PFIZER INC.

These results are supplied for informational purposes only.
Prescribing decisions should be made based on the approved package insert.

PROPRIETARY DRUG NAME® / GENERIC DRUG NAME: Prevnar 13® / Prevenar 13® / 13-Valent Pneumococcal Conjugate Vaccine

PROTOCOL NO.: 6115A1-3000 (B1851073)

PROTOCOL TITLE: A Phase 3, Open-Label, Single-Arm Trial Evaluating the Safety, Tolerability, and Reactogenicity of a 13-Valent Pneumococcal Conjugate Vaccine in Ambulatory Elderly Adults Aged 68 Years and Older Who Received 1 or More Doses of 23-Valent Pneumococcal Polysaccharide Vaccine at Least 3 Years Before Study Enrollment

Study Centers: A total of 68 centers took part in the study of which 61 sites enrolled subjects; 43 in the United States (US), 11 in Germany and 7 in Sweden.

Study Initiation Date and Final Completion Date: 27 May 2008 to 16 April 2009

Phase of Development: Phase 3

Study Objectives: The primary objective was to evaluate the acceptability of the safety profile of a single injection of 13-valent pneumococcal conjugate vaccine (13vPnC) administered at least 3 years after 1 or more nonstudy doses of 23-valent pneumococcal polysaccharide vaccine (23vPS) as measured by the incidence rates of local reactions, systemic events, and adverse events (AEs).

METHODS

Study Design: This was a single-arm, open-label, multicenter trial to evaluate the acceptability of the safety profile of a single injection of 13vPnC, administered at least 3 years after 1 or more nonstudy doses of 23vPS in healthy adults aged 68 years or older.

Eligible subjects participated in the study for approximately 6 months, including a vaccination visit (Day 1), a post-vaccination visit at approximately 1-month and a 6-month follow-up phone call.

The schedule of activities during the study is provided in Table 1.

Table 1. Schedule of Activities

Visit ID	1	2	3
Visit Description	**Vaccination**	**Post-Vaccination**	**6-Month Follow-Up Phone Call**
Visit Window	**Day 1**	**29 to 43 Days After Visit 1**	**166 to 194 Days After Visit 1**
Informed consent	X		
Review inclusion/exclusion criteria	X		
Demographics	X		
MMSE	X		
Medical history including tobacco use	X		
Physical examination	X		
Prevaccination body temperature (oral)	X		
Assess arm movement before vaccination	X		
Record concomitant medications, including any nonstudy vaccines administered	X		
Enrollment	X		
13vPnC administration	X		
Assess acute reactions (including pain at the injection site) for 30 minutes after vaccination	X		
Provide e-diary, thermometer, caliper, and appointment card	Days 1-14		
Subjects collect e-diary reactogenicity[a]	Days 1-14		
E-diary collection and review		X	
Record any new or change in concomitant medications since Visit 1		X	
Adverse event collection as appropriate for visit	X	X	X[b]

13vPnC = 13-valent pneumococcal conjugate vaccine; E-diary = electronic diary; ID = identity details; MMSE = Mini-Mental State Examination; SAE = serious adverse event.

a. Subjects were requested to contact the study staff if they experienced redness or swelling at the injection site measuring >10 cm (21/21+ caliper units) or severe limitation of arm movement in order to arrange an additional visit for local reaction(s) assessment by the Investigator or other medically qualified staff.

b. Only SAEs and any newly diagnosed chronic medical conditions (including autoimmune or neuroinflammatory diseases) and emergency room visits that met the criteria of an SAE and that had occurred since Visit 2 were collected at Visit 3.

Number of Subjects (Planned and Analyzed): Approximately 1053 subjects were planned to be enrolled to achieve 1000 evaluable subjects in this study. A total of 1077 subjects were screened, 1053 subjects (825 were enrolled in the US, 159 in Germany, and 69 in Sweden) were assigned study vaccine, 1049 subjects were actually vaccinated, and 1040 completed the study.

Diagnosis and Main Criteria for Inclusion: Male and female subjects, aged 68 years and older, with documented vaccination with 1 or more doses of 23vPS at least 3 years before study enrollment, healthy or with pre-existing stable disease (ie, not requiring significant change in therapy), and able to complete an electronic diary, in the opinion of the Investigator, were eligible to participate in the study.

Subjects were excluded if they had a history of severe reaction to a vaccine, received any vaccine (except influenza) within 28 days or a diphtheria-containing vaccine within 6 months prior to study vaccination, respectively, had documented *Streptococcus pneumoniae* infection within the past 5 years, were residents in a nursing home, had evidence of dementia or other severe cognitive impairment, as assessed by the Mini-Mental State Examination (MMSE) score of ≤21.

Study Vaccine: 13vPnC was provided by the Sponsor to each study site.

The 13vPnC vaccine was prefilled into single-dose syringes without preservatives, as a sterile liquid formulation of pneumococcal capsular polysaccharides of serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F, individually conjugated to nontoxic diphtheria toxoid cross reactive material 197 (CRM_{197}) protein. Each 0.5 mL dose contains 2.2 μg of each serotype, except for the 4.4 μg of serotype 6B, and is formulated in 5.0 mM succinate buffer and 0.85% sodium chloride (NaCl) at pH 5.8, with 0.125 mg aluminum as aluminum phosphate ($AlPO_4$) as adjuvant, and 0.02% polysorbate 80 (P80).

13vPnC was administered as a single dose of 13vPnC (0.5 mL) by intramuscular (IM) injection into the deltoid muscle.

Efficacy Endpoints: No efficacy or immunogenicity analyses were performed in this study.

Safety Endpoints: Safety endpoints were the incidence rates of local reactions, systemic events, and AEs.

Local reactions were pain at injection site, redness, swelling, and limitation of arm movement. Systemic events were fever, chills, fatigue, headache, vomiting, decreased appetite, rash, new, or aggravated generalized muscle pain, new or aggravated generalized joint pain.

Safety Evaluations: In the 14 days (Days 1 through 14) after 13vPnC administration, local reactions and systemic events were recorded in e-diaries by the subjects. AEs were recorded on the case report forms (CRFs) by the Investigator from Visit 1 to Visit 2. During the 6-month safety follow-up, only serious AEs (SAEs), any newly diagnosed chronic medical conditions (including autoimmune or neuroinflammatory diseases), and emergency room visits that met the criteria of an SAE, were recorded on the CRFs (ie, that had occurred since Visit 2 and were collected at Visit 3 phone call).

Statistical Methods: All participants who received at least 1 dose of study vaccine were included in the safety population.

The percentages of subjects with local reactions, systemic events, and use of antipyretic and pain medications reported on each day and any day within the 14-day period after vaccination were summarized.

AEs and SAEs were categorized according to Medical Dictionary for Regulatory Activities and summarized using descriptive statistics.

RESULTS

Subject Disposition and Demography: A summary of subject disposition is presented in Table 2. A total of 1077 subjects consented, of which 1053 subjects were assigned study vaccine and 1049 were actually vaccinated; 24 subjects were screened only and were not assigned study vaccine. A total of 1040 subjects were contacted at the 6-month follow-up

telephone contact and completed the study. Of the 1053 subjects who were assigned study vaccine, 13 subjects were withdrawn.

Table 2. Disposition of Subjects

	Screened Only		13vPnC	
	n[a]	%	n[a]	%
Consented[b]	24	100.0	1053	100.4
Vaccinated[c]	0	0.0	1049	100.0
Completed Visit 2	0	0.0	1046	99.7
Withdrawn before Visit 2	3	12.5	7	0.7
Reasons for withdrawal				
Subject request	0	0.0	4	0.4
Protocol violation	0	0.0	2	0.2
Other	3	12.5	1	0.1
Completed 6-month follow-up contact	0	0.0	1040	99.1
Withdrawn after Visit 2 and before 6-month follow-up contact	0	0.0	6	0.6
Reasons for withdrawal				
Death	0	0.0	3	0.3
Lost to follow-up	0	0.0	3	0.3

Four subjects were assigned to vaccine but did not receive vaccination.
13vPnC = 13-valent pneumococcal conjugate vaccine.
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 13vPnC.

The demographic characteristics for the 1049 subjects in the safety population are summarized in Table 3.

Table 3. Demographic Characteristics – Safety Population

	13vPnC N[a]=1049	
	n[b]	%
Sex		
Female	584	55.7
Male	465	44.3
Race		
White	1026	97.8
Black or African American	16	1.5
Asian	3	0.3
Other	3	0.3
American Indian or Alaska Native	1	0.1
Ethnicity		
Non-Hispanic and Non-Latino	1039	99.0
Hispanic or Latino	10	1.0
Age at vaccination (years)		
Mean (SD)	75.3 (5.1)	
Median	74.3	
Min, Max	68.0, 90.8	

13vPnC = 13-valent pneumococcal conjugate vaccine; Max = maximum; Min = minimum; SD = standard deviation.
a. N = Number of subjects in the specified group.
b. n = Number of subjects in the specified category.

Most subjects (98.67%) received 1 or more doses of 23vPS at least 3 years before study vaccination.

Safety Results:

Reactogenicity:

Local Reactions: The number and percentage of subjects with injection site pain within 30 minutes following vaccination are presented in Table 4; approximately 4.5% of subjects reported pain within 30 minutes post vaccination and most reports were mild (4.1%).

Table 4. Summary of Subjects With Injection Site Pain Within 30 Minutes Following Study Vaccination – Safety Population

	13vPnC N[a]=1049	
	n[b]	%
Pain at injection site within 30 minutes		
Yes	47	4.5
No	1002	95.5
Severity of pain		
Mild	43	4.1
Moderate	4	0.4

13vPnC = 13-valent pneumococcal conjugate vaccine.
a. N = Number of subjects in the vaccine group.
b. n = Number of subjects with the specified characteristic.

The number and percentage of subjects with injection site pain, redness, swelling, or limitation of arm movement during the 14 days after vaccination are presented in Table 5.

Table 5. Summary of Subjects Reporting Local Reactions Within 14 Days After Study Vaccination – Safety Population

	13vPnC			
Local Reaction	**N[a]**	**n[b]**	**%**	**(95% CI[c])**
Redness[d]				
Any	666	95	14.3	(11.7, 17.2)
Mild	660	83	12.6	(10.1, 15.3)
Moderate	649	42	6.5	(4.7, 8.6)
Severe	638	7	1.1	(0.4, 2.2)
Swelling[d]				
Any	664	85	12.8	(10.4, 15.6)
Mild	658	72	10.9	(8.7, 13.6)
Moderate	651	36	5.5	(3.9, 7.6)
Severe	636	4	0.6	(0.2, 1.6)
Pain[e]				
Any	777	396	51.0	(47.4, 54.5)
Mild	770	380	49.4	(45.8, 52.9)
Moderate	656	59	9.0	(6.9, 11.4)
Severe	634	1	0.2	(0.0, 0.9)
Limitation of arm movement[f]				
Any	679	110	16.2	(13.5, 19.2)
Mild	674	100	14.8	(12.2, 17.7)
Moderate	636	10	1.6	(0.8, 2.9)
Severe	640	10	1.6	(0.8, 2.9)
Any local reaction[g]	802	454	56.6	(53.1, 60.1)
Any severe local reaction	643	17	2.6	(1.5, 4.2)

13vPnC = 13-valent pneumococcal conjugate vaccine; CI = confidence interval.
a. N = Number of subjects reporting "yes" for at least 1 day or as "no" for all days.
b. n = Number of subjects reporting the specific characteristic.
c. Exact 2-sided CI based upon the observed proportion of subjects.
d. Mild = 2.5 to 5.0 cm, moderate = 5.1 to 10.0 cm, and severe is >10.0 cm.
e. Mild = no interference with activity, moderate = some interference with activity, and severe = prevents routine daily activity.
f. 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.
g. Any local reaction = any pain, any swelling, any redness, or any limitation of arm movement.

Systemic Events:

The numbers and percentages of subjects with systemic events reported within 14 days after study vaccination and use of medication to prevent and/or treat symptoms are presented in Table 6. Systemic events were reported by 58.4% of the subjects.

Table 6. Summary of Subjects Reporting Systemic Events and Medication Use Within 14 Days After Study Vaccination – Safety Population

	13vPnC			
Systemic Event	**N[a]**	**n[b]**	**%**	**(95% C I[c])**
Fever				
Any (≥38°C)	641	13	2.0	(1.1, 3.4)
Mild (≥38°C but <38.5°C)	636	5	0.8	(0.3, 1.8)
Moderate (≥38.5°C but <39°C)	634	0	0.0	(0.0, 0.6)
Severe (≥39°C but ≤40°C)	635	2	0.3	(0.0, 1.1)
Potentially life threatening (>40°C)	638	6[d]	0.9	(0.3, 2.0)
Fatigue[e]	733	252	34.4	(30.9, 37.9)
Mild	710	204	28.7	(25.4, 32.2)
Moderate	683	104	15.2	(12.6, 18.1)
Severe	639	13	2.0	(1.1, 3.5)
Headache[e]	702	183	26.1	(22.9, 29.5)
Mild	696	168	24.1	(21.0, 27.5)
Moderate	655	59	9.0	(6.9, 11.5)
Severe	637	5	0.8	(0.3, 1.8)
Chills	651	49	7.5	(5.6, 9.8)
Rash	658	55	8.4	(6.4, 10.7)
Vomiting[f]	638	6	0.9	(0.3, 2.0)
Mild	637	5	0.8	(0.3, 1.8)
Moderate	635	1	0.2	(0.0, 0.9)
Severe	634	0	0.0	(0.0, 0.6)
Decreased appetite	668	75	11.2	(8.9, 13.9)
Diarrhea[g]	684	99	14.5	(11.9, 17.3)
Mild	678	87	12.8	(10.4, 15.6)
Moderate	644	22	3.4	(2.2, 5.1)
Severe	635	2	0.3	(0.0, 1.1)
New generalized muscle pain[e]	700	177	25.3	(22.1, 28.7)
Mild	679	139	20.5	(17.5, 23.7)
Moderate	658	52	7.9	(6.0, 10.2)
Severe	636	4	0.6	(0.2, 1.6)
Aggravated generalized muscle pain[e]	669	82	12.3	(9.9, 15.0)
Mild	650	49	7.5	(5.6, 9.8)
Moderate	655	42	6.4	(4.7, 8.6)
Severe	639	9	1.4	(0.6, 2.7)
New generalized joint pain[e]	665	85	12.8	(10.3, 15.6)
Mild	651	53	8.1	(6.2, 10.5)
Moderate	648	37	5.7	(4.1, 7.8)
Severe	637	5	0.8	(0.3, 1.8)
Aggravated generalized joint pain[e]	661	64	9.7	(7.5, 12.2)
Mild	647	37	5.7	(4.1, 7.8)
Moderate	647	33	5.1	(3.5, 7.1)
Severe	637	7	1.1	(0.4, 2.3)
Use of medication to treat pain	677	115	17.0	(14.2, 20.0)
Use of medication to treat fever	655	42	6.4	(4.7, 8.6)
Any systemic event[h]	832	486	58.4	(55.0, 61.8)

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

a. N = Number of subjects with the event as "yes" for at least 1 day or as "no" for all days.
b. n = Number of subjects with the given characteristic.
c. Exact 2-sided CI based upon the observed proportion of subjects.
d. All of these cases were data entry errors.
e. Mild = no interference with activity, moderate = some interference with activity, severe = prevents routine daily activity.
f. Mild = no interference with activity or 1 to 2 times in 24 hours, moderate = some interference with activity or >2 times in 24 hours, severe = prevents routine daily activity.
g. Mild = 2 to 3 loose stools in 24 hours, moderate = 4 to 5 loose stools in 24 hours, severe = 6 or more loose stools in 24 hours.
h. Any systemic event = any fever ≥38°C, any fatigue, headache, chills, rash, vomiting, diarrhea, decreased appetite, new or aggravated generalized muscle pain, and any new or aggravated joint pain.

All-Causality Non-serious Adverse Events: The percentage of subjects with non-serious AEs occurring during the period from Visit 1 (13vPnC) to Visit 2 (29 to 43 days after Visit 1) is summarized in Table 7. The most frequent non-serious AEs, each occurring in 0.6% of subjects, were diarrhea, nausea, bronchitis, arthralgia, and myalgia.

Table 7. All-Causality Non-Serious Adverse Events Reported From Visit 1 to Visit 2 – Safety Population

System Organ Class Preferred Term	13vPnC N=1049		
	Number of Subjects[a]	%	Number of Events[b]
Any event	121	11.5	168
Cardiac disorders	1	0.1	1
Bradycardia	1	0.1	1
Ear and labyrinth disorders	1	0.1	1
Vertigo	1	0.1	1
Eye disorders	3	0.3	3
Blepharitis	1	0.1	1
Conjunctivitis	1	0.1	1
Diabetic retinopathy	1	0.1	1
Gastrointestinal disorders	16	1.5	21
Diarrhoea	6	0.6	7
Nausea	6	0.6	6
Vomiting	3	0.3	3
Constipation	2	0.2	2
Abdominal discomfort	1	0.1	1
Haemorrhoidal haemorrhage	1	0.1	1
Retching	1	0.1	1
General disorders and administration site conditions	11	1.0	11
Fatigue	4	0.4	4
Injection site pain	2	0.2	2
Injection site haematoma	1	0.1	1
Injection site pruritus	1	0.1	1
Injection site swelling	1	0.1	1
Oedema peripheral	1	0.1	1
Pain	1	0.1	1
Immune system disorders	1	0.1	1
Seasonal allergy	1	0.1	1
Infections and infestations	35	3.3	35
Bronchitis	6	0.6	6
Sinusitis	4	0.4	4
Upper respiratory tract infection	4	0.4	4
Urinary tract infection	4	0.4	4
Gastroenteritis	2	0.2	2
Gastroenteritis viral	2	0.2	2
Herpes zoster	2	0.2	2
Acute sinusitis	1	0.1	1
Cellulitis	1	0.1	1
Ear infection	1	0.1	1
Eye infection	1	0.1	1
Laryngitis	1	0.1	1
Localised infection	1	0.1	1
Nail infection	1	0.1	1
Nasopharyngitis	1	0.1	1
Staphylococcal skin infection	1	0.1	1
Tinea cruris	1	0.1	1
Viral infection	1	0.1	1
Injury, poisoning and procedural complications	9	0.9	11
Skin laceration	3	0.3	3
Contusion	2	0.2	2

Table 7. All-Causality Non-Serious Adverse Events Reported From Visit 1 to Visit 2 – Safety Population

System Organ Class Preferred Term	13vPnC N=1049		
	Number of Subjects[a]	%	Number of Events[b]
Limb injury	2	0.2	2
Electric shock	1	0.1	1
Excoriation	1	0.1	1
Fall	1	0.1	1
Joint sprain	1	0.1	1
Investigations	1	0.1	1
Blood glucose increased	1	0.1	1
Metabolism and nutrition disorders	1	0.1	1
Dehydration	1	0.1	1
Musculoskeletal and connective tissue disorders	27	2.6	31
Arthralgia	6	0.6	6
Myalgia	6	0.6	7
Musculoskeletal pain	3	0.3	3
Pain in extremity	3	0.3	3
Spinal osteoarthritis	2	0.2	2
Back pain	1	0.1	1
Bone pain	1	0.1	1
Bursitis	1	0.1	1
Musculoskeletal chest pain	1	0.1	1
Musculoskeletal discomfort	1	0.1	1
Neck pain	1	0.1	1
Osteoarthritis	1	0.1	1
Osteoporosis	1	0.1	1
Plantar fasciitis	1	0.1	1
Rotator cuff syndrome	1	0.1	1
Neoplasms benign, malignant and unspecified (including cysts and polyps)	3	0.3	3
Benign breast neoplasm	1	0.1	1
Endobronchial lipoma	1	0.1	1
Lung neoplasm	1	0.1	1
Nervous system disorders	11	1.0	15
Dizziness	3	0.3	4
Headache	3	0.3	3
Paraesthesia	3	0.3	3
Carotid artery stenosis	1	0.1	1
Carpal tunnel syndrome	1	0.1	1
Hypoaesthesia	1	0.1	1
Polyneuropathy	1	0.1	1
Tremor	1	0.1	1
Psychiatric disorders	2	0.2	4
Bipolar disorder	1	0.1	1
Depression	1	0.1	1
Stress	1	0.1	1
Suicidal ideation	1	0.1	1
Renal and urinary disorders	2	0.2	2
Bladder spasm	1	0.1	1
Renal failure	1	0.1	1
Respiratory, thoracic and mediastinal disorders	14	1.3	15
Cough	3	0.3	3
Oropharyngeal pain	2	0.2	2
Pleural effusion	2	0.2	2
Asthma	1	0.1	1
Nasal congestion	1	0.1	1
Pulmonary fibrosis	1	0.1	1
Respiratory disorder	1	0.1	1

Table 7. All-Causality Non-Serious Adverse Events Reported From Visit 1 to Visit 2 – Safety Population

System Organ Class Preferred Term	13vPnC N=1049		
	Number of Subjects[a]	%	Number of Events[b]
Rhinitis allergic	1	0.1	1
Rhinorrhoea	1	0.1	1
Sinus congestion	1	0.1	1
Upper respiratory tract congestion	1	0.1	1
Skin and subcutaneous tissue disorders	6	0.6	8
Actinic keratosis	1	0.1	1
Dermatitis allergic	1	0.1	1
Intertrigo	1	0.1	1
Rash	1	0.1	1
Rash pruritic	1	0.1	1
Skin discolouration	1	0.1	1
Skin lesion	1	0.1	1
Skin mass	1	0.1	1
Vascular disorders	4	0.4	4
Hypertension	3	0.3	3
Hypotension	1	0.1	1

Data presented were from Visit 1 (13vPnC) to Visit 2 (29 to 43 days after Visit 1).
13vPnC = 13-valent pneumococcal conjugate vaccine; N = total number of subjects who received study vaccine.
a. Number of subjects reporting at least 1 event of type specified. For "Any Event," it 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. For "Any Event," it represents the total number of events.

The percentage of subjects with protocol required reportable non-serious AEs occurring between Visit 2 and Visit 3, ie, the 6-month telephone contact is summarized in Table 8. The most frequent AEs were osteoarthritis and arthralgia.

Table 8. All-Causality Non-Serious Adverse Events Reported – 6-Month Follow-Up Telephone Contact – Safety Population

System Organ Class Preferred Term	13vPnC N=1049		
	Number of Subjects[a]	%	Number of Events[b]
Any event	77	7.3	106
Blood and lymphatic system disorders	2	0.2	2
Iron deficiency anaemia	1	0.1	1
Leukocytosis	1	0.1	1
Cardiac disorders	4	0.4	6
Angina unstable	1	0.1	1
Aortic valve incompetence	1	0.1	1
Arteriosclerosis coronary artery	1	0.1	1
Coronary artery disease	1	0.1	1
Left ventricular hypertrophy	1	0.1	1
Tricuspid valve incompetence	1	0.1	1
Ear and labyrinth disorders	1	0.1	1
Deafness neurosensory	1	0.1	1
Eye disorders	3	0.3	3
Cataract	3	0.3	3
Gastrointestinal disorders	8	0.8	8
Gastrooesophageal reflux disease	3	0.3	3
Diverticulum	2	0.2	2
Haemorrhoids	2	0.2	2
Constipation	1	0.1	1
General disorders and administration site conditions	3	0.3	3
Fatigue	1	0.1	1
Pain	1	0.1	1
Suprapubic pain	1	0.1	1
Hepatobiliary disorders	1	0.1	1
Cholelithiasis	1	0.1	1
Infections and infestations	6	0.6	6
Bronchitis	1	0.1	1
Oral herpes	1	0.1	1
Pneumonia	1	0.1	1
Sinusitis	1	0.1	1
Urinary tract infection	1	0.1	1
Viral infection	1	0.1	1
Injury, poisoning and procedural complications	4	0.4	6
Contusion	1	0.1	2
Facial bones fracture	1	0.1	1
Incisional hernia	1	0.1	1
Joint injury	1	0.1	1
Procedural pain	1	0.1	1
Investigations	2	0.2	2
Blood thyroid stimulating hormone increased	1	0.1	1
Cardiac murmur	1	0.1	1
Metabolism and nutrition disorders	3	0.3	3
Glucose tolerance impaired	1	0.1	1
Hyperlipidaemia	1	0.1	1
Type 2 diabetes mellitus	1	0.1	1
Musculoskeletal and connective tissue disorders	22	2.1	29
Osteoarthritis	5	0.5	6
Arthralgia	4	0.4	4
Osteopenia	3	0.3	3
Osteoporosis	3	0.3	3
Back pain	2	0.2	2
Musculoskeletal pain	2	0.2	2
Tendonitis	2	0.2	2
Bursitis	1	0.1	2

Table 8. All-Causality Non-Serious Adverse Events Reported – 6-Month Follow-Up Telephone Contact – Safety Population

System Organ Class Preferred Term	13vPnC N=1049 Number of Subjects[a]	 %	 Number of Events[b]
Joint range of motion decreased	1	0.1	1
Lumbar spinal stenosis	1	0.1	1
Rotator cuff syndrome	1	0.1	1
Sacroiliitis	1	0.1	1
Spinal osteoarthritis	1	0.1	1
Neoplasms benign, malignant and unspecified (including cysts and polyps)	1	0.1	1
Meningioma benign	1	0.1	1
Nervous system disorders	3	0.3	3
Carpal tunnel syndrome	1	0.1	1
Narcolepsy	1	0.1	1
Restless legs syndrome	1	0.1	1
Psychiatric disorders	3	0.3	3
Depression	2	0.2	2
Insomnia	1	0.1	1
Renal and urinary disorders	4	0.4	5
Renal failure	2	0.2	2
Haematuria	1	0.1	1
Hypertonic bladder	1	0.1	1
Renal mass	1	0.1	1
Reproductive system and breast disorders	3	0.3	3
Atrophic vulvovaginitis	1	0.1	1
Benign prostatic hyperplasia	1	0.1	1
Erectile dysfunction	1	0.1	1
Respiratory, thoracic and mediastinal disorders	9	0.9	9
Chronic obstructive pulmonary disease	3	0.3	3
Pulmonary fibrosis	3	0.3	3
Dyspnoea	1	0.1	1
Emphysema	1	0.1	1
Sleep apnoea syndrome	1	0.1	1
Skin and subcutaneous tissue disorders	5	0.5	5
Eczema	2	0.2	2
Erythema	1	0.1	1
Milia	1	0.1	1
Skin lesion	1	0.1	1
Social circumstances	1	0.1	1
Joint prosthesis user	1	0.1	1
Vascular disorders	6	0.6	6
Hypertension	3	0.3	3
Peripheral arterial occlusive disease	1	0.1	1
Peripheral vascular disorder	1	0.1	1
Temporal arteritis	1	0.1	1

Only any newly diagnosed chronic medical conditions (including autoimmune or neuroinflammatory diseases) were required to be recorded on the CRFs.
Data presented are for the period after Visit 2 (29 to 43 days after vaccination) to the 6-month telephone contact.
13vPnC = 13-valent pneumococcal conjugate vaccine; N = total number of subjects who received study vaccine; SAE = serious adverse event.

a. Number of subjects reporting at least 1 event of type specified. For "Any Event," it 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. For "Any Event," it represents.

Serious Adverse Events: SAEs that occurred during the period from Visit 1 (13vPnC) to Visit 2 (29 to 43 days after Visit 1) were reported by 1.0% of the subjects (11 events in 10 subjects) (Table 9). Most SAEs occurred in 1 (0.1%) subject only.

Table 9. Serious Adverse Events From Visit 1 to Visit 2 – Safety Population

System Organ Class Preferred Term	13vPnC N=1049		
	Number of Subjects[a]	%	Number of Events[b]
Any event	10	1.0	11
Cardiac disorders	1	0.1	2
Bradyarrhythmia	1	0.1	1
Tachyarrhythmia	1	0.1	1
Gastrointestinal disorders	2	0.2	2
Gastritis	1	0.1	1
Small intestinal obstruction	1	0.1	1
Infections and infestations	1	0.1	1
Appendicitis	1	0.1	1
Injury, poisoning and procedural complications	1	0.1	1
Hip fracture	1	0.1	1
Neoplasms benign, malignant and unspecified (including cysts and polyps)	2	0.2	2
Basal cell carcinoma	2	0.2	2
Nervous system disorders	1	0.1	1
Loss of consciousness	1	0.1	1
Skin and subcutaneous tissue disorders	1	0.1	1
Skin burning sensation	1	0.1	1
Vascular disorders	1	0.1	1
Peripheral arterial occlusive disease	1	0.1	1

Data presented are for the period after Visit 2 (29 to 43 days after vaccination) to the 6-month telephone contact.
13vPnC = 13-valent pneumococcal conjugate vaccine; N = total number of subjects who received study vaccine.

a. Number of subjects reporting at least 1 event of type specified. For "Any Event," it 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. For "Any Event," it represents the total number of events.

At the 6-month follow-up telephone contact, SAEs were reported by 3.9% of subjects (67 events in 41 subjects) (Table 10). Most SAEs were neoplasms (1.1%) or cardiac disorders (1%).

Table 10. Serious Adverse Events, Reported at the 6-Month Follow-Up Telephone Contact – Safety Population

System Organ Class Preferred Term	13vPnC N=1049		
	Number of Subjects[a]	%	Number of Events[b]
Any event	41	3.9	67
Cardiac disorders	11	1.0	12
Myocardial infarction	3	0.3	3
Atrial fibrillation	2	0.2	2
Acute coronary syndrome	1	0.1	1
Bradyarrhythmia	1	0.1	1
Cardiac arrest	1	0.1	1
Cardiac failure	1	0.1	1
Cardiac failure congestive	1	0.1	1
Coronary artery disease	1	0.1	1
Ischaemic cardiomyopathy	1	0.1	1
Infections and infestations	7	0.7	10
Pneumonia	3	0.3	3
Abscess limb	1	0.1	1
Bacteraemia	1	0.1	1
Bronchitis	1	0.1	1
Cellulitis	1	0.1	1
Enteritis infectious	1	0.1	1
Lower respiratory tract infection	1	0.1	1
Septic shock	1	0.1	1
Injury, poisoning and procedural complications	6	0.6	6
Fall	1	0.1	1
Fracture displacement	1	0.1	1
Hip fracture	1	0.1	1
Postoperative renal failure	1	0.1	1
Rib fracture	1	0.1	1
Wrist fracture	1	0.1	1
Metabolism and nutrition disorders	2	0.2	4
Diabetic ketoacidosis	1	0.1	1
Hyperkalaemia	1	0.1	2
Hypovolaemia	1	0.1	1
Musculoskeletal and connective tissue disorders	1	0.1	1
Osteoarthritis	1	0.1	1
Neoplasms benign, malignant and unspecified (including cysts and polyps)	12	1.1	13
Breast cancer	2	0.2	2
Bladder cancer	1	0.1	1
Breast cancer in situ	1	0.1	1
Colon cancer	1	0.1	1
Fibrosarcoma	1	0.1	1
Lung neoplasm malignant	1	0.1	1
Metastases to lymph nodes	1	0.1	1
Metastatic neoplasm	1	0.1	1
Non-small cell lung cancer	1	0.1	1
Ovarian cancer	1	0.1	1
Renal cancer	1	0.1	1
Renal neoplasm	1	0.1	1
Nervous system disorders	5	0.5	6
Carotid artery stenosis	1	0.1	1
Cerebral infarction	1	0.1	1
Cerebrovascular accident	1	0.1	2
Guillain-Barre syndrome	1	0.1	1
Transient ischaemic attack	1	0.1	1
Psychiatric disorders	2	0.2	2
Hallucination	1	0.1	1

Table 10. Serious Adverse Events, Reported at the 6-Month Follow-Up Telephone Contact – Safety Population

System Organ Class Preferred Term	13vPnC N=1049		
	Number of Subjects[a]	%	Number of Events[b]
Mental status changes	1	0.1	1
Renal and urinary disorders	2	0.2	2
Renal failure	1	0.1	1
Renal failure acute	1	0.1	1
Respiratory, thoracic and mediastinal disorders	6	0.6	9
Chronic obstructive pulmonary disease	3	0.3	4
Respiratory failure	2	0.2	2
Dyspnoea	1	0.1	1
Pleural effusion	1	0.1	1
Pulmonary oedema	1	0.1	1
Surgical and medical procedures	1	0.1	1
Percutaneous coronary intervention	1	0.1	1
Vascular disorders	1	0.1	1
Deep vein thrombosis	1	0.1	1

Data presented are for the period after Visit 2 (29 to 43 days after vaccination) to the 6-month telephone contact.
13vPnC = 13-valent pneumococcal conjugate vaccine; N = total number of subjects who received study vaccine.
a. Number of subjects reporting at least 1 event of type specified. For "Any Event," it 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. For "Any Event," it represents the total number of events.

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.

AEs after 13vPnC vaccination judged by the Investigator as possibly related to study vaccine are presented in Table 11.

Table 11. Adverse Events Judged by the Investigator as Possibly Related to Study Vaccine From Visit 1 to Visit 2 – Safety Population

System Organ Class Preferred Term	13vPnC N=1049		
	Number of Subjects[a]	%	Number of Events[b]
Any event	16	1.5	19
Gastrointestinal disorders	4	0.4	4
Nausea	2	0.2	2
Diarrhoea	1	0.1	1
Retching	1	0.1	1
General disorders and administration site conditions	6	0.6	6
Injection site pain	2	0.2	2
Fatigue	1	0.1	1
Injection site haematoma	1	0.1	1
Injection site pruritus	1	0.1	1
Injection site swelling	1	0.1	1
Infections and infestations	1	0.1	1
Cellulitis	1	0.1	1
Investigations	1	0.1	1
Blood glucose increased	1	0.1	1
Musculoskeletal and connective tissue disorders	4	0.4	4
Myalgia	2	0.2	2
Musculoskeletal pain	1	0.1	1
Pain in extremity	1	0.1	1
Nervous system disorders	1	0.1	1
Paraesthesia	1	0.1	1
Skin and subcutaneous tissue disorders	2	0.2	2
Dermatitis allergic	1	0.1	1
Skin discolouration	1	0.1	1

Data presented were from Visit 1 (13vPnC) to Visit 2 (29 to 43 days after Visit 1).
13vPnC = 13-valent pneumococcal conjugate vaccine; N = total number of subjects who received study vaccine.

a. Number of subjects reporting at least 1 event of type specified. For "Any Event," it 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. For "Any Event," it represents the total number of events.

AEs judged by the Investigator as possibly related to 13vPnC at the 6-month follow-up telephone contact are presented in Table 12.

Table 12. Adverse Events Judged by the Investigator as Possibly Related to Study Vaccine as Reported at the 6-Month Follow-Up Telephone Contact – Safety Population

System Organ Class Preferred Term	13vPnC N=1049		
	Number of Subjects[a]	%	Number of Events[b]
Any event	2	0.2	5
Musculoskeletal and connective tissue disorders	1	0.1	4
Arthralgia	1	0.1	1
Bursitis	1	0.1	2
Tendonitis	1	0.1	1
Nervous system disorders	1	0.1	1
Guillain-Barre syndrome	1	0.1	1

Non-serious and serious adverse events are not separated out.
Data presented are for the period after Visit 2 (29 to 43 days after vaccination) to the 6-month telephone contact.
13vPnC = 13-valent pneumococcal conjugate vaccine; N = total number of subjects who received study vaccine.
a. Number of subjects reporting at least 1 event of type specified. For "Any Event," it 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. For "Any Event," it represents the total number of events.

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

No SAEs were assessed by the Investigator as at least possibly related to 13vPnC during the period from Visit 1 (13vPnC) to Visit 2 (29 to 43 days after Visit 1).

At the 6-month follow-up telephone contact, only 1 SAE was assessed by the Investigator as possibly related to 13vPnC. This subject was a 78-year-old female subject who developed Guillain-Barre syndrome on Day 123 after vaccination with 13vPnC. Other possible risk factors included vaccination with influenza vaccine (on day 29 after vaccination with 13vPnC), and an infectious origin (varicella zoster was suspected because of eczema in scapula area, but diagnosis was not confirmed).

Discontinuations due to Adverse Events (Excluding Deaths): In this study, subjects received 1 dose of 13vPnC and were followed up for safety only. None of the subjects withdrew from the study because of safety-related reasons.

Deaths: Three subjects died during the study (Table 13). None of the deaths were related to vaccination with 13vPnC.

Table 13. Summary of Deaths

Serial Number/Age/Sex	Cause of Death	Days Since Vaccination
1/69/Female	Metastatic adenocarcinoma	145
2/70/Male	Lung cancer	191
3/78/Male	Septic shock	185

CONCLUSION: The analysis of safety identified no notable safety concerns; the incidence of local reactions and systemic events were consistent with those reported from other studies with 13vPnC to date. These results indicate that 13vPnC may be given safely to adults after prior vaccination with 1 or more doses of 23vPS.