Protocol B7471027

A PHASE 3, RANDOMIZED, PARTIALLY DOUBLE-BLIND TRIAL TO EVALUATE THE SAFETY AND IMMUNOGENICITY OF 20-VALENT PNEUMOCOCCAL CONJUGATE VACCINE IN HEALTHY TODDLERS 12 THROUGH 23 MONTHS OF AGE WITH 2 PRIOR INFANT DOSES OF PREVENAR 13

Statistical Analysis Plan (SAP)

Version: 1

Date: 04 May 2022

[redacted]

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1. VERSION HISTORY

Table 1. Summary of Changes

Version/ Date	Associated Protocol Amendment	Rationale	Specific Changes
1 04 May 2022	Original 10 Dec 2021	N/A	N/A

2. INTRODUCTION

This SAP provides the detailed methodology for summary and statistical analyses of the data collected in Study B7471027. This document may modify the plans outlined in the protocol; however, any major modifications of the primary endpoint definition or its analysis will also be reflected in a protocol amendment.

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2.2. Study Objectives, Endpoints, and Estimands

Objectives	Endpoints	Estimands
Primary Safety Objective	**Primary Safety Endpoints**	**Primary Safety Estimands**
• To describe the safety profile of 20vPnC	• Prompted local reactions (redness, swelling, and pain at the injection site) • Prompted systemic events (fever, decreased appetite, drowsiness/increased sleep, and irritability) • AEs • SAEs	In participants receiving at least 1 dose of study intervention with safety follow-up after the assigned vaccination: • The percentage of participants reporting prompted local reactions within 7 days after the last assigned vaccination in each group • The percentage of participants reporting prompted systemic events within 7 days after the last assigned vaccination in each group • The percentage of participants reporting AEs within 1 month after the last assigned vaccination in each group • The percentage of participants reporting SAEs within 1 month after the last assigned vaccination in each group
Primary Immunogenicity Objective	**Primary Immunogenicity Endpoint**	**Primary Immunogenicity Estimand**
• To describe the immune responses to the additional 7 serotypes after 1 or 2 doses of 20vPnC	• Pneumococcal serotype-specific IgG concentration	In participants complying with the key protocol criteria (evaluable participants) in each group: • Percentages of participants with predefined serotype-specific IgG concentrations for the 7 additional serotypes 1 month after the last assigned vaccination
Secondary Immunogenicity Objective	**Secondary Immunogenicity Endpoints**	**Secondary Immunogenicity Estimands**
• To further describe the immune response of 20vPnC after 1 or 2 doses	• Pneumococcal serotype-specific IgG concentration • Pneumococcal serotype-specific OPA titers	In evaluable participants in each group: • IgG GMCs for the vaccine serotypes 1 month after the last assigned vaccination • Percentages of participants with predefined IgG concentrations for the 13 matched serotypes 1 month after the last assigned vaccination • OPA GMTs for the vaccine serotypes 1 month after the last assigned vaccination

2.3. Study Design

This Phase 3, multicenter, randomized, partially double-blind study will be conducted at investigator sites in Europe.

Approximately 360 toddlers ≥12 to <24 months of age at the time of consent, who previously received 2 infant doses of 13vPnC (prior to 12 months of age), will be enrolled and randomized in a 1:1:1 ratio to receive either 1 or 2 doses of 20vPnC, or 1 dose of 13vPnC (control). The vaccine in toddlers randomized to receive 1 dose will be double-blind, as 20vPnC and 13vPnC have the same appearance and a single dose will be administered at Visit 1 of the study. Toddlers randomized to receive 1 dose are to return approximately 1 month later for Visit 2 for collection of safety information and a blood draw. For participants randomized to 2 doses of 20vPnC, the parent(s)/legal guardian(s) and site staff will know that these participants will need to return for a second vaccination visit and that they will receive 20vPnC at both Visit 1 and Visit 2 (approximately 2 months later), and after the second dose will return approximately 1 month later for Visit 3 for collection of safety information and a blood draw. The last assigned vaccinations will be the single vaccination at Visit 1 in the groups randomized to receive 1 dose of 20vPnC or 13vPnC (control) and the second vaccination given at Visit 2 in the group randomized to receive 2 doses.

Blood will be drawn from all participants for immunogenicity assessments before administration of the study intervention and 1 month after the vaccination (last vaccination in the group receiving 2 doses) in each vaccine group.

Participants will be observed for 30 minutes after each vaccination and any reactions occurring during that time will be recorded as immediate AEs. Prompted local reactions (redness, swelling, and pain at the 20vPnC or 13vPnC injection site), systemic events (fever, decreased appetite, drowsiness/increased sleep, and irritability), and use of antipyretic/pain medications occurring within 7 days after each vaccination will be collected via a provided

e-diary (or e-diary application). AEs and SAEs will be collected from the signing of informed consent to 1 month after the last dose.

3. ENDPOINTS AND BASELINE VARIABLES: DEFINITIONS AND CONVENTIONS

3.1. Primary Endpoints

3.1.1. Primary Safety Endpoints

- Prompted local reactions (redness, swelling, and pain at the injection site) within 7 days after the last assigned vaccination.
- Prompted systemic events (fever, decreased appetite, drowsiness/increased sleep, and irritability) within 7 days after the last assigned vaccination.
- AEs from vaccination to 1 month after the last assigned vaccination.
- SAEs from vaccination to 1 month after the last assigned vaccination.

3.1.1.1. Local Reactions

The local reactions assessed and reported in the e-diary are redness, swelling, and pain at the 20vPnC or 13vPnC injection site, from Day 1 through Day 7 after each dose, where Day 1 is the day of each dose. This section describes derivations with details for the assessment of local reactions: severity level, duration, and onset day.

Severity and Maximum Severity

Redness and swelling will be measured and recorded in measuring device (caliper) units (range: 1 to 14, and >14), and then categorized during analysis as mild, moderate, or severe based on the grading scale in Table 2. Grade 4 will not be collected in the e-diary but as an AE on the CRF. Measuring device units can be converted to centimeters according to the following scale: 1 measuring device unit = 0.5 cm. Pain at the vaccine injection site will be assessed by the participant's parent(s)/legal guardian(s) as mild, moderate, or severe according to the grading scale in Table 2.

Table 2. Grading Scales for Local Reactions

Local Reaction	GRADE 1 Mild	GRADE 2 Moderate	GRADE 3[a] Severe	GRADE 4[b]
Redness	1 to 4 caliper units (or measuring device units) = >0 to 2.0 cm	5 to 14 caliper units (or measuring device units) = >2.0 to 7.0 cm	>14 caliper units (or measuring device units) = >7.0 cm	Necrosis or exfoliative dermatitis
Swelling	1 to 4 caliper units (or measuring device units) = >0 to 2.0 cm	5 to 14 caliper units (or measuring device units) = >2.0 to 7.0 cm	>14 caliper units (or measuring device units) = >7.0 cm	Necrosis
Pain at injection site	Hurts if gently touched (eg, whimpers, winces, protests, or withdraws)	Hurts if gently touched, with crying	Causes limitation of limb movement	Emergency room visit or hospitalization for severe pain (tenderness) at injection site

Note: If the size of the redness and/or swelling falls between 2 measuring device units, the higher measuring device unit number will be recorded in the e-diary.

a. Parents/legal guardians of the participants experiencing local reactions >14 caliper units (>7.0 cm) are to be contacted by the study site. An unscheduled visit may be required.
b. Grade 4 assessment should be made by the investigator. Grade 4 will not be collected in the e-diary but as an AE on the CRF.

For each local reaction after each dose, the maximum severity grade will be derived for the e-diary collection period (Day 1 through Day 7, where Day 1 is the day of each dose) as follows:

> maximum severity grade = highest grade (maximum severity) within 7 days after the last assigned vaccination (Day 1 through Day 7) among severity grades reported for that local reaction in the e-diary.

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3.1.1.2. Systemic Events (Systemic Event Symptoms and Fever)

The systemic events assessed and recorded in the e-diary are fever, decreased appetite, drowsiness/increased sleep, and irritability from Day 1 through Day 7, where Day 1 is the day of each dose. The derivations for systemic events will be handled similarly to the way local reactions are handled for severity level, duration, and onset day (see Section 3.1.1.1).

The systemic events of decreased appetite, irritability, and drowsiness/increased sleep will be assessed by participant's parent(s)/legal guardian(s) as mild, moderate, or severe according to the grading scale in Table 3. Grade 4 will not be collected in the e-diary but will be collected as an AE on the CRF.

Table 3. Grading Scales for Systemic Events

Systemic Event	Mild Grade 1	Moderate Grade 2	Severe Grade 3	Grade 4[a]
Decreased appetite (loss of appetite)	Decreased interest in eating	Decreased oral intake	Refusal to feed	Emergency room visit or hospitalization for severe decreased appetite (loss of appetite)
Drowsiness (increased sleep)	Increased or prolonged sleeping bouts	Slightly subdued interfering with daily activity	Disabling not interested in usual daily activity	Emergency room visit or hospitalization for severe drowsiness (increased sleep)
Irritability (fussiness) (synonymous with restless sleep; decreased sleep)	Easily consolable	Requiring increased attention	Inconsolable; crying cannot be comforted	Emergency room visit or hospitalization for severe irritability (fussiness)

Abbreviation: CRF = case report form.

a. Grade 4 assessment should be made by the investigator. Grade 4 will not be collected in the e-diary but will be collected as an AE on the CRF.

Maximum temperature range over the period from Day 1 through Day 7 will be mapped into the ranges described in Table 4 for summary of maximum temperature. Fever will be grouped into ranges for the analysis according to Table 4.

Table 4. Ranges for Fever

≥38.0°C to 38.4°C
>38.4°C to 38.9°C
>38.9°C to 40.0°C
>40.0°C

Note: Fever is defined as temperature ≥38.0°C.

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3.1.1.4. Adverse Events

AEs will be categorized according to MedDRA terms. AEs will be assessed from the time of informed consent through 1 month after the last assigned vaccination.

The primary endpoint "AEs from vaccination through 1 month after the last assigned vaccination" and other supportive AE endpoints will be summarized by SOC and PT on a participant level.

This primary endpoint will be supported by summaries and listings of related AEs, severe AEs, and immediate AEs (within the first 30 minutes after each dose).

AE reporting will be based on the specific reporting period. Missing AE start dates will be imputed following the Pfizer data standard rules as described in Section 5.3.

A 3-tier approach will be used to summarize AEs from vaccination through 1 month after the last assigned vaccination. Under this approach, AEs are classified into 1 of 3 tiers. Different analyses will be performed for different tiers (see Section 6.1.1.3.1). The control group for both the 1-dose and 2-dose 20vPnC groups (after the last assigned dose) is the 13vPnC group.

- Tier 1 events: These are prespecified events of clinical importance and are identified in a list in the product's Safety Review Plan. No Tier 1 events have been identified to date for 20vPnC.

- Tier 2 events: These are events that are not Tier 1, but are "common." A MedDRA PT is defined as a Tier 2 event if there are at least 4 participants with the AE term in at least 1 vaccine group.

- Tier 3 events: These are events that are neither Tier 1 nor Tier 2.

3.1.1.5. Serious Adverse Events

SAEs will be categorized according to MedDRA terms. SAEs will be collected from the signing of the ICD through the end of the study.

3.1.2. Primary Pneumococcal Immunogenicity Endpoints

- Pneumococcal serotype-specific IgG concentration 1 month after the last dose.

Concentrations of anticapsular IgG for the 7 additional serotypes (8, 10A, 11A, 12F, 15B, 22F, and 33F) will be determined in all participants at 1 month after the last assigned vaccination using the Luminex assay. Results will be reported as IgG concentrations.

To support the primary pneumococcal immunogenicity estimands, IgG concentrations for the 7 additional serotypes will be classified based on a serotype-specific IgG reference concentration of 0.35 µg/mL.

3.2. Secondary Endpoints

- Pneumococcal serotype-specific IgG concentration 1 month after the last assigned vaccination.

To support the secondary pneumococcal immunogenicity estimands, IgG concentrations for the 13 matched serotypes will be classified based on serotype-specific IgG reference concentrations of 0.35 µg/mL, except for 0.23 µg/mL for serotype 5, 0.10 µg/mL for serotype 6B, and 0.12 µg/mL for serotype 19A.

- Pneumococcal serotype-specific OPA titers 1 month after the last assigned vaccination.

OPA titers will be determined in a random subset of participants from each vaccine group. Further details of the subsetting will be described in a memo to the unblinded statistical team before any testing proceeds.

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3.4. Baseline Variables

Measurements or samples collected prior to Dose 1 are considered the baseline data for the assessments.

3.4.1. Demographics and Medical History

The demographic variables are age at each dose (in months), sex (male or female), race (Black or African American, American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, White, multiracial, and not reported), and ethnicity (Hispanic/Latino, non-Hispanic/non-Latino, and not reported). Age at vaccination in months will be derived

based on the participant's birth date. For example, if a participant's birth date is 30 Jan 2021, the participant will be 12 months old from 30 Jan 2022 through 28 Feb 2022 and will be 13 months old from 1 Mar 2022 through 29 Mar 2022. In cases where more than 1 category is selected for race, the participant would be counted under the category "multiracial" for analysis.

For participants who were randomized but not vaccinated, the randomization date will be used in place of the date of vaccination for age calculation. If the randomization date is also missing, then the informed consent date will be used for age calculation.

Medical history will be categorized according to MedDRA.

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3.4.3. Prior/Concomitant Vaccines and Concomitant Medications

Other vaccines licensed and recommended for this age group may be administered as specified in the protocol. Concomitant medications will be recorded only if they were used to treat SAEs. Concomitant and prior vaccines and concomitant medications will be coded using the WHO Drug Dictionary.

Participants' time since the last 13vPnC vaccination will be calculated.

3.5. Safety Endpoints

Local reactions, systemic events, AEs, and SAEs have been described above in the Primary Endpoints section.

4. ANALYSIS SETS (POPULATIONS FOR ANALYSIS)

Analysis populations are defined for the statistical analysis of safety and immunogenicity results in the table below.

Population	Description
Enrolled	"Enrolled" means all participants who sign the ICD.
Randomized	All participants who are assigned a randomization number in the IWR system.
Evaluable immunogenicity	All participants who: 1. Are eligible, 2. Receive vaccinations to which they were randomized, 3. Have at least 1 valid immunogenicity result from 1 month after the last assigned vaccination collected within 27 to 56 days after the dose, and

Population	Description
	4. Have no other major protocol deviations as determined by the clinician The evaluable immunogenicity population will be used as the primary analysis population for the pneumococcal immunogenicity results. Participants will be grouped according to the vaccine as randomized in the analysis based on the evaluable immunogenicity population.
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Safety	All participants who receive at least 1 dose of the study intervention and have safety data reported after any dose. Participants will be grouped according to the vaccine as administered in the analysis based on the safety population.

For the evaluable immunogenicity population definition, the blood collection window has been expanded by 1 extra day before and 14 days after the protocol-specified blood collection window of 28 to 42 days defined in the protocol, for consistency with established rules in the Prevenar 13® development program. A major protocol deviation is a protocol deviation that, in the opinion of the Pfizer clinician or medical monitor, would materially affect assessment of immunogenicity, eg participant receipt of a prohibited vaccine or medication that might affect immune response, or a medication error with suspected decrease in potency of the vaccine.

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5. GENERAL METHODOLOGY AND CONVENTIONS

The planned statistical analyses will be carried out when all safety and immunogenicity data for all participants are available and released.

5.1. Hypotheses and Decision Rules

No hypothesis testing will be performed and no formal statistical decision rules apply in this study. A descriptive estimation approach will be used to assess all safety and immunogenicity objectives.

5.2. General Methods

Time points for local reactions and systemic events refer to data within 7 days after each dose.

CIs for all endpoints in the statistical analysis will be presented as 2-sided at the 95% level.

5.2.1. Analyses for Binary Endpoints

Descriptive statistics for categorical variables (eg, proportions) are the percentage (%), the numerator (n) and the denominator (N) used in the percentage calculation, and the 95% CI where applicable.

The exact 95% CI for binary endpoints for each group will be computed using the F distribution (Clopper-Pearson).[1]

The 3-tier approach will be used to summarize AEs. For both Tier 1 (if any are identified during the study) and Tier 2 events, a 95% CI for the between-group difference in proportions will be calculated based on the Miettinen and Nurminen method.[2] In addition, for Tier 1 events (if any), the asymptotic p-values will also be presented for the difference in proportions, based on the same test statistic and under the assumption that the test statistic is asymptotically normally distributed. For Tier 3 events, counts and percentages for each vaccine group will be provided.

5.2.2. Analyses for Continuous Endpoints

Unless otherwise stated, descriptive statistics for continuous variables are n, mean, median, standard deviation, minimum, and maximum.

5.2.2.1. Geometric Means

For immunogenicity results of serotype-specific IgG concentrations and OPA titers, the geometric means will be computed along with associated 95% CIs. The GM and associated 2-sided 95% CI will be calculated as the mean of the assay results on the natural logarithmic scale based on the t distribution, and then exponentiating the results.

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5.3. Methods to Manage Missing Data

A partial AE start date (missing day or missing both month and day) will be imputed by assigning the earliest possible start date using all available information, such as the stop date of the AE and the vaccination date(s) from the same participant, following the Pfizer standard of handling incomplete AE start date. A complete missing start date for an AE is not allowed in the data collection.

The LLOQ for each assay will be provided by Vaccines Research and Development as part of the electronic data transfer or within the Clinical Testing Completion Memo prior to statistical analysis. Assay results above the LLOQ will be reported, and values below the LLOQ, denoted as BLQ, will be imputed as 0.5 × LLOQ for analysis.

No additional imputation will be applied to other missing data.

6. ANALYSES AND SUMMARIES

6.1. Primary Endpoints

6.1.1. Primary Safety Endpoints

6.1.1.1. Local Reactions

6.1.1.1.1. Main Analysis

- Estimand: Proportions of participants reporting prompted local reactions (redness, swelling, and pain at the injection site) within 7 days after the last assigned vaccination.
- Analysis set**:** Safety population (Section 4).
- Analysis time point**:** Within 7 days after the last assigned vaccination.
- Analysis methodology**:** Descriptive statistics.
- Reporting results: Proportions of participants reporting prompted local reactions will be summarized by maximum severity level. The percentage (%), the numerator (n), and the denominator (N) used in the percentage calculation, and the corresponding 95% Clopper-Pearson CI will be presented for each vaccination group.

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6.1.1.2. Systemic Events

6.1.1.2.1. Main Analysis

- Estimand: Proportions of participants reporting prompted systemic events (fever, decreased appetite, irritability, and drowsiness/increased sleep) within 7 days after the last assigned vaccination.
- Analysis set**:** Safety population (Section 4).
- Analysis time point**:** Within 7 days after the last assigned vaccination.
- Analysis methodology**:** Descriptive statistics.
- Reporting results: The percentage (%), the numerator (n), and the denominator (N) used in the percentage calculation, and the corresponding 95% Clopper-Pearson CI will be presented for each vaccination group.

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6.1.1.3. Adverse Events

6.1.1.3.1. Main Analysis

- Estimand: Proportions of participants reporting AEs.
- Analysis set: Safety population (Section 4).
- Analysis time point: Vaccination to 1 month after the last assigned vaccination (in the 2-dose group this will be the last vaccination to 1 month after the last assigned vaccination for reporting).
- Analysis methodology: Descriptive statistics.
- Reporting results: For all 3 tiers, the numerator (n) and the denominator (N) used in the percentage calculation, the percentage (%), and the corresponding 2-sided 95% CI for participants reporting any AE, each SOC, and each PT within each SOC will be presented by vaccine group.

In addition, for AEs classified as Tier 2 events, the differences in percentages and associated 2-sided 95% CIs for between-group comparisons (20vPnC - 13vPnC control) will be provided for each of the 20vPnC vaccine groups (the comparison will be the percentage from the last vaccination to 1 month after the last vaccination in the 2-dose group).

Further, for Tier 1 events, if any are identified, the difference in percentages, the associated 2-sided 95% CI for the risk difference, and the asymptotic p-values will also be provided.

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6.1.1.4. Serious Adverse Events

6.1.1.4.1. Main Analysis

- Estimand: Proportions of participants reporting SAEs.
- Analysis set: Safety population (Section 4).
- Analysis time point: Vaccination to 1 month after the last assigned vaccination (the last vaccination to 1 month after the last vaccination in the 2-dose group).
- Analysis methodology: Descriptive statistics.
- Reporting results: The numerator (n), and the denominator (N) used in the percentage calculation, the percentage (%), and corresponding 2-sided 95% CI will be presented for each vaccination group.

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6.1.2. Primary Immunogenicity Endpoints

6.1.2.1. Participants With Predefined Pneumococcal Serotype-Specific IgG Concentrations at 1 Month After the Last Assigned Vaccination for the 7 Additional Serotypes

- Estimand: For each of the 7 additional serotypes in 20vPnC, the percentages of participants with predefined serotype-specific IgG concentrations.
- Analysis set: Evaluable immunogenicity population (Section 4).
- Analysis time point: 1 Month after the last assigned vaccination.
- Analysis methodology: Descriptive statistics.
- Reporting results: For each of the 7 additional serotypes, the numerator (n) and the denominator (N) used in the percentage calculation, the percentage (%), and the corresponding 2-sided 95% CI for participants with predefined IgG concentrations from each vaccine group.

Figures:

Percentages (and corresponding 95% CIs) of participants achieving predefined serotype-specific IgG concentrations 1 month after the last dose will be presented in a vertical bar chart.

6.2. Secondary Endpoints

6.2.1. IgG Concentration

6.2.1.1. Pneumococcal Serotype-Specific IgG Concentrations

- Estimand: Pneumococcal serotype-specific IgG concentrations 1 month after the last assigned vaccination.
- Analysis set: Evaluable immunogenicity population (Section 4).
- Analysis time point: 1 Month after the last assigned vaccination.
- Analysis methodology: Descriptive statistics.

- Reporting results: IgG GMCs with their associated 95% CIs will be summarized at 1 month after the last assigned vaccination for each 20vPnC serotype by each vaccination group.

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6.2.1.2. Participants With Predefined Pneumococcal Serotype-Specific IgG Concentrations at 1 Month After the Last Assigned Vaccination for the 13 Matched Serotypes

- Estimand: For each of the 13 matched serotypes in 20vPnC, the percentages of participants with predefined serotype-specific IgG concentrations.
- Analysis set: Evaluable immunogenicity population (Section 4).
- Analysis time point: 1 Month after the last assigned vaccination.
- Analysis methodology: Descriptive statistics.
- Reporting results: For each of the 13 matched serotypes, the numerator (n) and the denominator (N) used in the percentage calculation, the percentage (%), and the corresponding 2-sided 95% CI for participants with predefined IgG concentrations from each vaccine group.

Figures:

Percentages (and corresponding 95% CIs) of participants achieving predefined serotype-specific IgG concentrations 1 month after the last dose will be presented in a vertical bar chart.

6.2.2. OPA Titers

- Estimand: Pneumococcal serotype-specific OPA titers 1 month after the last dose.
- Analysis set: Evaluable immunogenicity population (Section 4).
- Analysis time point: 1 Month after the last assigned vaccination.
- Analysis methodology: Descriptive statistics.
- Reporting results: OPA GMTs with their associated 95% CIs will be summarized separately before and 1 month after vaccination for each 20vPnC serotype by each vaccination group.

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6.5. Baseline and Other Summaries and Analyses

6.5.1. Baseline Summaries

6.5.1.1. Demographic Characteristics

Demographic characteristics, including age at vaccination, sex, race, and ethnicity, will be summarized for the safety population and the evaluable immunogenicity population by vaccination group.

6.5.1.2. Medical History

Each reported medical history term will be mapped to an SOC and PT according to MedDRA. The number and percentage of participants with an assigned vaccine having at least 1 diagnosis, overall and at each SOC and PT level, will be summarized by vaccination group for the safety population.

6.5.2. Study Conduct and Participant Disposition

6.5.2.1. Participant Disposition

The number and percentage of randomized participants will be included in the participant disposition summary. In addition, the numbers and percentages of participants who receive each vaccination (Dose 1 or 2), who completed the follow-up visits (1 month after the last assigned vaccination), who completed all visits, and who withdrew, along with the reasons for withdrawal, will be tabulated by vaccine group (according to randomized group assignment). The reasons for withdrawal will be those as specified in the database.

Randomized participants excluded from the safety or immunogenicity analysis populations will also be summarized separately, along with the reasons for exclusion, by vaccine group.

6.5.2.2. Blood Samples for Assay

The number and percentage of enrolled participants providing blood samples within and outside of protocol-specified time frames will be tabulated.

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6.5.3. Investigational Vaccine

6.5.3.1. Vaccination Timing and Administration

The number and percentage of participants enrolled and receiving vaccine (2-dose group only) within the protocol-specified time frame, as well as before and after the specified time frame, will be tabulated for the 2-dose group. The denominator for the percentages is the total number of participants in the given vaccination group.

6.5.4. Concomitant Vaccines, Medications, and Nondrug Treatments

Each prior/concomitant vaccine will be summarized according to the ATC fourth-level classification. The number and percentage of enrolled participants receiving concomitant vaccines will be summarized according to vaccination group.

Concomitant medications used to treat SAEs will be summarized from the time of vaccination to 1 month after the last vaccination (safety population).

Participants' time since each previous dose of 13vPnC will be summarized descriptively.

6.6. Safety Summaries and Analyses

The summaries and analyses of the safety measures local reactions, systemic events, AEs, and SAEs are described under the Primary Safety Endpoints section (see Section 6.1.1).

7. INTERIM ANALYSES

No interim analysis is planned in this study. Statistical analyses will be carried out when the final data for the specified analyses are available.

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7.1. Introduction

Not applicable.

7.2. Interim Analyses and Summaries

Not applicable.

8. REFERENCES

1 Collett D. Statistical inference for binary data. Chapter 2. In: Modelling binary data. London, England: Chapman & Hall; 1991:17-42.

2 Miettinen O, Nurminen M. Comparative analysis of two rates. Stat Med. 1985;4(2):213-26.

9. APPENDICES

Appendix 1. List of Abbreviations

Abbreviation	Term
13vPnC	13-valent pneumococcal conjugate vaccine
20vPnC	20-valent pneumococcal conjugate vaccine
AE	adverse event
ATC	Anatomic Therapeutic Chemical
BLQ	below the limit of quantitation
CI	confidence interval
CRF	case report form
e-diary	electronic diary
CCI	[redacted]
GMC	geometric mean concentration
CCI	[redacted]
GMT	geometric mean titer
ICD	informed consent document
IgG	immunoglobulin G
IWR	interactive Web-based response
LLOQ	lower limit of quantitation
MedDRA	Medical Dictionary for Regulatory Activities
N/A	not applicable
OPA	opsonophagocytic activity
PT	preferred term
CCI	[redacted]
SAE	serious adverse event
SAP	statistical analysis plan
SOC	system organ class
WHO	World Health Organization