)	1848.8 (1350.5 to 2530.9)	
Anti-4 OPA Titers, Y1 (N=340;26;86)	59.8 (45.7 to 78.3)	192.9 (82.4 to 452)	88.9 (54.6 to 144.6)	
Anti-5 OPA Titers, M1 (N=162;25;40)	156.8 (125.9 to 195.3)	4.5 (3.5 to 5.7)	9.9 (6.3 to 15.7)	
Anti-5 OPA Titers, Y1 (N=335;27;89)	24.2 (20.8 to 28.2)	5.1 (3.6 to 7.4)	11.2 (8.7 to 14.3)	
Anti-6B OPA Titers, M1 (N=164;24;38)	999.8 (799.1 to 1250.9)	4966.3 (3594.5 to 6861.7)	819.7 (479.8 to 1400.4)	
Anti-6B OPA Titers, Y1 (N=354;25;88)	35.5 (26.5 to 47.5)	476.9 (175.3 to 1298)	44.7 (24 to 83.3)	
Anti-7F OPA Titers, M1 (N=164;22;38)	4620.2 (3898.5 to 5475.7)	65.5 (15.7 to 273)	3146.4 (1965.9 to 5035.6)	
Anti-7F OPA Titers, Y1 (N=346;25;89)	1855.7 (1644.4 to 2094.1)	350.4 (121.8 to 1008)	1617.2 (1152.9 to 2268.3)	
Anti-9V OPA Titers, M1 (N=164;23;39)	2551.3 (2198.3 to 2960.8)	5234.5 (3688.7 to 7428.2)	991.5 (692.4 to 1419.8)	
Anti-9V OPA Titers, Y1 (N=352;26;94)	791.5 (701.8 to 892.8)	1240.7 (829.4 to 1855.9)	370.5 (281.8 to 487.2)	
Anti-14 OPA Titers, M1 (N=170;24;40)	2129 (1836.4 to 2468.3)	1852.9 (1191.9 to 2880.6)	1184.3 (911.4 to 1538.9)	
Anti-14 OPA Titers, Y1 (N=343;25;91)	551.9 (486.5 to 626.2)	607.3 (385.3 to 957.1)	456.6 (361.1 to 577.3)	
Anti-18C OPA Titers, M1 (N=167;23;39)	901.6 (751.7 to 1081.4)	1071.6 (682.1 to 1683.3)	544.2 (334.7 to 884.8)	
Anti-18C OPA Titers, Y1 (N=319;22;84)	23.5 (18.6 to 29.8)	15.5 (6.1 to 39.2)	10.4 (7.1 to 15.4)	
Anti-19F OPA Titers, M1 (N=161;24;39)	668 (514.8 to 866.7)	634.9 (380.3 to 1059.9)	486 (247.1 to 956.1)	
Anti-19F OPA Titers, Y1 (N=359;27;93)	53.4 (44.7 to 63.9)	35.4 (15.9 to 78.6)	58 (41.6 to 80.7)	
Anti-23F OPA Titers, M1 (N=166;23;40)	2807 (2342.3 to 3363.9)	17273.9 (11313.6 to 26374.3)	2701 (1656.9 to 4403.2)	
Anti-23F OPA Titers, Y1 (N=336;27;93)	784.9 (625.4 to 985)	3013.1 (1349.5 to 6727.2)	552.3 (362.1 to 842.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic activity (OPA) titers against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F – Persistence Analysis in 111346 Year 2 Follow-Up Study.

End point title	Opsonophagocytic activity (OPA) titers against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F – Persistence Analysis in 111346 Year 2 Follow-Up Study.

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. For this endpoint, the analysis was a persistence analysis performed for the time point specified, on the evaluable subjects for this persistence analysis at the specified time point, that is, subjects enrolled in the applicable 111346 Year 2 Follow-Up Study, evaluated as evaluable and for whom for whom assay results were available for the antibodies against at least one vaccine antigen component for the blood sampling taken at Year 1 and/or Year 2 time points.

End point type	Secondary

End point timeframe:

At Year 1 (Y1) and Year 2 (Y2) time points, e. g. one year (12 to 14 months) and two years (24 to 26 months) post booster vaccination in study 10PN-PD-DIT-007.

End point values	Primed 10Pn-10Pn Group	Primed 7Pn-7Pn Group	Primed 7Pn-10Pn Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	354	27	92	
Units: Titer				
geometric mean (confidence interval 95%)				
Anti-1 OPA Titers, Y1 (N=333;26;88)	15.7 (13.4 to 18.5)	4.9 (3.6 to 6.5)	7.3 (5.9 to 9.1)	
Anti-1 OPA Titers, Y2 (N=354;27;92)	8.4 (7.3 to 9.7)	4 (4 to 4)	6.3 (4.9 to 8)	
Anti-4 OPA Titers, Y1 (N=320;25;83)	59.3 (45 to 78.3)	225.3 (98.9 to 513.2)	83.7 (52.3 to 134.1)	
Anti-4 OPA Titers, Y2 (N=335;27;84)	29 (22.1 to 38)	33.5 (11.9 to 94.6)	39.3 (23.7 to 65.2)	
Anti-5 OPA Titers, Y1 (N=318;26;85)	23.4 (20.1 to 27.3)	5.2 (3.6 to 7.5)	11.1 (8.6 to 14.4)	
Anti-5 OPA Titers, Y2 (N=351;27;91)	11.4 (10 to 13)	4.3 (3.9 to 4.7)	7.4 (6 to 9.1)	
Anti-6B OPA Titers, Y1 (N=333;24;86)	34.9 (25.9 to 47.2)	534.5 (193.3 to 1477.7)	45.4 (24 to 85.8)	
Anti-6B OPA Titers, Y2 (N=342;27;88)	167.2 (124.1 to 225.2)	526.1 (210.5 to 1314.4)	213.7 (117.8 to 387.6)	
Anti-7F OPA Titers, Y1 (N=326;24;87)	1890.2 (1676.1 to 2131.8)	347.9 (115.3 to 1049.7)	1611.3 (1141 to 2275.5)	
Anti-7F OPA Titers, Y2 (N=350;27;91)	1488.7 (1358.3 to 1631.6)	1068.3 (619.5 to 1842.4)	1387.8 (1096.2 to 1756.9)	
Anti-9V OPA Titers, Y1 (N=332;25;90)	812 (717.6 to 918.8)	1252.1 (823 to 1904.8)	360 (271.3 to 477.8)	
Anti-9V OPA Titers, Y2 (N=349;27;92)	648.5 (570 to 737.7)	730.4 (457.7 to 1165.7)	391 (279.2 to 547.5)	
Anti-14 OPA Titers, Y1 (N=323;24;88)	543.3 (476.6 to 619.3)	593.1 (369.7 to 951.4)	455.9 (357.7 to 581.2)	
Anti-14 OPA Titers, Y2 (N=341;25;90)	660.2 (567.2 to 768.4)	651 (348.6 to 1215.5)	534.4 (381.6 to 748.4)	
Anti-18C OPA Titers, Y1 (N=300;23;80)	22.4 (17.6 to 28.4)	16.4 (6.3 to 43)	10 (6.8 to 14.8)	
Anti-18C OPA Titers, Y2 (N=325;27;83)	34.9 (26.6 to 45.7)	34.8 (11.7 to 103.2)	17.7 (10.7 to 29.2)	
Anti-19F OPA Titers, Y1 (N=338;26;89)	52 (43.2 to 62.5)	38.5 (17.1 to 86.6)	58.8 (41.7 to 83)	
Anti-19F OPA Titers, Y2 (N=349;27;92)	78.1 (60.9 to 100.2)	49.2 (21.2 to 113.9)	105.4 (65.8 to 168.7)	
Anti-23F OPA Titers, Y1 (N=315;26;89)	747.6 (590.2 to 947.1)	3097.1 (1344.7 to 7133)	521.3 (337.9 to 804.3)	

Anti-23F OPA Titers, Y2 (N=342;26;91)	632 (483 to 827)	1923 (952.2 to 3883.7)	435 (250.5 to 755.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic activity (OPA) titers against cross-reactive pneumococcal serotypes 6A and 19 A – Persistence Analysis in 111345 Year 1 Follow-Up Study.

End point title	Opsonophagocytic activity (OPA) titers against cross-reactive pneumococcal serotypes 6A and 19 A – Persistence Analysis in 111345 Year 1 Follow-Up Study.

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. For this endpoint, the analysis was a persistence analysis performed for the time point specified, on the evaluable subjects for this persistence analysis at the specified time point, that is, subjects enrolled in the applicable 111345 Year 1 Follow-Up Study, evaluated as evaluable and for whom for whom assay results were available for the antibodies against at least one vaccine antigen component for the blood sampling taken at Month 1 and/or Year 1.

End point type	Secondary

End point timeframe:

At Month 1 (M1) and Year 1 (Y1) time points, e.g. one month and one year (12 to 14 months) post booster vaccination in study 10PN-PD-DIT-007.

End point values	Primed 10Pn-10Pn Group	Primed 7Pn-7Pn Group	Primed 7Pn-10Pn Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	352	26	93	
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-6A OPA Titers, M1 (N=156;24;36)	290.7 (213.8 to 395.3)	1624.1 (1038.6 to 2539.9)	120.4 (58.4 to 248.3)	
Anti-6A OPA Titers, Y1 (N=323;25;75)	59 (45.9 to 76)	610.2 (317.7 to 1171.9)	46.6 (28.3 to 76.8)	
Anti-19A OPA Titers, M1 (N=155;22;39)	30.2 (20.9 to 43.7)	12.5 (5.1 to 30.7)	11.6 (6.1 to 21.8)	
Anti-19A OPA Titers, Y1 (N=352;26;93)	6 (5.2 to 6.8)	5.9 (3.7 to 9.5)	5.5 (4.5 to 6.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic activity (OPA) titers against cross-reactive pneumococcal serotypes 6A and 19 A – Persistence Analysis in 111346 Year 2

Follow-Up Study.

End point title	Opsonophagocytic activity (OPA) titers against cross-reactive pneumococcal serotypes 6A and 19 A – Persistence Analysis in 111346 Year 2 Follow-Up Study.

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. For this endpoint, the analysis was a persistence analysis performed for the time point specified, on the evaluable subjects for this persistence analysis at the specified time point, that is, subjects enrolled in the applicable 111346 Year 2 Follow-Up Study, evaluated as evaluable and for whom for whom assay results were available for the antibodies against at least one vaccine antigen component for the blood sampling taken at Year 1 and/or Year 2 time points.

End point type	Secondary

End point timeframe:

At Year 1 (Y1) and Year 2 (Y2) time points, e. g. one year (12 to 14 months) and two years (24 to 26 months) post booster vaccination in study 10PN-PD-DIT-007.

End point values	Primed 10Pn-10Pn Group	Primed 7Pn-7Pn Group	Primed 7Pn-10Pn Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	351	27	91	
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-6A OPA Titers, Y1 (N=302;24;74)	57.8 (44.6 to 75)	653.6 (335.9 to 1271.8)	46.1 (27.8 to 76.4)	
Anti-6A OPA Titers, Y2 (N=314;25;82)	121.8 (95.2 to 156)	356.5 (134.6 to 944.6)	133.7 (81.8 to 218.7)	
Anti-19A OPA Titers, Y1 (N=332;25;90)	6 (5.2 to 6.9)	6 (3.7 to 9.8)	5.3 (4.3 to 6.5)	
Anti-19A OPA Titers, Y2 (N=351;27;91)	12.8 (10.4 to 15.7)	10.9 (5.2 to 22.8)	11.1 (7.6 to 16.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations to protein D (Anti-PD) – Persistence Analysis in 111345 Year 1 Follow-Up Study.

End point title	Antibody concentrations to protein D (Anti-PD) – Persistence Analysis in 111345 Year 1 Follow-Up Study.

End point description:

Anti-protein D (Anti-PD) antibody concentrations by Enzyme-Linked Immunosorbent Assay (ELISA) were calculated, expressed as geometric mean concentrations (GMCs) in ELISA unit per milli-liter (EL.U/mL) and tabulated. The seropositivity cut-off for the assay was ≥ 100 EL.U/mL. For this endpoint, the analysis was a persistence analysis performed for the time point specified, on the evaluable subjects for this persistence analysis at the specified time point, that is, subjects enrolled in the applicable 111345 Year 1 Follow-Up Study, evaluated as evaluable and for whom for whom assay results were available for the antibodies against at least one vaccine antigen component for the blood sampling taken at Month 1 and/or Year 1.

End point type	Secondary

End point timeframe:

At Month 1 (M1) and Year 1 (Y1) time points, e.g. one month and one year (12 to 14 months) post booster vaccination in study 10PN-PD-DIT-007.

End point values	Primed 10Pn-10Pn Group	Primed 7Pn-7Pn Group	Primed 7Pn-10Pn Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	390	30	102	
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD antibodies, M1 (N=194;30;48)	3283 (2845.9 to 3787.1)	113 (60.1 to 212.4)	152.2 (111.9 to 207.2)	
Anti-PD antibodies, Y1 (N=390;30;102)	822.1 (731.5 to 923.9)	93.9 (66.6 to 132.3)	193.6 (155.9 to 240.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations to protein D (Anti-PD) – Persistence Analysis in 111346 Year 2 Follow-Up Study.

End point title	Antibody concentrations to protein D (Anti-PD) – Persistence Analysis in 111346 Year 2 Follow-Up Study.

End point description:

Anti-protein D (Anti-PD) antibody concentrations by Enzyme-Linked Immunosorbent Assay (ELISA) were calculated, expressed as geometric mean concentrations (GMCs) in ELISA unit per milli-liter (EL.U/mL) and tabulated. The seropositivity cut-off for the assay was ≥ 100 EL.U/mL. For this endpoint, the analysis was a persistence analysis performed for the time point specified, on the evaluable subjects for this persistence analysis at the specified time point, that is, subjects enrolled in the applicable 111346 Year 2 Follow-Up Study, evaluated as evaluable and for whom for whom assay results were available for the antibodies against at least one vaccine antigen component for the blood sampling taken at Year 1 and/or Year 2 time points.

End point type	Secondary

End point timeframe:

At Year 1 (Y1) and Year 2 (Y2) time points, e. g. one year (12 to 14 months) and two years (24 to 26 months) post booster vaccination in study 10PN-PD-DIT-007.

End point values	Primed 10Pn-10Pn Group	Primed 7Pn-7Pn Group	Primed 7Pn-10Pn Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	368	29	96	
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD antibodies, Y1	815.8 (723.2 to 920.2)	95.9 (67.4 to 136.5)	182.6 (146.9 to 227)	
Anti-PD antibodies, Y2	573.2 (509.6 to 644.8)	116.7 (80.9 to 168.3)	157.5 (128.7 to 192.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reported with solicited local symptoms.

End point title	Number of subjects reported with solicited local symptoms.

End point description:

Solicited local symptoms assessed were Pain, Redness and Swelling. Follow-up period was of 4 days (Days 0-3) after 10Pn-PD-Dit vaccination in Year 4 Persistence and Immunological Memory 111347 Study, thus one period of 4 days for primed subjects and 2 periods of 4 days for unprimed subjects.

End point type	Secondary

End point timeframe:

Within 4 days (Days 0-3) period(s) after 10Pn-PD-Dit vaccination in Year 4 Persistence and Immunological Memory 111347 Study, across doses for Primed 10Pn-10Pn, Primed 7Pn-7Pn and Primed 7Pn-10Pn groups.

End point values	Primed 10Pn-10Pn Group	Primed 7Pn-7Pn Group	Primed 7Pn-10Pn Group	Unprimed Group
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	264	20	64	100
Units: Subjects				
Pain	157	9	34	54
Redness	90	5	14	21
Swelling	67	4	15	20

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reported with solicited general symptoms.

End point title	Number of subjects reported with solicited general symptoms.

End point description:

Solicited general symptoms assessed were Drowsiness, Irritability, Loss of appetite and Fever (defined as temperature by axillary measurement of 37.5°C and above). Follow-up period was of 4 days (Days 0-3) after 10Pn-PD-Dit vaccination in Year 4 Persistence and Immunological Memory 111347 Study, thus one period of 4 days for primed subjects and 2 periods of 4 days for unprimed subjects.

End point type	Secondary

End point timeframe:

Within 4 days (Days 0-3) period(s) after 10Pn-PD-Dit vaccination in Year 4 Persistence and Immunological Memory 111347 Study, across doses for Primed 10Pn-10Pn, Primed 7Pn-7Pn and Primed 7Pn-10Pn groups.

End point values	Primed 10Pn-10Pn Group	Primed 7Pn-7Pn Group	Primed 7Pn-10Pn Group	Unprimed Group
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	263	20	64	100
Units: Subjects				
Drowsiness	49	2	12	12
Irritability	35	4	6	8
Loss of appetite	30	3	6	13
Fever	13	0	2	5

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

An AE is any untoward medical occurrence in a clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. "Any" is defined an incidence of an unsolicited AE regardless of intensity or relationship to study vaccination. Follow-up period was of 31 days (Days 0-30) after 10Pn-PD-Dit vaccination in Year 4 Persistence and Immunological Memory 111347 Study, thus one period of 31 days for primed subjects and 2 periods of 31 days for unprimed subjects.

End point type	Secondary

End point timeframe:

Within 31 days (Day 0-30) after 10Pn-PD-Dit vaccination in Year 4 Persistence and Immunological Memory 111347 Study, across doses for Primed 10Pn-10Pn, Primed 7Pn-7Pn and Primed 7Pn-10Pn groups.

End point values	Primed 10Pn-10Pn Group	Primed 7Pn-7Pn Group	Primed 7Pn-10Pn Group	Unprimed Group
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	264	20	65	100
Units: Subjects				
Subject(s) with Any Unsolicited AE(s)	25	0	3	6

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs) – In 111345 Persistence Year 1 Follow-Up Study.

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

	111345 Persistence Year 1 Follow-Up Study.

End point description:

An SAE is any untoward medical occurrence that: results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, or may evolve into one of the outcomes listed above. "Any" is defined an incidence of a SAE regardless of intensity/severity. For this endpoint, the analysis was performed on the subjects enrolled in the applicable 111345 Year 1 Follow-Up Study.

End point type	Secondary

End point timeframe:

Between Month 1 and Year 1 time points, e.g. one month and one year (12 to 14 months) post booster vaccination in study 10PN-PD-DIT-007.

End point values	Primed 10Pn-10Pn Group	Primed 7Pn-7Pn Group	Primed 7Pn-10Pn Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	391	31	102	
Units: Subjects				
Subject(s) reported with SAE(s)	1	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs) – In 111346 Persistence Year 2 Follow-Up Study.

End point title	Number of subjects with serious adverse events (SAEs) – In 111346 Persistence Year 2 Follow-Up Study.

End point description:

An SAE is any untoward medical occurrence that: results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, or may evolve into one of the outcomes listed above. "Any" is defined an incidence of a SAE regardless of intensity/severity. For this endpoint, the analysis was performed on subjects enrolled in the applicable 111346 Year 2 Follow-Up Study.

End point type	Secondary

End point timeframe:

Between Year 1 and Year 2 time point, e. g. one year (12 to 14 months) and two years (24 to 26 months) post booster vaccination in study 10PN-PD-DIT-007.

End point values	Primed 10Pn-10Pn Group	Primed 7Pn-7Pn Group	Primed 7Pn-10Pn Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	370	31	96	
Units: Subjects				
Subject(s) reported with SAE(s)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs) – Persistence Phase in 111347 Study.

End point title	Number of subjects with serious adverse events (SAEs) – Persistence Phase in 111347 Study.

End point description:

An SAE is any untoward medical occurrence that: results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, or may evolve into one of the outcomes listed above. "Any" is defined an incidence of a SAE regardless of intensity/severity. For this endpoint, analysis was performed on subjects enrolled in the applicable Year 4 Persistence and Immunological Memory 111347 Study.

End point type	Secondary

End point timeframe:

Between Year 2 and Year 4 time points, e. g. two years (24 to 26 months) and four years (48 to 50 months) post booster vaccination in study 10PN-PD-DIT-007.

End point values	Primed 10Pn-10Pn Group	Primed 7Pn-7Pn Group	Primed 7Pn-10Pn Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	316	25	85	
Units: Subjects				
Subject(s) reported with SAE(s)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs) – Immunological Memory Phase in 111347 Study.

End point title	Number of subjects with serious adverse events (SAEs) – Immunological Memory Phase in 111347 Study.

End point description:

An SAE is any untoward medical occurrence that: results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, or may evolve into one of the outcomes listed above. "Any" is defined an incidence of a SAE regardless of intensity/severity. For this endpoint, analysis was performed on subjects enrolled in the applicable Year 4 Persistence and Immunological Memory 111347 Study.

End point type	Secondary

End point timeframe:

From booster dose vaccination to study end in Year 4 Persistence and Immunological Memory 111347 Study (Month 1 for primed subjects and Month 3 for unprimed subjects).

End point values	Primed 10Pn-10Pn Group	Primed 7Pn-7Pn Group	Primed 7Pn-10Pn Group	Unprimed Group
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	264	20	65	100
Units: Subjects				
Subject(s) reported with SAE(s)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (Anti-1, -4, -5, -6B, -7F, 9V, -14, -18C, -19F and -23F) – Persistence Analysis in Year 4 Persistence and Immunological Memory 111347 Study.

End point title	Antibody concentrations against vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F (Anti-1, -4, -5, -6B, -7F, 9V, -14, -18C, -19F and -23F) – Persistence Analysis in Year 4 Persistence and Immunological Memory 111347 Study.

End point description:

Anti-vaccine pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antibody concentrations (Anti-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F) were calculated, expressed as geometric mean concentrations (GMCs), in microgram per milliliter (µg/mL). The seropositivity cut-off for the assay was ≥ 0.05 µg/mL. For this endpoint, the analysis was a persistence analysis performed for the time point specified, on the evaluable subjects for this persistence analysis at the specified time points, that is, subjects enrolled in the applicable Year 4 Persistence and Immunological Memory 111347 Study, evaluated as evaluable and for whom for whom assay results were available for the antibodies against at least one vaccine antigen component for the blood sampling taken at Year 2 and/or Year 4 time points.

End point type	Secondary

End point timeframe:

At Years 2 and 4 (Y2 and Y4) time points, e.g. two years (24 to 26 months) and four years (48 to 50 months) post booster vaccination in study 10PN-PD-DIT-007.

End point values	Primed 10Pn-10Pn Group	Primed 7Pn-7Pn Group	Primed 7Pn-10Pn Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	264	19	75	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-1 antibodies, Y2 (N=263;18;75)	0.19 (0.17 to 0.22)	0.07 (0.04 to 0.12)	0.17 (0.14 to 0.21)	
Anti-1 antibodies, Y4 (N=263;19;75)	0.2 (0.17 to 0.24)	0.17 (0.07 to 0.43)	0.23 (0.17 to 0.32)	
Anti-4 antibodies, Y2 (N=264;19;75)	0.27 (0.24 to 0.31)	0.3 (0.22 to 0.4)	0.53 (0.43 to 0.66)	
Anti-4 antibodies, Y4 (N=263;18;74)	0.19 (0.16 to 0.22)	0.23 (0.12 to 0.41)	0.31 (0.25 to 0.38)	
Anti-5 antibodies, Y2 (N=264;18;75)	0.41 (0.37 to 0.46)	0.07 (0.04 to 0.13)	0.35 (0.28 to 0.44)	

Anti-5 antibodies, Y4 (N=263;19;74)	0.36 (0.31 to 0.4)	0.19 (0.1 to 0.35)	0.35 (0.28 to 0.43)	
Anti-6B antibodies, Y2 (N=264;19;75)	0.66 (0.54 to 0.82)	0.77 (0.38 to 1.59)	0.9 (0.61 to 1.32)	
Anti-6B antibodies, Y4 (N=263;19;75)	1.3 (1.1 to 1.55)	1.19 (0.68 to 2.07)	0.97 (0.74 to 1.27)	
Anti-7F antibodies, Y2 (N=264;19;75)	0.5 (0.45 to 0.56)	0.13 (0.07 to 0.25)	0.62 (0.5 to 0.76)	
Anti-7F antibodies, Y4 (N=263;19;75)	0.44 (0.38 to 0.52)	0.16 (0.08 to 0.36)	0.49 (0.37 to 0.65)	
Anti-9V antibodies, Y2 (N=264;19;75)	0.64 (0.52 to 0.78)	0.65 (0.33 to 1.31)	0.55 (0.39 to 0.79)	
Anti-9V antibodies, Y4 (N=263;19;75)	1.17 (0.92 to 1.47)	1.19 (0.43 to 3.27)	0.67 (0.46 to 0.99)	
Anti-14 antibodies, Y2 (N=264;19;75)	1.67 (1.38 to 2.01)	1.76 (0.85 to 3.65)	1.7 (1.22 to 2.37)	
Anti-14 antibodies, Y4 (N=263;19;75)	3.66 (3.01 to 4.45)	2.57 (1.22 to 5.42)	2.94 (2.11 to 4.12)	
Anti-18C antibodies, Y2 (N=264;18;75)	0.55 (0.47 to 0.65)	0.47 (0.32 to 0.69)	0.54 (0.42 to 0.7)	
Anti-18C antibodies, Y4 (N=263;18;74)	0.7 (0.58 to 0.84)	0.87 (0.4 to 1.88)	0.63 (0.45 to 0.89)	
Anti-19F antibodies, Y2 (N=264;19;74)	2.12 (1.67 to 2.7)	0.97 (0.47 to 2)	2.19 (1.5 to 3.2)	
Anti-19F antibodies, Y4 (N=263;19;75)	4.17 (3.4 to 5.1)	4.74 (2.24 to 10)	4.05 (3.03 to 5.41)	
Anti-23F antibodies, Y2 (N=264;19;75)	0.67 (0.54 to 0.84)	1.21 (0.72 to 2.03)	0.66 (0.48 to 0.91)	
Anti-23F antibodies, Y4 (N=262;19;75)	1.57 (1.26 to 1.96)	1.64 (1.15 to 2.34)	1.12 (0.79 to 1.58)	

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A and -19A) – Persistence Analysis in Year 4 Persistence and Immunological Memory 111347 Study.

End point title	Antibody concentrations against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A and -19A) – Persistence Analysis in Year 4 Persistence and Immunological Memory 111347 Study.

End point description:

Anti-pneumococcal serotypes 6A and 19A antibody concentrations (Anti-6A and -19A) were calculated, expressed as geometric mean concentrations (GMCs), in microgram per milliliter (µg/mL). The seropositivity cut-off for the assay was ≥ 0.05 µg/mL. For this endpoint, the analysis was a persistence analysis performed for the time point specified, on the evaluable subjects for this persistence analysis at the specified time points, that is, subjects enrolled in the applicable Year 4 Persistence and Immunological Memory 111347 Study, evaluated as evaluable and for whom for whom assay results were available for the antibodies against at least one vaccine antigen component for the blood sampling taken at Year 2 and/or Year 4 time points.

End point type	Secondary

End point timeframe:

At Years 2 and 4 (Y2 and Y4) time points, e.g. two years (24 to 26 months) and four years (48 to 50 months) post booster vaccination in study 10PN-PD-DIT-007.

End point values	Primed 10Pn-10Pn Group	Primed 7Pn-7Pn Group	Primed 7Pn-10Pn Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	264	19	75	
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-6A antibodies, Y2 (N=264;19;75)	0.34 (0.27 to 0.42)	0.41 (0.18 to 0.96)	0.39 (0.25 to 0.59)	
Anti-6A antibodies, Y4 (N=263;19;74)	0.92 (0.77 to 1.1)	0.69 (0.34 to 1.38)	0.75 (0.55 to 1.03)	
Anti-19A antibodies, Y2 (N=264;19;75)	0.35 (0.28 to 0.44)	0.18 (0.08 to 0.4)	0.31 (0.21 to 0.45)	
Anti-19A antibodies, Y4 (N=263;19;75)	1.3 (1.07 to 1.59)	1.08 (0.5 to 2.33)	1.14 (0.77 to 1.68)	

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against vaccine pneumococcal serotypes – Immunological Memory Analysis in Year 4 Persistence and Immunological Memory 111347 Study.

End point title	Antibody concentrations against vaccine pneumococcal serotypes – Immunological Memory Analysis in Year 4 Persistence and Immunological Memory 111347 Study.

End point description:

Anti-pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F antibody concentrations (Anti-1, -4, -5, -6B, -7F, -9V, -14, -18C, -19F and -23F) were calculated, expressed as geometric mean concentrations (GMCs), in microgram per milliliter (µg/mL). The seropositivity cut-off for the assay was >= 0.05 µg/mL. For this endpoint, the results presented are those of the immunological memory analysis part of the Year 4 Persistence and Immunological Memory 111347 Study. Subjects analyzed were subjects vaccinated subjects in the 111347 study assessed as evaluable and for whom assay results were available for antibodies against at least one study vaccine antigen component for the blood sample taken 7-10 days after vaccination for primed subjects and for any of blood samples taken from unprimed subjects (i.e. before vaccination, 7-10 days post-dose 1 and 1 month post-dose 2).

End point type	Secondary

End point timeframe:

Prior to Dose 1 of 10Pn-PD-DiT vaccination in 111347 study (PRE), and at Day 7 (D7) and Month 3 (M3), e.g. 7 days post Dose 1 of 10Pn-PD-DiT vaccination in 111347 study, and at one month post Dose 2 of 10Pn-PD-DiT vaccination in 111347 study.

End point values	Primed 10Pn-10Pn Group	Primed 7Pn-7Pn Group	Primed 7Pn-10Pn Group	Unprimed Group
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	210	14	55	98
Units: µg/mL				
geometric mean (confidence interval 95%)				

Anti-1 antibodies, PRE (N=210;14;55;97)	0.2 (0.17 to 0.25)	0.19 (0.05 to 0.68)	0.24 (0.16 to 0.37)	0.1 (0.08 to 1.69)
Anti-1 antibodies, D7 (N=208;14;54;98)	5.36 (4.54 to 6.33)	3.04 (1.22 to 7.56)	5 (3.72 to 6.71)	1.35 (1.08 to 1.69)
Anti-1 antibodies, M3 (N=0;0;0;98)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	2.39 (2.06 to 2.78)
Anti-4 antibodies, PRE (N=210;14;54;97)	0.18 (0.15 to 0.21)	0.19 (0.08 to 0.43)	0.32 (0.25 to 0.41)	0.04 (0.03 to 0.05)
Anti-4 antibodies, D7 (N=208;14;54;98)	12.11 (10.08 to 14.54)	10.45 (6.49 to 16.81)	7.13 (5.18 to 9.82)	4.74 (3.77 to 5.95)
Anti-4 antibodies, M3 (N=0;0;0;98)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	7.32 (6.7 to 8)
Anti-5 antibodies, PRE (N=210;14;54;97)	0.36 (0.31 to 0.41)	0.17 (0.08 to 0.38)	0.34 (0.26 to 0.44)	0.1 (0.08 to 0.12)
Anti-5 antibodies, D7 (N=208;14;54;98)	6.23 (5.19 to 7.49)	3.24 (1.44 to 7.29)	8.15 (5.71 to 11.63)	1.2 (0.97 to 1.49)
Anti-5 antibodies, M3 (N=0;0;0;98)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	3.1 (2.7 to 3.55)
Anti-6B antibodies, PRE (N=210;14;55;97)	1.27 (1.04 to 1.55)	1.2 (0.56 to 2.55)	0.97 (0.71 to 1.33)	0.21 (0.15 to 0.29)
Anti-6B antibodies, D7 (N=208;14;54;97)	3.68 (3.16 to 4.29)	2.85 (1.89 to 4.3)	2.15 (1.62 to 2.85)	0.53 (0.4 to 0.71)
Anti-6B antibodies, M3 (N=0;0;0;98)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	1.25 (1.01 to 1.54)
Anti-7F antibodies, PRE (N=210;14;55;97)	0.43 (0.36 to 0.5)	0.17 (0.07 to 0.44)	0.49 (0.36 to 0.66)	0.12 (0.09 to 0.16)
Anti-7F antibodies, D7 (N=208;14;54;97)	7.16 (6.11 to 8.39)	3.26 (1.67 to 6.35)	7.57 (5.84 to 9.81)	1.67 (1.33 to 2.09)
Anti-7F antibodies, M3 (N=0;0;0;98)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	4.55 (3.93 to 5.26)
Anti-9V antibodies, PRE (N=210;14;55;97)	1.28 (0.98 to 1.67)	0.86 (0.24 to 3.05)	0.54 (0.34 to 0.86)	0.19 (0.12 to 0.28)
Anti-9V antibodies, D7 (N=208;14;54;97)	9.94 (8.59 to 11.51)	9 (5.49 to 14.77)	5.32 (4.08 to 6.94)	0.9 (0.66 to 1.23)
Anti-9V antibodies, M3 (N=0;0;0;98)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	2.2 (1.85 to 2.62)
Anti-14 antibodies, PRE (N=210;14;55;96)	3.67 (2.94 to 4.57)	2.16 (0.95 to 4.93)	3.54 (2.35 to 5.34)	0.58 (0.38 to 0.87)
Anti-14 antibodies, D7 (N=208;14;54;98)	19.38 (16.74 to 22.43)	13.26 (6.91 to 25.43)	18.61 (14.23 to 24.34)	1.72 (1.2 to 2.46)
Anti-14 antibodies, M3 (N=0;0;0;98)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	7.81 (6.34 to 9.63)
Anti-18C antibodies, PRE (N=210;14;54;96)	0.66 (0.53 to 0.82)	0.53 (0.23 to 1.21)	0.63 (0.41 to 0.96)	0.1 (0.07 to 0.15)
Anti-18C antibodies, D7 (N=208;14;54;98)	15.51 (13.06 to 18.43)	19.71 (11.87 to 32.74)	13.34 (9.34 to 19.05)	2.26 (1.66 to 3.09)
Anti-18C antibodies, M3 (N=0;0;0;98)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	13.21 (11.44 to 15.25)
Anti-19F antibodies, PRE (N=210;14;55;96)	4.04 (3.22 to 5.07)	3.69 (1.38 to 9.87)	4.18 (2.93 to 5.96)	0.6 (0.4 to 0.89)
Anti-19F antibodies, D7 (N=208;14;54;98)	11.63 (10 to 13.51)	16.44 (10.68 to 25.29)	8.09 (6.29 to 10.42)	5.12 (3.97 to 6.62)
Anti-19F antibodies, M3 (N=0;0;0;98)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	15.47 (13.08 to 18.29)
Anti-23F antibodies, PRE (N=209;14;55;97)	1.44 (1.12 to 1.84)	1.62 (1.02 to 2.57)	1.09 (0.72 to 1.65)	0.1 (0.07 to 0.14)
Anti-23F antibodies, D7 (N=208;14;54;98)	6.5 (5.61 to 7.53)	9.34 (5.62 to 15.54)	4.7 (3.43 to 6.45)	0.42 (0.3 to 0.59)
Anti-23F antibodies, M3 (N=0;0;0;98)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	1.63 (1.32 to 2.01)

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A and 19A) – Immunological Memory Analysis in Year 4 Persistence and Immunological Memory 111347 Study.

End point title	Antibody concentrations against cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A and 19A) – Immunological Memory Analysis in Year 4 Persistence and Immunological Memory 111347 Study.

End point description:

Anti-cross-reactive pneumococcal serotypes 6A and 19A (Anti-6A and 19A) were calculated, expressed as geometric mean concentrations (GMCs), in microgram per milliliter (µg/mL). The seropositivity cut-off for the assay was >= 0.05 µg/mL. For this endpoint, the results presented are those of the immunological memory analysis part of the Year 4 Persistence and Immunological Memory 111347 Study. Subjects analyzed were subjects vaccinated subjects in the 111347 study assessed as evaluable and for whom assay results were available for antibodies against at least one study vaccine antigen component for the blood sample taken 7-10 days after vaccination for primed subjects and for any of blood samples taken from unprimed subjects (i.e. before vaccination, 7-10 days post-dose 1 and 1 month post-dose 2).

End point type	Secondary

End point timeframe:

Prior to Dose 1 of 10Pn-PD-DiT vaccination in 111347 study (PRE), and at Day 7 and Month 3, e.g. 7 days post Dose 1 of 10Pn-PD-DiT vaccination in 111347 study, and at one month post Dose 2 of 10Pn-PD-DiT vaccination in 111347 study (Unprimed Group only).

End point values	Primed 10Pn-10Pn Group	Primed 7Pn-7Pn Group	Primed 7Pn-10Pn Group	Unprimed Group
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	210	14	54	98
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-6A antibodies, PRE (N=210;14;54;97)	0.91 (0.74 to 1.11)	0.73 (0.32 to 1.68)	0.76 (0.52 to 1.11)	0.2 (0.15 to 0.27)
Anti-6A antibodies, D7 (N=208;14;54;98)	2.2 (1.85 to 2.6)	1.67 (1 to 2.8)	1.33 (0.96 to 1.83)	0.44 (0.33 to 0.58)
Anti-6A antibodies, M3 (N=0;0;0;98)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0.92 (0.73 to 1.16)
Anti-19A antibodies, PRE (N=210;14;55;97)	1.21 (0.97 to 1.5)	0.79 (0.3 to 2.12)	1.04 (0.65 to 1.65)	0.44 (0.32 to 0.6)
Anti-19A antibodies, D7 (N=208;14;54;98)	2.79 (2.33 to 3.35)	2.44 (1.2 to 4.96)	1.72 (1.14 to 2.61)	1.1 (0.84 to 1.45)
Anti-19A antibodies, M3 (N=0;0;0;98)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	2.39 (1.9 to 3.01)

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic activity (OPA) titers against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F – Persistence Analysis in Year 4 Persistence and Immunological Memory 111347 Study.

End point title	Opsonophagocytic activity (OPA) titers against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F – Persistence Analysis in Year 4 Persistence and Immunological Memory 111347 Study.

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. For this endpoint, the analysis was a persistence analysis performed for the time point specified, on the evaluable subjects for this persistence analysis at the specified time points, that is, subjects enrolled in the applicable Year 4 Persistence and Immunological Memory 111347 Study, evaluated as evaluable and for whom for whom assay results were available for the antibodies against at least one vaccine antigen component for the blood sampling taken at Year 2 and/or Year 4 time points.

End point type	Secondary

End point timeframe:

At Years 2 and 4 (Y2 and Y4) time points, e.g. two years (24 to 26 months) and four years (48 to 50 months) post booster vaccination in study 10PN-PD-DIT-007.

End point values	Primed 10Pn-10Pn Group	Primed 7Pn-7Pn Group	Primed 7Pn-10Pn Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	253	16	72	
Units: Titer				
geometric mean (confidence interval 95%)				
Anti-1 OPA Titers, Y2 (N=253;16;71)	8.5 (7.2 to 10.1)	4 (4 to 4)	6.4 (4.9 to 8.4)	
Anti-1 OPA Titers, Y4 (N=250;16;72)	8.8 (7.1 to 10.9)	4.6 (3.4 to 6.4)	8.9 (5.9 to 13.2)	
Anti-4 OPA Titers, Y2 (N=240;16;65)	32.5 (23.5 to 45.2)	41.6 (9.5 to 182.2)	39.9 (22.3 to 71.5)	
Anti-4 OPA Titers, Y4 (N=232;16;63)	37.9 (27.2 to 52.8)	62.2 (13.6 to 284.7)	50.7 (26.5 to 97)	
Anti-5 OPA Titers, Y2 (N=251;16;71)	11.9 (10.1 to 13.9)	4.2 (3.8 to 4.6)	7.3 (5.7 to 9.4)	
Anti-5 OPA Titers, Y4 (N=243;15;68)	7.7 (6.8 to 8.9)	5.3 (3.5 to 8.1)	5.5 (4.5 to 6.6)	
Anti-6B OPA Titers, Y2 (N=245;16;68)	172.3 (120.8 to 245.6)	550.1 (180 to 1681.7)	248.1 (127.3 to 483.7)	
Anti-6B OPA Titers, Y4 (N=250;16;68)	875.7 (658.7 to 1164.3)	978.3 (395.3 to 2421.3)	716.4 (417.4 to 1229.7)	

Anti-7F OPA Titers, Y2 (N=250;16;70)	1557.5 (1399.6 to 1733.3)	1285.8 (794.7 to 2080.3)	1428.7 (1080.1 to 1889.8)	
Anti-7F OPA Titers, Y4 (N=249;15;71)	1693.1 (1489.3 to 1924.8)	965.8 (666.8 to 1398.9)	1602.1 (1286.9 to 1994.5)	
Anti-9V OPA Titers, Y2 (N=249;16;71)	661.2 (568.2 to 769.4)	743.7 (353.4 to 1565)	463.3 (318.4 to 674.2)	
Anti-9V OPA Titers, Y4 (N=250;15;70)	747.4 (624.9 to 894.1)	563.8 (220.2 to 1444)	558.6 (403 to 774.2)	
Anti-14 OPA Titers, Y2 (N=242;15;70)	678 (559.1 to 822.1)	387.9 (164.6 to 913.9)	579 (403.6 to 830.5)	
Anti-14 OPA Titers, Y4 (N=250;15;71)	1139.8 (961.9 to 1350.5)	687.9 (267.8 to 1767.4)	849.4 (645.4 to 1117.8)	
Anti-18C OPA Titers, Y2 (N=229;16;65)	29.4 (21.3 to 40.6)	34 (8.4 to 137.8)	20.7 (11.4 to 37.6)	
Anti-18C OPA Titers, Y4 (N=226;16;63)	46.4 (33.3 to 64.5)	35.3 (8.8 to 142.5)	26.6 (14.3 to 49.3)	
Anti-19F OPA Titers, Y2 (N=249;16;71)	81.2 (60.4 to 109.2)	38.1 (14.1 to 102.8)	93.1 (56.8 to 152.7)	
Anti-19F OPA Titers, Y4 (N=247;16;69)	151.7 (115.9 to 198.4)	178.8 (64.6 to 495.1)	129.3 (83.1 to 201.4)	
Anti-23F OPA Titers, Y2 (N=244;16;70)	577.5 (418.7 to 796.7)	2820.1 (1365.9 to 5822.8)	467.9 (254.4 to 860.6)	
Anti-23F OPA Titers, Y4 (N=239;15;65)	1518.4 (1107.9 to 2080.9)	3366.1 (1599.2 to 7085.1)	1146.2 (596.8 to 2201.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic activity (OPA) titers against cross-reactive pneumococcal serotypes 6A and 19 A – Persistence Analysis in Year 4 Persistence and Immunological Memory 111347 Study.

End point title	Opsonophagocytic activity (OPA) titers against cross-reactive pneumococcal serotypes 6A and 19 A – Persistence Analysis in Year 4 Persistence and Immunological Memory 111347 Study.

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. For this endpoint, the analysis was a persistence analysis performed for the time point specified, on the evaluable subjects for this persistence analysis at the specified time points, that is, subjects enrolled in the applicable Year 4 Persistence and Immunological Memory 111347 Study, evaluated as evaluable and for whom for whom assay results were available for the antibodies against at least one vaccine antigen component for the blood sampling taken at Year 2 and/or Year 4 time points.

End point type	Secondary

End point timeframe:

At Years 2 and 4 (Y2 and Y4) time points, e.g. two years (24 to 26 months) and four years (48 to 50 months) post booster vaccination in study 10PN-PD-DIT-007.

End point values	Primed 10Pn-10Pn Group	Primed 7Pn-7Pn Group	Primed 7Pn-10Pn Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	251	16	71	
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-6A OPA Titers, Y2 (N=223;15;65)	129.4 (96.8 to 172.8)	283.4 (91.6 to 876.3)	167.3 (99.8 to 280.3)	
Anti-6A OPA Titers, Y4 (N=231;14;66)	213.5 (165.4 to 275.7)	227.8 (72.1 to 720)	153.5 (90.5 to 260.2)	
Anti-19A OPA Titers, Y2 (N=251;16;71)	12.6 (9.9 to 16)	8.8 (3.6 to 21.5)	8.9 (6 to 13.1)	
Anti-19A OPA Titers, Y4 (N=246;15;68)	31.2 (23.6 to 41.3)	14.3 (5.6 to 36.8)	21.8 (13.3 to 35.7)	

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 – Immunological Memory Analysis in Year 4 Persistence and Immunological Memory 111347 Study.

End point title	Opsonophagocytic activity (OPA) titers against pneumococcal serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F and 23F – Immunological Memory Analysis in Year 4 Persistence and Immunological Memory 111347 Study.

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. For this endpoint, the results presented are those of the immunological memory analysis part of the Year 4 Persistence and Immunological Memory 111347 Study. Subjects analysed were subjects vaccinated subjects in the 111347 study assessed as evaluable and for whom assay results were available for antibodies against at least one study vaccine antigen component for the blood sample taken 7-10 days after vaccination for primed subjects and for any of blood samples taken from unprimed subjects (i.e. before vaccination, 7-10 days post-dose 1 and 1 month post-dose 2).

End point type	Secondary

End point timeframe:

Prior to Dose 1 of 10Pn-PD-DiT vaccination in 111347 study (PRE), and at Day 7 and Month 3, e.g. 7 days post Dose 1 of 10Pn-PD-DiT vaccination in 111347 study, and at one month post Dose 2 of 10Pn-PD-DiT vaccination in 111347 study (Unprimed Group only).

End point values	Primed 10Pn-10Pn Group	Primed 7Pn-7Pn Group	Primed 7Pn-10Pn Group	Unprimed Group
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	204	13	54	96
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-1 OPA Titers, PRE (N=204;11;54;94)	8.7 (6.9 to 10.9)	4 (4 to 4)	9.9 (6 to 16.4)	5 (4.2 to 5.9)

Anti-1 OPA Titers, D7 (N=197;13;50;92)	2920.8 (2353.5 to 3624.7)	1331 (586.7 to 3019.5)	1816.1 (1090 to 3025.8)	605 (462.7 to 791.2)
Anti-1 OPA Titers, M3 (N=0;0;0;95)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	128.3 (97.3 to 169.1)
Anti-4 OPA Titers, PRE (N=189;11;45;81)	37.3 (25.8 to 54.1)	45.9 (6.9 to 305.4)	53 (24.1 to 116.2)	11.5 (7.2 to 18.3)
Anti-4 OPA Titers, D7 (N=196;13;51;93)	23633.7 (19118.5 to 29215.3)	10650.3 (3969.2 to 28577.6)	8592.8 (5609.3 to 13163.1)	18262.1 (15571.6 to 21417.4)
Anti-4 OPA Titers, M3 (N=0;0;0;94)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	4451.3 (3962.4 to 5000.6)
Anti-5 OPA Titers, PRE (N=196;10;51;92)	7.7 (6.6 to 9)	4 (4 to 4)	5.2 (4.2 to 6.5)	4.9 (4.3 to 5.7)
Anti-5 OPA Titers, D7 (N=193;13;48;91)	822.3 (662.7 to 1020.3)	375.6 (217.4 to 648.9)	683.6 (428.6 to 1090.2)	295.6 (219.4 to 398.3)
Anti-5 OPA Titers, M3 (N=0;0;0;92)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	93.2 (73.7 to 117.8)
Anti-6B OPA Titers, PRE (N=203;11;51;79)	909.7 (664.3 to 1245.7)	884.7 (242.4 to 3229.6)	712 (401.4 to 1263)	70.7 (33.5 to 149.2)
Anti-6B OPA Titers, D7 (N=198;13;50;93)	3513.1 (2858.1 to 4318.1)	3566.6 (2446.1 to 5200.3)	1590.5 (942.8 to 2683.3)	1971.4 (1238 to 3139.2)
Anti-6B OPA Titers, M3 (N=0;0;0;95)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	2536.9 (2014.1 to 3195.5)
Anti-7F OPA Titers, PRE (N=203;11;53;74)	1676.4 (1454.6 to 1932)	1017 (616.6 to 1677.4)	1503.1 (1152.4 to 1960.5)	1368.2 (849.6 to 2185.8)
Anti-7F OPA Titers, D7 (N=199;13;50;93)	25196.4 (21149.5 to 30017.6)	17828.8 (10270.4 to 30949.7)	13098.6 (9715.5 to 17659.8)	19243.4 (15701.4 to 23584.5)
Anti-7F OPA Titers, M3 (N=0;0;0;93)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	9692 (8299.3 to 11318.4)
Anti-9V OPA Titers, PRE (N=203;11;52;87)	806.3 (665.5 to 976.9)	443.6 (121.3 to 1621.7)	459.7 (307.8 to 686.5)	398.2 (253.8 to 624.9)
Anti-9V OPA Titers, D7 (N=201;13;51;93)	9419.4 (7586 to 11695.9)	12234.7 (8280.5 to 18077.3)	7730.3 (5361.8 to 11145.2)	8322.7 (6605.7 to 10486.1)
Anti-9V OPA Titers, M3 (N=0;0;0;94)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	6456.1 (5458.1 to 7636.6)
Anti-14 OPA Titers, PRE (N=203;10;54;83)	1207.7 (999.2 to 1459.7)	507.2 (137 to 1878.1)	955.9 (682.8 to 1338.4)	586.5 (439 to 783.6)
Anti-14 OPA Titers, D7 (N=197;13;51;94)	8572.3 (7145.4 to 10284.3)	4192.8 (2218.6 to 7923.7)	6883.1 (5057.3 to 9368)	4678.2 (3788 to 5777.5)
Anti-14 OPA Titers, M3 (N=0;0;0;95)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	4891.1 (4178.8 to 5724.8)
Anti-18C OPA Titers, PRE (N=183;11;46;89)	49.6 (34.1 to 72)	16.2 (3.2 to 82.5)	31.3 (14.8 to 66.1)	5.3 (4.2 to 6.6)
Anti-18C OPA Titers, D7 (N=194;13;50;92)	3378.9 (2652.2 to 4304.8)	3478.6 (1788.5 to 6765.8)	1663.2 (970.5 to 2850.2)	2503.1 (1692.6 to 3701.6)
Anti-18C OPA Titers, M3 (N=0;0;0;92)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	2255.9 (1876.9 to 2711.4)
Anti-19F OPA Titers, PRE (N=200;11;51;92)	141.2 (104.4 to 190.9)	104.9 (29.1 to 378.1)	132.2 (77 to 226.9)	12 (8.3 to 17.5)
Anti-19F OPA Titers, D7 (N=196;13;50;93)	1346.4 (1068.6 to 1696.5)	2340.4 (654.8 to 8365.2)	662.3 (430 to 1020.1)	700.2 (456.1 to 1074.9)

Anti-19F OPA Titers, M3 (N=0;0;0;93)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	1437.7 (1146.9 to 1802.3)
Anti-23F OPA Titers, PRE (N=194;11;48;83)	1477.4 (1046.2 to 2086.2)	2931 (1904.8 to 7847.3)	1314.1 (612.5 to 2819.7)	176.4 (83.4 to 373.2)
Anti-23F OPA Titers, D7 (N=199;13;50;96)	8700.4 (7021.7 to 10780.5)	11341.1 (5374.6 to 23931)	7871.9 (4965.3 to 12480.1)	6813.9 (5249.5 to 8844.6)
Anti-23F OPA Titers, M3 (N=0;0;0;95)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	5586.1 (4666.1 to 6687.5)

Statistical analyses

No statistical analyses for this end point

Secondary: Opsonophagocytic activity (OPA) titers against pneumococcal serotypes 6A and 19A – Immunological Memory Analysis in Year 4 Persistence and Immunological Memory 111347 Study.

End point title	Opsonophagocytic activity (OPA) titers against pneumococcal serotypes 6A and 19A – Immunological Memory Analysis in Year 4 Persistence and Immunological Memory 111347 Study.

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. For this endpoint, the results presented are those of the immunological memory analysis part of the Year 4 Persistence and Immunological Memory 111347 Study. Subjects analyzed were subjects vaccinated subjects in the 111347 study assessed as evaluable and for whom assay results were available for antibodies against at least one study vaccine antigen component for the blood sample taken 7-10 days after vaccination for primed subjects and for any of blood samples taken from unprimed subjects (i.e. before vaccination, 7-10 days post-dose 1 and 1 month post-dose 2).

End point type	Secondary

End point timeframe:

Prior to Dose 1 of 10Pn-PD-DiT vaccination in 111347 study (PRE), and at Day 7 (D7) and Month 3 (M3), e.g. 7 days post Dose 1 of 10Pn-PD-DiT vaccination in 111347 study, and at one month post Dose 2 of 10Pn-PD-DiT vaccination in 111347 study.

End point values	Primed 10Pn-10Pn Group	Primed 7Pn-7Pn Group	Primed 7Pn-10Pn Group	Unprimed Group
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	201	13	50	92
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-6A OPA Titers, PRE (N=192;10;50;82)	211.2 (160.2 to 278.5)	195.2 (39.8 to 958)	130.1 (69.5 to 243.6)	102.6 (61.5 to 171.2)
Anti-6A OPA Titers, D7 (N=189;12;49;90)	1217.7 (957.8 to 1548.2)	1490.2 (681.6 to 3257.8)	467.7 (293.8 to 744.5)	826.5 (593.9 to 1150.2)
Anti-6A OPA Titers, M3 (N=0;0;0;91)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	943.4 (691.3 to 1287.4)
Anti-19A OPA Titers, PRE (N=201;11;50;92)	31.5 (23.2 to 42.9)	7.3 (4 to 13.1)	19.6 (11.2 to 34.3)	9.9 (7 to 13.8)

Anti-19A OPA Titers, D7 (N=194;13;48;90)	467 (335 to 651.1)	437.6 (81.3 to 2356.3)	106.1 (54.1 to 208.3)	431.2 (269.4 to 689.9)
Anti-19A OPA Titers, M3 (N=0;0;0;91)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	376.4 (256.3 to 552.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations to protein D (Anti-PD) – Persistence Analysis in Year 4 Persistence and Immunological Memory 111347 Study.

End point title	Antibody concentrations to protein D (Anti-PD) – Persistence Analysis in Year 4 Persistence and Immunological Memory 111347 Study.

End point description:

Anti-protein D (Anti-PD) antibody concentrations by Enzyme-Linked Immunosorbent Assay (ELISA) were calculated, expressed as geometric mean concentrations (GMCs) in ELISA unit per milli-liter (EL.U/mL) and tabulated. The seropositivity cut-off for the assay was ≥ 100 EL.U/mL. For this endpoint, the analysis was a persistence analysis performed for the time point specified, on the evaluable subjects for this persistence analysis at the specified time points, that is, subjects enrolled in the applicable Year 4 Persistence and Immunological Memory 111347 Study, evaluated as evaluable and for whom for whom assay results were available for the antibodies against at least one vaccine antigen component for the blood sampling taken at Year 2 and/or Year 4 time points.

End point type	Secondary

End point timeframe:

At Years 2 and 4 (Y2 and Y4) time points, e.g. two years (24 to 26 months) and four years (48 to 50 months) post booster vaccination in study 10PN-PD-DIT-007.

End point values	Primed 10Pn-10Pn Group	Primed 7Pn-7Pn Group	Primed 7Pn-10Pn Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	264	19	75	
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD antibodies, Y2 (N=264;18;75)	595.1 (514.7 to 688.1)	131.4 (78.5 to 219.9)	158.4 (125.7 to 199.6)	
Anti-PD antibodies, Y4 (N=261;19;74)	372.4 (329.6 to 420.9)	144.9 (86.3 to 243.2)	161.4 (128.4 to 203)	

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations to protein D (Anti-PD) – Immunological Memory Analysis in Year 4 Persistence and Immunological Memory 111347 Study.

End point title	Antibody concentrations to protein D (Anti-PD) – Immunological Memory Analysis in Year 4 Persistence and Immunological Memory 111347 Study.

End point description:

Anti-protein D (Anti-PD) antibody concentrations by Enzyme-Linked Immunosorbent Assay (ELISA) were calculated, expressed as geometric mean concentrations (GMCs) in ELISA unit per milli-liter (EL.U/mL) and tabulated. The seropositivity cut-off for the assay was ≥ 100 EL.U/mL. For this endpoint, the results presented are those of the immunological memory analysis part of the Year 4 Persistence and Immunological Memory 111347 Study. Subjects analyzed were subjects vaccinated subjects in the 111347 study assessed as evaluable and for whom assay results were available for antibodies against at least one study vaccine antigen component for the blood sample taken 7-10 days after vaccination for primed subjects and for any of blood samples taken from unprimed subjects (i.e. before vaccination, 7-10 days post-dose 1 and 1 month post-dose 2).

End point type	Secondary

End point timeframe:

Prior to Dose 1 of 10Pn-PD-DiT vaccination in 111347 study (PRE), and at Day 7 and Month 3, e.g. 7 days post Dose 1 of 10Pn-PD-DiT vaccination in 111347 study, and at one month post Dose 2 of 10Pn-PD-DiT vaccination in 111347 study (Unprimed Group only).

End point values	Primed 10Pn-10Pn Group	Primed 7Pn-7Pn Group	Primed 7Pn-10Pn Group	Unprimed Group
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	208	14	54	96
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PD antibodies, PRE (N=208;14;54;95)	374.3 (324.8 to 431.3)	133.3 (78.3 to 227)	141.6 (109.1 to 183.8)	106 (91.1 to 123.4)
Anti-PD antibodies, D7 (N=208;14;54;96)	2106 (1806.7 to 2454.9)	718.2 (442.5 to 1165.7)	680.7 (522.9 to 886.2)	382.9 (320.7 to 457.2)
Anti-PD antibodies, M3 (N=0;0;0;98)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	708.6 (604.6 to 830.4)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

SAEs: from Month 1, e.g. one month post booster vaccination in study 10PN-PD-DIT-007, to one (primed subjects) and 3 months (unprimed subjects) post Dose 1 of 10Pn-PD-DiT vaccine in study 111347.

Adverse event reporting additional description:

Solicited & Unsolicited AEs: within 4 days (Days 0-3) & 31 days (Day 0-30) post 10Pn-PD-DiT vaccination in 111347 Study, respectively, across doses when applicable (Primed 10Pn-10Pn, Primed 7Pn-7Pn & Primed 7Pn-10Pn groups). The occurrence of reported AEs (all/related) was not available and is encoded as equal to the number of subjects affected.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.1

Reporting groups

Reporting group title	Primed 10Pn-10Pn Group

Reporting group description:

This group consisted of subjects primed with 10Pn-PD-DiT vaccine in the 10PN-PD-DIT-001 (1105553) and 007 (107046) studies (EudraCT: 2005-003300-11 & 2006-001628-38). In 105553 study, subjects had been primed with 3 doses of 10Pn vaccine at 2, 3 and 4 months of age co-administered with DTPa-related vaccines. In 107046 study, subjects had received a booster dose of 10Pn vaccine at 12-18 months of age co-administered with DTPa-HBV-IPV/Hib vaccine. In this study, in the Year 4 111347 study, subjects received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of 10Pn-PD-DiT vaccine intramuscularly in the right of left deltoid muscle. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix™) and/or against varicella (a single dose of Varilrix™). These vaccines were to be given after the blood sampling procedure.

Reporting group title	Primed 7Pn-7Pn Group

Reporting group description:

This group consisted of subjects vaccinated with 7Pn (Prevenar™) vaccine in the 10PN-PD-DIT-001 (105553) and 007 (107046) studies (EudraCT: 2005-003300-11 & 2006-001628-38). In 105553 study, subjects had been primed with 3 doses of 7Pn vaccine at 2, 3 and 4 months of age co-administered with DTPa-related vaccines. In 107046 study, subjects had received a booster dose at 12-18 months of age of 7Pn vaccine co-administered with DTPa-HBV-IPV/Hib vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one dose of 10Pn-PD-DiT vaccine intramuscularly in the right of left deltoid muscle. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix™ and/or against varicella (a single dose of Varilrix™). These vaccines were to be given after the blood sampling procedure.

Reporting group title	Primed 7Pn-10Pn Group

Reporting group description:

This group consisted of subjects vaccinated with 7Pn (Prevenar™) and 10Pn-PD-DiT vaccines in the 10PN-PD-DIT-001 (105553) and 10PN-PD-DIT-007 (107046) studies (EudraCT: 2005-003300-11 and 2006-001628-38). In 105553 study, subjects had been primed with 3 doses 7Pn vaccine at 2, 3 and 4 months of age co-administered with DTPa-related vaccines. In the 107046 study, subjects had received at 12-18 months of age a booster dose of 10Pn-PD-DiT vaccine co-administered with DTPa-HBV-IPV/Hib vaccine. In this study, in the Year 4 111347 study, subjects had received at Month 48 (4 years post Dose 1 in study 105553) one additional dose of 10Pn-PD-DiT vaccine intramuscularly in the right of left deltoid muscle. In addition, subjects were also offered vaccination against hepatitis A (2 doses of Havrix™ and/or against varicella (a single dose of Varilrix™). These vaccines were to be given after the blood sampling procedure.

Reporting group title	Unprimed Group

Reporting group description:

This group consisted of age-matched subjects enrolled at the time of and in the Year 4 111347 study alone aged between 64 and 68 months previously unprimed with any pneumococcal vaccine who received 2 doses of the 10Pn-PD-DiT vaccine in their 6th year of life at Months 48 and 50 (timing by reference to Month 0 as Dose 1 of vaccine in study 10PN-PD-DIT-001 (105553) by GSK Biologicals (EudraCT: 2005-003300-11). The 10Pn-PD-DiT vaccine was injected intramuscularly in the right of left deltoid muscle. Age-matching to Primed Subjects was met by first vaccination of unprimed subjects at 64-68 months of age, time when primed subjects received an additional dose of 10Pn-PD-DiT vaccine.

Two doses of 10Pn vaccine by intramuscular use were administered in the left thigh or deltoid at 64-68 (= Day 0 in the 111347 study) and 65-69 months of age (= Month 1 in the 111347 study).

Serious adverse events	Primed 10Pn-10Pn Group	Primed 7Pn-7Pn Group	Primed 7Pn-10Pn Group
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 391 (0.26%)	0 / 31 (0.00%)	0 / 102 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Infections and infestations			
Broncopneumonia			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 391 (0.26%)	0 / 31 (0.00%)	0 / 102 (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

Serious adverse events	Unprimed Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 100 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Infections and infestations			
Broncopneumonia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 100 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Primed 10Pn-10Pn Group	Primed 7Pn-7Pn Group	Primed 7Pn-10Pn Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	157 / 391 (40.15%)	9 / 31 (29.03%)	34 / 102 (33.33%)
General disorders and administration site conditions			
Pain			

subjects affected / exposed[1]	157 / 264 (59.47%)	9 / 20 (45.00%)	34 / 64 (53.13%)
occurrences (all)	157	9	34
Redness			
subjects affected / exposed[2]	90 / 264 (34.09%)	5 / 20 (25.00%)	14 / 64 (21.88%)
occurrences (all)	90	5	14
Swelling			
subjects affected / exposed[3]	67 / 264 (25.38%)	4 / 20 (20.00%)	15 / 64 (23.44%)
occurrences (all)	67	4	15
Drowsiness			
subjects affected / exposed[4]	49 / 263 (18.63%)	2 / 20 (10.00%)	12 / 64 (18.75%)
occurrences (all)	49	2	12
irritability			
subjects affected / exposed[5]	35 / 263 (13.31%)	4 / 20 (20.00%)	6 / 64 (9.38%)
occurrences (all)	35	4	6
Loss of appetite			
subjects affected / exposed[6]	30 / 263 (11.41%)	3 / 20 (15.00%)	6 / 64 (9.38%)
occurrences (all)	30	3	6
Fever (Axillary temperature >= 37.5°C)			
subjects affected / exposed[7]	13 / 263 (4.94%)	0 / 20 (0.00%)	2 / 64 (3.13%)
occurrences (all)	13	0	2

Non-serious adverse events	Unprimed Group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	54 / 100 (54.00%)		
General disorders and administration site conditions			
Pain			
subjects affected / exposed[1]	54 / 100 (54.00%)		
occurrences (all)	54		
Redness			
subjects affected / exposed[2]	21 / 100 (21.00%)		
occurrences (all)	21		
Swelling			
subjects affected / exposed[3]	20 / 100 (20.00%)		
occurrences (all)	20		
Drowsiness			

subjects affected / exposed[4]	12 / 100 (12.00%)		
occurrences (all)	12		
irritability			
subjects affected / exposed[5]	8 / 100 (8.00%)		
occurrences (all)	8		
Loss of appetite			
subjects affected / exposed[6]	13 / 100 (13.00%)		
occurrences (all)	13		
Fever (Axillary temperature >= 37.5°C)			
subjects affected / exposed[7]	5 / 100 (5.00%)		
occurrences (all)	5		

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Analysis for solicited symptoms post vaccination was done solely on subjects participating to the Immunological Memory phase of the 111347 study, on subjects with results available for the specified symptom.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Analysis for solicited symptoms post vaccination was done solely on subjects participating to the Immunological Memory phase of the 111347 study, on subjects with results available for the specified symptom.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Analysis for solicited symptoms post vaccination was done solely on subjects participating to the Immunological Memory phase of the 111347 study, on subjects with results available for the specified symptom.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Analysis for solicited symptoms post vaccination was done solely on subjects participating to the Immunological Memory phase of the 111347 study, on subjects with results available for the specified symptom.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Analysis for solicited symptoms post vaccination was done solely on subjects participating to the Immunological Memory phase of the 111347 study, on subjects with results available for the specified symptom.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Analysis for solicited symptoms post vaccination was done solely on subjects participating to the Immunological Memory phase of the 111347 study, on subjects with results available for the specified symptom.

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: Analysis for solicited symptoms post vaccination was done solely on subjects participating to the Immunological Memory phase of the 111347 study, on subjects with results available for the specified symptom.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 June 2010	The protocol was amended on 22 June 2010 in response to a request from Committee on Human Medicinal Products (CHMP) to obtain data on immunological memory in children previously vaccinated with four doses of pneumococcal conjugate vaccine. In addition, information on the storage conditions for the study vaccine, the contact details for the back-up study contact for reporting SAEs and the list of the contributing authors were updated. Changes made also included some amendments to the phrasing of the study detailed title.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported