



## 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        | <ul style="list-style-type: none"><li>• Correction of full data set</li></ul> 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)                    | EMA-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 to 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:

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**Subjects enrolled per age group**

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|   |     |
|---|-----|
| 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   |

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## 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.

|                  |                      |
|------------------|----------------------|
| <b>Arm title</b> | 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.

|                  |                       |
|------------------|-----------------------|
| <b>Arm title</b> | 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.

|                  |                      |
|------------------|----------------------|
| <b>Arm title</b> | 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.

|                  |                       |
|------------------|-----------------------|
| <b>Arm title</b> | 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 <sup>[1]</sup> | 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.

|                  |                      |
|------------------|----------------------|
| <b>Arm title</b> | 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.

|                  |                       |
|------------------|-----------------------|
| <b>Arm title</b> | 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.

| <b>Number of subjects in period 3[2]</b> | 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 |
|------------------------------|-----|

|  |  |
|--|--|
| <b>Arm title</b>   | 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.

|   |  |
|---|--|
| <b>Arm title</b>  | 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.

|                  |                       |
|------------------|-----------------------|
| <b>Arm title</b> | 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.

| <b>Number of subjects in period 4<sup>[3]</sup></b> | 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<br>Units: Subjects |     |    |    |
| Female                                | 203 | 14 | 52 |
| Male                                  | 188 | 17 | 50 |

|  |       |  |  |
|--|-------|--|--|
| <b>Reporting group values</b>  | Total |  |  |
| Number of subjects   | 524   |  |  |
| Age categorical<br>Units: Subjects                                       |       |  |  |
| In utero   | 0     |  |  |
| Preterm newborn infants<br>(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<br>Units: months<br>arithmetic mean<br>standard deviation | -     |  |  |
| Gender categorical<br>Units: Subjects                                    |       |  |  |
| Female   | 269   |  |  |
| Male   | 255   |  |  |



## End points

### 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  $\geq 0.05$  microgram per millilitre ( $\mu\text{g/mL}$ ) – Persistence Analysis in 111345 Year 1 Follow-up study.**

|                 |   |
|-----------------|---|
| End point title | Number of subjects with anti-vaccine pneumococcal serotypes antibody concentrations $\geq 0.05$ microgram per millilitre ( $\mu\text{g/mL}$ ) – Persistence Analysis in 111345 Year 1 Follow-up study. <sup>[1]</sup> |
|-----------------|---|

End point description:

Analysis was performed using the 22F-inhibition Enzyme-linked immunosorbent assay (ELISA), using  $\geq 0.05 \mu\text{g/mL}$  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 $\geq 0.05 \mu\text{g/mL}$ , M1 (N=195;29;47)  | 195                    | 11                   | 45                    |  |
| Anti-1 $\geq 0.05 \mu\text{g/mL}$ , Y1 (N=387;29;102) | 372                    | 7                    | 99                    |  |
| Anti-4 $\geq 0.05 \mu\text{g/mL}$ , M1 (N=196;30;47)  | 196                    | 30                   | 47                    |  |

|  |     |    |     |  |
|--|-----|----|-----|--|
| Anti-4 $\geq$ 0.05 $\mu\text{g/mL}$ , Y1<br>(N=387;31;102)   | 384 | 31 | 102 |  |
| Anti-5 $\geq$ 0.05 $\mu\text{g/mL}$ , M1<br>(N=195;30;47)    | 195 | 17 | 45  |  |
| Anti-5 $\geq$ 0.05 $\mu\text{g/mL}$ , Y1 (N=387<br>;30;101)  | 386 | 19 | 101 |  |
| Anti-6B $\geq$ 0.05 $\mu\text{g/mL}$ , M1<br>(N=193;30;47)   | 191 | 30 | 47  |  |
| Anti-6B $\geq$ 0.05 $\mu\text{g/mL}$ , Y1<br>(N=389;31;102)  | 384 | 31 | 100 |  |
| Anti-7F $\geq$ 0.05 $\mu\text{g/mL}$ , M1<br>(N=194;29;47)   | 194 | 12 | 46  |  |
| Anti-7F $\geq$ 0.05 $\mu\text{g/mL}$ , Y1<br>(N=387;31;102)  | 387 | 17 | 102 |  |
| Anti-9V $\geq$ 0.05 $\mu\text{g/mL}$ , M1<br>(N=193;31;47)   | 193 | 31 | 47  |  |
| Anti-9V $\geq$ 0.05 $\mu\text{g/mL}$ , Y1<br>(N=388;31;102)  | 388 | 31 | 102 |  |
| Anti-14 $\geq$ 0.05 $\mu\text{g/mL}$ , M1<br>(N=192;30;47)   | 192 | 30 | 47  |  |
| Anti-14 $\geq$ 0.05 $\mu\text{g/mL}$ , Y1<br>(N=388;31;102)  | 387 | 31 | 102 |  |
| Anti-18C $\geq$ 0.05 $\mu\text{g/mL}$ , M1<br>(N=195;30;48)  | 195 | 30 | 48  |  |
| Anti-18C $\geq$ 0.05 $\mu\text{g/mL}$ , Y1<br>(N=384;31;102) | 384 | 31 | 102 |  |
| Anti-19F $\geq$ 0.05 $\mu\text{g/mL}$ , M1<br>(N=196;30;48)  | 196 | 30 | 48  |  |
| Anti-19F $\geq$ 0.05 $\mu\text{g/mL}$ , Y1<br>(N=387;30;102) | 387 | 30 | 102 |  |
| Anti-23F $\geq$ 0.05 $\mu\text{g/mL}$ , M1<br>(N=194;30;46)  | 193 | 30 | 46  |  |
| Anti-23F $\geq$ 0.05 $\mu\text{g/mL}$ , Y1<br>(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 $\geq$ 0.05 microgram per millilitre ( $\mu\text{g/mL}$ ) – Persistence Analysis in 111346 Year 2 Follow-Up Study.

|                 |   |
|-----------------|---|
| End point title | Number of subjects with anti-vaccine pneumococcal serotypes antibody concentrations $\geq$ 0.05 microgram per millilitre ( $\mu\text{g/mL}$ ) – Persistence Analysis in 111346 Year 2 Follow-Up Study. <sup>[2]</sup> |
|-----------------|---|

### End point description:

Analysis was performed using the 22F-inhibition Enzyme-linked immunosorbent assay (ELISA), using  $\geq$  0.05  $\mu\text{g/mL}$  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-<br>10Pn Group | Primed 7Pn-<br>7Pn Group | Primed 7Pn-<br>10Pn Group |  |
|---|----------------------------|--------------------------|---------------------------|--|
| Subject group type                              | Reporting group            | Reporting group          | Reporting group           |  |
| Number of subjects analysed                     | 368                        | 30                       | 96                        |  |
| Units: Subjects                                 |                            |                          |                           |  |
| Anti-1 $\geq$ 0.05 µg/mL, Y1<br>(N=365;28;96)   | 351                        | 7                        | 93                        |  |
| Anti-1 $\geq$ 0.05 µg/mL, Y2<br>(N=367;29;96)   | 354                        | 18                       | 90                        |  |
| Anti-4 $\geq$ 0.05 µg/mL, Y1<br>(N=365;30;96)   | 362                        | 30                       | 96                        |  |
| Anti-4 $\geq$ 0.05 µg/mL, Y2<br>(N=368;30;96)   | 356                        | 30                       | 96                        |  |
| Anti-5 $\geq$ 0.05 µg/mL, Y1<br>(N=365;29;95)   | 364                        | 18                       | 95                        |  |
| Anti-5 $\geq$ 0.05 µg/mL, Y2<br>(N=368;29;95)   | 362                        | 21                       | 95                        |  |
| Anti-6B $\geq$ 0.05 µg/mL, Y1<br>(N=367;30;96)  | 362                        | 30                       | 94                        |  |
| Anti-6B $\geq$ 0.05 µg/mL, Y2<br>(N=368;30;96)  | 355                        | 30                       | 95                        |  |
| Anti-7F $\geq$ 0.05 µg/mL, Y1<br>(N=365;30;96)  | 365                        | 16                       | 96                        |  |
| Anti-7F $\geq$ 0.05 µg/mL, Y2<br>(N=368;30;96)  | 367                        | 19                       | 95                        |  |
| Anti-9V $\geq$ 0.05 µg/mL, Y1<br>(N=366;30;96)  | 366                        | 30                       | 96                        |  |
| Anti-9V $\geq$ 0.05 µg/mL, Y2<br>(N=368;30;96)  | 362                        | 30                       | 96                        |  |
| Anti-14 $\geq$ 0.05 µg/mL, Y1<br>(N=366;30;96)  | 365                        | 30                       | 96                        |  |
| Anti-14 $\geq$ 0.05 µg/mL, Y2<br>(N=368;30;96)  | 367                        | 30                       | 96                        |  |
| Anti-18C $\geq$ 0.05 µg/mL, Y1<br>(N=362;30;96) | 362                        | 30                       | 96                        |  |
| Anti-18C $\geq$ 0.05 µg/mL, Y2<br>(N=368;30;96) | 365                        | 30                       | 96                        |  |
| Anti-19F $\geq$ 0.05 µg/mL, Y1<br>(N=365;29;96) | 365                        | 29                       | 96                        |  |
| Anti-19F $\geq$ 0.05 µg/mL, Y2<br>(N=368;30;95) | 368                        | 30                       | 95                        |  |
| Anti-23F $\geq$ 0.05 µg/mL, Y1<br>(N=366;30;96) | 364                        | 30                       | 96                        |  |
| Anti-23F $\geq$ 0.05 µg/mL, Y2<br>(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  $\geq 0.05$  microgram per millilitre ( $\mu\text{g/mL}$ ) – Persistence Analysis in Year 4 Persistence and Immunological Memory 111347 Study.**

|                 |  |
|-----------------|--|
| End point title | Number of subjects with anti-vaccine pneumococcal serotypes antibody concentrations $\geq 0.05$ microgram per millilitre ( $\mu\text{g/mL}$ ) – Persistence Analysis in Year 4 Persistence and Immunological Memory 111347 Study. <sup>[3]</sup> |
|-----------------|--|

End point description:

Analysis was performed using the 22F-inhibition Enzyme-linked immunosorbent assay (ELISA), using  $\geq 0.05 \mu\text{g/mL}$  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 $\geq 0.05 \mu\text{g/mL}$ , Y2 (N=263;18;75)   | 250                    | 11                   | 70                    |  |
| Anti-1 $\geq 0.05 \mu\text{g/mL}$ , Y4 (N=263;19;75)   | 238                    | 14                   | 71                    |  |
| Anti-4 $\geq 0.05 \mu\text{g/mL}$ , Y2 (N=264;19;75)   | 254                    | 19                   | 75                    |  |
| Anti-4 $\geq 0.05 \mu\text{g/mL}$ , Y4 (N=263;18;74)   | 238                    | 18                   | 72                    |  |
| Anti-5 $\geq 0.05 \mu\text{g/mL}$ , Y2 (N=264;18;75)   | 260                    | 10                   | 75                    |  |
| Anti-5 $\geq 0.05 \mu\text{g/mL}$ , Y4 (N=263;19;74)   | 257                    | 19                   | 73                    |  |
| Anti-6B $\geq 0.05 \mu\text{g/mL}$ , Y2 (N=264;19;75)  | 255                    | 19                   | 74                    |  |
| Anti-6B $\geq 0.05 \mu\text{g/mL}$ , Y4 (N=263;19;75)  | 258                    | 19                   | 74                    |  |
| Anti-7F $\geq 0.05 \mu\text{g/mL}$ , Y2 (N=264;19;75)  | 263                    | 15                   | 75                    |  |
| Anti-7F $\geq 0.05 \mu\text{g/mL}$ , Y4 (N=263;19;75)  | 260                    | 13                   | 73                    |  |
| Anti-9V $\geq 0.05 \mu\text{g/mL}$ , Y2 (N=264;19;75)  | 259                    | 19                   | 75                    |  |
| Anti-9V $\geq 0.05 \mu\text{g/mL}$ , Y4 (N=263;19;75)  | 255                    | 19                   | 72                    |  |
| Anti-14 $\geq 0.05 \mu\text{g/mL}$ , Y2 (N=264;19;75)  | 263                    | 19                   | 75                    |  |
| Anti-14 $\geq 0.05 \mu\text{g/mL}$ , Y4 (N=263;19;75)  | 263                    | 19                   | 75                    |  |
| Anti-18C $\geq 0.05 \mu\text{g/mL}$ , Y2 (N=264;18;75) | 262                    | 19                   | 75                    |  |
| Anti-18C $\geq 0.05 \mu\text{g/mL}$ , Y4 (N=263;18;74) | 256                    | 19                   | 73                    |  |

|   |     |    |    |  |
|---|-----|----|----|--|
| Anti-19F $\geq$ 0.05 $\mu\text{g/mL}$ , Y2<br>(N=264;19;74) | 264 | 19 | 74 |  |
| Anti-19F $\geq$ 0.05 $\mu\text{g/mL}$ , Y4<br>(N=263;19;75) | 260 | 19 | 75 |  |
| Anti-23F $\geq$ 0.05 $\mu\text{g/mL}$ , Y2<br>(N=264;19;75) | 259 | 19 | 74 |  |
| Anti-23F $\geq$ 0.05 $\mu\text{g/mL}$ , Y4<br>(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 ( $\mu\text{g/mL}$ ). The seropositivity cut-off for the assay was  $\geq$  0.05  $\mu\text{g/mL}$ . 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: $\mu\text{g/mL}$                  |                        |                      |                       |  |
| 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  $\geq 0.05$  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 |
|-----------------|---|

## 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 ( $\mu\text{g/mL}$ ). The seropositivity cut-off for the assay was  $\geq 0.05 \mu\text{g/mL}$ . 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: $\mu\text{g/mL}$                  |                        |                      |                       |  |
| 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 ( $\mu\text{g/mL}$ ). The seropositivity cut-off for the assay was  $\geq 0.05 \mu\text{g/mL}$ . 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  $\geq 8$ . 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 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  $\geq 8$ . 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 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  $\geq 8$ . 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  $\geq 8$ . 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  $\geq 100$  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  $\geq 100$  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 as 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 |
|-----------------|--|

## 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 as 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 as 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 as 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 as 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  $\geq 0.05$  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  $\geq 0.05$  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 $\geq 0.05$ 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<br>(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<br>(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<br>(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<br>(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<br>(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<br>(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<br>(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<br>(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<br>(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<br>(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<br>(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<br>(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<br>(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<br>(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<br>(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<br>(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<br>(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<br>(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<br>(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<br>(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  $\geq 0.05$  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  $\geq 8$ . 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  $\geq 8$ . 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  $\geq 8$ . 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<br>(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<br>(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<br>(N=196;13;51;93)    | 23633.7<br>(19118.5 to 29215.3) | 10650.3<br>(3969.2 to 28577.6)  | 8592.8 (5609.3 to 13163.1)     | 18262.1<br>(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<br>(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<br>(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<br>(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<br>(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<br>(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<br>(N=199;13;50;93)   | 25196.4<br>(21149.5 to 30017.6) | 17828.8<br>(10270.4 to 30949.7) | 13098.6<br>(9715.5 to 17659.8) | 19243.4<br>(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<br>(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<br>(N=201;13;51;93)   | 9419.4 (7586 to 11695.9)        | 12234.7<br>(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<br>(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<br>(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<br>(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<br>(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<br>(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<br>(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  $\geq 8$ . 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<br>(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  $\geq 100$  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. |
|-----------------|---|

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**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  $\geq 100$  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).

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|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

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**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).

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| 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) |

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**Statistical analyses**

No statistical analyses for this end point

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## 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).

| <b>Serious adverse events</b>                     | 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                 |

| <b>Serious adverse events</b>                     | 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 %

| <b>Non-serious adverse events</b>                     | 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 <sup>[1]</sup> | 157 / 264 (59.47%) | 9 / 20 (45.00%) | 34 / 64 (53.13%) |
| occurrences (all)                          | 157                | 9               | 34               |
| Redness                                    |                    |                 |                  |
| subjects affected / exposed <sup>[2]</sup> | 90 / 264 (34.09%)  | 5 / 20 (25.00%) | 14 / 64 (21.88%) |
| occurrences (all)                          | 90                 | 5               | 14               |
| Swelling                                   |                    |                 |                  |
| subjects affected / exposed <sup>[3]</sup> | 67 / 264 (25.38%)  | 4 / 20 (20.00%) | 15 / 64 (23.44%) |
| occurrences (all)                          | 67                 | 4               | 15               |
| Drowsiness                                 |                    |                 |                  |
| subjects affected / exposed <sup>[4]</sup> | 49 / 263 (18.63%)  | 2 / 20 (10.00%) | 12 / 64 (18.75%) |
| occurrences (all)                          | 49                 | 2               | 12               |
| irritability                               |                    |                 |                  |
| subjects affected / exposed <sup>[5]</sup> | 35 / 263 (13.31%)  | 4 / 20 (20.00%) | 6 / 64 (9.38%)   |
| occurrences (all)                          | 35                 | 4               | 6                |
| Loss of appetite                           |                    |                 |                  |
| subjects affected / exposed <sup>[6]</sup> | 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 <sup>[7]</sup> | 13 / 263 (4.94%)   | 0 / 20 (0.00%)  | 2 / 64 (3.13%)   |
| occurrences (all)                          | 13                 | 0               | 2                |

| <b>Non-serious adverse events</b>                     | 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 <sup>[1]</sup>            | 54 / 100 (54.00%) |  |  |
| occurrences (all)                                     | 54                |  |  |
| Redness   |                   |  |  |
| subjects affected / exposed <sup>[2]</sup>            | 21 / 100 (21.00%) |  |  |
| occurrences (all)                                     | 21                |  |  |
| Swelling  |                   |  |  |
| subjects affected / exposed <sup>[3]</sup>            | 20 / 100 (20.00%) |  |  |
| occurrences (all)                                     | 20                |  |  |
| Drowsiness  |                   |  |  |

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

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported