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PROPRIETARY DRUG NAME® / GENERIC DRUG NAME: Prevnar 13® / Prevenar 13® / 13-Valent pneumococcal conjugate vaccine

PROTOCOL NO.: 6115A1-3005 (B1851024)

PROTOCOL TITLE: A Phase 3, Randomized, Active-Controlled, Modified Double-Blind Trial, Evaluating the Safety, Tolerability, and Immunogenicity of a 13-Valent Pneumococcal Conjugate Vaccine Compared With a 23-Valent Pneumococcal Polysaccharide Vaccine (23vPS) in Ambulatory Elderly Individuals Aged 70 Years and Older Who Received 1 Dose of 23vPS at Least 5 Years Before Study Enrollment

Study Centers: A total of 61 centers took part in the study and enrolled subjects; 54 in the United States (US) and 7 in Sweden.

Study Initiation and Final Completion Dates: 15 November 2007 to 06 May 2010;

Final Serology Date: 15 July 2010

Phase of Development: Phase 3

Study Objectives:

Primary Objectives:

- To demonstrate that 13-valent pneumococcal conjugate vaccine (13vPnC) was as immunogenic as 23vPS for the 12 common serotypes contained in 13vPnC as measured by serotype-specific opsonophagocytic assay (OPA) titers 1 month after initial study vaccination (Year 0);

- To show that the proportion of subjects receiving 13vPnC and exhibiting a 4-fold rise in the 6A OPA titer was statistically significantly greater than the proportion of subjects receiving 23vPS exhibiting the same 4-fold rise, measured 1 month after initial study vaccination (Year 0).

Secondary Objectives:

At Year 0:

- To demonstrate that 13vPnC was statistically significantly more immunogenic than 23vPS for at least some of the 12 common serotypes contained in 13vPnC as measured by serotype-specific OPA titers 1 month after initial study vaccination;

- To demonstrate that the anti-6A OPA titer in the 13vPnC recipients was statistically significantly greater than the anti-6A titer in 23vPS recipients measured 1 month after initial study vaccination.

At Year 1:

- To demonstrate that the immune response to a second dose of 13vPnC administered 1 year after an initial study dose of 13vPnC was noninferior to the immune response to the initial study dose of 13vPnC as measured by serotype-specific OPA titers obtained 1 month after vaccination;

- To demonstrate that the immune response to a second dose of 13vPnC administered 1 year after an initial study dose of 13vPnC was noninferior to the immune response to 23vPS (Year 0) for the 12 common serotypes contained in the 13vPnC as measured by serotype-specific OPA titers obtained 1 month after vaccination;

- To demonstrate that the anti-6A titer in recipients of a second dose of 13vPnC administered 1 year after the initial study dose of 13vPnC was statistically significantly greater than the anti-6A titer in recipients of an initial study dose of 23vPS (Year 0), measured 1 month after vaccination.

Safety Objectives:

- To evaluate the acceptability of the safety profile of 13vPnC as measured by the incidence rates of local reactions, systemic events, and adverse events (AEs);

- To evaluate clinical and statistical differences between 23vPS and 13vPnC groups at Year 0 for injection site pain, redness and swelling, limitation of arm movement, and generalized muscle pain.

METHODS

Study Design: This was a Phase 3, randomized, active-controlled, modified double-blind multicenter trial to compare the safety, tolerability, and immunogenicity of 13vPnC with that of 23vPS in healthy adults aged 70 years or older. All subjects had to have received 1 dose of 23vPS at least 5 years before study enrollment.

Subjects were randomly assigned in a 1:1 ratio to receive 13vPnC or 23vPS at Vaccination 1 (Year 0). All subjects were to receive 13vPnC at Vaccination 2 (Year 1).

Subjects received either 13vPnC or 23vPS at Vaccination 1, followed by immunogenicity and safety assessments at approximately 1 month after Vaccination 1 and safety assessments at approximately 6 months after Vaccination 1. At approximately 1 year after Vaccination 1, all subjects received 13vPnC at Vaccination 2. The immunogenicity and safety of the 2 treatment sequences (13vPnC/13vPnC and 23vPS/13vPnC) were assessed at approximately 1 month after Vaccination 2 and safety was assessed approximately 6 months after Vaccination 2. Subjects participated in the study for approximately 18 months. The study flow chart is presented in Table 1.

Table 1. Study Flowchart

Visit ID	1	2	3	4	5	6
Visit Description	**Vaccination 1**	**Postvaccination 1**	**6-Month FUP**	**Vaccination 2**	**Postvaccination 2**	**6-Month FUP**
Visit Window	**Day 1**	**29 to 43 Days After Visit 1**	**166 to 194 Days After Visit 1/ Telephone Call**	**351 to 379 Days After Visit 1**	**29 to 43 Days After Visit 4**	**166 to 194 Days After Visit 4/ Telephone Call**
Informed consent	X					
Review inclusion/exclusion criteria	X					
Confirm continued eligibility				X		
MMSE	X			X		
Demography	X					
Medical history including tobacco use	X					
Physical examination	X					
Obtain blood sample	X	X		X	X	
Prevaccination body temperature (oral)	X			X		
Assess arm movement before vaccination	X			X		
Record concomitant non-study vaccines	X			X		
Randomization	X					
Test article administration and accountability	X			X		
Assess acute reactions 30 min after vaccination, including pain at 30 minutes	X			X		
Provide e-diary, thermometer, caliper and appointment card	X			X		
Postvaccination contact			Telephone call			Telephone call
Subjects collect diary reactogenicity information[a]	Days 1-14			Days 1-14		
Electronic diary collection and review		X			X	
Adverse event collection	X----------X			X----------X		
SAE reporting[b]	X----------X		X	X----------X		X
Death	X----------	----------	----------	----------	----------	----------X

e-dairy = electronic dairy; FUP = follow-up; ID = identification; MMSE = Mini-Mental State Examination; SAEs = serious adverse events.

a. Subjects were requested to contact the study staff to arrange an additional visit for local reaction(s) assessment by the Investigator, if they experience redness or swelling >10 cm (21/21+ caliper units) or severe limitation of arm movement in the arm the test article was administered.

b. At Visit 3 and Visit 6, SAEs, any newly diagnosed chronic medical conditions (including autoimmune or neuroinflammatory diseases) and emergency room visits that meet the criteria of an SAE would be collected. A subject's SAEs would be recorded and reported on SAE form 7443-V. SAEs would be recorded from the signing of the informed consent form (ICF) through the completion of Visit 2, and from Visit 2 to the Visit 3 phone call. SAE information captured at the time of the Visit 3 phone call would be reported at Visit 3. SAEs were also recorded and reported from Visit 4 through the completion of Visit 5, and from Visit 5 to the Visit 6 phone call. SAE information captured at the Visit 6 phone call was reported at Visit 6. Death would be recorded and reported from the signing of the ICF until completion of the study.

Number of Subjects (Planned and Analyzed): The study was planned to be conducted in approximately 924 subjects at approximately 60 sites throughout the US and Sweden. Nine hundred and thirty eight (938) subjects from 61 sites were randomly assigned in a 1:1 ratio to the 2 vaccine groups (464 subjects to 13vPnC and 474 subjects to 23vPS).

Diagnosis and Main Criteria for Inclusion: The study included healthy male and female subjects aged ≥70 years who had documented vaccination with 1 dose of 23vPS at least 5 years before study enrollment.

Subjects who had history of severe adverse reaction to a vaccine; receipt of >1 dose of 23vPS before study enrollment; subjects with immunodeficiency were excluded.

Study Vaccine:

13vPnC contains saccharides from pneumococcal serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F individually conjugated to nontoxic diphtheria cross-reactive material 197 (CRM_{197}). The vaccine was formulated to contain 2.2 μg of each saccharide, except for 4.4 μg of 6B, per 0.5-mL dose. The final vaccine was formulated at pH 5.8 with 5 mM succinate buffer, 0.85% sodium chloride, 0.02% polysorbate 80, and 0.125 mg aluminum as aluminum phosphate ($AlPO_4$), per 0.5-mL dose.

23vPS is a licensed product that consists of a mixture of purified capsular polysaccharides from 23 types of *Streptococcus pneumoniae*: 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, and 33F. The vaccine is formulated to contain 25 μg of each of the 23 purified polysaccharide serotypes per 0.5-mL dose of vaccine. Phenol is added as a preservative.

Only a medically qualified member of the Investigator's staff was to administer the study vaccines. 13vPnC (0.5 mL) or 23vPS (0.5 mL) was administered into a deltoid muscle of either arm.

Standard vaccination practices were to be observed and appropriate medications and other supportive measures for management of an acute hypersensitivity reaction were to be available in accordance with local guidelines on standard immunization practices.

Immunogenicity Endpoints:

The primary immunologic comparisons were the pneumococcal responses to the 13 serotypes contained in 13vPnC in subjects who received 13vPnC relative to the pneumococcal responses in subjects who received 23vPS at Vaccination 1. The primary endpoint for the 12 common serotypes was the serotype-specific geometric mean OPA titer 1 month after the initial study vaccination. The primary endpoint for serotype 6A was the proportion of subjects exhibiting a 4-fold rise in anti-6A OPA titer 1 month after the initial study vaccination.

The OPA geometric mean titer (GMT) 1 month after Vaccination 1 was the endpoint for secondary immunologic comparison of whether 13vPnC was more immunogenic than 23vPS for some of the 12 common serotypes and for serotype 6A.

Safety Evaluations: To evaluate the acceptability of the safety profile of 13vPnC as measured by the incidence of local reactions, systemic events, and AEs. Local reactions included pain, redness, and swelling at the injection site, and limitation of arm movement. Systemic events included fever, chills, fatigue, headache, vomiting, decreased appetite, rash, new generalized muscle pain, aggravated generalized muscle pain, new generalized joint pain, and aggravated generalized joint pain.

Statistical Methods: For immunogenicity analyses, 2 analysis populations (evaluable dose immunogenicity and all-available dose immunogenicity) were defined for Dose 1 (13vPnC or 23vPS) and Dose 2 (13vPnC/13vPnC or 23vPS/13vPnC).

Dose 1 evaluable immunogenicity population included subjects who:

- Were eligible for the study and randomized;
- Were 70 years of age or older on the day of first vaccination;
- Received the vaccine Dose 1 to which they were randomized;
- Had prevaccination blood drawn on the same day as the day of vaccination of Dose 1 or within 15 days prior to Day 1;
- Had postvaccination blood drawn within the required time window. Blood draw window specified would be expanded by 1 extra day before and 14 days after. For example, the blood draw time window of Days 29-43 after Visit 1 would be expanded to Days 28-57 after Visit 1, for reporting purposes;
- Have at least 1 valid and determinate assay result for antibody response to any pneumococcal serotype;
- Received no prohibited vaccinations after Dose 1 and prior to Dose 1 postvaccination blood drawn;
- Had no major protocol violations as determined by the global clinical program leader (GCPL) or global medical monitor (GMM).

Dose 2 evaluable immunogenicity population includes subjects who:

- Were eligible for the study;
- Were 70 years of age or older on the day of first vaccination at Dose 1;
- Received the treatment to which they were randomized at Dose 1;
- Received vaccine 13vPnC at Dose 2;
- Had prevaccination blood drawn on the same day as the day of vaccination of Dose 2 (351 to 379 days after Visit 1) or within 15 days prior to Dose 2;

- Had postvaccination blood drawn within the required time window. Blood draw window specified would be expanded by 1 extra day before and 14 days after. For example, the blood draw time window of days 29-43 after Visit 4 would be expanded to Days 28-57 after Visit 4, for reporting purposes;

- Have at least 1 valid and determinate assay result for antibody response to any pneumococcal serotype;

- Received no prohibited vaccinations after Dose 2 and prior to Dose 2 postvaccination blood drawn;

- Had no major protocol violations as determined by GCPL or GMM.

The all-available immunogenicity population for each dose included, a subject with at least 1 valid and determinate assay result related to that dose.

The safety population included all subjects who received at least 1 dose of test article.

Opsonophagocytic Assay Geometric Mean Titers

For the 13 serotypes contained in 13vPnC, the serotype-specific OPA titers were logarithmically transformed for analysis. Within each vaccine group and for each antibody titer separately, geometric means of the antibody titers at both visits (before vaccination and 1 month after vaccination) were calculated for each vaccination (Year 0 and Year 1) separately. Two -sided 95% confidence intervals (CIs) were constructed by back transformation of the CIs for the mean of the logarithmically transformed assay results computed using the Student t-distribution. In the 13vPnC/13vPnC treatment sequence, where subjects received 2 successive doses of 13vPnC, geometric mean fold rises (GMFR) were calculated based on GMTs obtained 1 month after each dose.

Noninferiority and statistically significant differences were evaluated using the ratio of the GMTs and corresponding 2-sided 95% CIs. For the geometric mean ratio (GMR), the CIs were computed using the Student t-distribution for the mean difference of the measures on the log scale (test group relative to reference group). Noninferiority was declared if the lower limit of the CI for the GMR was >0.5 (2-fold criterion) for the 12 common serotypes. If the lower limit of the CI for the GMR was >1 for the 12 common serotypes, or >2 for serotype 6A, then 13vPnC was declared statistically significantly more immunogenic than 23vPS for that serotype. For comparison of 13vPnC/13vPnC to 23vPS/13vPnC or 23vPS, statistical significance was declared if the lower limit of the CI for the GMR was >1. Results were also provided for these comparisons for circumstances in which the GMFR was statistically lower (upper bound of the 2-sided 95% CI was <1) or statistically higher (lower bound of the 2-sided 95% CI was >1).

The GMRs or GMFRs for the 13 serotypes were calculated for the following pairs:

- 13vPnC at Year 0 versus 23vPS at Year 0;

- 13vPnC/13vPnC at Year 1 versus 13vPnC at Year 0;

- 13vPnC/13vPnC at Year 1 versus 23vPS at Year 0;
- 13vPnC/13vPnC at Year 1 versus 13vPnC/23vPS at Year 1;
- 23vPS/13vPnC at Year 1 versus 13vPnC at Year 0.

Proportion of Subjects Exhibiting a 4-Fold Rise in Anti-6A OPA titer: For serotype 6A, superiority of the response for 13vPnC was declared if the lower bound of the 2-sided, 95% CI for the difference in proportions of subjects achieving a 4-fold rise in OPA titer (from before vaccination to 1 month after vaccination) (13vPnC - 23vPS) was >0. This was assessed for 13vPnC at Year 0 versus 23vPS at Year 0.

OPA titers for 13vPnC were to be declared noninferior to those for 23vPS if the lower limit of the 2-sided, 95% CI for the GMR (13vPnC GMT/23vPS GMT) was >0.5, 2-fold criterion.

A secondary objective of the study was to demonstrate that, based on OPA titers measured 1 month after vaccination, 13vPnC was statistically significantly more immunogenic than 23vPS for at least some of the 12 serotypes contained in 13vPnC. For the 12 common serotypes, statistical significance was demonstrated if the lower limit of the 2-sided, 95% CI for the GMR (13vPnC GMT/23vPS GMT) was >1.

RESULTS

Subject Disposition and Demography: Approximately 924 subjects were planned to be enrolled in this study. A total of 1008 subjects consented to participate in the study. Of these, 938 subjects were randomly assigned in a 1:1 ratio to the 2 vaccine groups. The disposition of subjects for Vaccination 1 is presented in Table 2.

Table 2. Disposition of All Subjects – Vaccination 1 (Year 0)

	Vaccine Group (as Randomized)			
	Screened Only	13vPnC	23vPS	Total
	n[a] (%)	n[a] (%)	n[a] (%)	n[a] (%)
Consented[b]	70 (100.0)	464 (100.0)	474 (100.0)	1008 (107.5)
Randomized[c]	N/A	464 (100.0)	474 (100.0)	938 (100.0)
Not randomized/not assigned	71 (101.4)	0 (0.0)	0 (0.0)	71 (7.6)
Vaccinated	0 (0.0)	463 (99.8)	473 (99.8)	936 (99.8)
Completed vax 1 blood draw visit	0 (0.0)	460 (99.1)	473 (99.8)	933 (99.5)
Withdrawn before vax 1 blood draw visit	0 (0.0)	3 (0.6)	0 (0.0)	3 (0.3)
Reason for withdrawal				
Subject request	0 (0.0)	3 (0.6)	0 (0.0)	3 (0.3)
Completed vax 1, 6-month contact	0 (0.0)	455 (98.1)	463 (97.7)	918 (97.9)
Withdrawn after vax 1 blood draw visit and before 6-month contact	0 (0.0)	5 (1.1)	10 (2.1)	15 (1.6)
Reason for withdrawal				
Protocol violation	0 (0.0)	3 (0.6)	4 (0.8)	7 (0.7)
Death	0 (0.0)	2 (0.4)	2 (0.4)	4 (0.4)
Subject request	0 (0.0)	0 (0.0)	2 (0.4)	2 (0.2)
Adverse event	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.1)
Lost to follow-up	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.1)

One subject had no consent and no randomization information. Two subjects were randomized but not vaccinated. One subject did not provide a blood sample after Vaccination 1 but continued in the study and completed the 6-month telephone contact after Vaccination 1.
13vPnC = 13-valent pneumococcal conjugate vaccine; 23vPS = 23-valent pneumococcal polysaccharide vaccine; N/A = not applicable; vax= vaccination.
a. n = number of subjects in the specified category.
b. The values in this row are used as the denominators for percentages for screened only.
c. The values in this row are used as the denominators for percentages for vaccine groups.

The disposition of subjects from the 6-month contact for Vaccination 1 to the 6-month contact for Vaccination 2 is summarized in Table 3.

Table 3. Disposition of All Subjects - Vaccination 2 (Year 1)

	Vaccine Group (as Randomized)		
	13vPnC/13vPnC	23vPS/13vPnC	Total
	n[a] (%)	n[a] (%)	n[a] (%)
Randomized[b]	464 (100.0)	474 (100.0)	938 (100.0)
Completed vax 1, 6-month contact	455 (98.1)	463 (97.7)	918 (97.9)
Withdrawn after vax 1, 6-month contact and before vax 2	63 (13.6)	59 (12.4)	122 (13.0)
Unknown[c]	1 (0.2)	0 (0.0)	1 (0.1)
Reason for withdrawal			
Other	31 (6.7)	25 (5.3)	56 (6.0)
Subject request	11 (2.4)	20 (4.2)	31 (3.3)
Protocol violation	10 (2.2)	4 (0.8)	14 (1.5)
Adverse event	4 (0.9)	5 (1.1)	9 (1.0)
Death	2 (0.4)	2 (0.4)	4 (0.4)
Investigator request	3 (0.6)	1 (0.2)	4 (0.4)
Failed to return	1 (0.2)	2 (0.4)	3 (0.3)
Lost to follow-up	1 (0.2)	0 (0.0)	1 (0.1)
Received vax 2	391 (84.3)	404 (85.2)	795 (84.8)
Completed vax 2 blood draw visit	389 (83.8)	403 (85.0)	792 (84.4)
Withdrawn after vax 2 and before vax 2 blood draw visit	2 (0.4)	1 (0.2)	3 (0.3)
Reason for withdrawal			
Other	1 (0.2)	1 (0.2)	2 (0.2)
Adverse event	1 (0.2)	0 (0.0)	1 (0.1)
Completed vax 2, 6-month contact	387 (83.4)	402 (84.8)	789 (84.1)
Withdrawn after vax 2 blood draw visit and before vax 2, 6-month contact	2 (0.4)	1 (0.2)	3 (0.3)
Reason for withdrawal			
Death	1 (0.2)	0 (0.0)	1 (0.1)
Lost to follow-up	1 (0.2)	0 (0.0)	1 (0.1)
Protocol violation	0 (0.0)	1 (0.2)	1 (0.1)

Two subjects did not provide a blood sample after Vaccination 2 but continued in the study.
13vPnC = 13-valent pneumococcal conjugate vaccine; 23vPS = 23-valent pneumococcal polysaccharide vaccine; vax = vaccination.

a. n = number of subjects in the specified category.
b. The values in this row are used as the denominators for percentages.
c. One subject completed Vaccination 1 6-month follow-up telephone contact but did not receive Vaccination 2. The subject was erroneously marked as completing the study and so has unknown final disposition.

The demographic characteristics of the 936 subjects in the Vaccination 1 safety population are summarized in Table 4.

Table 4. Demographic Characteristics - Vaccination 1 Safety Population

	Vaccine Group (as Administered)		
	13vPnC N[a]=463	23vPS N[a]=473	Total N[a]=936
Characteristic	n[b] (%)	n[b] (%)	n[b] (%)
Sex			
Male	242 (52.3)	238 (50.3)	480 (51.3)
Female	221 (47.7)	235 (49.7)	456 (48.7)
Age at vaccination (in years)			
Mean (SD)	76.7 (4.6)	76.7 (4.5)	76.7 (4.6)
Median	75.9	75.7	75.8
Range	70.1, 95.5	70.0, 94.7	70.0, 95.5
Race			
White	444 (95.9)	454 (96.0)	898 (95.9)
Black or African American	12 (2.6)	10 (2.1)	22 (2.4)
Asian	3 (0.6)	8 (1.7)	11 (1.2)
American Indian or Alaska native	1 (0.2)	1 (0.2)	2 (0.2)
Other	2 (0.4)	0 (0.0)	2 (0.2)
Native Hawaiian or other Pacific Islander	1 (0.2)	0 (0.0)	1 (0.1)
Ethnicity			
Non-Hispanic and non-Latino	460 (99.4)	468 (98.9)	928 (99.1)
Hispanic or Latino	3 (0.6)	5 (1.1)	8 (0.9)

13vPnC = 13-valent pneumococcal conjugate vaccine; 23vPS = 23-valent pneumococcal polysaccharide vaccine; SD = standard deviation.
a. N = number of subjects in the vaccine group, or total sample.
b. n = number of subjects in the specified category.

The demographic characteristics of the 795 subjects in the Vaccination 2 safety population are summarized in Table 5.

Table 5. Demographic Characteristics - Vaccination 2 Safety Population

	Vaccine Sequence (as Administered)		
	13vPnC/13vPnC N[a]=391	23vPS/13vPnC N[a]=404	Total N[a]=795
Characteristic	**n[b] (%)**	**n[b] (%)**	**n[b] (%)**
Sex			
Male	206 (52.7)	202 (50.0)	408 (51.3)
Female	185 (47.3)	202 (50.0)	387 (48.7)
Age at vaccination (in years)			
Mean (SD)	77.4 (4.5)	77.4 (4.4)	77.4 (4.5)
Median	76.7	76.4	76.5
Range	71.1, 93.1	71.1, 95.8	71.1, 95.8
Race			
White	378 (96.7)	387 (95.8)	765 (96.2)
Black or African American	8 (2.0)	8 (2.0)	16 (2.0)
Asian	2 (0.5)	8 (2.0)	10 (1.3)
Other	2 (0.5)	0 (0.0)	2 (0.3)
American Indian or Alaska native	0 (0.0)	1 (0.2)	1 (0.1)
Native Hawaiian or other Pacific Islander	1 (0.3)	0 (0.0)	1 (0.1)
Ethnicity			
Non-Hispanic and Non-Latino	388 (99.2)	401 (99.3)	789 (99.2)
Hispanic or Latino	3 (0.8)	3 (0.7)	6 (0.8)

13vPnC = 13-valent pneumococcal conjugate vaccine; 23vPS = 23-valent pneumococcal polysaccharide vaccine; SD = standard deviation.
a. N = number of subjects in the vaccine sequence, or total sample.
b. n = number of subjects in the specified category.

The all-available and evaluable immunogenicity populations for Vaccination 1 and 2 are presented in Table 6 and Table 7 respectively.

Table 6. All-Available and Evaluable Immunogenicity Populations for Vaccination 1 (Year 0)

	Vaccine Group (as Randomized)					
	13vPnC		23vPS		Total	
	n[a]	%	n[a]	%	n[a]	%
Randomized	464	100.0	474	100.0	938	100.0
Vaccination 1 all-available immunogenicity population	463	99.8	473	99.8	936	99.8
Subjects excluded from the vaccination 1 all-available immunogenicity population	1	0.2	1	0.2	2	0.2
No prevaccination 1 or postvaccination 1 assay result for any serotype/antibody	1	0.2	1	0.2	2	0.2
Vaccination 1 evaluable immunogenicity population	431	92.9	448	94.5	879	93.7
Subjects excluded from the evaluable immunogenicity population[b]	33	7.1	26	5.5	59	6.3
Other protocol violation	17	3.7	12	2.5	29	3.1
Received prohibited vaccine after vaccination 1 and prior to vaccination 1 postvaccination blood draw	8	1.7	12	2.5	20	2.1
Not eligible for the study	10	2.2	8	1.7	18	1.9
No postvaccination 1 blood drawn	4	0.9	0	0.0	4	0.4
Postvaccination 1 sample <28 days after vaccination 1	2	0.4	1	0.2	3	0.3
Not in vaccination 1 all-available immunogenicity population	1	0.2	1	0.2	2	0.2
Postvaccination 1 sample >57 days after vaccination 1	2	0.4	0	0.0	2	0.2

13vPnC = 13-valent pneumococcal conjugate vaccine; 23vPS = 23-valent pneumococcal polysaccharide vaccine.
a. n = number of subjects with the specified characteristic.
b. Subjects may have been excluded for >1 reason.

Table 7. All-Available and Evaluable Immunogenicity Populations for Vaccination 2 (Year 1)

	Vaccine Sequence (as Randomized)					
	13vPnC/13vPnC		23vPS/13vPnC		Total	
	n[a]	%	n[a]	%	n[a]	%
Randomized	464	100.0	474	100.0	938	100.0
Vaccination 2 all-available immunogenicity population	394	84.9	403	85.0	797	85.0
Subjects excluded from the vaccination 2 all-available immunogenicity population	70	15.1	71	15.0	141	15.0
No prevaccination 2 or postvaccination 2 assay result for any serotype/antibody	70	15.1	71	15.0	141	15.0
Vaccination 2 evaluable immunogenicity population	372	80.2	373	78.7	745	79.4
Subjects excluded from the vaccination 2 evaluable immunogenicity population[b]	92	19.8	101	21.3	193	20.6
Not in vaccination 2 all-available immunogenicity population	70	15.1	71	15.0	141	15.0
Other protocol violation	11	2.4	9	1.9	20	2.1
Received prohibited vaccines after vaccination 2 and prior to vaccination 2 postvaccination blood drawn	4	0.9	11	2.3	15	1.6
Not eligible for the study	5	1.1	3	0.6	8	0.9
Did not receive 13vPnC at vaccination 2	4	0.9	2	0.4	6	0.6
No postvaccination 2 blood drawn	3	0.6	2	0.4	5	0.5
Postvaccination 2 blood draw <28 days after vaccination 2	0	0.0	5	1.1	5	0.5
Postvaccination 2 blood draw >57 days after vaccination 2	1	0.2	2	0.4	3	0.3
Prevaccination 2 blood draw not 15 days prior to vaccination 2 or the same day as vaccination 2	1	0.2	0	0.0	1	0.1

13vPnC = 13-valent pneumococcal conjugate vaccine; 23vPS = 23-valent pneumococcal polysaccharide vaccine.
a. n = number of subjects with the specified characteristic.
b. Subjects may have been excluded for >1 reason.

Immunogenicity Results:

Comparison of Pneumococcal OPA GMTs, 13vPnC Relative to 23vPS: Noninferiority was met by all 12 common serotypes and 10 of the 12 common serotypes were statistically significantly higher in 13vPnC compared to 23vPS (Table 8).

Table 8. Comparison of Pneumococcal OPA GMTs, 13vPnC Relative to 23vPS (Year 0) - Vaccination 1 Evaluable Immunogenicity Population

	Vaccine Group (as Randomized)						Vaccine Comparison	
	13vPnC			23vPS				
Serotype	n[a]	GMT[b]	(95% CI[c])	n[a]	GMT[b]	(95% CI[c])	Ratio[d]	(95% CI[e])
1	426	81	(68.4, 95.9)	445	55	(46.2, 64.8)	1.5	(1.17, 1.88)
3	405	55	(47.7, 62.9)	424	49	(42.9, 56.9)	1.1	(0.91, 1.35)
4	400	545	(441.9, 672.3)	395	203	(157.1, 262.2)	2.7	(1.93, 3.74)
5	422	72	(59.7, 86.6)	442	36	(29.5, 43.1)	2.0	(1.55, 2.63)
6B	411	1261	(1024.7, 1552.6)	411	417	(330.5, 526.7)	3.0	(2.21, 4.13)
7F	420	245	(191.9, 312.4)	431	160	(123.5, 207.9)	1.5	(1.07, 2.18)
9V	402	181	(138.0, 237.0)	402	90	(67.8, 119.7)	2.0	(1.36, 2.97)
14	411	280	(227.5, 345.5)	410	285	(228.9, 354.3)	1.0	(0.73, 1.33)
18C	411	907	(761.9, 1080.1)	416	481	(385.1, 600.7)	1.9	(1.42, 2.50)
19A	420	354	(307.7, 408.4)	442	200	(170.0, 234.4)	1.8	(1.43, 2.20)
19F	414	333	(273.2, 404.8)	417	214	(174.3, 262.8)	1.6	(1.17, 2.06)
23F	403	158	(126.0, 198.6)	417	43	(34.2, 53.5)	3.7	(2.69, 5.09)
6A	421	903	(726.7, 1121.3)	433	94	(74.1, 118.5)	9.6	(7.00 , 13.26)

13vPnC = 13-valent pneumococcal conjugate vaccine; 23vPS = 23-valent pneumococcal polysaccharide vaccine; CIs = confidence intervals; GMTs = geometric mean titers; OPA = opsonophagocytic assay.

a. n = number of subjects with a determinate OPA antibody titer to the given serotype.
b. GMTs were calculated using all subjects with available data for both the specified blood draws.
c. CIs were back transformations of a CI based on the Student t-distribution for the mean logarithm of the titers.
d. Ratio of GMT (13vPnC to 23vPS), was calculated by back transforming the mean difference between vaccine groups on the logarithmic scale.
e. CIs for the ratio are back transformations of a CI based on the Student t-distribution for the mean difference of the logarithms of the measures (13vPnC – 23vPS).

Proportion of Subjects Achieving a ≥4-Fold Increase in OPA Titer: As shown in Table 9, the proportion of subjects was statistically higher (lower limit of the 95%CI for the difference in proportions of subjects achieving a 4-fold increase in OPA titer >0) in the 13vPnC group (71.1%) than in the 23vPS group (27.3%) (lower limit of CI of 37.4%).

Table 9. Comparison of Subjects Achieving a ≥4-Fold Increase in Titer for Serotype 6A, 13vPnC Relative to 23vPS (Year 0) - Vaccination 1 Evaluable Immunogenicity Population

	Vaccine Group (as Randomized)					
	13vPnC N[a]=408		23vPS N[a]=411			
Serotype	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])	Difference[d]	(95% CI[e])
6A	290 (71.1)	(66.4, 75.4)	112 (27.3)	(23.0, 31.8)	43.8	(37.4, 49.9)

13vPnC = 13-valent pneumococcal conjugate vaccine; 23vPS = 23-valent pneumococcal polysaccharide vaccine; CIs = confidence intervals.

a. N = number of subjects with a determinate antibody titer to the given serotype.
b. n = number of subjects with an antibody titer who meet the comparison level for the given serotype.
c. Exact 2-sided CI (Clopper and Pearson) based upon the observed proportion of subjects.
d. Difference in proportions, 13vPnC – 23vPS, expressed as a percentage.
e. Exact 2-sided CI (based on Chan and Zhang) for the difference in proportions, 13vPnC – 23vPS, expressed as a percentage.

Pneumococcal OPA Geometric Mean Titers: A secondary objective of the study was to demonstrate that, based on OPA titers measured 1 month after Vaccination 1, 13vPnC was statistically significantly more immunogenic than 23vPS for serotype 6A. For serotype 6A, statistical significance was demonstrated if the lower limit of the 2-sided, 95% CI for the GMR (13vPnC GMT/23vPS GMT) was >2. In the evaluable immunogenicity population, 13vPnC was statistically significantly more immunogenic than 23vPS for serotype 6A (Table 8).

Vaccination 2 Comparisons:

Pneumococcal OPA Geometric Mean Titers: For 3 of the 13 serotypes (serotypes 6A, 6B, and 23F), the lower limit of the 95% CI for the GMFRs exceeded 1.0, indicating that the OPA response was statistically significantly greater after 13vPnC/13vPnC than after 13vPnC. For 2 of 13 serotypes (serotypes 4 and 5), OPA GMTs were statistically significantly lower (ie, a upper limit of the 95% CI for the GMFR of <1.0) after 13vPnC/13vPnC than after 13vPnC (Table 10).

Table 10. Comparison of Pneumococcal OPA GMTs and GMFRs, 13vPnC/13vPnC (Year 1) Relative to 13vPnC (Year 0) - Evaluable Immunogenicity Population

	13vPnC/13vPnC (as Randomized)								
	Vaccination 1 (Year 0)			Vaccination 2 (Year 1)			Fold Rise		
Serotype	n[a]	GMT[b]	(95% CI[c])	n[a]	GMT[b]	(95% CI[c])	n[a]	GMFR[d]	(95% CI[c])
1	361	79	(65.3, 94.6)	361	76	(64.8, 89.7)	361	1.0	(0.85, 1.10)
3	337	55	(47.2, 64.0)	337	55	(48.4, 63.1)	337	1.0	(0.91, 1.11)
4	324	614	(489.8, 768.8)	324	487	(393.9, 603.3)	324	0.8	(0.68, 0.92)
5	355	69	(56.2, 84.2)	355	57	(46.9, 68.5)	355	0.8	(0.73, 0.94)
6A	354	971	(771.0, 1222.1)	354	1169	(974.0, 1403.0)	354	1.2	(1.03, 1.40)
6B	339	1358	(1085.4, 1700.2)	339	1590	(1316.9, 1919.8)	339	1.2	(1.02, 1.35)
7F	351	222	(170.2, 290.2)	351	180	(138.1, 233.8)	351	0.8	(0.65, 1.01)
9V	331	187	(139.3, 250.4)	331	166	(124.2, 220.8)	331	0.9	(0.69, 1.15)
14	348	265	(209.9, 333.6)	348	241	(194.4, 299.1)	348	0.9	(0.79, 1.05)
18C	342	918	(763.4, 1104.3)	342	1003	(850.2, 1182.1)	342	1.1	(0.97, 1.23)
19A	349	349	(299.7, 405.5)	349	341	(297.2, 390.5)	349	1.0	(0.89, 1.07)
19F	340	329	(265.6, 408.6)	340	322	(266.3, 389.6)	340	1.0	(0.83, 1.15)
23F	335	167	(130.9, 213.0)	335	309	(251.6, 380.1)	335	1.9	(1.60, 2.14)

13vPnC = 13-valent pneumococcal conjugate vaccine; 23vPS = 23-valent pneumococcal polysaccharide vaccine; CIs = confidence intervals; GMFRs = geometric mean fold rises; GMTs = geometric mean titers; OPA = opsonophagocytic assay.

a. n = number of subjects with a determinate OPA antibody titer to the given serotype at both the Postvaccination 1 and Postvaccination 2 blood draws.
b. GMTs were calculated using all subjects with available data from both the Postvaccination 1 and Postvaccination 2 blood draws.
c. CIs are back transformations of a CI based on the Student t-distribution for the mean logarithm of the titers.
d. GMFRs ([13vPnC/13vPnC]/[13vPnC]) were calculated using all subjects with available data from both the Postvaccination 1 and Postvaccination 2 blood draws.

A secondary objective of the study was to demonstrate that the immune response to a second dose of 13vPnC administered 1 year after an initial study dose of 13vPnC was noninferior to the immune response after the initial dose of 23vPS for the 12 common serotypes (lower limit of 95% CI was >0.5), based on serotype-specific OPA titers. The criterion for noninferiority was met for all 12 common serotypes in the evaluable population. For the 12 common serotypes, statistical significance was demonstrated if the lower limit of the 2-sided, 95% CI for the GMR was >1 (Table 11).

Table 11. Comparison of Pneumococcal OPA GMTs, 13vPnC/13vPnC (Year 1) Relative to 23vPS (Year 0) - Evaluable Immunogenicity Population

	Vaccine Sequence (as Randomized)						Vaccine Comparison	
	13vPnC/13vPnC			23vPS				
Serotype	n[a]	GMT[b]	(95% CI[c])	n[a]	GMT[b]	(95% CI[c])	Ratio[d]	(95% CI[e])
1	370	76	(64.9, 89.5)	445	55	(46.2, 64.8)	1.4	(1.10, 1.76)
3	362	55	(47.9, 62.0)	424	49	(42.9, 56.9)	1.1	(0.91, 1.34)
4	347	472	(383.5, 580.2)	395	203	(157.1, 262.2)	2.3	(1.66, 3.25)
5	365	56	(46.6, 67.7)	442	36	(29.5, 43.1)	1.6	(1.21, 2.06)
6B	356	1565	(1306.1, 1875.9)	411	417	(330.5, 526.7)	3.8	(2.78, 5.07)
7F	365	185	(142.9, 239.7)	431	160	(123.5, 207.9)	1.2	(0.80, 1.67)
9V	356	158	(119.5, 209.5)	402	90	(67.8, 119.7)	1.8	(1.18, 2.62)
14	366	238	(192.3, 293.8)	410	285	(228.9, 354.3)	0.8	(0.62, 1.13)
18C	361	975	(829.0, 1147.3)	416	481	(385.1, 600.7)	2.0	(1.53, 2.69)
19A	362	339	(296.4, 386.9)	442	200	(170.0, 234.4)	1.7	(1.37, 2.10)
19F	354	311	(257.1, 375.9)	417	214	(174.3, 262.8)	1.5	(1.09, 1.93)
23F	360	310	(254.1, 378.0)	417	43	(34.2, 53.5)	7.3	(5.36, 9.82)
6A	366	1134	(943.6, 1363.7)	433	94	(74.1, 118.5)	12.1	(8.92, 16.44)

13vPnC = 13-valent pneumococcal conjugate vaccine; 23vPS = 23-valent pneumococcal polysaccharide vaccine; CIs = confidence intervals; GMTs = geometric mean titers; OPA = opsonophagocytic assay.

a. n = number of subjects with a determinate OPA antibody titer to the given serotype.
b. GMTs were calculated using all subjects with available data for both the specified blood draws.
c. CIs were back transformations of a CI based on the Student t-distribution for the mean logarithm of the titers.
d. Ratio of GMT (13vPnC/13vPnC to 23vPS), was calculated by back transforming the mean difference between vaccine group/sequence on the logarithmic scale.
e. CIs for the ratio were back transformations of a CI based on the Student t-distribution for the mean difference of the logarithms of the measures ([13vPnC/13vPnC]–[23vPS]).

Results from the all-available immunogenicity population are similar, and are not presented here.

Safety Results:

Local Reactions After Vaccination 1:

The percentages of subjects with any redness, any swelling, and any limitation of arm movement were significantly higher for the 23vPS group (22.2%, 23.1%, and 27.6%, respectively) compared with the 13vPnC group (10.8%, 10.4%, and 10.5%, respectively). The percentage of subjects with any pain was slightly higher in the 23vPS group (58.5%) compared with the 13vPnC group (51.7%); however, this difference was not statistically significant. The local reactions within 14 days after Vaccination 1 are presented in Table 12.

Table 12. Subjects Reporting Local Reactions Within 14 Days After Vaccination 1 (Year 0) - Safety Population

Local Reaction	Vaccine Group (as Administered) 13vPnC N[a]	13vPnC n[b] (%)	13vPnC (95% CI[c])	23vPS N[a]	23vPS n[b] (%)	23vPS (95% CI[c])	Difference[d]	(95% CI[e])	p-Value[e]
Redness[f]									
Any	306	33 (10.8)	(7.5, 14.8)	324	72 (22.2)	(17.8, 27.1)	-11.4	(-17.3, -5.6)	<0.001
Mild	304	29 (9.5)	(6.5, 13.4)	311	42 (13.5)	(9.9, 17.8)	-4.0	(-9.1, 1.1)	0.129
Moderate	301	14 (4.7)	(2.6, 7.7)	314	36 (11.5)	(8.2, 15.5)	-6.8	(-11.3, -2.3)	0.002
Severe	299	5 (1.7)	(0.5, 3.9)	310	15 (4.8)	(2.7, 7.9)	-3.2	(-6.3, -0.3)	0.028
Swelling[f]									
Any	307	32 (10.4)	(7.2, 14.4)	333	77 (23.1)	(18.7, 28.0)	-12.7	(-18.5, -7.0)	<0.001
Mild	305	27 (8.9)	(5.9, 12.6)	315	44 (14.0)	(10.3, 18.3)	-5.1	(-10.2, -0.1)	0.048
Moderate	299	12 (4.0)	(2.1, 6.9)	323	44 (13.6)	(10.1, 17.9)	-9.6	(-14.2, -5.1)	<0.001
Severe	297	0 (0.0)	(0.0, 1.2)	310	15 (4.8)	(2.7, 7.9)	-4.8	(-7.9, -2.7)	<0.001
Pain[g]									
Any	362	187 (51.7)	(46.4, 56.9)	383	224 (58.5)	(53.4, 63.5)	-6.8	(-14.0, 0.4)	0.062
Mild	359	180 (50.1)	(44.8, 55.4)	377	204 (54.1)	(48.9, 59.2)	-4.0	(-11.3, 3.3)	0.284
Moderate	306	23 (7.5)	(4.8, 11.1)	330	78 (23.6)	(19.2, 28.6)	-16.1	(-21.7, -10.6)	<0.001
Severe	299	4 (1.3)	(0.4, 3.4)	306	7 (2.3)	(0.9, 4.7)	-0.9	(-3.5, 1.4)	0.539
Limitation of arm movement[h]									
Any	313	33 (10.5)	(7.4, 14.5)	326	90 (27.6)	(22.8, 32.8)	-17.1	(-23.1, -11.1)	<0.001
Mild	312	32 (10.3)	(7.1, 14.2)	322	81 (25.2)	(20.5, 30.3)	-14.9	(-20.8, -9.0)	<0.001
Moderate	297	1 (0.3)	(0.0, 1.9)	303	8 (2.6)	(1.1, 5.1)	-2.3	(-4.8, -0.4)	0.020
Severe	298	2 (0.7)	(0.1, 2.4)	305	9 (3.0)	(1.4, 5.5)	-2.3	(-4.9, -0.1)	0.042
Any local reaction[i]	370	209 (56.5)	(51.3, 61.6)	387	248 (64.1)	(59.1, 68.9)	-7.6	(-14.6, -0.6)	0.033

Data presented are from the Vaccination 1 safety population.
13vPnC = 13-valent pneumococcal conjugate vaccine; 23vPS = 23-valent pneumococcal polysaccharide vaccine; CI = confidence interval.

a. N = number of subjects with known values.
b. n = number of subjects with the specified characteristic.
c. Exact 2-sided CI (Clopper and Pearson) based upon the observed proportion of subjects.
d. Difference in proportions, (13vPnC) – (23vPS), expressed as a percentage.
e. Exact 2-sided CI and corresponding p-value (based on Chan and Zhang) for the difference in proportions, [13vPnC] – [23vPS], expressed as a percentage.
f. Mild = 2.5 to 5.0 cm, moderate = 5.1 to 10.0 cm, and severe is >10.0 cm.
g. Mild = awareness of symptom but easily tolerated, moderate = discomfort enough to cause interference with usual activity, severe = incapacitating with inability to do usual activity.
h. Mild = some limitation of arm movement, moderate = unable to move arm above head but able to move arm above shoulder, and severe = unable to move arm above shoulder.
i. Any local reaction = any pain, any swelling, any redness, or any limitation of arm movement.

Local Reactions After Vaccination 2: The percentages of subjects with mild, moderate or severe redness, swelling, pain, and limitation of arm movement were similar for the 13vPnC/13vPnC (Year 1) group compared with the 13vPnC (Year 0) group (Table 13). The percentages of subjects with any redness, any swelling, and any pain were similar between the treatment groups (23vPS/13vPnC [Year 1] compared with 13vPnC [Year 0]); the percentage of subjects with any limitation of arm movement was significantly higher for the 23vPS/13vPnC (Year 1) group (19.9%) compared with the 13vPnC (Year 0) (10.5%) group (p=0.002).

Table 13. Subjects Reporting Local Reactions Within 14 Days After Vaccination, 13vPnC (Year 0) and 13vPnC/13vPnC (Year 1) - Safety Population

	Vaccine Group/Sequence (as Administered)							
	13vPnC			13vPnC/13vPnC				
Local Reaction	N[a]	n[b] (%)	(95% CI[c])	N[a]	n[b] (%)	(95% CI[c])	Difference[d]	(95% CI[e])
Redness[f]								
Any	185	18 (9.7)	(5.9, 14.9)	185	23 (12.4)	(8.0, 18.1)	2.7	(-2.0, 7.3)
Mild	182	15 (8.2)	(4.7, 13.2)	182	11 (6.0)	(3.1, 10.6)	-2.2	(-6.3, 1.9)
Moderate	182	8 (4.4)	(1.9, 8.5)	182	13 (7.1)	(3.9, 11.9)	2.7	(-1.2, 6.7)
Severe	179	2 (1.1)	(0.1, 4.0)	179	3 (1.7)	(0.3, 4.8)	0.6	(-1.0, 2.1)
Swelling[f]								
Any	185	17 (9.2)	(5.4, 14.3)	185	20 (10.8)	(6.7, 16.2)	1.6	(-2.8, 6.0)
Mild	182	12 (6.6)	(3.5, 11.2)	182	16 (8.8)	(5.1, 13.9)	2.2	(-1.7, 6.0)
Moderate	179	6 (3.4)	(1.2, 7.2)	179	5 (2.8)	(0.9, 6.4)	-0.6	(-4.0, 2.9)
Severe	177	0 (0.0)	(0.0, 2.1)	177	0 (0.0)	(0.0, 2.1)	0	(-1.1, 1.1)
Pain[g]								
Any	258	142 (55.0)	(48.7, 61.2)	258	148 (57.4)	(51.1, 63.5)	2.3	(-4.4, 9.0)
Mild	251	133 (53.0)	(46.6, 59.3)	251	136 (54.2)	(47.8, 60.5)	1.2	(-5.7, 8.0)
Moderate	187	16 (8.6)	(5.0, 13.5)	187	21 (11.2)	(7.1, 16.7)	2.7	(-2.6, 7.9)
Severe	179	3 (1.7)	(0.3, 4.8)	179	1 (0.6)	(0.0, 3.1)	-1.1	(-3.5, 1.3)
Limitation of arm movement[h]								
Any	195	19 (9.7)	(6.0, 14.8)	195	26 (13.3)	(8.9, 18.9)	3.6	(-1.9, 9.0)
Mild	194	18 (9.3)	(5.6, 14.3)	194	26 (13.4)	(8.9, 19.0)	4.1	(-1.3, 9.4)
Moderate	178	1 (0.6)	(0.0, 3.1)	178	1 (0.6)	(0.0, 3.1)	0	(-1.9, 1.9)
Severe	178	1 (0.6)	(0.0, 3.1)	178	0 (0.0)	(0.0, 2.1)	-0.6	(-2.1, 1.0)
Any local reaction[i]	265	155 (58.5)	(52.3, 64.5)	265	165 (62.3)	(56.1, 68.1)	3.8	(-2.8, 10.3)

Data presented are from the safety populations.
13vPnC = 13-valent pneumococcal conjugate vaccine; CI = confidence interval.

a. N = number of subjects with known values.
b. n = number of subjects with the specified characteristic.
c. Exact 2-sided CI (Clopper and Pearson) based upon the observed proportion of subjects.
d. Difference in proportions, (13vPnC/13vPnC) – (13vPnC), expressed as a percentage.
e. Adjusted Wald 2-sided CI for the difference in dependent proportions, (13vPnC/13vPnC) – (13vPnC), expressed as a percentage.
f. Mild = 2.5 to 5.0 cm, moderate = 5.1 to 10.0 cm, and severe is >10.0 cm.
g. Mild = awareness of symptom but easily tolerated, moderate = discomfort enough to cause interference with usual activity, severe = incapacitating with inability to do usual activity.
h. Mild = some limitation of arm movement, moderate = unable to move arm above head but able to move arm above shoulder, and severe = unable to move arm above shoulder.
i. Any local reaction = any pain, any swelling, any redness, or any limitation of arm movement.

Local reactions occurring within 14 days after administration of vaccine were reported by a similar percentage of subjects in the 23vPS (Year 0) group compared with the 13vPnC/13vPnC (Year 1) group (64.1% of subjects for the 23vPS [Year 0] group and 62.8% of subjects for the 13vPnC/13vPnC [Year 1] group) (Table 14).

Table 14. Subjects Reporting Local Reactions Within 14 Days After Vaccination, 23vPS (Year 0) and 13vPnC/13vPnC (Year 1) - Safety Population

Local Reaction	Vaccine Group/Sequence (as Administered) 23vPS N[a]	23vPS n[b] (%)	23vPS (95% CI[c])	13vPnC/13vPnC N[a]	13vPnC/13vPnC n[b] (%)	13vPnC/13vPnC (95% CI[c])	Diff[d]	(95% CI[e])	p-Value[e]
Redness[f]									
Any	324	72 (22.2)	(17.8, 27.1)	236	30 (12.7)	(8.7, 17.6)	-9.5	(-15.7, -3.1)	0.004
Mild	311	42 (13.5)	(9.9, 17.8)	233	16 (6.9)	(4.0, 10.9)	-6.6	(-11.7, -1.4)	0.012
Moderate	314	36 (11.5)	(8.2, 15.5)	231	16 (6.9)	(4.0, 11.0)	-4.5	(-9.4, 0.5)	0.074
Severe	310	15 (4.8)	(2.7, 7.9)	227	4 (1.8)	(0.5, 4.5)	-3.1	(-6.4, 0.1)	0.058
Swelling[f]									
Any	333	77 (23.1)	(18.7, 28.0)	236	29 (12.3)	(8.4, 17.2)	-10.8	(-17.0, -4.5)	<0.001
Mild	315	44 (14.0)	(10.3, 18.3)	234	24 (10.3)	(6.7, 14.9)	-3.7	(-9.2, 1.9)	0.194
Moderate	323	44 (13.6)	(10.1, 17.9)	229	8 (3.5)	(1.5, 6.8)	-10.1	(-14.8, -5.3)	<0.001
Severe	310	15 (4.8)	(2.7, 7.9)	227	2 (0.9)	(0.1, 3.1)	-4.0	(-7.1, -1.1)	0.008
Pain[g]									
Any	383	22 (58.5)	(53.4, 63.5)	297	173 (58.2)	(52.4, 63.9)	-0.2	(-7.7, 7.2)	0.953
Mild	377	20 (54.1)	(48.9, 59.2)	291	158 (54.3)	(48.4, 60.1)	0.2	(-7.4, 7.8)	0.965
Moderate	330	78 (23.6)	(19.2, 28.6)	239	31 (13.0)	(9.0, 17.9)	-10.7	(-16.9, -4.2)	0.001
Severe	306	7 (2.3)	(0.9, 4.7)	226	1 (0.4)	(0.0, 2.4)	-1.8	(-4.3, 0.3)	0.085
Limitation of arm movement[h]									
Any	326	90 (27.6)	(22.8, 32.8)	247	40 (16.2)	(11.8, 21.4)	-11.4	(-18.1, -4.6)	0.001
Mild	322	81 (25.2)	(20.5, 30.3)	245	38 (15.5)	(11.2, 20.7)	-9.6	(-16.2, -2.9)	0.005
Moderate	303	8 (2.6)	(1.1, 5.1)	228	2 (0.9)	(0.1, 3.1)	-1.8	(-4.4, 0.7)	0.165
Severe	305	9 (3.0)	(1.4, 5.5)	228	2 (0.9)	(0.1, 3.1)	-2.1	(-4.8, 0.4)	0.100
Any local reaction[i]	387	24 (64.1)	(59.1, 68.9)	304	191 (62.8)	(57.1, 68.3)	-1.3	(-8.5, 6.0)	0.737

Data presented are from the Vaccination 1 and Vaccination 2 safety population.
13vPnC = 13-valent pneumococcal conjugate vaccine; 23vPS = 23-valent pneumococcal polysaccharide vaccine; CI = confidence interval; Diff = difference.

a. N = number of subjects with known values.
b. n = number of subjects with the specified characteristic.
c. Exact 2-sided CI (Clopper and Pearson) based upon the observed proportion of subjects.
d. Difference in proportions, (13vPnC/13vPnC) – (23vPS), expressed as a percentage.
e. Exact 2-sided CI and corresponding p-value (based on Chan and Zhang) for the difference in proportions, (13vPnC/13vPnC) – (23vPS), expressed as a percentage.
f. Mild = 2.5 to 5.0 cm, moderate = 5.1 to 10.0 cm, and severe is >10.0 cm.
g. Mild = awareness of symptom but easily tolerated, moderate = discomfort enough to cause interference with usual activity, severe = incapacitating with inability to do usual activity.
h. Mild = some limitation of arm movement, moderate = unable to move arm above head but able to move arm above shoulder, and severe = unable to move arm above shoulder.
i. Any local reaction = any pain, any swelling, any redness, or any limitation of arm movement.

The percentages of subjects with any redness, any swelling, any pain, and any limitation of arm movement were also similar between the treatment groups (13vPnC/13vPnC [Year 1] compared with 23vPS/13vPnC [Year 1]). The percentages of subjects with mild, moderate, and severe redness, swelling, pain, and limitation of arm movement were similar for the 13vPnC/13vPnC (Year 1) group compared with the percentages of subjects for the 23vPS/13vPnC (Year 1) group; there were no significant differences between the vaccine groups (Table 15).

Table 15. Subjects Reporting Local Reactions Within 14 Days After Vaccination 2 (Year 1) - Safety Population

Local Reaction	Vaccine Group/Sequence (as Administered) 13vPnC/13vPnC N[a]	n[b] (%)	(95% CI[c])	23vPS/13vPnC N[a]	n[b] (%)	(95% CI[c])	Diff[d]	(95% CI[e])	p-Value[e]
Redness[f]									
Any	236	30 (12.7)	(8.7, 17.6)	228	23 (10.1)	(6.5, 14.8)	2.6	(-3.2, 8.6)	0.381
Mild	233	16 (6.9)	(4.0, 10.9)	226	20 (8.8)	(5.5, 13.3)	-2.0	(-7.2, 3.0)	0.447
Moderate	231	16 (6.9)	(4.0, 11.0)	223	8 (3.6)	(1.6, 6.9)	3.3	(-0.9, 7.8)	0.138
Severe	227	4 (1.8)	(0.5, 4.5)	222	2 (0.9)	(0.1, 3.2)	0.9	(-1.6, 3.6)	0.542
Swelling[f]									
Any	236	29 (12.3)	(8.4, 17.2)	241	34 (14.1)	(10.0, 19.2)	-1.8	(-8.0, 4.3)	0.577
Mild	234	24 (10.3)	(6.7, 14.9)	236	28 (11.9)	(8.0, 16.7)	-1.6	(-7.4, 4.2)	0.594
Moderate	229	8 (3.5)	(1.5, 6.8)	229	11 (4.8)	(2.4, 8.4)	-1.3	(-5.3, 2.6)	0.533
Severe	227	2 (0.9)	(0.1, 3.1)	222	1 (0.5)	(0.0, 2.5)	0.4	(-1.7, 2.7)	0.696
Pain[g]									
Any	297	173 (58.2)	(52.4, 63.9)	302	171 (56.6)	(50.8, 62.3)	1.6	(-6.4, 9.6)	0.702
Mild	291	158 (54.3)	(48.4, 60.1)	297	159 (53.5)	(47.7, 59.3)	0.8	(-7.3, 8.9)	0.872
Moderate	239	31 (13.0)	(9.0, 17.9)	236	31 (13.1)	(9.1, 18.1)	-0.2	(-6.3, 6.0)	>0.999
Severe	226	1 (0.4)	(0.0, 2.4)	221	2 (0.9)	(0.1, 3.2)	-0.5	(-2.8, 1.6)	0.670
Limitation of arm movement[h]									
Any	247	40 (16.2)	(11.8, 21.4)	251	50 (19.9)	(15.2, 25.4)	-3.7	(-10.6, 3.1)	0.287
Mild	245	38 (15.5)	(11.2, 20.7)	249	47 (18.9)	(14.2, 24.3)	-3.4	(-10.1, 3.3)	0.326
Moderate	228	2 (0.9)	(0.1, 3.1)	222	2 (0.9)	(0.1, 3.2)	-0.0	(-2.4, 2.3)	>0.999
Severe	228	2 (0.9)	(0.1, 3.1)	222	3 (1.4)	(0.3, 3.9)	-0.5	(-3.1, 1.9)	0.734
Any local reaction[i]	304	191 (62.8)	(57.1, 68.3)	311	189 (60.8)	(55.1, 66.2)	2.1	(-5.7, 9.8)	0.612

Data presented are from the Vaccination 2 safety population.
13vPnC = 13-valent pneumococcal conjugate vaccine; 23vPS = 23-valent pneumococcal polysaccharide vaccine; CI = confidence interval; Diff = difference.

a. N = number of subjects with known values.
b. n = number of subjects with the specified characteristic.
c. Exact 2-sided CI (Clopper and Pearson) based upon the observed proportion of subjects.
d. Difference in proportions, (13vPnC/13vPnC) – (23vPS/13vPnC), expressed as a percentage.
e. Exact 2-sided CI and corresponding p-value (based on Chan and Zhang) for the difference in proportions, (13vPnC/13vPnC) – (23vPS/13vPnC), expressed as a percentage.
f. Mild = 2.5 to 5.0 cm, moderate = 5.1 to 10.0 cm, and severe is >10.0 cm.
g. Mild = awareness of symptom but easily tolerated, moderate = discomfort enough to cause interference with usual activity, severe = incapacitating with inability to do usual activity.
h. Mild = some limitation of arm movement, moderate = unable to move arm above head but able to move arm above shoulder, and severe = unable to move arm above shoulder.
i. Any local reaction = any pain, any swelling, any redness, or any limitation of arm movement.

The percentages of subjects with any redness, any swelling, and any pain were similar between the treatment groups (23vPS/13vPnC [Year 1] compared with 13vPnC [Year 0]); the percentage of subjects with any limitation of arm movement was significantly higher for the 23vPS/13vPnC (Year 1) group (19.9%) compared with the 13vPnC (Year 0) (10.5%) group (p=0.002) (Table 16).

Table 16. Subjects Reporting Local Reactions Within 14 Days After Vaccination, 13vPnC (Year 0) and 23vPS/13vPnC (Year 1) - Safety Population

Local Reaction	Vaccine Group/Sequence (as Administered) 13vPnC N[a]	n[b] (%)	(95% CI[c])	23vPS/13vPnC N	n (%)	(95% CI)	Diff[d]	(95% CI[e])	p-Value[e]
Redness[f]									
Any	306	33 (10.8)	(7.5, 14.8)	228	23 (10.1)	(6.5, 14.8)	-0.7	(-5.9, 4.8)	0.806
Mild	304	29 (9.5)	(6.5, 13.4)	226	20 (8.8)	(5.5, 13.3)	-0.7	(-5.7, 4.5)	0.821
Moderate	301	14 (4.7)	(2.6, 7.7)	223	8 (3.6)	(1.6, 6.9)	-1.1	(-4.6, 2.7)	0.665
Severe	299	5 (1.7)	(0.5, 3.9)	222	2 (0.9)	(0.1, 3.2)	-0.8	(-3.1, 1.7)	0.618
Swelling[f]									
Any	307	32 (10.4)	(7.2, 14.4)	241	34 (14.1)	(10.0, 19.2)	3.7	(-1.9, 9.5)	0.195
Mild	305	27 (8.9)	(5.9, 12.6)	236	28 (11.9)	(8.0, 16.7)	3.0	(-2.2, 8.5)	0.256
Moderate	299	12 (4.0)	(2.1, 6.9)	229	11 (4.8)	(2.4, 8.4)	0.8	(-2.8, 4.7)	0.670
Severe	297	0 (0.0)	(0.0, 1.2)	222	1 (0.5)	(0.0, 2.5)	0.5	(-0.9, 2.5)	0.422
Pain[g]									
Any	362	187 (51.7)	(46.4, 56.9)	302	171 (56.6)	(50.8, 62.3)	5.0	(-2.7, 12.5)	0.203
Mild	359	180 (50.1)	(44.8, 55.4)	297	159 (53.5)	(47.7, 59.3)	3.4	(-4.3, 11.1)	0.388
Moderate	306	23 (7.5)	(4.8, 11.1)	236	31 (13.1)	(9.1, 18.1)	5.6	(0.4, 11.1)	0.035
Severe	299	4 (1.3)	(0.4, 3.4)	221	2 (0.9)	(0.1, 3.2)	-0.4	(-2.7, 2.0)	0.713
Limitation of arm movement[h]									
Any	313	33 (10.5)	(7.4, 14.5)	251	50 (19.9)	(15.2, 25.4)	9.4	(3.3, 15.6)	0.002
Mild	312	32 (10.3)	(7.1, 14.2)	249	47 (18.9)	(14.2, 24.3)	8.6	(2.7, 14.7)	0.004
Moderate	297	1 (0.3)	(0.0, 1.9)	222	2 (0.9)	(0.1, 3.2)	0.6	(-1.1, 2.9)	0.527
Severe	298	2 (0.7)	(0.1, 2.4)	222	3 (1.4)	(0.3, 3.9)	0.7	(-1.4, 3.3)	0.562
Any local reaction[i]	370	209 (56.5)	(51.3, 61.6)	311	189 (60.8)	(55.1, 66.2)	4.3	(-3.2, 11.7)	0.260

Data presented are from the Vaccination 2 safety population.
13vPnC = 13-valent pneumococcal conjugate vaccine; 23vPS = 23-valent pneumococcal polysaccharide vaccine; CI = confidence interval; Diff = difference.

a. N = number of subjects with known values.
b. n = number of subjects with the specified characteristic.
c. 2-sided CI (Clopper and Pearson) based upon the observed proportion of subjects.
d. Difference in proportions, (23vPS/13vPnC) – (13vPnC), expressed as a percentage.
e. Exact 2-sided CI and corresponding p-value (based on Chan and Zhang) for the difference in proportions, (23vPS/13vPnC) – (13vPnC), expressed as a percentage.
f. Mild = 2.5 to 5.0 cm, moderate = 5.1 to 10.0 cm, and severe is >10.0 cm.
g. Mild = awareness of symptom but easily tolerated, moderate = discomfort enough to cause interference with usual activity, severe = incapacitating with inability to do usual activity.
h. Mild = some limitation of arm movement, moderate = unable to move arm above head but able to move arm above shoulder, and severe = unable to move arm above shoulder.
i. Any local reaction = any pain, any swelling, any redness, or any limitation of arm movement.

Systemic Events:

Systemic Events After Vaccination 1: 13vPnC Versus 23vPS: The numbers and percentages of subjects with systemic events reported within 14 days after Vaccination 1 (Year 0) are shown in Table 17.

Significantly fewer 13vPnC recipients (60.3%) reported any systemic event compared with 23vPS recipients (68.2%; p=0.020) after Vaccination 1.

Table 17. Subjects Reporting Systemic Events Within 14 Days After Vaccination 1 (Year 0) - Safety Population

	Vaccine Group (as Administered)								
	13vPnC			23vPS					
Event	N[a]	n[b] (%)	(95% CI[c])	N[a]	n[b] (%)	(95% CI[c])	Diff[d]	(95% CI[e])	p-Value[e]
Fever									
Any (≥38°C)	299	3 (1.0)	(0.2, 2.9)	309	13 (4.2)	(2.3, 7.1)	-3.2	(-6.2, -0.7)	0.013
Mild (≥38°C but <38.5°C)	299	3 (1.0)	(0.2, 2.9)	303	6 (2.0)	(0.7, 4.3)	-1.0	(-3.4, 1.2)	0.535
Moderate (≥38.5°C but <39°C)	297	0 (0.0)	(0.0, 1.2)	301	0 (0.0)	(0.0, 1.2)	0.0	(-1.2, 1.3)	>0.999
Severe (≥39°C but ≤40°C)	297	0 (0.0)	(0.0, 1.2)	301	1 (0.3)	(0.0, 1.8)	-0.3	(-1.8, 0.9)	0.509
Potentially life threatening (>40°C)	297	0 (0.0)	(0.0, 1.2)	307	6[f] (2.0)	(0.7, 4.2)	-2.0	(-4.2, -0.5)	0.015
Fatigue	350	119 (34.0)	(29.0, 39.2)	367	159 (43.3)	(38.2, 48.6)	-9.3	(-16.4, -2.2)	0.011
Headache	329	78 (23.7)	(19.2, 28.7)	331	86 (26.0)	(21.3, 31.1)	-2.3	(-8.9, 4.3)	0.510
Chills	305	24 (7.9)	(5.1, 11.5)	312	35 (11.2)	(7.9, 15.3)	-3.3	(-8.1, 1.3)	0.162
Rash	303	22 (7.3)	(4.6, 10.8)	323	53 (16.4)	(12.5, 20.9)	-9.1	(-14.3, -4.0)	<0.001
Vomiting	300	5 (1.7)	(0.5, 3.8)	304	4 (1.3)	(0.4, 3.3)	0.4	(-1.9, 2.7)	0.808
Decreased appetite	317	33 (10.4)	(7.3, 14.3)	313	36 (11.5)	(8.2, 15.6)	-1.1	(-6.1, 3.9)	0.688
New generalized muscle pain	345	127 (36.8)	(31.7, 42.1)	358	160 (44.7)	(39.5, 50.0)	-7.9	(-15.2, -0.6)	0.034
Aggravated generalized muscle pain	320	66 (20.6)	(16.3, 25.5)	334	92 (27.5)	(22.8, 32.7)	-6.9	(-13.6, -0.3)	0.039
New generalized joint pain	310	39 (12.6)	(9.1, 16.8)	323	48 (14.9)	(11.2, 19.2)	-2.3	(-7.7, 3.1)	0.413
Aggravated generalized joint pain	310	36 (11.6)	(8.3, 15.7)	322	53 (16.5)	(12.6, 21.0)	-4.8	(-10.3, 0.6)	0.081
Use of medication to treat pain	327	72 (22.0)	(17.6, 26.9)	342	91 (26.6)	(22.0, 31.6)	-4.6	(-11.2, 1.9)	0.169
Use of medication to treat fever	304	9 (3.0)	(1.4, 5.5)	308	19 (6.2)	(3.8, 9.5)	-3.2	(-6.8, 0.2)	0.059
Any systemic event[g]	388	234 (60.3)	(55.2, 65.2)	403	275 (68.2)	(63.4, 72.8)	-7.9	(-14.6, -1.2)	0.020

Data presented are from the Vaccination 1 safety population.

13vPnC = 13-valent pneumococcal conjugate vaccine; 23vPS = 23-valent pneumococcal polysaccharide vaccine; CI = confidence interval; Diff = difference.

a. N = number of subjects with known values.
b. n = number of subjects with the specified characteristic.
c. Exact 2-sided CI (Clopper and Pearson) based upon the observed proportion of subjects.
d. Difference in proportions, (13vPnC) – (23vPS), expressed as a percentage.
e. Exact 2-sided CI and corresponding p-value (based on Chan and Zhang) for the difference in proportions, (13vPnC) – (23vPS), expressed as a percentage.
f. All reports of fever >40°C were confirmed as data entry errors.
g. Any systemic event = any fever ≥38°C, any fatigue, any headache, any chills, any rash, any vomiting, any decreased appetite, any new or aggravated generalized muscle pain, and any new or aggravated joint pain.

Comparisons of Systemic Events After Vaccination 2: A comparison of subjects reporting systemic events after 1 vaccination of 13vPnC during Year 0 and those who subsequently received another 13vPnC vaccination in Year 1 (13vPnC/13vPnC group) is shown in Table 18.

Except in 1 case, the 95% CIs for the differences included 0, indicating that there were no statistically significant differences between the vaccination groups being compared. The exception was for chills (9.3% for 13vPnC and 4.4% for 13vPnC/13vPnC).

Table 18. Subjects Reporting Systemic Events Within 14 Days After Vaccination, 13vPnC (Year 0) and 13vPnC/13vPnC (Year 1) - Safety Population

	Vaccine Group/Sequence (as Administered)							
	13vPnC			13vPnC/13vPnC				
Event	N[a]	n[b] (%)	(95% CI[c])	N[a]	n[b] (%)	(95% CI[c])	Difference[d]	(95% CI[e])
Fever								
Any (≥38°C)	179	3 (1.7)	(0.3, 4.8)	179	4 (2.2)	(0.6, 5.6)	0.6	(-2.5, 3.6)
Mild (≥38°C but <38.5°C)	179	3 (1.7)	(0.3, 4.8)	179	1 (0.6)	(0.0, 3.1)	-1.1	(-3.5, 1.3)
Moderate (≥38.5°C but <39°C)	177	0 (0.0)	(0.0, 2.1)	177	0 (0.0)	(0.0, 2.1)	0	(-1.1, 1.1)
Severe (≥39°C but ≤40°C)	177	0 (0.0)	(0.0, 2.1)	177	1 (0.6)	(0.0, 3.1)	0.6	(-1.0, 2.1)
Potentially life threatening (>40°C)	177	0 (0.0)	(0.0, 2.1)	177	2 (1.1)	(0.1, 4.0)	1.1	(-0.8, 3.0)
Fatigue	215	72 (33.5)	(27.2, 40.2)	215	61 (28.4)	(22.5, 34.9)	-5.1	(-11.5, 1.4)
Headache	200	46 (23.0)	(17.4, 29.5)	200	38 (19.0)	(13.8, 25.1)	-4	(-10.0, 2.1)
Chills	182	17 (9.3)	(5.5, 14.5)	182	8 (4.4)	(1.9, 8.5)	-4.9	(-9.6, -0.2)
Rash	183	15 (8.2)	(4.7, 13.2)	183	11 (6.0)	(3.0, 10.5)	-2.2	(-6.3, 1.9)
Vomiting	178	2 (1.1)	(0.1, 4.0)	178	0 (0.0)	(0.0, 2.1)	-1.1	(-3.0, 0.8)
Decreased appetite	190	16 (8.4)	(4.9, 13.3)	190	15 (7.9)	(0.0, 2.1)	-0.5	(-4.9, 3.8)
New generalized muscle pain	219	83 (37.9)	(31.4, 44.7)	219	78 (35.6)	(29.3, 42.3)	-2.3	(-9.7, 5.2)
Aggravated generalized muscle pain	198	41 (20.7)	(15.3, 27.0)	198	32 (16.2)	(11.3, 22.0)	-4.5	(-11.3, 2.3)
New generalized joint pain	187	21 (11.2)	(7.1, 16.7)	187	14 (7.5)	(4.2, 12.2)	-3.7	(-8.8, 1.3)
Aggravated generalized joint pain	188	21 (11.2)	(7.0, 16.6)	188	19 (10.1)	(6.2, 15.3)	-1.1	(-6.4, 4.3)
Use of medication to treat pain	206	45 (21.8)	(16.4, 28.1)	206	38 (18.4)	(13.4, 24.4)	-3.4	(-9.9, 3.1)
Use of medication to treat fever	184	6 (3.3)	(1.2, 7.0)	184	4 (2.2)	(0.6, 5.5)	-1.1	(-4.6, 2.4)
Any systemic event[f]	259	156 (60.2)	(54.0, 66.2)	259	146 (56.4)	(50.1, 62.5)	-3.9	(-10.7, 3.0)

Data presented are from the Vaccination 1 and Vaccination 2 safety population.

13vPnC = 13-valent pneumococcal conjugate vaccine; 23vPS = 23-valent pneumococcal polysaccharide vaccine; CI = confidence interval.

a. N = number of subjects with known values.

b. n = number of subjects with the specified characteristic.

c. Exact 2-sided CI (Clopper and Pearson) based upon the observed proportion of subjects.

d. Difference in proportions, (13vPnC/13vPnC) – (13vPnC), expressed as a percentage.

e. Adjusted Wald 2-sided CI for the difference in dependent proportions, (13vPnC/13vPnC) – (13vPnC), expressed as a percentage.

f. Any systemic event = any fever ≥38°C, any fatigue, any headache, any chills, any rash, any vomiting, any decreased appetite, any new or aggravated generalized muscle pain, and any new or aggravated joint pain.

The comparison of 23vPS in Year 0 with the 13vPnC/13vPnC group in Year 1 is shown in Table 19. The results suggest that administering 13vPnC 1 year after a vaccination with 13vPnC produced slightly fewer systemic events compared to those after a single dose of 23vPS. The incidences of any systemic event were significantly different between groups (68.2% for 23vPS and 55.5% for 13vPnC/13vPnC, $p<0.001$).

Table 19. Subjects Reporting Systemic Events Within 14 Days After Vaccination, 23vPS (Year 0) and 13vPnC/13vPnC (Year 1) - Safety Population

	Vaccine Group/Sequence (as Administered)								
	23vPS			13vPnC/13vPnC					
Event	N[a]	n[b] (%)	(95% CI[c])	N[a]	n[b] (%)	(95% CI[c])	Difference[d]	(95% CI[e])	p-Value[e]
Fever									
Any (≥38°C)	309	13 (4.2)	(2.3, 7.1)	229	8 (3.5)	(1.5, 6.8)	-0.7	(-4.1, 2.9)	0.711
Mild (≥38°C but <38.5°C)	303	6 (2.0)	(0.7, 4.3)	227	2 (0.9)	(0.1, 3.1)	-1.1	(-3.6, 1.3)	0.384
Moderate (≥38.5°C but <39°C)	301	0 (0.0)	(0.0, 1.2)	227	2 (0.9)	(0.1, 3.1)	0.9	(-0.4, 3.1)	0.160
Severe (≥39°C but ≤40°C)	301	1 (0.3)	(0.0, 1.8)	226	1 (0.4)	(0.0, 2.4)	0.1	(-1.5, 2.1)	0.955
Potentially life threatening (>40°C)	307	6 (2.0)	(0.7, 4.2)	227	3 (1.3)	(0.3, 3.8)	-0.6	(-3.2, 2.0)	0.666
Fatigue	367	159 (43.3)	(38.2, 48.6)	255	73 (28.6)	(23.2, 34.6)	-14.7	(-22.1, -7.0)	<0.001
Headache	331	86 (26.0)	(21.3, 31.1)	246	47 (19.1)	(14.4, 24.6)	-6.9	(-13.7, 0.1)	0.053
Chills	312	35 (11.2)	(7.9, 15.3)	234	17 (7.3)	(4.3, 11.4)	-4.0	(-8.9, 1.1)	0.120
Rash	323	53 (16.4)	(12.5, 20.9)	232	14 (6.0)	(3.3, 9.9)	-10.4	(-15.6, -4.8)	<0.001
Vomiting	304	4 (1.3)	(0.4, 3.3)	226	1 (0.4)	(0.0, 2.4)	-0.9	(-3.0, 1.3)	0.371
Decreased appetite	313	36 (11.5)	(8.2, 15.6)	237	21 (8.9)	(5.6, 13.2)	-2.6	(-7.7, 2.6)	0.331
New generalized muscle pain	358	160 (44.7)	(39.5, 50.0)	260	90 (34.6)	(28.8, 40.7)	-10.1	(-17.8, -2.2)	0.012
Aggravated generalized muscle pain	334	92 (27.5)	(22.8, 32.7)	245	44 (18.0)	(13.4, 23.3)	-9.6	(-16.3, -2.7)	0.007
New generalized joint pain	323	48 (14.9)	(11.2, 19.2)	238	25 (10.5)	(6.9, 15.1)	-4.4	(-9.9, 1.3)	0.133
Aggravated generalized joint pain	322	53 (16.5)	(12.6, 21.0)	239	30 (12.6)	(8.6, 17.4)	-3.9	(-9.7, 2.1)	0.205
Use of medication to treat pain	342	91 (26.6)	(22.0, 31.6)	247	47 (19.0)	(14.3, 24.5)	-7.6	(-14.3, -0.7)	0.032
Use of medication to treat fever	308	19 (6.2)	(3.8, 9.5)	232	9 (3.9)	(1.8, 7.2)	-2.3	(-6.2, 1.6)	0.303
Any systemic event[f]	403	275 (68.2)	(63.4, 72.8)	290	161 (55.5)	(49.6, 61.3)	-12.7	(-20.0, -5.4)	<0.001

Data presented are from the Vaccination 1 and Vaccination 2 safety population.

13vPnC = 13-valent pneumococcal conjugate vaccine; 23vPS = 23-valent pneumococcal polysaccharide vaccine; CI = confidence interval.

a. N = number of subjects with known values.
b. n = number of subjects with the specified characteristic.
c. Exact 2-sided CI (Clopper and Pearson) based upon the observed proportion of subjects.
d. Difference in proportions, (13vPnC/13vPnC) – (23vPS), expressed as a percentage.
e. Exact 2-sided CI and corresponding p-value (based on Chan and Zhang) for the difference in proportions, (13vPnC/13vPnC) – (23vPS), expressed as a percentage.
f. Any systemic event = any fever ≥38°C, any fatigue, any headache, any chills, any rash, any vomiting, any decreased appetite, any new or aggravated generalized muscle pain, and any new or aggravated joint pain.

Table 20 shows the comparison of systemic events in subjects for both treatment sequences (13vPnC/13vPnC versus 23vPS/13vPnC) at Year 1. The results suggest that administering 13vPnC 1 year after a vaccination with 13vPnC produced systemic events comparable to those observed with administering 13vPnC 1 year after a vaccination with 23vPS. Vomiting was the only systemic event that was significantly different between groups (0.4% for 13vPnC/13vPnC and 3.1% for 23vPS/13vPnC, p=0.032). There were no other incidences of systemic events that were significantly different between groups.

Table 20. Subjects Reporting Systemic Events Within 14 Days After Vaccination 2 (Year 1) - Safety Population

	Vaccine Group/Sequence (as Administered)								
	13vPnC/13vPnC			23vPS/13vPnC					
Event	N[a]	n[b] (%)	(95% CI[c])	N[a]	n[b] (%)	(95% CI[c])	Difference[d]	(95% CI[e])	p-Value[e]
Fever									
Any (≥38°C)	229	8 (3.5)	(1.5, 6.8)	224	5 (2.2)	(0.7, 5.1)	1.3	(-2.0, 4.8)	0.539
Mild (≥38°C but <38.5°C)	227	2 (0.9)	(0.1, 3.1)	224	4 (1.8)	(0.5, 4.5)	-0.9	(-3.7, 1.6)	0.527
Moderate (≥38.5°C but <39°C)	227	2 (0.9)	(0.1, 3.1)	221	0 (0.0)	(0.0, 1.7)	0.9	(-0.8, 3.1)	0.218
Severe (≥39°C but ≤40°C)	226	1 (0.4)	(0.0, 2.4)	222	1 (0.5)	(0.0, 2.5)	-0.0	(-2.1, 2.1)	>0.999
Potentially life threatening (>40°C)	227	3[f] (1.3)	(0.3, 3.8)	221	1[f] (0.5)	(0.0, 2.5)	0.9	(-1.3, 3.4)	0.541
Fatigue	255	73 (28.6)	(23.2, 34.6)	265	91 (34.3)	(28.6, 40.4)	-5.7	(-13.7, 2.3)	0.163
Headache	246	47 (19.1)	(14.4, 24.6)	248	56 (22.6)	(17.5, 28.3)	-3.5	(-10.7, 3.7)	0.348
Chills	234	17 (7.3)	(4.3, 11.4)	233	23 (9.9)	(6.4, 14.4)	-2.6	(-7.9, 2.6)	0.363
Rash	232	14 (6.0)	(3.3, 9.9)	226	16 (7.1)	(4.1, 11.2)	-1.0	(-5.8, 3.6)	0.718
Vomiting	226	1 (0.4)	(0.0, 2.4)	226	7 (3.1)	(1.3, 6.3)	-2.7	(-5.8, -0.2)	0.032
Decreased appetite	237	21 (8.9)	(5.6, 13.2)	230	17 (7.4)	(4.4, 11.6)	1.5	(-3.6, 6.6)	0.594
New generalized muscle pain	260	90 (34.6)	(28.8, 40.7)	263	92 (35.0)	(29.2, 41.1)	-0.4	(-8.6, 7.8)	0.955
Aggravated generalized muscle pain	245	44 (18.0)	(13.4, 23.3)	248	52 (21.0)	(16.1, 26.6)	-3.0	(-10.1, 4.0)	0.407
New generalized joint pain	238	25 (10.5)	(6.9, 15.1)	234	28 (12.0)	8.1, 16.8)	-1.5	(-7.3, 4.3)	0.644
Aggravated generalized joint pain	239	30 (12.6)	(8.6, 17.4)	231	27 (11.7)	(7.8, 16.5)	0.9	(-5.2, 6.9)	0.797
Use of medication to treat pain	247	47 (19.0)	(14.3, 24.5)	240	37 (15.4)	(11.1, 20.6)	3.6	(-3.2, 10.4)	0.296
Use of medication to treat fever	232	9 (3.9)	(1.8, 7.2)	231	17 (7.4)	(4.3, 11.5)	-3.5	(-8.0, 0.8)	0.126
Any systemic event[g]	290	161 (55.5)	(49.6, 61.3)	299	174 (58.2)	(52.4, 63.8)	-2.7	(-10.7, 5.4)	0.524

Data presented are from the Vaccination 2 safety population.

13vPnC = 13-valent pneumococcal conjugate vaccine; 23vPS = 23-valent pneumococcal polysaccharide vaccine; CI = confidence interval.

a. N = number of subjects with known values.
b. n = number of subjects with the specified characteristic.
c. Exact 2-sided CI (Clopper and Pearson) based upon the observed proportion of subjects.
d. Difference in proportions, (13vPnC/13vPnC) – (23vPS/13vPnC), expressed as a percentage.
e. Exact 2-sided CI and corresponding p-value (based on Chan and Zhang) for the difference in proportions, (13vPnC/13vPnC) – (23vPS/13vPnC), expressed as a percentage.
f. Two of the reports of fever >40°C in the 13vPnC/13vPnC group and the report of fever >40°C in the 23vPS/13vPnC group were confirmed as data entry errors
g. Any systemic event = any fever ≥38°C, any fatigue, any headache, any chills, any rash, any vomiting, any decreased appetite, any new or aggravated generalized muscle pain, and any new or aggravated joint pain.

The comparison of 13vPnC in Year 0 with the 23vPS/13vPnC group in Year 1 is shown in Table 21. The results suggest that administering 13vPnC 1 year after a vaccination with 23vPS produced systemic events comparable to those after a single dose of 13vPnC. There were few significant differences between the groups. The significant differences observed were for the use of medication to treat pain (22.0% for 13vPnC, 15.4% for 23vPS/13vPnC, p=0.049) and the use of medication to treat fever (3.0% for 13vPnC, 7.4% for 23vPS/13vPnC, p=0.022). These statistical differences were not considered clinically important.

Table 21. Subjects Reporting Systemic Events Within 14 Days After Vaccination, 13vPnC (Year 0) and 23vPS/13vPnC (Year 1) - Safety Population

	Vaccine Group/Sequence (as Administered)								
	13vPnC			23vPS/13vPnC					
Event	N[a]	n[b] (%)	(95% CI[c])	N[a]	n[b] (%)	(95% CI[c])	Difference[d]	(95% CI[e])	p-Value[e]
Fever									
Any (≥38°C)	299	3 (1.0)	(0.2, 2.9)	224	5 (2.2)	(0.7, 5.1)	1.2	(-1.0, 4.2)	0.423
Mild (≥38°C but <38.5°C)	299	3 (1.0)	(0.2, 2.9)	224	4 (1.8)	(0.5, 4.5)	0.8	(-1.4, 3.6)	0.580
Moderate (≥38.5°C but <39°C)	297	0 (0.0)	(0.0, 1.2)	221	0 (0.0)	(0.0, 1.7)	0.0	(-1.3, 1.7)	>0.999
Severe (≥39°C but ≤40°C)	297	0 (0.0)	(0.0, 1.2)	222	1 (0.5)	(0.0, 2.5)	0.5	(-0.9, 2.5)	0.422
Potentially life threatening (>40°C)	297	0 (0.0)	(0.0, 1.2)	221	1 (0.5)	(0.0, 2.5)	0.5	(-0.9, 2.5)	0.421
Fatigue	350	119 (34.0)	(29.0, 39.2)	265	91 (34.3)	(28.6, 40.4)	0.3	(-7.2, 8.0)	0.933
Headache	329	78 (23.7)	(19.2, 28.7)	248	56 (22.6)	(17.5, 28.3)	-1.1	(-8.0, 5.9)	0.760
Chills	305	24 (7.9)	(5.1, 11.5)	233	23 (9.9)	(6.4, 14.4)	2.0	(-2.9, 7.2)	0.424
Rash	303	22 (7.3)	(4.6, 10.8)	226	16 (7.1)	(4.1, 11.2)	-0.2	(-4.7, 4.6)	0.959
Vomiting	300	5 (1.7)	(0.5, 3.8)	226	7 (3.1)	(1.3, 6.3)	1.4	(-1.3, 4.7)	0.425
Decreased appetite	317	33 (10.4)	(7.3, 14.3)	230	17 (7.4)	(4.4, 11.6)	-3.0	(-7.8, 2.0)	0.270
New generalized muscle pain	345	127 (36.8)	(31.7, 42.1)	263	92 (35.0)	(29.2, 41.1)	-1.8	(-9.5, 5.9)	0.648
Aggravated generalized muscle pain	320	66 (20.6)	(16.3, 25.5)	248	52 (21.0)	(16.1, 26.6)	0.3	(-6.5, 7.2)	0.923
New generalized joint pain	310	39 (12.6)	(9.1, 16.8)	234	28 (12.0)	8.1, 16.8)	-0.6	(-6.2, 5.2)	0.840
Aggravated generalized joint pain	310	36 (11.6)	(8.3, 15.7)	231	27 (11.7)	(7.8, 16.5)	0.1	(-5.4, 5.8)	0.986
Use of medication to treat pain	327	72 (22.0)	(17.6, 26.9)	240	37 (15.4)	(11.1, 20.6)	-6.6	(-13.0, -0.0)	0.049
Use of medication to treat fever	304	9 (3.0)	(1.4, 5.5)	231	17 (7.4)	(4.3, 11.5)	4.4	(0.5, 8.7)	0.022
Any systemic event[f]	388	234 (60.3)	(55.2, 65.2)	299	174 (58.2)	(52.4, 63.8)	-2.1	(-9.6, 5.3)	0.582

Data presented are from the Vaccination 1 and Vaccination 2 safety population.

13vPnC = 13-valent pneumococcal conjugate vaccine; 23vPS = 23-valent pneumococcal polysaccharide vaccine; CI = confidence interval.

a. N = number of subjects with known values.

b. n = number of subjects with the specified characteristic.

c. Exact 2-sided CI (Clopper and Pearson) based upon the observed proportion of subjects.

d. Difference in proportions, (23vPS/13vPnC) – (13vPnC), expressed as a percentage.

e. Exact 2-sided CI and corresponding p-value (based on Chan and Zhang) for the difference in proportions, (23vPS/13vPnC) – (13vPnC), expressed as a percentage.

f. Any systemic event = any fever ≥38°C, any fatigue, any headache, any chills, any rash, any vomiting, any decreased appetite, any new or aggravated generalized muscle pain, and any new or aggravated joint pain.

Adverse Events: AEs were to be recorded within 29 days (Day 1 through Day 29) after each study vaccination for all vaccine groups. Local reactions lasting longer than 14 days after vaccination, any redness or swelling at the injection site >10 cm, and severe limitation of arm movement were to be recorded as AEs.

Non-Serious Adverse Events After Vaccination 1: The incidence of AEs occurring from Visit 1 through Visit 2 (after Vaccination 1 [Year 0]) was higher in the 23vPS group than in the 13vPnC group. In both vaccine groups, the most frequently reported types of AEs were infections and infestations. The non-serious AEs reported after Vaccination 1 (Year 0) are presented in Table 22.

Table 22. Non-Serious Adverse Events Reported After Vaccination 1 (Year 0) – Safety Population

	Vaccine Group (as Administered)								
	13vPnC N=463			23vPS N=473					
System Organ Class/ Preferred Term	No. of Subjects[a]	%	No. of Events[b]	No. of Subjects[a]	%	No. of Events[b]	Difference[c]	(95% CI[d])	p-Value[d]
Any event	66	14.3	82	83	17.5	102	-3.3	(-8.0, 1.4)	0.169
Cardiac disorders	0	0.0	0	3	0.6	3	-0.6	(-1.8, 0.2)	0.086
Angina pectoris	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Cardiac failure congestive	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Sinus bradycardia	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Ear and labyrinth disorders	2	0.4	2	2	0.4	2	0.0	(-1.1, 1.2)	0.983
Cerumen impaction	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Ear pain	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Hypoacusis	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Vertigo positional	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Endocrine disorders	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Hyperthyroidism	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Eye disorders	1	0.2	1	3	0.6	4	-0.4	(-1.7, 0.6)	0.327
Conjunctival haemorrhage	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Conjunctivitis	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Eye discharge	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Eye pain	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Vision blurred	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Gastrointestinal disorders	11	2.4	14	3	0.6	3	1.7	(0.2, 3.6)	0.028
Diarrhoea	4	0.9	4	0	0.0	0	0.9	(0.1, 2.2)	0.043
Abdominal pain lower	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Abdominal pain upper	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Colonic polyp	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Constipation	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Diverticulum	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Duodenal ulcer	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Dyspepsia	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Dysphagia	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Haemorrhoidal haemorrhage	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Lip pain	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Melaena	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312

Table 22. Non-Serious Adverse Events Reported After Vaccination 1 (Year 0) – Safety Population

	Vaccine Group (as Administered)								
	13vPnC N=463			23vPS N=473					
System Organ Class/ Preferred Term	No. of Subjects[a]	%	No. of Events[b]	No. of Subjects[a]	%	No. of Events[b]	Difference[c]	(95% CI[d])	p-Value[d]
Nausea	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Toothache	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
General disorders and administration site conditions	3	0.6	3	16	3.4	17	-2.7	(-4.9, -1.0)	0.003
Injection site pruritus	1	0.2	1	3	0.6	3	-0.4	(-1.7, 0.6)	0.327
Fatigue	0	0.0	0	3	0.6	3	-0.6	(-1.8, 0.2)	0.086
Injection site induration	0	0.0	0	2	0.4	2	-0.4	(-1.5, 0.4)	0.161
Injection site movement impairment	0	0.0	0	2	0.4	2	-0.4	(-1.5, 0.4)	0.161
Oedema peripheral	1	0.2	1	1	0.2	1	0.0	(-1.0, 1.0)	0.988
Chest discomfort	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Injection site erythema	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Injection site haematoma	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Injection site mass	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Injection site pain	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Vaccination site haematoma	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Vaccination site pain	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Infections and infestations	19	4.1	19	24	5.1	25	-1.0	(-3.8, 1.8)	0.478
Upper respiratory tract infection	10	2.2	10	6	1.3	6	0.9	(-0.9, 2.8)	0.293
Bronchitis	1	0.2	1	3	0.6	3	-0.4	(-1.7, 0.6)	0.327
Gastroenteritis	0	0.0	0	3	0.6	3	-0.6	(-1.8, 0.2)	0.086
Urinary tract infection	2	0.4	2	1	0.2	1	0.2	(-0.8, 1.4)	0.551
Cellulitis	0	0.0	0	2	0.4	2	-0.4	(-1.5, 0.4)	0.161
Eye infection	0	0.0	0	2	0.4	2	-0.4	(-1.5, 0.4)	0.161
Herpes zoster	0	0.0	0	2	0.4	2	-0.4	(-1.5, 0.4)	0.161
Labyrinthitis	1	0.2	1	1	0.2	1	0.0	(-1.0, 1.0)	0.988
Nasopharyngitis	0	0.0	0	2	0.4	2	-0.4	(-1.5, 0.4)	0.161
Acute sinusitis	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Borrelia infection	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Diverticulitis	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Folliculitis	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Sinusitis	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312

Table 22. Non-Serious Adverse Events Reported After Vaccination 1 (Year 0) – Safety Population

	Vaccine Group (as Administered)								
	13vPnC N=463			23vPS N=473					
System Organ Class/ Preferred Term	No. of Subjects[a]	%	No. of Events[b]	No. of Subjects[a]	%	No. of Events[b]	Difference[c]	(95% CI[d])	p-Value[d]
Tinea cruris	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Vulvovaginal candidiasis	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Wound infection	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Injury, poisoning and procedural complications	5	1.1	5	8	1.7	9	-0.6	(-2.4, 1.0)	0.424
Animal bite	1	0.2	1	1	0.2	1	0.0	(-1.0, 1.0)	0.988
Hand fracture	1	0.2	1	1	0.2	1	0.0	(-1.0, 1.0)	0.988
Muscle strain	0	0.0	0	2	0.4	2	-0.4	(-1.5, 0.4)	0.161
Fall	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Foreign body in eye	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Joint sprain	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Ligament rupture	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Limb injury	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Skin laceration	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Tendon rupture	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Tibia fracture	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Investigations	1	0.2	2	2	0.4	2	-0.2	(-1.3, 0.8)	0.576
Alanine aminotransferase increased	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Aspartate aminotransferase increased	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Biopsy skin	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Blood parathyroid hormone increased	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Metabolism and nutrition disorders	2	0.4	2	2	0.4	2	0.0	(-1.1, 1.2)	0.983
Gout	1	0.2	1	1	0.2	1	0.0	(-1.0, 1.0)	0.988
Decreased appetite	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Hyperlipidaemia	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Musculoskeletal and connective tissue disorders	11	2.4	12	12	2.5	14	-0.2	(-2.3, 2.0)	0.873
Osteoarthritis	2	0.4	2	2	0.4	2	0.0	(-1.1, 1.2)	0.983
Pain in extremity	1	0.2	1	2	0.4	2	-0.2	(-1.3, 0.8)	0.576
Arthralgia	0	0.0	0	2	0.4	2	-0.4	(-1.5, 0.4)	0.161
Bursitis	2	0.4	2	0	0.0	0	0.4	(-0.4, 1.6)	0.152

Table 22. Non-Serious Adverse Events Reported After Vaccination 1 (Year 0) – Safety Population

	Vaccine Group (as Administered)								
	13vPnC N=463			23vPS N=473					
System Organ Class/ Preferred Term	No. of Subjects[a]	%	No. of Events[b]	No. of Subjects[a]	%	No. of Events[b]	Difference[c]	(95% CI[d])	p-Value[d]
Joint swelling	2	0.4	2	0	0.0	0	0.4	(-0.4, 1.6)	0.152
Musculoskeletal chest pain	1	0.2	1	1	0.2	1	0.0	(-1.0, 1.0)	0.988
Myalgia	1	0.2	1	1	0.2	1	0.0	(-1.0, 1.0)	0.988
Back pain	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Joint range of motion decreased	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Monarthritis	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Musculoskeletal pain	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Neck pain	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Osteoporosis	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Pelvic deformity	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Rotator cuff syndrome	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Spinal column stenosis	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Neoplasms benign, malignant and unspecified (including cysts and polyps)	2	0.4	2	0	0.0	0	0.4	(-0.4, 1.6)	0.152
Lipoma	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Seborrhoeic keratosis	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Nervous system disorders	3	0.6	3	4	0.8	4	-0.2	(-1.6, 1.1)	0.726
Dizziness	1	0.2	1	1	0.2	1	0.0	(-1.0, 1.0)	0.988
Headache	1	0.2	1	1	0.2	1	0.0	(-1.0, 1.0)	0.988
Balance disorder	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Sciatica	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Sinus headache	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Psychiatric disorders	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Depression	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Reproductive system and breast disorders	0	0.0	0	2	0.4	2	-0.4	(-1.5, 0.4)	0.161
Benign prostatic hyperplasia	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Prostatitis	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Respiratory, thoracic and mediastinal disorders	2	0.4	4	3	0.6	3	-0.2	(-1.5, 1.0)	0.671
Cough	2	0.4	2	1	0.2	1	0.2	(-0.8, 1.4)	0.551

Table 22. Non-Serious Adverse Events Reported After Vaccination 1 (Year 0) – Safety Population

	Vaccine Group (as Administered)								
	13vPnC N=463			23vPS N=473					
System Organ Class/ Preferred Term	No. of Subjects[a]	%	No. of Events[b]	No. of Subjects[a]	%	No. of Events[b]	Difference[c]	(95% CI[d])	p-Value[d]
Bronchospasm	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Nasal congestion	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Sinus congestion	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Throat irritation	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Skin and subcutaneous tissue disorders	10	2.2	10	9	1.9	9	0.3	(-1.7, 2.3)	0.780
Rash	1	0.2	1	6	1.3	6	-1.1	(-2.6, 0.1)	0.062
Dermatitis contact	1	0.2	1	1	0.2	1	0.0	(-1.0, 1.0)	0.988
Rash erythematous	2	0.4	2	0	0.0	0	0.4	(-0.4, 1.6)	0.152
Actinic keratosis	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Campbell de Morgan spots	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Cutis laxa	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Ecchymosis	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Eczema	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Eczema nummular	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Ingrowing nail	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Swelling face	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Vascular disorders	2	0.4	2	2	0.4	2	0.0	(-1.1, 1.2)	0.983
Hypertension	1	0.2	1	1	0.2	1	0.0	(-1.0, 1.0)	0.988
Flushing	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Hypotension	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322

Data presented are from the Vaccination 1 safety population. Vaccination 1 is defined as the period from the first study vaccination to the blood draw, 1 month after Vaccination 1.

13vPnC = 13-valent pneumococcal conjugate vaccine; 23vPS = 23-valent pneumococcal polysaccharide vaccine; CI = confidence interval; N = number of subjects; No. = number.

a. Number of subjects reporting at least 1 event of type specified. "Any event" represents the number of subjects reporting at least 1 event of any kind.
b. The total number of events of the type specified. Subjects can be represented more than once. "Any event" represents the total number of events.
c. Difference in proportions, 13vPnC – 23vPS, expressed as a percentage, of the subjects reporting at least 1 event of type specified.
d. Exact 2-sided CI and corresponding p-value for the difference in proportions using the Miettinen and Nurminen method, 13vPnC – 23vPS, expressed as a percentage.

Non-Serious Adverse Events After Vaccination 2: The incidence of AEs occurring from Visit 4 through Visit 5 (after Vaccination 2 [Year 1]) was similar between the 13vPnC/13vPnC group and the 23vPS/13vPnC group. There were no statistically significant differences between the 2 vaccine groups for individual preferred terms. The non-serious AEs reported after Vaccination 2 (Year 1) are presented in Table 23.

Table 23. Non-Serious Adverse Events Reported After Vaccination 2 (Year 1) – Safety Population

System Organ Class/ Preferred Term	Vaccine Sequence (as Administered) 13vPnC/13vPnC N=391 No. of Subjects[a]	%	No. of Events[b]	23vPS/13vPnC N=404 No. of Subjects[a]	%	No. of Events[b]	Difference[c]	(95% CI[d])	p-Value[d]
Any event	69	17.6	81	62	15.3	85	2.3	(-2.9, 7.5)	0.382
Cardiac disorders	1	0.3	1	2	0.5	2	-0.2	(-1.6, 1.0)	0.582
Atrial fibrillation	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Bradycardia	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Coronary artery disease	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Ear and labyrinth disorders	1	0.3	1	2	0.5	2	-0.2	(-1.6, 1.0)	0.582
Vertigo	1	0.3	1	1	0.2	1	0.0	(-1.2, 1.2)	0.982
Ear discomfort	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Eye disorders	2	0.5	2	1	0.2	3	0.3	(-0.9, 1.6)	0.544
Astigmatism	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Cataract	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Hypermetropia	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Keratitis	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Presbyopia	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Gastrointestinal disorders	6	1.5	7	7	1.7	7	-0.2	(-2.2, 1.8)	0.826
Diarrhoea	1	0.3	1	4	1.0	4	-0.7	(-2.3, 0.5)	0.190
Abdominal pain upper	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Constipation	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Faecal incontinence	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Food poisoning	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Gastrooesophageal reflux disease	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Haemorrhoids	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Nausea	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Swollen tongue	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Toothache	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
General disorders and administration site conditions	10	2.6	10	5	1.2	5	1.3	(-0.6, 3.6)	0.171
Injection site haematoma	3	0.8	3	3	0.7	3	0.0	(-1.5, 1.6)	0.968
Fatigue	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Inflammation	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Influenza like illness	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325

Table 23. Non-Serious Adverse Events Reported After Vaccination 2 (Year 1) – Safety Population

	Vaccine Sequence (as Administered)								
	13vPnC/13vPnC N=391			23vPS/13vPnC N=404					
System Organ Class/ Preferred Term	No. of Subjects[a]	%	No. of Events[b]	No. of Subjects[a]	%	No. of Events[b]	Difference[c]	(95% CI[d])	p-Value[d]
Injection site pain	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Injection site pruritus	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Injection site reaction	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Local swelling	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Pyrexia	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Vaccination site pain	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Immune system disorders	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Allergy to arthropod sting	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Infections and infestations	13	3.3	13	17	4.2	18	-0.9	(-3.7, 1.9)	0.514
Upper respiratory tract infection	3	0.8	3	7	1.7	7	-1.0	(-2.9, 0.7)	0.222
Urinary tract infection	3	0.8	3	2	0.5	2	0.3	(-1.1, 1.8)	0.627
Sinusitis	2	0.5	2	2	0.5	2	0.0	(-1.3, 1.4)	0.974
Cellulitis	0	0.0	0	2	0.5	2	-0.5	(-1.8, 0.5)	0.164
Bronchitis	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Cystitis	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Diverticulitis	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Eye infection	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Fungal skin infection	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Nasopharyngitis	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Otitis externa	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Pneumonia	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Skin infection	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Viral upper respiratory tract infection	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Injury, poisoning and procedural complications	6	1.5	6	8	2.0	10	-0.4	(-2.5, 1.6)	0.633
Contusion	2	0.5	2	1	0.2	1	0.3	(-0.9, 1.6)	0.544
Arthropod bite	1	0.3	1	1	0.2	1	0.0	(-1.2, 1.2)	0.982
Excoriation	1	0.3	1	1	0.2	1	0.0	(-1.2, 1.2)	0.982
Arthropod sting	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Fall	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Foot fracture	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Joint injury	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325

Table 23. Non-Serious Adverse Events Reported After Vaccination 2 (Year 1) – Safety Population

System Organ Class/ Preferred Term	Vaccine Sequence (as Administered) 13vPnC/13vPnC N=391 No. of Subjects[a]	%	No. of Events[b]	23vPS/13vPnC N=404 No. of Subjects[a]	%	No. of Events[b]	Difference[c]	(95% CI[d])	p-Value[d]
Joint sprain	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Ligament rupture	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Procedural pain	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Skin injury	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Skin laceration	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Investigations	2	0.5	2	3	0.7	3	-0.2	(-1.7, 1.2)	0.680
Blood glucose increased	1	0.3	1	1	0.2	1	0.0	(-1.2, 1.2)	0.982
Heart rate irregular	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Occult blood positive	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Red blood cell sedimentation rate increased	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Metabolism and nutrition disorders	0	0.0	0	2	0.5	2	-0.5	(-1.8, 0.5)	0.164
Fluid retention	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Gout	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Musculoskeletal and connective tissue disorders	7	1.8	12	11	2.7	11	-0.9	(-3.2, 1.3)	0.377
Arthralgia	1	0.3	3	1	0.2	1	0.0	(-1.2, 1.2)	0.982
Myalgia	1	0.3	1	3	0.7	3	-0.5	(-1.9, 0.8)	0.332
Neck pain	2	0.5	2	0	0.0	0	0.5	(-0.4, 1.8)	0.150
Osteoarthritis	1	0.3	1	1	0.2	1	0.0	(-1.2, 1.2)	0.982
Plantar fasciitis	1	0.3	1	1	0.2	1	0.0	(-1.2, 1.2)	0.982
Spinal column stenosis	1	0.3	1	1	0.2	1	0.0	(-1.2, 1.2)	0.982
Tendonitis	1	0.3	2	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Back pain	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Muscle spasms	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Musculoskeletal pain	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Pain in extremity	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Rotator cuff syndrome	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Neoplasms benign, malignant and unspecified (including cysts and polyps)	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Seborrhoeic keratosis	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Nervous system disorders	6	1.5	6	3	0.7	3	0.8	(-0.8, 2.7)	0.291
Headache	1	0.3	1	2	0.5	2	-0.2	(-1.6, 1.0)	0.582

Table 23. Non-Serious Adverse Events Reported After Vaccination 2 (Year 1) – Safety Population

System Organ Class/ Preferred Term	Vaccine Sequence (as Administered) 13vPnC/13vPnC N=391 No. of Subjects[a]	%	No. of Events[b]	23vPS/13vPnC N=404 No. of Subjects[a]	%	No. of Events[b]	Difference[c]	(95% CI[d])	p-Value[d]
Sciatica	2	0.5	2	0	0.0	0	0.5	(-0.4, 1.8)	0.150
Dizziness	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Hemianopia	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Loss of consciousness	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Narcolepsy	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Psychiatric disorders	2	0.5	2	2	0.5	2	0.0	(-1.3, 1.4)	0.974
Depression	2	0.5	2	0	0.0	0	0.5	(-0.4, 1.8)	0.150
Insomnia	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Nervousness	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Renal and urinary disorders	2	0.5	2	2	0.5	3	0.0	(-1.3, 1.4)	0.974
Haematuria	1	0.3	1	1	0.2	1	0.0	(-1.2, 1.2)	0.982
Bladder spasm	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Dysuria	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Urinary retention	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Reproductive system and breast disorders	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Breast calcifications	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Respiratory, thoracic and mediastinal disorders	6	1.5	8	8	2.0	9	-0.4	(-2.5, 1.6)	0.633
Cough	3	0.8	3	4	1.0	4	-0.2	(-1.8, 1.4)	0.737
Nasal congestion	2	0.5	2	2	0.5	2	0.0	(-1.3, 1.4)	0.974
Chronic obstructive pulmonary disease	1	0.3	1	1	0.2	1	0.0	(-1.2, 1.2)	0.982
Oropharyngeal pain	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Rhinitis allergic	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Rhinorrhoea	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Upper respiratory tract congestion	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Skin and subcutaneous tissue disorders	3	0.8	3	4	1.0	4	-0.2	(-1.8, 1.4)	0.737
Dermatitis	1	0.3	1	1	0.2	1	0.0	(-1.2, 1.2)	0.982
Actinic keratosis	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Dermatitis contact	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Ecchymosis	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Pruritus generalised	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Urticaria	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325

Table 23. Non-Serious Adverse Events Reported After Vaccination 2 (Year 1) – Safety Population

System Organ Class/ Preferred Term	Vaccine Sequence (as Administered) 13vPnC/13vPnC N=391 No. of Subjects[a]	%	No. of Events[b]	23vPS/13vPnC N=404 No. of Subjects[a]	%	No. of Events[b]	Difference[c]	(95% CI[d])	p-Value[d]
Vascular disorders	3	0.8	3	1	0.2	1	0.5	(-0.7, 2.0)	0.300
Hypertension	2	0.5	2	0	0.0	0	0.5	(-0.4, 1.8)	0.150
Haematoma	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Venous insufficiency	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309

Data presented are from the Vaccination 2 safety population. Vaccination 2 is defined as the period from the second study vaccination to the blood draw, 1 month after Vaccination 2.

13vPnC = 13-valent pneumococcal conjugate vaccine; 23vPS = 23-valent pneumococcal polysaccharide vaccine; CI = confidence interval; N = number of subjects; No. = number.

a. Number of subjects reporting at least 1 event of type specified. "Any event" represents the number of subjects reporting at least 1 event of any kind.
b. The total number of events of the type specified. Subjects can be represented more than once. "Any event" represents the total number of events.
c. Difference in proportions, 13vPnC/13vPnC – 23vPS/13vPnC, expressed as a percentage, of the subjects reporting at least 1 event of type specified.
d. Exact 2-sided CI and corresponding p-value for the difference in proportions using the Miettinen and Nurminen method, 13vPnC/13vPnC – 23vPS/13vPnC, expressed as a percentage.

Non-Serious Adverse Events at the 6-Month Follow-Up After Vaccination 1: The incidence of AEs was similar between the 2 vaccine groups, the most frequently reported types of AEs were musculoskeletal and connective tissue disorders. The non-serious adverse events reported at the 6-month follow-up telephone contact after Vaccination 1 are presented in Table 24.

Table 24. Non-Serious Adverse Events Reported at the 6-Month Follow-Up Telephone Contact After Vaccination 1 (Year 0) – Safety Population

System Organ Class/ Preferred Term	Vaccine Group (as Administered) 13vPnC N=463 No. of Subjects[a]	%	No. of Events[b]	23vPS N=473 No. of Subjects[a]	%	No. of Events[b]	Difference[c]	(95% CI[d])	p-Value[d]
Any event	60	13	87	59	12.5	86	0.5	(-3.8, 4.8)	0.824
Blood and lymphatic system disorders	2	0.4	2	1	0.2	1	0.2	(-0.8, 1.4)	0.551
Iron deficiency anaemia	1	0.2	1	1	0.2	1	0	(-1.0, 1.0)	0.988
Anaemia	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Cardiac disorders	2	0.4	2	2	0.4	2	0	(-1.1, 1.2)	0.983
Coronary artery disease	1	0.2	1	1	0.2	1	0	(-1.0, 1.0)	0.988
Atrial fibrillation	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Mitral valve incompetence	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Ear and labyrinth disorders	4	0.9	4	2	0.4	3	0.4	(-0.8, 1.8)	0.398
Vertigo	1	0.2	1	1	0.2	2	0	(-1.0, 1.0)	0.988
Deafness	2	0.4	2	0	0	0	0.4	(-0.4, 1.6)	0.152
Deafness neurosensory	1	0.2	1	1	0.2	1	0	(-1.0, 1.0)	0.988
Endocrine disorders	2	0.4	2	1	0.2	1	0.2	(-0.8, 1.4)	0.551
Goitre	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Hyperparathyroidism	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Hypothyroidism	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Eye disorders	4	0.9	4	2	0.4	2	0.4	(-0.8, 1.8)	0.398
Cataract	2	0.4	2	2	0.4	2	0	(-1.1, 1.2)	0.983
Eye pain	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Macular degeneration	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Gastrointestinal disorders	5	1.1	5	8	1.7	10	-0.6	(-2.4, 1.0)	0.424
Gastrooesophageal reflux disease	1	0.2	1	2	0.4	2	-0.2	(-1.3, 0.8)	0.576
Abdominal pain	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Barrett's oesophagus	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Coeliac disease	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Constipation	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Diarrhoea	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Diverticulum	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Gastric mucosal lesion	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Gastric polyps	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322

Table 24. Non-Serious Adverse Events Reported at the 6-Month Follow-Up Telephone Contact After Vaccination 1 (Year 0) – Safety Population

	Vaccine Group (as Administered)								
	13vPnC N=463			23vPS N=473					
System Organ Class/ Preferred Term	No. of Subjects[a]	%	No. of Events[b]	No. of Subjects[a]	%	No. of Events[b]	Difference[c]	(95% CI[d])	p-Value[d]
Hiatus hernia	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Oesophageal ulcer	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Oesophagitis	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Vomiting	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
General disorders and administration site conditions	1	0.2	1	1	0.2	1	0	(-1.0, 1.0)	0.988
Cyst	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Gait disturbance	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Immune system disorders	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Drug hypersensitivity	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Infections and infestations	3	0.6	3	5	1.1	6	-0.4	(-1.9, 1.0)	0.497
Pneumonia	1	0.2	1	1	0.2	1	0	(-1.0, 1.0)	0.988
Urinary tract infection	1	0.2	1	1	0.2	1	0	(-1.0, 1.0)	0.988
Bronchitis	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Genital herpes	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Herpes zoster	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Nasopharyngitis	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Staphylococcal infection	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Injury, poisoning and procedural complications	4	0.9	5	3	0.6	4	0.2	(-1.1, 1.6)	0.683
Meniscus lesion	1	0.2	1	1	0.2	1	0	(-1.0, 1.0)	0.988
Back injury	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Fall	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Fractured sacrum	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Hand fracture	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Joint dislocation	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Joint sprain	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Skin injury	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Investigations	1	0.2	1	1	0.2	1	0	(-1.0, 1.0)	0.988
Heart rate irregular	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Prostatic specific antigen increased	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Metabolism and nutrition disorders	7	1.5	7	10	2.1	10	-0.6	(-2.5, 1.2)	0.49

Table 24. Non-Serious Adverse Events Reported at the 6-Month Follow-Up Telephone Contact After Vaccination 1 (Year 0) – Safety Population

	Vaccine Group (as Administered)								
	13vPnC N=463			23vPS N=473					
System Organ Class/ Preferred Term	No. of Subjects[a]	%	No. of Events[b]	No. of Subjects[a]	%	No. of Events[b]	Difference[c]	(95% CI[d])	p-Value[d]
Hypercholesterolaemia	2	0.4	2	3	0.6	3	-0.2	(-1.5, 1.0)	0.671
Hyperlipidaemia	0	0	0	3	0.6	3	-0.6	(-1.8, 0.2)	0.086
Type 2 diabetes mellitus	3	0.6	3	0	0	0	0.6	(-0.2, 1.9)	0.08
Diabetes mellitus	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Diabetic foot	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Gout	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Hyponatraemia	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Type 1 diabetes mellitus	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Vitamin D deficiency	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Musculoskeletal and connective tissue disorders	13	2.8	19	17	3.6	20	-0.8	(-3.2, 1.6)	0.495
Osteoarthritis	3	0.6	3	4	0.8	4	-0.2	(-1.6, 1.1)	0.726
Arthralgia	2	0.4	3	2	0.4	2	0	(-1.1, 1.2)	0.983
Arthritis	1	0.2	1	3	0.6	3	-0.4	(-1.7, 0.6)	0.327
Back pain	1	0.2	1	2	0.4	3	-0.2	(-1.3, 0.8)	0.576
Plantar fasciitis	2	0.4	2	1	0.2	1	0.2	(-0.8, 1.4)	0.551
Bursitis	2	0.4	2	0	0	0	0.4	(-0.4, 1.6)	0.152
Osteoporosis	0	0	0	2	0.4	2	-0.4	(-1.5, 0.4)	0.161
Tendonitis	2	0.4	2	0	0	0	0.4	(-0.4, 1.6)	0.152
Dupuytren's contracture	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Muscular weakness	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Musculoskeletal pain	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Myalgia	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Osteopenia	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Rotator cuff syndrome	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Sacroiliitis	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Spinal column stenosis	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Synovial cyst	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Trigger finger	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Neoplasms benign, malignant and unspecified (including cysts and polyps)	3	0.6	3	2	0.4	2	0.2	(-1.0, 1.5)	0.637

Table 24. Non-Serious Adverse Events Reported at the 6-Month Follow-Up Telephone Contact After Vaccination 1 (Year 0) – Safety Population

	Vaccine Group (as Administered)								
	13vPnC N=463			23vPS N=473					
System Organ Class/ Preferred Term	No. of Subjects[a]	%	No. of Events[b]	No. of Subjects[a]	%	No. of Events[b]	Difference[c]	(95% CI[d])	p-Value[d]
Melanocytic naevus	2	0.4	2	0	0	0	0.4	(-0.4, 1.6)	0.152
Benign breast neoplasm	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Bladder neoplasm	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Lipoma	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Nervous system disorders	5	1.1	6	4	0.8	4	0.2	(-1.2, 1.8)	0.713
Amnesia	1	0.2	1	1	0.2	1	0	(-1.0, 1.0)	0.988
Sciatica	1	0.2	1	1	0.2	1	0	(-1.0, 1.0)	0.988
Anosmia	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Dementia Alzheimer's type	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Dizziness	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Neuropathy peripheral	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Restless legs syndrome	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Senile dementia	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Psychiatric disorders	2	0.4	2	0	0	0	0.4	(-0.4, 1.6)	0.152
Depression	2	0.4	2	0	0	0	0.4	(-0.4, 1.6)	0.152
Renal and urinary disorders	4	0.9	5	3	0.6	3	0.2	(-1.1, 1.6)	0.683
Nephrolithiasis	1	0.2	2	0	0	0	0.2	(-0.6, 1.2)	0.312
Hypertonic bladder	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Renal artery occlusion	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Renal failure	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Renal failure chronic	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Urethral stenosis	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Urinary incontinence	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Reproductive system and breast disorders	0	0	0	3	0.6	3	-0.6	(-1.8, 0.2)	0.086
Benign prostatic hyperplasia	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Breast mass	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Erectile dysfunction	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Respiratory, thoracic and mediastinal disorders	4	0.9	4	4	0.8	5	0	(-1.4, 1.5)	0.976
Sleep apnoea syndrome	2	0.4	2	1	0.2	1	0.2	(-0.8, 1.4)	0.551
Cough	1	0.2	1	1	0.2	1	0	(-1.0, 1.0)	0.988

Table 24. Non-Serious Adverse Events Reported at the 6-Month Follow-Up Telephone Contact After Vaccination 1 (Year 0) – Safety Population

	Vaccine Group (as Administered)								
	13vPnC N=463			23vPS N=473					
System Organ Class/ Preferred Term	No. of Subjects[a]	%	No. of Events[b]	No. of Subjects[a]	%	No. of Events[b]	Difference[c]	(95% CI[d])	p-Value[d]
Diaphragmatic hernia	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Dyspnoea	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Emphysema	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Rhinitis allergic	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Skin and subcutaneous tissue disorders	6	1.3	8	1	0.2	1	1.1	(-0.0, 2.6)	0.054
Rash	2	0.4	2	0	0	0	0.4	(-0.4, 1.6)	0.152
Actinic keratosis	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Dermatitis	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Eczema asteatotic	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Lichenoid keratosis	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Rosacea	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Skin lesion	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Skin wrinkling	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Vascular disorders	4	0.9	4	6	1.3	6	-0.4	(-2.0, 1.1)	0.547
Hypertension	3	0.6	3	3	0.6	3	0	(-1.3, 1.3)	0.979
Aortic disorder	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Peripheral vascular disorder	1	0.2	1	0	0	0	0.2	(-0.6, 1.2)	0.312
Vasoconstriction	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Venous insufficiency	0	0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322

Data presented are from the Vaccination 1 safety population. The 6-month follow-up period for Vaccination 1 includes data from Vaccination 1 to the telephone contact, 6 months after Vaccination 1.

13vPnC = 13-valent pneumococcal conjugate vaccine; 23vPS = 23-valent pneumococcal polysaccharide vaccine; CI = confidence interval; N = number of subjects; No. = number.

a. Number of subjects reporting at least 1 event of type specified. "Any event" represents the number of subjects reporting at least 1 event of any kind.
b. The total number of events of the type specified. Subjects can be represented more than once. "Any event" represents the total number of events.
c. Difference in proportions, 13vPnC – 23vPS, expressed as a percentage, of the subjects reporting at least 1 event of type specified.
d. Exact 2-sided CI and corresponding p-value for the difference in proportions using the Miettinen and Nurminen method, 13vPnC – 23vPS, expressed as a percentage.

Non-Serious Adverse Events at the 6-Month Follow-Up After Vaccination 2: The incidence of AEs was similar between the 2 vaccine groups. In the 13vPnC/13vPnC group, the most frequent categories of AEs were neoplasms benign, malignant and unspecified (including cysts and polyps), and nervous system disorders. In the 23vPS/13vPnC group, the most frequent categories of AEs were infections and infestations and neoplasms benign, malignant and unspecified (including cysts and polyps).

The non-serious adverse events reported at the 6-month follow-up telephone contact after Vaccination 2 are presented in Table 25.

Table 25. Non-Serious Adverse Events Reported at the 6-Month Follow-Up Telephone Contact After Vaccination 2 (Year 1) – Safety Population

System Organ Class/ Preferred Term	Vaccine Sequence (as Administered) 13vPnC/13vPnC N=391 No. of Subjects[a]	%	No. of Events[b]	23vPS/13vPnC N=404 No. of Subjects[a]	%	No. of Events[b]	Difference[c]	(95% CI[d])	p-Value[d]
Any event	29	7.4	34	30	7.4	38	-0.0	(-3.7, 3.7)	>.99
Blood and lymphatic system disorders	1	0.3	1	2	0.5	2	-0.2	(-1.6, 1.0)	0.582
Anaemia	1	0.3	1	1	0.2	1	0.0	(-1.2, 1.2)	0.982
Lymphadenopathy	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Cardiac disorders	2	0.5	3	2	0.5	3	0.0	(-1.3, 1.4)	0.974
Angina pectoris	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Atrial fibrillation	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Atrioventricular block first degree	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Coronary artery disease	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Hypertensive heart disease	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Sick sinus syndrome	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Ear and labyrinth disorders	1	0.3	1	1	0.2	1	0.0	(-1.2, 1.2)	0.982
Cerumen impaction	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Deafness	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Endocrine disorders	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Hypothyroidism	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Eye disorders	1	0.3	1	3	0.7	3	-0.5	(-1.9, 0.8)	0.332
Cataract	1	0.3	1	1	0.2	1	0.0	(-1.2, 1.2)	0.982
Open angle glaucoma	0	0.0	0	2	0.5	2	-0.5	(-1.8, 0.5)	0.164
Gastrointestinal disorders	3	0.8	3	1	0.2	1	0.5	(-0.7, 2.0)	0.300
Gastrooesophageal reflux disease	1	0.3	1	1	0.2	1	0.0	(-1.2, 1.2)	0.982
Colonic polyp	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Dysphagia	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
General disorders and administration site conditions	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Fatigue	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Infections and infestations	2	0.5	2	2	0.5	2	0.0	(-1.3, 1.4)	0.974
Cystitis	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Gastroenteritis viral	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Staphylococcal infection	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Urinary tract infection	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309

Table 25. Non-Serious Adverse Events Reported at the 6-Month Follow-Up Telephone Contact After Vaccination 2 (Year 1) – Safety Population

System Organ Class/ Preferred Term	Vaccine Sequence (as Administered) 13vPnC/13vPnC N=391 No. of Subjects[a]	%	No. of Events[b]	23vPS/13vPnC N=404 No. of Subjects[a]	%	No. of Events[b]	Difference[c]	(95% CI[d])	p-Value[d]
Injury, poisoning and procedural complications	2	0.5	2	0	0.0	0	0.5	(-0.4, 1.8)	0.150
Open wound	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Upper limb fracture	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Investigations	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Blood pressure increased	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Metabolism and nutrition disorders	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Hypercholesterolaemia	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Musculoskeletal and connective tissue disorders	5	1.3	5	6	1.5	7	-0.2	(-2.1, 1.7)	0.803
Dupuytren's contracture	1	0.3	1	1	0.2	1	0.0	(-1.2, 1.2)	0.982
Osteoarthritis	1	0.3	1	1	0.2	1	0.0	(-1.2, 1.2)	0.982
Plantar fasciitis	1	0.3	1	1	0.2	1	0.0	(-1.2, 1.2)	0.982
Arthritis	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Bursitis	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Monarthritis	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Rotator cuff syndrome	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Spinal column stenosis	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Synovial cyst	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Neoplasms benign, malignant and unspecified (including cysts and polyps)	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Benign neoplasm of thyroid gland	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Nervous system disorders	6	1.5	6	4	1.0	4	0.5	(-1.2, 2.4)	0.491
Amnesia	2	0.5	2	0	0.0	0	0.5	(-0.4, 1.8)	0.150
Neuropathy peripheral	1	0.3	1	1	0.2	1	0.0	(-1.2, 1.2)	0.982
Hypertonia	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Memory impairment	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Migraine	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Post herpetic neuralgia	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Restless legs syndrome	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Sciatica	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Psychiatric disorders	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309

Table 25. Non-Serious Adverse Events Reported at the 6-Month Follow-Up Telephone Contact After Vaccination 2 (Year 1) – Safety Population

	Vaccine Sequence (as Administered)								
	13vPnC/13vPnC N=391			23vPS/13vPnC N=404					
System Organ Class/ Preferred Term	No. of Subjects[a]	%	No. of Events[b]	No. of Subjects[a]	%	No. of Events[b]	Difference[c]	(95% CI[d])	p-Value[d]
Insomnia	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Renal and urinary disorders	3	0.8	3	2	0.5	3	0.3	(-1.1, 1.8)	0.627
Bladder neck obstruction	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Haematuria	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Renal artery arteriosclerosis	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Renal impairment	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Stress urinary incontinence	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Urinary retention	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Reproductive system and breast disorders	1	0.3	1	2	0.5	2	-0.2	(-1.6, 1.0)	0.582
Benign prostatic hyperplasia	0	0.0	0	2	0.5	2	-0.5	(-1.8, 0.5)	0.164
Prostatomegaly	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Respiratory, thoracic and mediastinal disorders	0	0.0	0	5	1.2	5	-1.2	(-2.9, -0.3)	0.027
Sleep apnoea syndrome	0	0.0	0	3	0.7	3	-0.7	(-2.2, 0.2)	0.088
Bronchial hyperreactivity	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Nasal septum perforation	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Skin and subcutaneous tissue disorders	0	0.0	0	2	0.5	2	-0.5	(-1.8, 0.5)	0.164
Ecchymosis	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Erythema	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Vascular disorders	2	0.5	2	1	0.2	1	0.3	(-0.9, 1.6)	0.544
Aortic stenosis	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Hypertension	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Venous insufficiency	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325

Table 25. Non-Serious Adverse Events Reported at the 6-Month Follow-Up Telephone Contact After Vaccination 2 (Year 1) – Safety Population

	Vaccine Sequence (as Administered)								
	13vPnC/13vPnC N=391			23vPS/13vPnC N=404					
System Organ Class/ Preferred Term	No. of Subjects[a]	%	No. of Events[b]	No. of Subjects[a]	%	No. of Events[b]	Difference[c]	(95% CI[d])	p-Value[d]

Data presented are from the Vaccination 2 safety population. The 6-month follow-up period for Vaccination 2 includes data from Vaccination 2 to the telephone contact, 6 months after Vaccination 2.

13vPnC = 13-valent pneumococcal conjugate vaccine; 23vPS = 23-valent pneumococcal polysaccharide vaccine; CI = confidence interval; N = number of subjects; No. = number.

a. Number of subjects reporting at least 1 event of type specified. "Any event" represents the number of subjects reporting at least 1 event of any kind.
b. The total number of events of the type specified. Subjects can be represented more than once. "Any event" represents the total number of events.
c. Difference in proportions, 13vPnC/13vPnC – 23vPS/13vPnC, expressed as a percentage, of the subjects reporting at least 1 event of type specified.
d. Exact 2-sided CI and corresponding p-value for the difference in proportions using the Miettinen and Nurminen method, 13vPnC/13vPnC – 23vPS/13vPnC, expressed as a percentage.

Related Adverse Events: Related AEs are defined as AEs where there is a reasonable possibility that the AE is associated with the investigational product, according to the assessment of the Investigator.

Related Adverse Events After Vaccination 1: The incidence of related AEs was higher in the 23vPS group (16 subjects, 3.4%) than in the 13vPnC group (8 subjects, 1.7%), however the difference was not statistically significant (Table 26).

Table 26. Related Adverse Events Reported After Vaccination 1 (Year 0) – Safety Population

System Organ Class/ Preferred Term	Vaccine Group (as Administered) 13vPnC N=463 No. of Subjects[a]	%	No. of Events[b]	23vPS N=473 No. of Subjects[a]	%	No. of Events[b]	Difference[c]	(95% CI[d])	p-Value[d]
Any event	8	1.7	9	16	3.4	19	-1.7	(-3.9, 0.4)	0.109
Gastrointestinal disorders	2	0.4	2	0	0.0	0	0.4	(-0.4, 1.6)	0.152
Diarrhoea	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Nausea	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
General disorders and administration site conditions	2	0.4	2	12	2.5	13	-2.1	(-4.0, -0.6)	0.008
Injection site pruritus	1	0.2	1	3	0.6	3	-0.4	(-1.7, 0.6)	0.327
Injection site induration	0	0.0	0	2	0.4	2	-0.4	(-1.5, 0.4)	0.161
Injection site movement impairment	0	0.0	0	2	0.4	2	-0.4	(-1.5, 0.4)	0.161
Fatigue	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Injection site erythema	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Injection site haematoma	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Injection site mass	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Injection site pain	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Vaccination site haematoma	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Vaccination site pain	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Musculoskeletal and connective tissue disorders	2	0.4	2	3	0.6	5	-0.2	(-1.5, 1.0)	0.671
Myalgia	1	0.2	1	1	0.2	1	0.0	(-1.0, 1.0)	0.988
Arthralgia	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Joint range of motion decreased	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Joint swelling	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Pain in extremity	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Spinal column stenosis	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Nervous system disorders	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Dizziness	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Skin and subcutaneous tissue disorders	2	0.4	2	0	0.0	0	0.4	(-0.4, 1.6)	0.152
Eczema	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Rash erythematous	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Vascular disorders	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Flushing	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312

Table 26. Related Adverse Events Reported After Vaccination 1 (Year 0) – Safety Population

	Vaccine Group (as Administered)								
	13vPnC N=463			23vPS N=473					
System Organ Class/ Preferred Term	No. of Subjects[a]	%	No. of Events[b]	No. of Subjects[a]	%	No. of Events[b]	Difference[c]	(95% CI[d])	p-Value[d]

Data presented are from the Vaccination 1 safety population. Vaccination 1 is defined as the period from the first study vaccination to the blood draw, 1 month after Vaccination 1.

13vPnC = 13-valent pneumococcal conjugate vaccine; 23vPS = 23-valent pneumococcal polysaccharide vaccine; CI = confidence interval; N = number of subjects in a treatment group; No. = number.

a. Number of subjects reporting at least 1 event of type specified. "Any event" represents the number of subjects reporting at least 1 event of any kind.

b. The total number of events of the type specified. Subjects can be represented more than once. "Any event" represents the total number of events.

c. Difference in proportions, 13vPnC – 23vPS, expressed as a percentage, of the subjects reporting at least 1 event of type specified.

d. Exact 2-sided CI and corresponding p-value for the difference in proportions using the Miettinen and Nurminen method, 13vPnC – 23vPS, expressed as a percentage.

Non-Serious Adverse Events After Vaccination 2: The incidence of related AEs was similar between the 13vPnC/13vPnC group (2.6%) and the 23vPS/13vPnC group (1.5%). There were no significant differences between the subjects in the 2 vaccine groups in related AEs after Vaccination 2 (Table 27).

Table 27. Related Adverse Events Reported After Vaccination 2 (Year 1) – Safety Population

System Organ Class/ Preferred Term	Vaccine Sequence (as Administered) 13vPnC/13vPnC N=391 No. of Subjects[a]	%	No. of Events[b]	23vPS/13vPnC N=404 No. of Subjects[a]	%	No. of Events[b]	Difference[c]	(95% CI[d])	p-Value[d]
Any event	10	2.6	14	6	1.5	6	1.1	(-1.0, 3.3)	0.282
Ear and labyrinth disorders	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Ear discomfort	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Gastrointestinal disorders	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Diarrhoea	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
General disorders and administration site conditions	8	2.0	8	4	1.0	4	1.1	(-0.7, 3.1)	0.222
Injection site haematoma	3	0.8	3	3	0.7	3	0	(-1.5, 1.6)	0.968
Influenza like illness	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Injection site pain	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Injection site pruritus	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Injection site reaction	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Pyrexia	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Vaccination site pain	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Musculoskeletal and connective tissue disorders	1	0.3	4	1	0.2	1	0	(-1.2, 1.2)	0.982
Arthralgia	1	0.3	3	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Myalgia	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Neck pain	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Skin and subcutaneous tissue disorders	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Pruritus generalised	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309

Data presented are from the vaccination 2 safety population. Vaccination 2 is defined as the period from the second study vaccination to the blood draw, 1 month after Vaccination 2.

13vPnC = 13-valent pneumococcal conjugate vaccine; 23vPS = 23-valent pneumococcal polysaccharide vaccine; CI = confidence interval; N = number of subjects in a treatment group; No. = number.

a. Number of subjects reporting at least 1 event of type specified. "Any event" represents the number of subjects reporting at least 1 event of any kind.

b. The total number of events of the type specified. Subjects can be represented more than once. "Any event" represents the total number of events.

c. Difference in proportions, 13vPnC/13vPnC – 23vPS/13vPnC, expressed as a percentage, of the subjects reporting at least 1 event of type specified.

d. Exact 2-sided CI and corresponding p-value for the difference in proportions using the Miettinen and Nurminen method, 13vPnC/13vPnC – 23vPS/13vPnC, expressed as a percentage.

Non-Serious Adverse Events at the 6-Month Follow-Up After Vaccination 1 and 2: One (1) AE (idiopathic thrombocytopenic purpura in 23vPS/13vPnC group) was assessed as related at the 6-month follow-ups after Vaccination 1 and Vaccination 2.

Serious Adverse Events:

Serious Adverse Events After Vaccination 1: After Vaccination 1, SAEs were reported in 3 (0.6%) subjects in the 13vPnC group and in 8 (1.7%) subjects in the 23vPS group (Table 28). None of the SAEs were considered vaccine related.

Table 28. Serious Adverse Events Reported After Vaccination 1 (Year 0) - Safety Population

	Vaccine Group (as Administered)								
	13vPnC N=463			23vPS N=473					
System Organ Class/ Preferred Term	No. of Subjects [a]	%	No. of Events[b]	No. of Subjects [a]	%	No. of Events[b]	Difference[c]	(95% CI[d])	p-Value[d]
Any event	3	0.6	5	8	1.7	9	-1.0	(-2.7, 0.4)	0.139
Cardiac disorders	2	0.4	4	1	0.2	1	0.2	(-0.8, 1.4)	0.551
Angina pectoris	1	0.2	1	1	0.2	1	0.0	(-1.0, 1.0)	0.988
Atrial fibrillation	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Atrial flutter	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Ischaemic cardiomyopathy	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Gastrointestinal disorders	1	0.2	1	1	0.2	1	0.0	(-1.0, 1.0)	0.988
Diverticulum intestinal haemorrhagic	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Pancreatitis	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Infections and infestations	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Pneumonia	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Neoplasms benign, malignant and unspecified (including cysts and polyps)	0	0.0	0	4	0.8	5	-0.8	(-2.2, -0.0)	0.047
Basal cell carcinoma	0	0.0	0	2	0.4	2	-0.4	(-1.5, 0.4)	0.161
Bladder cancer	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Prostate cancer	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Renal cancer	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Nervous system disorders	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Cerebrovascular accident	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322

Data presented are from the Vaccination 1 safety population. Vaccination 1 is defined as the period from the first study vaccination to the blood draw, 1 month after Vaccination 1.

13vPnC = 13-valent pneumococcal conjugate vaccine; 23vPS = 23-valent pneumococcal polysaccharide vaccine; CI = confidence interval; N = number of subjects; No. = number.

a. Number of subjects reporting at least 1 event of type specified. "Any event" represents the number of subjects reporting at least 1 event of any kind.
b. The total number of events of the type specified. Subjects can be represented more than once. "Any event" represents the total number of events.
c. Difference in proportions, 13vPnC – 23vPS, expressed as a percentage, of the subjects reporting at least 1 event of type specified.
d. Exact 2-sided CI and corresponding p-value for the difference in proportions using the Miettinen and Nurminen method, 13vPnC – 23vPS, expressed as a percentage.

Serious Adverse Events After Vaccination 2: SAEs were reported in 4 (1.0%) subjects in the 13vPnC/13vPnC group and in 7 (1.7%) subjects in the 23vPS/13vPnC group. None of the SAEs were considered vaccine related. The SAEs reported after Vaccination 2 are summarized in Table 29.

Table 29. Serious Adverse Events Reported After Vaccination 2 (Year 1) - Safety Population

	Vaccine Group (as Administered)								
	13vPnC/13vPnC N=391			23vPS/13vPnC N=404					
System Organ Class/ Preferred Term	No. of Subjects[a]	%	No. of Events[b]	No. of Subjects[a]	%	No. of Events[b]	Difference[c]	(95% CI[d])	p-Value[d]
Any event	4	1.0	5	7	1.7	9	-0.7	(-2.6, 1.1)	0.392
Cardiac disorders	1	0.3	2	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Angina pectoris	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Sick sinus syndrome	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
General disorders and administration site conditions	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Asthenia	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Hepatobiliary disorders	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Cholecystitis chronic	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Infections and infestations	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Appendicitis	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Injury, poisoning and procedural complications	0	0.0	0	2	0.5	2	-0.5	(-1.8, 0.5)	0.164
Muscle rupture	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Spinal fracture	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Musculoskeletal and connective tissue disorders	0	0.0	0	2	0.5	2	-0.5	(-1.8, 0.5)	0.164
Lumbar spinal stenosis	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Osteoarthritis	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Neoplasms benign, malignant and unspecified (including cysts and polyps)	1	0.3	1	1	0.2	1	0.0	(-1.2, 1.2)	0.982
Basal cell carcinoma	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Breast cancer	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Nervous system disorders	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Syncope	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Renal and urinary disorders	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Urinary retention	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Respiratory, thoracic and mediastinal disorders	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Chronic obstructive pulmonary disease	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309

Table 29. Serious Adverse Events Reported After Vaccination 2 (Year 1) - Safety Population

Data presented are from the Vaccination 2 safety population. Vaccination 2 is defined as the period from the second study vaccination to the blood draw, 1 month after Vaccination 2.

13vPnC = 13-valent pneumococcal conjugate vaccine; 23vPS = 23-valent pneumococcal polysaccharide vaccine; CI = confidence interval; N = number of subjects; No. = number.

a. Number of subjects reporting at least 1 event of type specified. "Any event" represents the number of subjects reporting at least 1 event of any kind.
b. The total number of events of the type specified. Subjects can be represented more than once. "Any event" represents the total number of events.
c. Difference in proportions, 13vPnC/13vPnC – 23vPS/13vPnC, expressed as a percentage, of the subjects reporting at least 1 event of type specified.
d. Exact 2-sided CI and corresponding p-value for the difference in proportions using the Miettinen and Nurminen method, 13vPnC/13vPnC – 23vPS/13vPnC, expressed as a percentage.

Serious Adverse Events at the 6-Month Follow-Up After Vaccination 1: At the 6-month follow-up telephone contact after Vaccination 1, SAEs were reported for 27 (5.8%) subjects in the 13vPnC group and 26 (5.5%) subjects in the 23vPS group (Table 30). None of the SAEs in either group were considered vaccine related.

Table 30. Serious Adverse Events Reported at the 6-Month Follow-Up Telephone Contact After Vaccination 1 (Year 0) - Safety Population

	Vaccine Group (as Administered)								
	13vPnC N=463			23vPS N=473					
System Organ Class/ Preferred Term	No. of Subjects[a]	%	No. of Events[b]	No. of Subjects[a]	%	No. of Events[b]	Difference[c]	(95% CI[d])	p-Value[d]
Any event	27	5.8	34	26	5.5	43	0.3	(-2.7, 3.4)	0.825
Cardiac disorders	11	2.4	12	4	0.8	7	1.5	(-0.1, 3.5)	0.062
Cardiac failure congestive	1	0.2	1	1	0.2	4	0.0	(-1.0, 1.0)	0.988
Angina pectoris	3	0.6	3	0	0.0	0	0.6	(-0.2, 1.9)	0.080
Coronary artery disease	2	0.4	2	1	0.2	1	0.2	(-0.8, 1.4)	0.551
Myocardial infarction	2	0.4	2	1	0.2	1	0.2	(-0.8, 1.4)	0.551
Acute myocardial infarction	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Atrial fibrillation	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Cardiac arrest	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Diastolic dysfunction	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Ventricular tachycardia	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Endocrine disorders	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Hyperthyroidism	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Gastrointestinal disorders	0	0.0	0	4	0.8	9	-0.8	(-2.2, -0.0)	0.047
Small intestinal obstruction	0	0.0	0	1	0.2	3	-0.2	(-1.2, 0.6)	0.322
Abdominal mass	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Colonic stenosis	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Constipation	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Gastrointestinal haemorrhage	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Small intestinal haemorrhage	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Upper gastrointestinal haemorrhage	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Hepatobiliary disorders	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Cholelithiasis	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Infections and infestations	3	0.6	3	2	0.4	2	0.2	(-1.0, 1.5)	0.637
Device related infection	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Gastroenteritis	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Labyrinthitis	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Pneumonia	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Streptococcal bacteraemia	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Injury, poisoning and procedural complications	2	0.4	3	2	0.4	3	0.0	(-1.1, 1.2)	0.983

Table 30. Serious Adverse Events Reported at the 6-Month Follow-Up Telephone Contact After Vaccination 1 (Year 0) - Safety Population

System Organ Class/ Preferred Term	Vaccine Group (as Administered) 13vPnC N=463 No. of Subjects[a]	%	No. of Events[b]	23vPS N=473 No. of Subjects[a]	%	No. of Events[b]	Difference[c]	(95% CI[d])	p-Value[d]
Concussion	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Fall	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Hip fracture	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Post procedural pulmonary embolism	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Subdural haematoma	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Wrist fracture	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Metabolism and nutrition disorders	2	0.4	2	1	0.2	1	0.2	(-0.8, 1.4)	0.551
Dehydration	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Diabetes mellitus inadequate control	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Gout	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Musculoskeletal and connective tissue disorders	2	0.4	2	3	0.6	3	-0.2	(-1.5, 1.0)	0.671
Osteoarthritis	0	0.0	0	2	0.4	2	-0.4	(-1.5, 0.4)	0.161
Arthralgia	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Monarthritis	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Musculoskeletal pain	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Neoplasms benign, malignant and unspecified (including cysts and polyps)	4	0.9	4	10	2.1	12	-1.3	(-3.1, 0.4)	0.115
Basal cell carcinoma	3	0.6	3	4	0.8	4	-0.2	(-1.6, 1.1)	0.726
Squamous cell carcinoma of skin	0	0.0	0	2	0.4	2	-0.4	(-1.5, 0.4)	0.161
B-cell lymphoma recurrent	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Breast cancer	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Colon cancer	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Lung neoplasm malignant	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Neuroendocrine carcinoma of the skin	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Prostate cancer	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Squamous cell carcinoma	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Nervous system disorders	2	0.4	2	1	0.2	1	0.2	(-0.8, 1.4)	0.551
Cerebrovascular accident	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Parkinson's disease	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Syncope	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322

Table 30. Serious Adverse Events Reported at the 6-Month Follow-Up Telephone Contact After Vaccination 1 (Year 0) - Safety Population

System Organ Class/ Preferred Term	Vaccine Group (as Administered) 13vPnC N=463 No. of Subjects[a]	%	No. of Events[b]	23vPS N=473 No. of Subjects[a]	%	No. of Events[b]	Difference[c]	(95% CI[d])	p-Value[d]
Psychiatric disorders	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Mental status changes	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Renal and urinary disorders	2	0.4	2	0	0.0	0	0.4	(-0.4, 1.6)	0.152
Neurogenic bladder	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Renal failure acute	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Reproductive system and breast disorders	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Uterovaginal prolapse	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Respiratory, thoracic and mediastinal disorders	2	0.4	2	2	0.4	2	0.0	(-1.1, 1.2)	0.983
Pleural effusion	1	0.2	1	1	0.2	1	0.0	(-1.0, 1.0)	0.988
Obstructive airways disorder	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Pneumothorax	0	0.0	0	1	0.2	1	-0.2	(-1.2, 0.6)	0.322
Vascular disorders	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312
Aortic aneurysm	1	0.2	1	0	0.0	0	0.2	(-0.6, 1.2)	0.312

Data presented are from the Vaccination 1 safety population. The 6-month follow-up period for Vaccination 1 includes data from Vaccination 1 to the telephone contact, 6 months after Vaccination 1.

13vPnC = 13-valent pneumococcal conjugate vaccine; 23vPS = 23-valent pneumococcal polysaccharide vaccine; CI = confidence interval; N = number of subjects; No. = number.

a. Number of subjects reporting at least 1 event of type specified. "Any event" represents the number of subjects reporting at least 1 event of any kind.
b. The total number of events of the type specified. Subjects can be represented more than once. "Any event" represents the total number of events.
c. Difference in proportions, 13vPnC – 23vPS, expressed as a percentage, of the subjects reporting at least 1 event of type specified.
d. Exact 2-sided CI and corresponding p-value for the difference in proportions using the Miettinen and Nurminen method, 13vPnC – 23vPS, expressed as a percentage.

Serious Adverse Events at the 6-Month Follow-Up After Vaccination 2: At the 6-month follow-up telephone contact after Vaccination 2, SAEs were reported for 17 (4.3%) subjects in the 13vPnC/13vPnC group and for 21 (5.2%) subjects in the 23vPS/13vPnC group (Table 31). None of the SAEs in the 13vPnC/13vPnC group were considered vaccine related.

In the 23vPS/13vPnC group, 1 SAE (idiopathic thrombocytopenic purpura) was considered vaccine related. There were no significant differences between the 2 vaccine groups.

Table 31. Serious Adverse Events Reported at the 6-Month Follow-Up Telephone Contact After Vaccination 2 (Year 1) - Safety Population

	Vaccine Group (as Administered)								
	13vPnC/13vPnC N=391			23vPS/13vPnC N=404					
System Organ Class/ Preferred Term	No. of Subjects[a]	%	No. of Events[b]	No. of Subjects[a]	%	No. of Events[b]	Difference[c]	(95% CI[d])	p-Value[d]
Any event	17	4.3	22	21	5.2	29	-0.9	(-3.9, 2.2)	0.574
Blood and lymphatic system disorders	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Idiopathic thrombocytopenic purpura	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Cardiac disorders	4	1.0	6	4	1.0	4	0.0	(-1.6, 1.7)	0.963
Atrial fibrillation	0	0.0	0	3	0.7	3	-0.7	(-2.2, 0.2)	0.088
Bradycardia	2	0.5	2	0	0.0	0	0.5	(-0.4, 1.8)	0.150
Cardiac failure congestive	1	0.3	1	1	0.2	1	0.0	(-1.2, 1.2)	0.982
Arteriosclerosis coronary artery	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Sinus arrest	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Ventricular fibrillation	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Ear and labyrinth disorders	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Vertigo	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Gastrointestinal disorders	2	0.5	2	4	1.0	4	-0.5	(-2.1, 1.0)	0.436
Rectal haemorrhage	1	0.3	1	1	0.2	1	0.0	(-1.2, 1.2)	0.982
Diverticular perforation	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Dysphagia	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Small intestinal obstruction	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Subileus	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Infections and infestations	1	0.3	1	5	1.2	5	-1.0	(-2.6, 0.3)	0.110
Pneumonia	0	0.0	0	2	0.5	2	-0.5	(-1.8, 0.5)	0.164
Diverticulitis	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Gangrene	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Pneumonia primary atypical	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Pneumonia viral	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Injury, poisoning and procedural complications	1	0.3	1	2	0.5	2	-0.2	(-1.6, 1.0)	0.582
Hip fracture	1	0.3	1	1	0.2	1	0.0	(-1.2, 1.2)	0.982
Spinal compression fracture	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Musculoskeletal and connective tissue disorders	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Osteoarthritis	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309

Table 31. Serious Adverse Events Reported at the 6-Month Follow-Up Telephone Contact After Vaccination 2 (Year 1) - Safety Population

	Vaccine Group (as Administered)								
	13vPnC/13vPnC N=391			23vPS/13vPnC N=404					
System Organ Class/ Preferred Term	No. of Subjects[a]	%	No. of Events[b]	No. of Subjects[a]	%	No. of Events[b]	Difference[c]	(95% CI[d])	p-Value[d]
Neoplasms benign, malignant and unspecified (including cysts and polyps)	7	1.8	9	6	1.5	7	0.3	(-1.6, 2.3)	0.735
Basal cell carcinoma	3	0.8	4	0	0.0	0	0.8	(-0.2, 2.2)	0.078
Bowen's disease	1	0.3	1	1	0.2	1	0.0	(-1.2, 1.2)	0.982
Breast cancer	0	0.0	0	2	0.5	2	-0.5	(-1.8, 0.5)	0.164
Squamous cell carcinoma of skin	0	0.0	0	2	0.5	2	-0.5	(-1.8, 0.5)	0.164
Breast cancer in situ	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Gastrointestinal tract adenoma	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Laryngeal cancer	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Metastatic neoplasm	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Non-small cell lung cancer metastatic	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Squamous cell carcinoma	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Nervous system disorders	1	0.3	1	2	0.5	2	-0.2	(-1.6, 1.0)	0.582
Cerebrovascular accident	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Syncope	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Transient ischaemic attack	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Reproductive system and breast disorders	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Benign prostatic hyperplasia	1	0.3	1	0	0.0	0	0.3	(-0.7, 1.4)	0.309
Respiratory, thoracic and mediastinal disorders	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Orthopnoea	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Vascular disorders	0	0.0	0	2	0.5	2	-0.5	(-1.8, 0.5)	0.164
Hypertension	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325
Peripheral vascular disorder	0	0.0	0	1	0.2	1	-0.2	(-1.4, 0.7)	0.325

Table 31. Serious Adverse Events Reported at the 6-Month Follow-Up Telephone Contact After Vaccination 2 (Year 1) - Safety Population

	Vaccine Group (as Administered)								
	13vPnC/13vPnC N=391			23vPS/13vPnC N=404					
System Organ Class/ Preferred Term	No. of Subjects[a]	%	No. of Events[b]	No. of Subjects[a]	%	No. of Events[b]	Difference[c]	(95% CI[d])	p-Value[d]

Data presented are from the Vaccination 2 safety population. The 6-month follow-up period for Vaccination 2 includes data from Vaccination 2 to the telephone contact, 6 months after Vaccination 2.

13vPnC = 13-valent pneumococcal conjugate vaccine; 23vPS = 23-valent pneumococcal polysaccharide vaccine; CI = confidence interval; N = number of subjects; No. = number.

a. Number of subjects reporting at least 1 event of type specified. "Any event" represents the number of subjects reporting at least 1 event of any kind.
b. The total number of events of the type specified. Subjects can be represented more than once. "Any event" represents the total number of events.
c. Difference in proportions, 13vPnC/13vPnC – 23vPS/13vPnC, expressed as a percentage, of the subjects reporting at least 1 event of type specified.
d. Exact 2-sided CI and corresponding p-value for the difference in proportions using the Miettinen and Nurminen method, 13vPnC/13vPnC – 23vPS/13vPnC, expressed as a percentage.

Safety-Related Discontinuations: Five (5) subjects in the 13vPnC/13vPnC group were withdrawn from the study due to AEs. Six (6) subjects in the 23vPS/13vPnC group were withdrawn from the study due to AEs. None of the AEs were considered vaccine related.

Deaths: Nine (9) subjects died during the study. Eight (8) of the subjects (4 in the 13vPnC group and 4 in the 23vPS group) died after Vaccination 1; the day of death for these subjects ranged from Day 72 to Day 309 after vaccination. The remaining subject died after Vaccination 2; subject was in the 13vPnC/13vPnC group and died on Day 85 after vaccination. None of the events leading to the deaths were considered related to study vaccine.

CONCLUSIONS: In subjects 70 years of age or older immunized at least 5 years earlier with 23vPS, 13vPnC was as immunogenic as 23vPS for the 12 common serotypes, and was significantly more immunogenic for most of the common serotypes and for serotype 6A. The immune response to a second dose of 13vPnC administered 1 year after an initial study dose of 13vPnC was similar to the immune response to the initial study dose of 13vPnC, and the immune response to a second dose of 13vPnC administered 1 year after an initial study dose of 13vPnC was noninferior to the immune response to 23vPS (Year 0). Furthermore, the 13vPnC/13vPnC sequence had a statistically significantly greater OPA GMT response than the 23vPS/13vPnC sequence after Vaccination 2 for most of the serotypes. An acceptable safety profile was demonstrated for the administration of 13vPnC to 23vPS preimmunized subjects 70 years of age or older.