GlaxoSmithKline	**Statistical Analysis Plan**
Detailed Title:	A Phase IIIB, randomized, open-label, multicenter clinical trial to assess the immunogenicity and safety of GSK Biologicals' Herpes Zoster vaccine GSK1437173A when co-administered with *Prevenar13* in adults aged 50 years and older.
eTrack study number and Abbreviated Title	204487 (ZOSTER-059 PRI)
Scope:	All analyses planned per protocol.
Date of Statistical Analysis Plan	Final: 13 April 2018 Amendment 1: 11 June 2019 Amendment 2: 20 November 2019 ***Amendment 3 Final: 23 November 2020***

APP 9000058193 Statistical Analysis Plan Template V4 (Effective date: 3 June 2019)

CONFIDENTIAL

TABLE OF CONTENTS

PAGE

LIST OF TABLES

PAGE

LIST OF FIGURES

PAGE

LIST OF TEMPLATES

PAGE

LIST OF ABBREVIATIONS

AE	Adverse event
AES	***Adverse Event Screen***
ANCOVA	Analysis of Covariance
$AS01_B$:	MPL, QS21, liposome based Adjuvant System (50 μg MPL and 50 μg QS21)
BS	Blood Sampling
CDR	Clinical Data Reviewer
CI	Confidence Interval
Co-Ad	Co-administration
CRDL	Clinical Research and Development Lead
CRF	Case Report Form
CSR	Clinical Study Report
CTRS	Clinical Trial Registry Summary
EL.U/ml	ELISA unit per milliliter
Eli Type	Internal GSK database code for type of elimination code
ELISA	Enzyme-linked immunosorbent assay
EoS	End of Study
ES	Exposed Set (formally called 'Total Vaccinated Cohort')
GMC	Geometric mean antibody concentration
GMT	Geometric mean antibody titre
GSK	GlaxoSmithKline
IU/ml	International units per milliliter
LL	Lower Limit of the confidence interval
LLOQ	Lower Limit of Quantification

MedDRA	Medical Dictionary for Regulatory Activities
MGI	***Mean Geometric Increase***
MOPA	***Multiplex Opsonophagocytosis Assay***
PCD	Primary Completion Date
PD	Protocol Deviation
PDMP	Protocol Deviation Management Plan
PPS	Per-Protocol Set (formally called 'According to Protocol')
PT	***Preferred Term***
SAE	Serious adverse event
SAP	Statistical Analysis Plan
SBIR	GSK Internet Randomization System
SD	Standard Deviation
SHS	Study Headline Summary
SOC	***System Organ Class***
SUSAR	Suspected Unexpected Serious Adverse Reactions
TFL	Tables Figures and Listings
TOC	Table of Content
UL	Upper Limit of the confidence interval
ULOQ	Upper Limit of Quantification
VRR	Vaccine response rate
YOA	***Years of Age***

1. DOCUMENT HISTORY

Date	Description	Protocol Version
13 APR 2018	First Version	Amendment 2: 30 JAN 2018
11 JUN 2019	Amendment 1 - Summary of changes as below: - As per new process applicable, the front page has been modified to remove the names of all the contributing author and reviewers. Also, sign-off is only required to be done by Lead Statistician - Updated LLOQ and newly calculated ULOQ for the 13 pneumococcal serotypes tested by MOPA have been added and accordingly analysis of immunogenicity section has been updated. - Consort table have been added for subject disposition. - Additional tables for fatal serious adverse events (SAEs) and grade 3 non-serious unsolicited adverse events (AEs) have been added. - The term "symptom" has been changed to "adverse event (AE)" in endpoints, table titles and content for solicited AEs, unsolicited AEs, SAEs, and potential immune mediated diseases (pIMDs). - Table 'Summary of temperature value by half degree increment reported during the 7-day (Days 1-7) post-vaccination following each dose' has been removed - Sequence of analysis has been updated - Inclusion of Enrolled and Randomized Set definition - Code 1500 in elimination codes has been removed and added under code 1070. Also, mandatory columns have been added in the elimination table under 'Elimination from PPS section.	Amendment 2: 30 JAN 2018
20-NOV-2019	Amendment 2 - Summary of changes as below: - The active phase analysis has been removed as a request for a CTRS posting extension has been submitted to NIH; complete CTRS posting will be done at Last Subject Last Visit (LSLV) + 12 months rather than Primary Completion Date (PCD) +12 months as previously planned - Titles and Footnotes of selected templates have been updated following the Dry run kick-off meeting - Two new safety templates have been added (Templates 49 and 50)	Amendment 2: 30 JAN 2018
23-NOV-2020	***Amendment 3 – Summary of changes: -*** ***Few templates have been edited for better presentation*** ***Removal of template for vaccine response table with only one group for primary objective assessment; Addition of separate template for anti-gE seropositivity rate and GMC, list of PT codes to identify suspected HZ episode***	***Amendment 2: 30 JAN 2018***

2. STUDY DESIGN

Figure 1 Overview of Study Design

Vacc: vaccination; BS: blood sample; Pre-Vacc: pre-vaccination; FU: follow-up

Experimental design: Phase IIIB, open-label, randomized, controlled, multi-centric, and multi-country, with two parallel groups.

Duration of the study: The intended duration of the study per subject is approximately 14 months for subjects from the Co-Ad group and approximately 16 months for subjects from the Control group.

- Epoch 001: Primary starting at Visit Day 1 and ending with the phone contact at Month 16.

Primary completion date (PCD): Visit Month 5.

End of Study (EoS): Last testing results released of samples collected at Visit Month 3 (Co-Ad group) or at Visit Month 5 (Control group).

Study groups:

Table 1 Study groups and epochs foreseen in the study

Study groups	Number of subjects	Age	Epochs
			Epoch 001
Co-Ad	456	≥ 50 years	x
Control	456	≥ 50 years	x

Table 2 Study groups and treatment foreseen in the study

Treatment name	Vaccine/Product name	Study Groups	
		Co-Ad	Control
HZ/su	VZV gE	x	x
	AS01B	x	x
Prevenar13	*Prevenar 13*	x	x

Control: active control.

Vaccination schedule(s):

- Co-Ad Group:
  - at Visit Day 1: first dose of HZ/su and one dose of Prevenar13,
  - at Visit Month 2: second dose of HZ/su.
- Control Group:
  - at Visit Day 1: one dose of *Prevenar13*,
  - at Visit Month 2: first dose of HZ/su,
  - at Visit Month 4: second dose of HZ/su.

Treatment allocation: Subjects to be randomized in a 1:1 ratio at Visit Day 1 to either Co-Ad or Control group. Subjects in each group will be stratified by age with the following approximate distribution (not less than 25% in each age strata):

- 171 subjects in the 50-59 Years of Age (YOA) stratum,
- 171 subjects in the 60-69 YOA stratum, and
- 114 subjects in the ≥ 70 YOA stratum.

Blinding: open-label.

Table 3 Blinding of study epochs

Study Epochs	Blinding
Epoch 001	open

3. OBJECTIVES

3.1. Co-Primary objectives

To determine the vaccine response rate (VRR) to HZ/su (based on humoral immune response) one month after the second vaccine dose, when the first dose of HZ/su is co-administered with *Prevenar13* (Co-Ad group).

Criterion to be used:

The objective is met if the lower limit (LL) of the 95% CI of the VRR for anti-gE antibody concentrations in the Co-Ad group one month after the second vaccine dose is ≥60%.

If the above objective is met in the Co-Ad group, then the following objective will be evaluated:

To demonstrate non-inferiority of the humoral immune response to two doses of HZ/su at one month after the last vaccine dose, when the first dose of HZ/su is co-administered with *Prevenar13* (Co-Ad group) compared to when two doses of HZ/su are administered subsequent to *Prevenar13* (Control Group).

Criterion for non-inferiority:

One month after the last vaccine dose in each study group, the upper limit (UL) of the 95% confidence interval (CI) for the anti-gE antibodies Geometric Mean Concentration (GMC) ratio between the Control group and the Co-Ad group is <1.5.

If the above non-inferiority objective is met, then the following objective will be evaluated:

To demonstrate non-inferiority of the humoral immune response to *Prevenar13* at one month after the vaccine dose, when *Prevenar13 is* co-administered with the first HZ/su dose (Co-Ad group) compared to when *Prevenar13* is administered separately from HZ/su (Control group), for the 13 serotypes included in *Prevenar13* analyzed sequentially.

Criterion for non-inferiority:

One month after the Prevenar13 vaccine dose in each study group, the UL of the 95% CI for each individual pneumococcal conjugate serotype Geometric Mean Titer (GMT) ratio of the Control group over the Co-Ad group is <2.

For the co-primary objectives, fixed sequence testing which allows for full alpha propagation in pre-ordered hypotheses families will be used (see section 6.3.2.1).

3.2. Secondary objective

To evaluate the safety and reactogenicity following administration of HZ/su and *Prevenar13* vaccines, up to one month post last vaccination and during the whole follow-up period, in the Control group and the Co-Ad group.

4. ENDPOINTS

4.1. Primary endpoints

HZ/su immunogenicity:

- Vaccine response for anti-gE humoral immunogenicity, as determined by ELISA, in subjects from the Co-Ad group at one month post-dose 2, at Visit Month 3.
- Anti-gE antibody concentrations as determined by ELISA at one month post-dose 2, at Visit Month 3 for the Co-Ad group and Visit Month 5 for the Control group.

Pneumococcal vaccine immunogenicity:

- Anti-pneumococcal antibody titers for the 13 following serotypes as determined by MOPA at one month post-dose at Visit Month 1: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F.

The criteria used to define the VRR is given in Section 12.1.2.

4.2. Secondary endpoints

Occurrence of solicited local and general adverse events:

- Occurrence, duration and intensity of each solicited local adverse event within 7 days (Days 1 - 7) after each vaccination,
- Occurrence, duration, intensity and relationship to vaccination of each solicited general adverse event within 7 days (Days 1 - 7) after each vaccination.

Occurrence of unsolicited AEs:

- Occurrence, intensity and relationship to vaccination of unsolicited AEs within 30 days (Days 1 - 30) after each vaccination, according to the Medical Dictionary for Regulatory Activities (MedDRA) classification.

Occurrence of SAEs:

- Occurrence and relationship to vaccination of all SAEs from first vaccination at Day 1 up to 30 days post last vaccination.
- Occurrence and relationship to vaccination of all SAEs during the period starting after 30 days post last vaccination up to study end.

Occurrence of pIMDs:

- Occurrence and relationship to vaccination of any pIMDs from first vaccination at Day 1 up to 30 days post last vaccination.
- Occurrence of any pIMDs during the period starting after 30 days post last vaccination up to study end.

5. ANALYSIS SETS

5.1. Definition

5.1.1. Enrolled Set

The Enrolled Set will include all the subjects for whom valid signed informed consent form is available.

5.1.2. Randomized Set

The Randomized Set will include all the subjects for whom valid signed informed consent form is available and treatment is allocated.

5.1.3. Exposed Set (ES)*

The Exposed set (ES) will include all subjects with at least one vaccine administration documented:

- The ES for analysis of solicited adverse events will include all subjects with at least one documented administered vaccine.
- The ES for analysis of unsolicited AEs, SAEs and pIMDs will include all subjects with at least one vaccine administered.
- The ES for analysis of immunogenicity will include vaccinated subjects for whom immunogenicity data are available.

The ES analysis will be performed per treatment actually administered (at Dose 1).

5.1.4. Per-protocol set (PPS)* for immunogenicity

The Per-protocol set for immunogenicity will include all evaluable subjects:

- who meet all eligibility criteria,
- who comply with the procedures and intervals allowed for the analysis,
- who do not meet any of the criteria for elimination during the study,
- for whom data concerning immunogenicity endpoint measures are available.

** Note that in order to align to ICH and cDISC terminology the Total Vaccinated Cohort and the Per- Protocol cohort have been renamed Exposed Set (ES) and Per-Protocol Set (PPS) respectively.*

The intervals allowed for the inclusion in the ***PPS for immunogenicity*** are defined as follows:

	Group	Interval	Allowed interval for PPS analysis of immunogenicity
Interval between vaccinations	Co-Ad	HZ/su (Dose 1) – HZ/su (Dose 2)	49-83 Days
	Control	*Prevenar13* (Dose 1) – HZ/su (Dose 2)	>= 60 days*
	Control	HZ/su (Dose 2) – HZ/su (Dose 3)	49-83 Days
Interval between vaccination and blood sample taken	Co-Ad	*Prevenar13* (Dose 1) – Visit Month 1 for BS	28-48 Days*
	Co-Ad	HZ/su (Dose 2) – Visit Month 3 for BS	28-48 days*
	Control	*Prevenar13* (Dose 1) – Visit Month 1 for BS	28-48 Days*
	Control	HZ/su (Dose 3)– Visit Month 5 for BS	28-48 days*

BS= blood sampling taken; *please note these intervals differ from protocol amendment 2 Table 8 and 9 to increase the number of evaluable subjects while not compromising the interpretation of immunogenicity data

5.2. Criteria for eliminating data from Analysis Sets

Elimination codes are used to identify subjects to be eliminated from analysis. Detail is provided below for each set.

5.2.1. Elimination from Enrolled Set

Code 900 (invalid informed consent or fraud data) will be used for identifying subjects eliminated from Enrolled Set.

5.2.2. Elimination from Randomized Set

Code 900 (invalid informed consent or fraud data) and code 1010 (vaccine number not allocated) will be used for identifying subjects eliminated from Randomized Set.

5.2.3. Elimination from Exposed Set (ES)

Code 1030 (Study vaccine not administered at all), code 1010 (vaccine number not allocated) and code 900 (invalid informed consent or fraud data) will be used for identifying subjects eliminated from ES.

5.2.4. Elimination from Per-protocol analysis Set (PPS)

A subject will be excluded from the PPS analysis under the following conditions:

Code	Condition under which the code is used	Visit (timepoints) where the code is applicable	Applicable for analysis set
900	Invalid informed consent or fraudulent data. Subjects excluded from all stat analysis Note: Subjects receiving a code 900 should not receive any other elimination codes.	All	All
1010	Vaccine number not allocated Note: Subjects receiving a code 1010 should not receive any other elimination codes	Day 1	Randomized Set, ES, PPS
1030	Study vaccine not administered AT ALL but subject number allocated Note: Subjects receiving a code 1030 should not receive any other elimination codes	Day 1	ES, PPS
1040*	Administration of concomitant vaccine(s) forbidden in the protocol Comment: Co-Ad group: From 30 days before 1st vaccination up to Month 3 blood sampling Control group: From 30 days before 1st vaccination up to Month 5 blood sampling	Co-Ad group: Day -30 to Month 3 Control group: Day -30 to Month 5	PPS
1050	Randomization failure (subject not randomized in the correct group) Comment: To check for manual randomisation, treatment not compatible with one assigned by SBIR	Day 1	PPS
1070	– Side, site or route of study vaccine administration wrong or unknown – Administration not according to protocol for reason specified by the investigator, other than side, site and route – Wrong replacement or study vaccine administered (not compatible with the vaccine regimen associated to the treatment number) – Administered study vaccine reported as being the correct one but is not compatible with the vaccine regimen associated to the treatment number.	Co-Ad group – Day 1, Month 2 Control group – Day 1, Month 2, Month 4	PPS
1080	Vaccine has been administered (effective treatment number) despite a temperature deviation qualified by Status QA GMP NON Use	Co-Ad group – Day 1, Month 2 Control group – Day 1, Month 2, Month 4	PPS
1090	Expired vaccine administered	Co-Ad group – Day 1, Month 2 Control group – Day 1, Month 2, Month 4	PPS
2010	Protocol violation (inclusion/exclusion criteria)	Day 1	PPS
2040*	Administration of any medication forbidden by the protocol Co-Ad group: From 1st vaccination up to Month 3 blood sampling Control group : From 1st vaccination up to Month 5 blood sampling	Co-Ad group – Day 1 up to Month 3 Control group – Day 1 up to Month 5	PPS

Code	Condition under which the code is used	Visit (timepoints) where the code is applicable	Applicable for analysis set
2050*	Underlying medical condition forbidden by the protocol Co-Ad group: From 1st vaccination up to Month 3 blood sampling Control group: From 1st vaccination up to Month 5 blood sampling	Co-Ad group – Day 1 up to Month 3 Control group – Day 1 up to Month 5	PPS
2060*	Concomitant infection related to the vaccine which may influence immune response Co-Ad group: From 1st vaccination up to Month 3 blood sampling Control group: From 1st vaccination up to Month 5 blood sampling	Co-Ad group – Day 1 up to Month 3 Control group – Day 1 up to Month 5	PPS
2070*	Concomitant infection not related to the vaccine which may influence immune response Comment: Co-Ad group: From 1st vaccination up to Month 3 blood sampling Control group: From 1st vaccination up to Month 5 blood sampling	Co-Ad group – Day 1 up to Month 3 Control group – Day 1 up to Month 5	PPS
2080	Subjects did not comply with vaccination schedule (dates of vaccination not corresponding to adapted protocol intervals provided in SAP or unknown vaccination dates) Comment: Co-Ad group: DOSE 1 – DOSE 2 Control group: DOSE 1 – DOSE 2 DOSE 2 – DOSE 3	Co-Ad group: Day 1, Month 2 Control group: Day 1, Month 2, Month 4	PPS
2090	Subjects did not comply with blood sample schedule (dates of BS not corresponding to adapted protocol intervals provided in SAP or unknown BS/vaccination dates) Comment: Co-Ad group: DOSE 1 – MONTH 1 BS DOSE 2 – MONTH 3 BS Control group: DOSE 1 – MONTH 1 BS DOSE 3 – MONTH 5 BS	Co-Ad group: Month 1, Month 3 Control group: Month 1, Month 5	PPS
2100	Serological results not available post-vaccination (including lost samples, blood sample not done, unable to test, absence of parallelism). Please specify the applicable rule: ☒ elimination code if ALL are missing for a subject Comment: Co-Ad group: Check for availability of anti-gE serological result at Month 3 and for pneumococcal serological results at Month 1 Control group: Check for availability of anti-gE serological result at Month 5 and for pneumococcal serological results at Month 1	Co-Ad – Month 1, Month 3 Control – Month 1, Month 5	PPS
2120	Obvious incoherence or abnormality or error in data (incoherence between CRF and results, wrong labelling) Comment: Co-Ad group: Check for above condition on anti-gE serological result at Month 3 and on pneumococcal serological results at Month 1	Co-Ad – Month 1, Month 3 Control – Month 1, Month 5	PPS

Code	Condition under which the code is used	Visit (timepoints) where the code is applicable	Applicable for analysis set
	Control group: Check for above condition on anti-gE serological result at Month 5 and on pneumococcal serological results at Month 1		
2500	Incomplete vaccination course. Comment: The subject should receive one dose of Prevenar 13 vaccine and 2 doses of Hz/su vaccine	Co-Ad – Day 1, Month 2 Control – Day 1, Month 2, Month 4	PPS

BS = Blood sample

** Attribution of these elimination codes are responsibility of CRDL following review of individual data listings*

5.3. Important protocol deviation not leading to elimination from per-protocol analysis set

For information on important protocol deviation not leading to elimination from the PPS set, refer to the study protocol deviation and management plan (PDMP).

6. STATISTICAL ANALYSES

Note that standard data derivation rule and stat methods are described in Section 12 and will not be repeated below. All analyses will be presented by study phase when there are data for both active and follow up phases.

6.1. Demography

6.1.1. Analysis of demographics/baseline characteristics planned in the protocol

Demographic characteristics (age at first vaccination, sex, race and ethnicity) will be tabulated per treatment group.

The mean age (plus range and standard deviation [SD]) of the subjects, as a whole, and per treatment group will be calculated for ES and PPS. The distribution of subjects enrolled among the study sites will be tabulated, as a whole, and per treatment group.

The same tabulations might be performed by age strata (50-59, 60-69 and ≥70 YOA) if deemed necessary.

6.1.2. Additional considerations

- The following additional tables will be generated:
  - The number of subjects enrolled into the study as well as the number of subjects excluded from PPS analyses will be presented through two consort tables:
  - Consort table 1 - Showing the subjects disposition from Enrolled Set to Randomized Set
  - Consort table 2 – Showing the subjects disposition from Randomised Set to ***Per Protocol Set for immunogenicity***
  - Withdrawal status will be summarized by group. The numbers of withdrawn subjects will be tabulated according to the reason for withdrawal

- The following table will be generated for CTRS:
  - Percentage of Enrolled subjects by country will be tabulated by group,
  - Percentage of Enrolled subjects in the following age categories ≤64, 65-84, ≥85 will be tabulated by group.
- For computation of age, following rule need to be considered:
  - Age will be calculated as the number of years between the date of birth and the date of first vaccination.
  - To ensure that the collection of date of birth will not jeopardise the privacy of Personally Identifiable Information (PII), only a partial date of birth (MMYYYY) will be collected.
  - Therefore, the 15th of the month will be used to replace the missing date.
  - In case the month is missing, the date will be replaced by the June 30th of the year.
- Summary of important protocol deviations leading to elimination will be presented.

6.2. Exposure

6.2.1. Analysis of exposure planned in the protocol

None

6.2.2. Additional considerations

The number of doses administered will be tabulated. The number of doses administered will be tabulated by age sub-group.

6.3. Immunogenicity

6.3.1. Analysis of immunogenicity planned in the protocol

The primary analysis will be based on the ***Per-protocol set (PPS) for immunogenicity.*** A second analysis based on the Exposed set will be performed to complement the per-protocol analysis (see section 9 for changes in the planned analysis).

Immunogenicity analyses for confirmatory objectives will be performed by age stratum (50-59, 60-69 and ≥ 70 YOA) on PPS, if the number of subjects enrolled is sufficient in each stratum.

6.3.1.1. Within group assessment

The following parameters will be tabulated by vaccine group at each time point when a blood sample result is available:

- Seropositivity with exact 95% CI for all antigens
- GMC/GMT with 95% CI for all antigens
- VRR with exact 95% CI for anti-gE
- Mean Geometric Increase (MGI) with exact 95% CI for anti-gE
- Descriptive statistics (N, mean, SD, min, Q1, median, Q3, max) of Mean Geometric Increase (MGI) for anti-gE
- Distribution of the fold increase i.e. Percentage of subjects with a more than X-fold (e.g. >2, >4, >6, -fold) increase will be tabulated for anti-gE per group with 95% CI.
- Antibody titre/concentration will be displayed using reverse cumulative curves.

6.3.1.2. Between group assessment

The following between group comparison will be performed:

- For the second co-primary objective for non-inferiority of the anti-gE humoral response, at one-month post-dose 2 of HZ/su vaccine:
  - The 95% CI of the group GMCs ratio (Control divided by Co-Ad) will be computed using an ANCOVA model on the log10 transformation of the concentrations. The pre-vaccination log-transformed antibody concentrations will be included as continuous covariate and the vaccine group and age strata as fixed effects in the model.
- For the third co-primary objective for non-inferiority of the humoral response to each vaccine pneumococcal serotype (according to the pre-specified order in the protocol), one month post-dose of *Prevenar13*:
  - The 95% CI of the group MOPA GMT ratios (Control divided by Co-Ad) will be computed using an ANCOVA model on the log10 transformation of the concentrations. The pre-vaccination log-transformed antibody concentrations will be included as continuous covariate and the vaccine group and age strata as fixed effects in the model.

6.3.2. Additional considerations

The following additional points need to be considered for immunogenicity analysis:

- Percentage of subjects above the pneumococcal serotype specific LLOQ will be calculated for each serotype with exact 95% Cis.
- Immunogenicity descriptive analyses will be performed by age stratum (50-59, 60-69 and ≥ 70 YOA), if the number of subjects enrolled is sufficient in each stratum.

- Two-sided 95% CIs for Seropositivity and VRR will be computed by Clopper-Pearson method [Clopper, 1934].
- The two-sided 95% CI for the mean of log-transformed titre/concentration will be first obtained assuming that log-transformed values were normally distributed with unknown variance. The 95% CI for the GMTs/GMCs/MGIs will be then obtained by exponential-transformation of the 95% CI for the mean of log-transformed titre/concentration.

6.3.2.1. Statistical considerations for confirmatory objectives

For the multiplicity adjustment, all hypotheses have been ranked into three families and one sub-family according to the following power of test:

Table 4 Power to demonstrate VRR objective and non-inferiority of the immunogenicity of HZ/su and *Prevenar13* co-administered compared to Control group

Family 1: HZ/su: VVR*(1-sided test with alpha = 2.5%)				
Endpoint	Threshold	VR assumed	Total β	Power
VRR in Co-Ad group	0.60	95%	0.001%	99.99%
Family 2: HZ/su: non-inferiority* (1-sided test with alpha = 2.5%) N=410				
Endpoint	Standard deviation	δ	Total β	Power
Anti-gE GMC ratio	0.35	1.5	0.001 %	99.99 %
Family 3: *Prevenar13*: Non-inferiority* (1-sided test with alpha = 2.5%) N=410				
Endpoint (13 vaccine pneumococcal serotypes)	Standard deviation	δ	Total β	Power
3 GMT ratio	0.660	2	0.001%	99.99%
19A GMT ratio	0.644	2	0.001%	99.99%
1 GMT ratio	0.798	2	0.029%	99.97%
18C GMT ratio	0.891	2	0.203%	99.80%
4 GMT ratio	0.906	2	0.260%	99.74%
6A GMT ratio	0.919	2	0.320%	99.68%
5 GMT ratio	0.931	2	0.383%	99.62%
19F GMT ratio	0.971	2	0.664%	99.33%
6B GMT ratio	0.995	2	0.891%	99.11%
7F GMT ratio	1.014	2	1.107%	98.89%
9V GMT ratio	1.021	2	1.194%	98.81%
14 GMT ratio	1.045	2	1.530%	98.47%
23F GMT ratio	1.094	2	2.398%	97.60%
Global β to show non-inferiority			~9%	
Global power				**~91%**

VRR: vaccine response rate; gE: Varicella Zoster Virus glycoprotein E; GMT: geometric mean titer; GMC: geometric mean concentration.
* Pass 12, alpha = 2.5%, for VRR: Exact test, for non-inferiority one-sided equivalence of means.
For gE: non-inferiority limit = 0.176 (=log10(1.5)), power under equal GMC
For each pneumococcal serotype: non-inferiority limit = 0.301 (=log10(2)), variability for each of the 13 vaccine pneumococcal serotype taken from the EMA assessment report for *Prevenar13* and multiplied by 1.1, power under equal GMT.

Fixed sequence testing which allows for full alpha propagation in pre-ordered hypotheses families will be applied in the following manner:

Family 1:

In the Co-Ad group, for anti-gE, at one month post-dose 2 of HZ/su vaccine:

- The VRR and 95% CI will be computed.

The objective is met if the LL of the 95% CI is ≥60%.

Family 2:

For anti-gE, at one month post-dose 2 of HZ/su vaccine:

- The 95% CI of the group GMCs ratio will be computed using an analysis of covariance (ANCOVA) model on the log10 transformation of the concentrations. The pre-vaccination log-transformed antibody concentrations will be included as continuous covariate and the vaccine group and age strata as fixed effects in the model.

In terms of concentrations, the Co-Ad group will be considered non-inferior to the Control group if the UL of the 95% CI for the GMC ratio of the Control group to the Co-Ad group is <1.5.

Family 3:

For each vaccine pneumococcal serotype (according to the pre-specified order), one month post-dose of *Prevenar13*:

- The 95% CI of the group MOPA GMT ratios will be computed using an analysis of covariance (ANCOVA) model on the log10 transformation of the concentrations. The pre-vaccination log-transformed antibody concentrations will be included as continuous covariate and the vaccine group and age strata as fixed effects in the model.

In terms of MOPA GMTs, the Co-Ad group will be considered non-inferior to the Control group if the UL of the 95% CI for the MOPA GMTs ratio of the Control group to the Co-Ad group is <2 for each of the 13 vaccine serotypes.

In the ANCOVA models Adjusted Least Squares (LS) means and difference of LS means between the groups will be calculated together with the 2-sided 95% CIs and back-transformed to the original units to provide GMCs and GM ratios.

6.4. Analysis of safety

6.4.1. Analysis of safety planned in the protocol

The analysis for safety will be based on the Exposed set. All safety analyses may also be performed by age strata (50-59, 60-69 and ≥70 YOA), if deemed necessary.

When appropriate, tabulations will be presented overall and by time of occurrence relative to last vaccination (e.g. using windows such as Days 1 to 7, Days 1 to 30 and more than 30 days post-vaccination).

The results for the analysis of safety will be tabulated as follows:

- The number and percentage of subjects with at least one local solicited AE, with at least one general solicited AE, and with any solicited AE during the 7-day follow-up period with exact 95% CIs after each vaccine dose and overall by vaccination group will be provided;
- The percentage of subjects reporting each individual solicited local and general AE during the solicited 7-day follow-up period will be tabulated with exact 95% CI;
- For all solicited adverse events, the same tabulation will be performed for grade 3 solicited AEs and for solicited general AEs with relationship to vaccination;
- Number of days with each individual solicited local and general AE during the solicited 7-day follow-up period;
- The proportion of subjects with at least one report of unsolicited AE (containing both serious and non-serious unsolicited AEs) classified by the MedDRA Primary System Organ Class (SOC) and Preferred Terms (PTs) and reported up to 30 days after each vaccination will be tabulated with exact 95% CI;
- The same tabulation will be performed for grade 3 unsolicited AEs and for unsolicited AEs with a relationship to vaccination reported up to 30 days after each vaccination with exact 95% CI. The proportion of AEs resulting in a medically attended visit will also be tabulated;
- Total number/percentages of doses (per dose and overall) followed by AEs will be tabulated;
- Number of subjects with pIMDs will be tabulated;
- SAEs, including fatalities and withdrawal due to AE(s) will be described in detail.

6.4.2. Additional considerations

- The following additional tables will be generated:
  - The percentage of subjects with at least one local AE (solicited and unsolicited), with at least one general AE (solicited and unsolicited) and with any AE (solicited and unsolicited) during the 7-day follow-up period will be tabulated with exact 95% CI after each vaccine dose and overall. The same computations

will be done for Grade 3 AEs, for any AEs considered related to vaccination and for any Grade 3 AEs considered related to vaccination.

- The percentage of subjects with at least one local solicited AE, with at least one general solicited AE and with any solicited AE will also be done for Grade 3 solicited AEs, for any solicited AEs considered related to vaccination and for any Grade 3 solicited AEs considered related to vaccination.
- The percentage of subjects reporting each individual solicited local AE during the solicited 7-day follow-up period will be tabulated by study vaccine with exact 95% CI.
- Summary of temperature value by half degree increment taken by different routes reported during the 7-day (Days 1-7) post-vaccination following each dose.
- For fever, the number and percentage of subjects reporting fever by half degree (°C) cumulative increments during the 7-day follow-up period (Day 1-7) will be tabulated for each group after each vaccine dose and overall. Similar tabulations will be performed for Grade 3 (> 39.0°C) causally related fever.
- List of suspected HZ cases identified during the study will be presented.
- The number and percentage of subjects starting a concomitant medication during the 30-day post-vaccination period by dose and overall will be presented.
- The duration of solicited local adverse events (in days), not limited to the 7-day post-vaccination period, following each dose and overall/dose. The same tabulations after Prevenar13 and HZ/su vaccinations.
- The duration of solicited general adverse events (in days), not limited to the 7-day post-vaccination period, following each dose and overall/dose.
- Solicited local adverse events ongoing beyond the 7-day (Days 1-7) post-vaccination period, following each dose and overall/dose. The same tabulations after Prevenar13 and HZ/su vaccinations.
- Solicited general adverse events ongoing beyond the 7-day (Days 1-7) post-vaccination period, following each dose and overall/dose.
- Number and percentage of subjects with at least one report of a grade 3 non-serious unsolicited AE during the 30-day (Days 0–29) follow-up period after each vaccination classified according to the MedDRA Primary SOC and PTs will be tabulated, with exact 95% CI. The same will be generated for grade 3 non-serious unsolicited AE considered related to vaccination.
- Number and percentage of subjects with fatal SAEs, classified by MedDRA Primary SOC and PTs will be presented with exact 95% CI in two ways:
- With onset of fatal SAE during the period starting from first vaccination to 30 days post last vaccination dose, after 30 days post last vaccination dose to study end and from first vaccination to study end.

- Who died during the period starting from first vaccination to 30 days post last vaccination dose, after 30 days post last vaccination dose to study end and entire study period.
- The listing of all subjects who died during the entire study period and their fatal SAEs in the Enrolled Set

6.4.2.1. Combined Solicited and Unsolicited Adverse Events

A summary of subjects with all combined solicited (regardless of their duration) and unsolicited adverse events will be provided. Solicited adverse events will be coded by MedDRA as per the following codes:

Solicited adverse event	Lower level term name	Corresponding Lower level term code
Pain	Injection site pain	10022086
Redness	Redness at injection site	10022098
Swelling	Swelling at injection site	10053425
Fatigue	Fatigue	10016256
Gastrointestinal symptoms	Gastrointestinal disorder	10017944
Headache	Headache	10019211
Myalgia	Myalgia	10028411
Shivering	Shivering	10040558
Temperature	Fever	10016558

For clintrial.gov and EudraCT posting purposes, a summary of combined solicited and unsolicited non-serious adverse events will be produced by SOC and PTs and according to occurrence of each event.

7. ANALYSIS INTERPRETATION

All co-primary objectives will be evaluated using a one-sided Type I error of 2.5% (as already justified by fixed sequential testing procedure, no alpha adjustment needed). The trial will be considered conclusive if all co-primary objectives criteria are met.

8. CONDUCT OF ANALYSES

8.1. Sequence of analyses

The analysis will be performed in the following steps:

- The final analysis on immunogenicity, reactogenicity and safety data will be performed when all data up to study end (i.e., phone contact at Month 14 for Co-Ad group and phone contact at Month 16 for Control group) will be available and cleaned. Individual data listings will also be provided.

An integrated clinical study report containing all data will be written and made available to the investigators following the final analysis.

Table 5 Analysis and disclosure plan for the planned analysis

Description	Analysis ID	Disclosure Purpose (CTRS=public posting, CSR=clinical study report, internal)	Dry run review needed (Y/N)	Reference for TFL
Final analysis	E1_01	CTRS CSR	Y	***All tables from Section 13 of the SAP Amendment 3 23NOV2020***

8.2. Statistical considerations for interim analyses

Not applicable

9. CHANGES FROM PLANNED ANALYSES

- In Protocol Amendment 2 Final (30 Jan 2018), it was specified that a second analysis for immunogenicity of the ES would be performed only if, in any study group, the percentage of enrolled subjects with serological results excluded from the PPS for immunogenicity is 5% or more. At the request of Paul Ehrlich Institute, Germany (PEI), an analysis of the ES will be performed to complement the per-protocol analysis regardless of the percentage of enrolled subjects excluded from the PPS for immunogenicity.
- Updated LLOQ values (i.e. assay cut-off values) for the pneumococcal serotypes are provided in this version of SAP (section 12.1.2). The cut-off values presented in this SAP will be used to determine seropositivity rather than those presented in Protocol Amendment 2 Final (30 Jan 2018). Analysis of immunogenicity section has been updated accordingly.
- Additional tables on presentation of grade 3 non-serious unsolicited adverse events and fatal SAEs has been added based on CBER request.
- The sequence of analysis was updated from SAP amendment 1 to accommodate a delay in the availability of immunogenicity results. ***The active phase analysis has been removed as a request for a CTRS posting extension has been submitted to NIH; complete CTRS posting will be done at Last Subject Last Visit (LSLV) + 12 months rather than Primary Completion Date (PCD) +12 months as previously planned***
- Two new cohorts – Enrolled Set and Randomized Set has been defined as required for web disclosure and SAE tables presentation.
- Analysis of demography section has been updated to add consort table and summary of important protocol deviations.

10. NON-STANDARD DATA DERIVATION RULES AND STATISTICAL METHODS

10.1. Statistical Method

10.1.1. Safety

For the listing of suspected HZ episode, following list of PT_CODE has to be considered:-

PT_CODE	PT_NAME
10076667	Disseminated varicella zoster vaccine virus infection
10084396	Disseminated varicella zoster virus infection
10072210	Genital herpes zoster
10019974	Herpes zoster
10074297	Herpes zoster cutaneous disseminated
10061208	Herpes zoster infection neurological
10074259	Herpes zoster meningitis
10074248	Herpes zoster meningoencephalitis
10074251	Herpes zoster meningomyelitis
10079327	Herpes zoster meningoradiculitis
10074253	Herpes zoster necrotising retinopathy
10063491	Herpes zoster oticus
10074245	Herpes zoster pharyngitis
10080516	Herpes zoster reactivation
10030865	Ophthalmic herpes zoster
10074241	Varicella zoster gastritis
10074243	Varicella zoster oesophagitis
10074254	Varicella zoster pneumonia
10074298	Varicella zoster sepsis
10075611	Varicella zoster virus infection

11. LIST OF FINAL REPORT TABLES, LISTINGS AND FIGURES

The TFL TOC provides the list of tables/listings and figures to be included in the study report.

The following group names will be used in the TFLs, in line with the T-domains:

Group order in tables	Group label in tables	Group definition for footnote
1	Co-Ad	Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
2	Control	Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su

The following sub-groups will be used in the TFL, in line with the T-domains:

Table 6 Group Definitions to be used for the sub-group analysis by age (Analysis will be included in the clinical report)

Sub-group order in tables	Sub-group label in tables	Sub-group definition for footnote
1	50-59YOA	Subjects aged 50-59 years
2	60-69YOA	Subjects aged 60-69 years
3	≥70YOA	Subjects aged 70 years and over

YOA = Year of age

Please note that for table presentation in the sub-group analysis, the sequence maintained has to be each treatment group within each age sub-group.

12. ANNEX 1 STANDARD DATA DERIVATION RULE AND STATISTICAL METHODS

12.1. Standard data derivation

12.1.1. Dose number

The study dose number is defined in reference to the number of study visits at which vaccination occurred. More specifically dose 1 refers to all vaccines administered at the first vaccination visit while dose 2 corresponds to all vaccinations administered at the second vaccination visit even if this is the first time a product is administered to the subject.

Associated dose: the associated dose for an event (AE, medication, vaccination) is the most recent study dose given before an event. In case the event takes place on the day a study dose is given, the associated dose will be that of the study dose, even if the event actually took place before vaccination. For instance, if an adverse event begins on the day of the study vaccination but prior to administration of the vaccine, it will be assigned to this dose. In case a study dose is not administered and an event occurs after the

subsequent study dose (e.g. 2nd study dose), the associated dose of the event will be study dose associated to the subsequent study dose (e.g. dose 2).

The number of doses for a product is the number of times the product was administered to a subject.

The incidence per dose is the number of visits with vaccine administered at which an event was reported among all visits with vaccine administered.

12.1.2. Immunogenicity

- For a given subject and given immunogenicity measurement, missing or non-evaluable measurements will not be replaced. Therefore, an analysis will exclude subjects with missing or non-evaluable measurements.
- A seronegative subject is a subject whose antibodies concentration/titer is below the cut-off value (cut-off value is defined by the laboratory prior to the analysis).
- A seropositive subject is a subject whose antibodies concentration/titer is greater than or equal to the assay cut-off value.
- The seropositivity rate is defined as the percentage of seropositive subjects.
- The VRR for anti-gE is defined as the percentage of subjects who have at least:
  - a 4-fold increase in the anti-gE antibodies concentration as compared to the pre-vaccination anti-gE antibodies concentration, for subjects who are seropositive at baseline, or,
  - a 4-fold increase in the anti-gE antibodies concentration as compared to the anti-gE antibodies cut-off value for seropositivity, for subjects who are seronegative at baseline.
- The GMC calculations for anti-gE antibody concentration are performed by taking the anti-log of the mean of the log base 10 concentration transformations. Antibody concentrations below the cut-off of the assay will be given an arbitrary value equal to half the cut-off for the purpose of GMC/GMT calculation.
- All CI computed will be two-sided 95% CI.

- Updated LLOQ and ULOQ values for the MOPA assay are described below for each of the 13 pneumococcal serotypes:

Pneumococcal serotype	Method	Unit	LLOQ[1]	ULOQ	Laboratory
Streptococcus pneumoniae Serotype 01/37 Brugmann Hospital Ab	MOPA	1/ dilution	14	3504	University of Alabama at Birmingham
Streptococcus pneumoniae Serotype 03/1 Statens Serum Institut Ab			11	2822	
Streptococcus pneumoniae Serotype 04/2656 Brugmann Hospital Ab			40	18042	
Streptococcus pneumoniae Serotype 05 Ambrose- Statens Serum Institut Ab			15	13304	
Streptococcus pneumoniae Serotype 06A Centers for Disease Control Ab			45	15305	
Streptococcus pneumoniae Serotype 06B/DS2212/94 Centers for Disease Control Ab			29	20806	
Streptococcus pneumoniae Serotype 07F/46 Brugmann Hospital Ab			28	59809	
Streptococcus pneumoniae Serotype 09V/112 161/95 Statens Serum Institut Ab			39	28095	
Streptococcus pneumoniae Serotype 14/58 Brugmann Hospital Ab			16	47856	
Streptococcus pneumoniae Serotype 18C/4593/40 Statens Serum Institut Ab			40	13318	
Streptococcus pneumoniae Serotype 19A/DB18 Kansanterveyslaitos Folkhalsoinstitutet Ab			13	34881	
Streptococcus pneumoniae Serotype 19F/2737 Brugmann Hospital Ab			33	29352	
Streptococcus pneumoniae Serotype 23F Mac-Statens Serum Institut Ab			40	10662	

[1]LLOQ corresponds to serotype-specific assay cut-off value.

- The Geometric Mean Titres (GMTs) calculations for pneumococcal serotypes are performed by taking the anti-log of the mean of the log base 10 titre transformations. For GMT calculation for pneumococcal serotypes, antibody titres below the LLOQ of the assay will be given an arbitrary value of half the cut-off for GMT calculation. Antibody titres above the ULOQ of the assay will be given the value of ULOQ for GMT calculation.

12.1.3. Safety

For a given subject and the analysis of solicited adverse event during the 7 day follow-up period after vaccination, missing or non-evaluable measurements will not be replaced. Therefore, the analysis of the solicited adverse events based on the ES will include only vaccinated subjects with documented safety data (i.e., symptom screen completed). More specifically the following rules will be used:

- Subjects who documented the absence of a solicited adverse event after one dose will be considered not having that adverse event after that dose.
- Subjects who documented the presence of a solicited adverse event and fully or partially recorded daily measurement over the solicited period will be included in the summaries at that dose and classified according to their maximum observed daily recording over the solicited period.

- Subjects who documented the presence of a solicited adverse event after one dose without having recorded any daily measurement will be assigned to the lowest intensity category at that dose (i.e., 38°C for fever or grade 1 for other adverse events). The subject will only be presented in the subject with adverse event experienced and not in specific grade information.
- Doses without adverse event sheets documented will be excluded.

For analysis of unsolicited AEs, such as SAEs or adverse events by MedDRA Primary SOC and PTs term, and for the analysis of concomitant medications, all vaccinated subjects will be considered. Subjects who did not report the event or the concomitant medication will be considered as subjects without the event or the concomitant medication respectively.

Associated dose: The associated dose for an event (e.g., AE, medication, vaccination,…) is the study dose given before an event. In case the event takes place on a day a study dose is given, the associated dose will be that of the study dose even if the event actually took place before. For instance, for a conc. medication started on the day of study dose 2 but before dose 2 administrations, the associated dose will be dose 2

The way the percentage of subjects will be derived will depend on the event analysed (see the following table for details). As a result, the denominator (N) will differ from one table to another.

Event	N used for deriving %	Terminology used in the tables for N
Concomitant medication	All vaccinated subjects	Number of subjects with at least one administered dose
Solicited local adverse event	All vaccinated subjects with at least one solicited local adverse event documented as either present or absent	For each dose and overall/subject: N= number of subjects with at least one documented dose For overall/dose: N= number of documented doses
Solicited general adverse event	All vaccinated subjects with at least one solicited general adverse event documented as either present or absent	For each dose and overall/subject: N= number of subjects with at least one documented dose For overall/dose: N= number of documented doses
Unsolicited adverse event from day 0 to day X	All vaccinated subjects	Number of subjects with at least one administered dose
SAE	All vaccinated subjects	Number of subjects with at least one administered dose

- The maximum intensity of local injection site redness and swelling will be scored at GSK Biologicals as follows:
  - 0 : <20 mm
  - 1 : ≥ 20 mm to ≤ 50 mm diameter
  - 2 : > 50 mm to ≤ 100 mm diameter
  - 3 : > 100 mm diameter

Fever is defined as temperature ≥ 38.0 C / 100.4 F for oral, axillary, tympanic or rectal route. The preferred route for recording temperature in this study will be oral. For the analysis, temperatures will be coded as follows:

Grade	Temperature (oral, axillary, tympanic or rectal route)
0	< 38°C
1	≥ 38°C - ≤ 38.5°C
2	> 38.5°C - ≤ 39°C
3	> 39°C

- Conversion of temperature to °C -

  The following conversion rule is used for the conversion of temperature to °C

  – Temperature in °Celsius = ((Temperature in °Fahrenheit -32) *5)/9

The result is rounded to 1 decimal digit.

12.2. Statistical Method References

Clopper CJ, Pearson ES. The use of confidence or fiducial limits illustrated in the case of binomial. *Biometrika*. 1934; 26:404-413.

12.3. Number of decimals displayed:

The following decimal description from the decision rules will be used for the demography, immunogenicity and safety/reactogenicity.

Display Table	Parameters	Number of decimal digits
Demographic characteristics	Mean, median age	1
Demographic characteristics	SD (age)	1
Immunogenicity	Ratio of GMT/C	2
All summaries	% of count, including LL & UL of CI	1
All summaries	% of difference, including LL & UL of CI	2

13. ANNEX 2: STUDY SPECIFIC MOCK TFL

The study specific mocks are annexed to this SAP in a separate document.

The data display, title and footnote are for illustration purpose and will be adapted to the study specificity as indicated in the TFL TOC. Note that there may be few changes between the study specific SAP mock TFL and the final TFLs as editorial/minor changes do not require a SAP amendment

13.1. List of individual data listing

Following individual data listing will be generated. ***Please refer to TFL TOC for the numbering of these Appendices.***

- Elimination codes
- Demography
- Physical examination/vital signs
- Dates of birth, Informed consent, Vaccination and blood sampling, Contact
- Reason for visit not done
- General medical history - Physical examination
- Study Conclusion
- Notes (this appendix is provided for info only and should not be used for the clinical report)
- Vaccination procedure
- Reason for not administration of vaccine
- Reason for non-eligibility
- Previous history of vaccination
- Previous history of disease
- Solicited local adverse events
- Solicited general adverse events
- Unsolicited adverse events within (30) days post-vaccination
- Unsolicited adverse events after (30) days post-vaccination
- Concomitant medications
- Concomitant vaccinations
- Immunogenicity

13.2. Template of Tables and Figures

Template 1 Number of subjects by country and center <Exposed Set>

		<Each group> N=XXXX		<Each group> N=XXXX		Total N=XXXX	
Country	**Center**	**n**	**%**	**n**	**%**	**n**	**%**
<each country>	<each center >	XXX	XX.X	XXX	XX.X	XXX	XX.X
	All	XXX	XX.X	XXX	XX.X	XXX	XX.X

<each group>:
Co_Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
n = number of subjects in a given center or country
N = total number of subjects
% = n/N x 100
Center = GSK Biologicals assigned center number

Template 2 Number of enrolled subjects by country

	<Each group> N=XXXX		<Each group> N=XXXX		Total N=XXXX	
Country	**n**	**%**	**n**	**%**	**n**	**%**
<Each country>	XXX	XX.X	XXX	XX.X	XXX	XX.X

<each group>:
Co_Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
No Group= enrolled not vaccinated
n = number of subjects in a given country
N = total number of subjects
% = n/N x 100

Template 3 Number of enrolled subjects by age category

	<Each group> N=XXXX		<Each group> N=XXXX		Total N=XXXX	
Age category	**n**	**%**	**n**	**%**	**n**	**%**
Adults [18-64 years]	XXX	XX.X	XXX	XX.X	XXX	XX.X
From 65-84 years						
85 years and over						

<each group>:
Co_Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = number of enrolled subjects
n = number of enrolled subjects included in each group or in total for a given age category or for all age categories
% = n/N x 100

Template 4 Number of subjects by country and age category <Exposed Set>

		<Each group> N=XXXX		<Each group> N=XXXX		Total N=XXXX	
Country	**Age category**	**n**	**%**	**n**	**%**	**n**	**%**
<each country>	50-59YOA	XXX	XX.X	XXX	XX.X	XXX	XX.X
	60-69YOA						
	≥70YOA						
	All	XXX	XX.X	XXX	XX.X	XXX	XX.X

Co_Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
50-59YOA = subjects aged 50-59 years; 60-69YOA = subjects aged 60-69 years; ≥70YOA = subjects aged 70 years and over
n = number of subjects in a given center or country
N = total number of subjects
% = n/N x 100

Template 5 Number of subjects vaccinated, completed and withdrawn with reason for withdrawal – <end of active phase, study end> <Exposed set>

	<Each group> N=XXXX	<Each group> N=XXXX	Total N=XXXX
	n	**n**	**n**
Number of subjects vaccinated	xxx	xxx	xxx
End of study status			
[EACH CATEGORY]	xxx	xxx	xxx
Reasons for withdrawal:			
[REASONS]	xxx	xxx	xxx

Co_Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
Vaccinated = number of subjects who were vaccinated in the study
Completed = number of subjects who completed <end of active phase visit, last study visit>
Withdrawn = number of subjects who did not come for the <end of active phase visit, last study visit>
Unknown = number/percentage of subjects who have not come for the <end of active phase visit, last study visit> yet

Template 6 Visit attendance <Exposed set>

		<Each group> N=XXX	
Visit	**Status**	**n**	**%**
INFORMED CONSENT	Completed		
RANDOMIZATION	Completed		
<EACH VISIT>	Attended		
	Not attended yet		
	Permanent discontinuation prior to this visit		
	Not attended		
CONCLUSION	Completed		

Co_Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = Number of subjects in each group or in total
Conclusion = date of last visit or withdrawal

Template 7 Summary of important protocol deviations leading to elimination from any analyses

Category Sub-category	<Each group> N=XXXX			Total N=XXXX		
	occ	n	%	occ	n	%
At least one important protocol deviation	xxx	xxx	xx.x	xxx	xxx	xx.x
<Category 1>	xxx	xxx	xx.x	xxx	xxx	xx.x
<Sub-category 1>	xxx	xxx	xx.x	xxx	xxx	xx.x
<Sub-category 2>	xxx	xxx	xx.x	xxx	xxx	xx.x
…						
<Category 2>	xxx	xxx	xx.x	xxx	xxx	xx.x
…						
…						

Co_Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = Total number of subjects
Occ = number of occurrences = number of important protocol deviations
n/% = number / percentage of subjects with important protocol deviations

Template 8 Percentage of subjects with serological results who were eliminated from PPS for immunogenicity

	[each group]	
Number of subjects in Exposed Set with serological results available		
Number of subjects with serological results eliminated from PPS for immunogenicity		
Percentage of subjects with serological results eliminated from PPS for immunogenicity		

Co_Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su

Template 9 Deviations from specifications for age and intervals between study visits for Co-Ad group <Exposed Set>

		Age	Dose:1-PI (M1)		Dose:1-Dose:2	Dose:2-PII (M3)		Dose:2–PHC (M14)
Group		Protocol	Protocol	Adapted	Protocol	Protocol	Adapted	Protocol
		from ≥ 50 years	from 30 to 42 days	from 28 to 48 days	from 49 to 83 days	from 30 to 48 days	from 28 to 48 days	from 335 to 395 days
Co-Ad	N							
	n							
	%							
	range							

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Adapted = interval used for defining PPS for immunogenicity
N = total number of subjects with available results
n/% = number / percentage of subjects with results outside of the interval
range = minimum-maximum for age and intervals
PI (M1) = Blood sample at Month 1, post-vaccination Dose 1; PII (M3) = Blood sample at Month 3, post-vaccination Dose 2; PHC (M14) = Phone Contact MONTH 14

Template 10 Deviations from specifications for age and intervals between study visits - for Control group <Exposed Set>

		Age	Dose:1-PI(M1)		Dose:1-Dose:2		Dose:2-Dose:3	Dose:3-PIII(M5)		Dose:3-PHONE CONT M16
Group		**Protocol**	**Protocol**	**Adapted**	**Protocol**	**Adapted**	**Protocol**	**Protocol**	**Adapted**	**Protocol**
		from ≥ 50 years	from 30 to 42 days	from 28 to 48 days	from 60 to 83 days	≥ 60 days	from 49 to 83 days	from 30 to 48 days	from 28 to 48 days	from 335 to 395 days
Control	N									
	n									
	%									
	range									

Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
Adapted = interval used for defining the ***PPS for immunogenicity***
N = total number of subjects with available results
n/% = number / percentage of subjects with results outside of the interval
range = minimum-maximum for age and intervals
PI(M1) = Blood sample at Month 1, post-vaccination Dose 1; PIII(M5) = Blood sample at Month 5, post-vaccination Dose 3; PHC (M16) = Phone Contact Month 16

Template 11 Summary of demographic characteristics <Exposed Set, PPS for immunogenicity>

	<Each group> N=XXXX		<Each group> N=XXXX		Total N=XXXX	
	Value or n	**%**	**Value or n**	**%**	**Value or n**	**%**
Age in Years at <timepoint>						
N with data	xxx		xxx		xxx	
Mean	xxx.x		xxx.x		xxx.x	
SD	xxx.x		xxx.x		xxx.x	
Median	xxx.x		xxx.x		xxx.x	
Minimum	xxx		xxx		xxx	
Maximum	xxx		xxx		xxx	
Gender						
<EACH GENDER>	xxx	xx.x	xxx	xx.x	xxx	xx.x
…	xxx	xx.x	xxx	xx.x	xxx	xx.x
Ethnicity						
<EACH ETHNICITY>	xxx	xx.x	xxx	xx.x	xxx	xx.x
…	xxx	xx.x	xxx	xx.x	xxx	xx.x
Geographic Ancestry						
<EACH GEOGRAPHIC ANCESTRY>	xxx	xx.x	xxx	xx.x	xxx	xx.x
…	xxx	xx.x	xxx	xx.x	xxx	xx.x
Age category						
<EACH AGE CATEGORY>	xxx	xx.x	xxx	xx.x	xxx	xx.x
Country						
<EACH COUNTRY>	xxx	xx.x	xxx	xx.x	xxx	xx.x
…	xxx	xx.x	xxx	xx.x	xxx	xx.x

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = total number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
N with data = number of subjects with documentation of the corresponding data
SD = standard deviation; *YOA = years of age*

Template 12 Minimum and maximum activity dates <Exposed Set>

Group	Activity number	Activity Description	Minimum date	Maximum date
Co-Ad	10	VISIT DAY 1		
	20	VISIT MONTH 1		
	30	VISIT MONTH 2		
	40	VISIT MONTH 3		
	70	PHONE CONTACT MONTH 14		
Control	10	VISIT DAY 1		
	20	VISIT MONTH 1		
	30	VISIT MONTH 2		
	50	VISIT MONTH 4		
	60	VISIT MONTH 5		
	80	PHONE CONTACT MONTH 16		

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su

Template 13 Study Population <Exposed Set>

	<Each group> N=XXXX	<Each group> N=XXXX	Total N=XXXX
Number of subjects			
Planned, N	xxx	xxx	xxx
Randomised, N <cohort name>	xxx	xxx	xxx
Completed to visit Month 3, n (%)*	***xxx (xx.x)***	***xxx (xx.x)***	***xxx (xx.x)***
Completed to visit Month 5, n (%)**	***xxx (xx.x)***	***xxx (xx.x)***	***xxx (xx.x)***
Completed to Phone contact Month 14, n (%)*	***xxx (xx.x)***	***xxx (xx.x)***	***xxx (xx.x)***
Completed to Phone contact Month 16, n (%)**	***xxx (xx.x)***	***xxx (xx.x)***	***xxx (xx.x)***
<Unknown>	xxx	xxx	xxx
Demographics			
N <cohort name>	xxx	xxx	xxx
Females:Males	xxx:xxx	xxx:xxx	xxx:xxx
Mean Age, <unit> (SD)	xxx.x (xxx.x)	xxx.x (xxx.x)	xxx.x (xxx.x)
Median Age, <unit> (minimum, maximum)	xxx (xxx,xxx)	xxx (xxx,xxx)	xxx (xxx,xxx)
<MOST FREQUENT CATEGORY OF RACE>	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
<SECOND MOST FREQUENT CATEGORY OF RACE>	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
<THIRD MOST FREQUENT CATEGORY OF RACE>	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)

<each group>:
Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = Total number of subjects
SD = Standard deviation
applicable for Co-Ad group and ** applicable for Control group

Template 14 Exposure to study vaccines <Exposed Set>

	<Each group> N=XXXX		<Each group> N=XXXX		Total N=XXXX	
Number of subjects receiving	**n**	**%**	**n**	**%**	**n**	**%**
Exactly 1 Dose						
Exactly 2 Doses						
Exactly 3 Doses						
…						
At least 1 Dose						
Total number of doses administered during the study						

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = number of subjects in each group or in total included in the considered cohort
n = number of subjects/doses in the given category
% = percentage of subjects in the given category

Template 15 Compliance in completing solicited adverse events information <Exposed Set>

		<each group>			<each group>		
DOSE	**Adverse event information**	**N**	**n**	**Compliance (%)**	**N**	**n**	**Compliance (%)**
DOSE <each dose number>	General AES						
	Local AES						
TOTAL	General AES						
	Local AES						

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N=Number of administered doses
n = number of doses with AES returned
General AES = **AE** screens used for the collection of general solicited AEs
Local AES = **AE** screens used for the collection of local solicited AEs
Compliance (%) = (n / N) X 100

Template 16 Incidence and nature of <grade 3, related, grade 3 related, > adverse events (<unsolicited and solicited, solicited only>) reported <during the 7-day (Days 1-7), beyond the 7-day (Days 1-7)> post-vaccination period following each dose and overall *<Exposed Set>*

		<Each group>					<Each group>				
					95% CI					95% CI	
Dose	**Adverse event**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 1	Any adverse event										
	General adverse events										
	Local adverse events										
Dose 2	Any adverse event										
	General adverse events										
	Local adverse events										
Dose 3	Any adverse event										
	General adverse events										
	Local adverse events										
Overall/dose	Any adverse event										
	General adverse events										
	Local adverse events										
Overall/subject	Any adverse event										
	General adverse events										
	Local adverse events										

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
For each dose and overall/subject: N = number of subjects with at least one documented dose; n/% = number/percentage of subjects presenting at least one type of adverse event
For overall/dose: N = number of documented doses; n/% = number/percentage of doses followed by at least one type of adverse event
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

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204487 (ZOSTER-059 PRI)
Statistical Analysis Plan Amendment 3

Template 17 Incidence of solicited local adverse events reported during the 7-day (Days 1-7) post-vaccination period by study vaccine following each dose and overall <Exposed Set>

				Co-Ad					Control				
							95% CI					95% CI	
Dose	**Adverse event**	**Product**	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 1	Pain	HZ/su	All										
			Grade 2 or 3										
			Grade 3										
			Medical advice										
		Prevenar13	All										
			Grade 2 or 3										
			Grade 3										
			Medical advice										
	Redness (mm)	HZ/su	All										
			>50										
			>100										
			Medical advice										
		Prevenar 13	All										
			>50										
			>100										
			Medical advice										
	Swelling (mm)	HZ/su	All										
			>50										
			>100										
			Medical advice										
		Prevenar 13	All										
			>50										
			>100										
			Medical advice										
Dose 2													
Dose 3													
Overall/Dose													
Overall/Subject													

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
For each dose: N = number of subjects with the corresponding documented dose; n/% = number/percentage of subjects reporting the type of adverse event at least once following the corresponding dose
For Overall/dose: N = number of documented dose; n/% = number/percentage of doses followed by at least one type of adverse event
For Overall/subject: N = number of subjects with at least one documented dose; n/% = number/percentage of subjects reporting the type of adverse event at least once
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit

Template 18 Incidence of solicited general adverse events reported during the 7-day (Days 1-7) post-vaccination period following each dose and overall <Exposed Set>

			<each group>				
						95 % CI	
Dose	**Adverse event**	**Type**	**N**	**n**	**%**	**LL**	**UL**
Dose 1	Fatigue	All					
		Grade 3					
		Related					
		Grade 3*Related					
		Medical advice					
	Gastrointestinal symptoms	All					
		Grade 3					
		Related					
		Grade 3*Related					
		Medical advice					
	Headache	All					
		Grade 3					
		Related					
		Grade 3*Related					
		Medical advice					
	Myalgia	All					
		Grade 3					
		Related					
		Grade 3*Related					
		Medical advice					
	Shivering	All					
		Grade 3					
		Related					
		Grade 3*Related					
		Medical advice					
	Fever (Oral) (°C)	All (≥38.0)					
		>38.0					
		>38.5					
		>39.0					
		>39.5					
		>40.0					
		Related					
		>39.0*Related					
		Medical advice					
Dose 2		…					
Dose 3							
Overall/Dose							
Overall/Subject							

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
For each dose: N = number of subjects with the corresponding documented dose; n/% = number/percentage of subjects reporting the adverse event at least once following the corresponding dose
For Overall/dose: N = number of documented dose; n/% = number/percentage of doses followed by at least one type of adverse event
For Overall/subject: N = number of subjects with at least one documented dose; n/% = number/percentage of subjects reporting the type of adverse event at least once
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit

Template 19 Summary of temperature value by half degree increment taken by different routes reported during the 7-day (Days 1-7) post-vaccination following each dose <Exposed Set>

				Co-Ad					Control				
							95 % CI					95 % CI	
Dose	**Symptom**	**Route**	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 1	Temperature (°C)	Oral	≥35.0										
			>35.5										
			>36.0										
			>36.5										
			>37.0										
			>37.5										
			>38.0										
			>38.5										
			>39.0										
			>39.5										
			>40.0										
		Axillary	≥35.0										
			>35.5										
			>36.0										
			>36.5										
			>37.0										
			>37.5										
			>38.0										
			>38.5										
			>39.0										
			>39.5										
			>40.0										
Dose 2	Temperature (°C)	Oral	≥35.0										
			>35.5										
			>36.0										
			>36.5										
			>37.0										
			>37.5										
			>38.0										
			>38.5										
			>39.0										
			>39.5										
			>40.0										
Dose 3													

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su

Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su

For each dose: N = number of subjects with at least one documented dose; ***n/% = number/percentage of subjects reporting the temperature at least once***

95%CI = Exact 95% confidence interval; LL = lower limit, UL = upper limit

Template 20 Number and percentage of subjects reporting the occurrence of <grade 3> <non-serious> unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term <with causal relationship to vaccination, with medically attended visit>, within the 30-day (Days 1-30) post-vaccination period <,including numbers of events><Exposed Set>

		Each group N =				
					95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n***	**n**	**%**	**LL**	**UL**
	At least one adverse event					
Gastrointestinal disorders (10017947)	At least one PT related to the corresponding SOC					
	Diarrhoea (10012735)					
	Teething (10043183)					
	Vomiting (10047700)					
General disorders and administration site conditions (10018065)	At least one PT related to the corresponding SOC					
	Pyrexia (10037660)					
Immune system disorders (10021428)	Seasonal allergy (10048908)					
Infections and infestations (10021881)	Conjunctivitis (10010741)					
	Otitis media (10033078)					
	Paronychia (10034016)					
	Tonsillitis (10044008)					
	Tonsillitis streptococcal (10044013)					
	Viral upper respiratory tract infection (10047482)					
Injury, poisoning and procedural complications (10022117)	Arthropod bite (10003399)					
	Face injury (10050392)					
	Head injury (10019196)					
Skin and subcutaneous tissue disorders (10040785)	Miliaria (10027627)					

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
At least one adverse event = at least one adverse event experienced (regardless of the MedDRA Preferred Term)
N = number of subjects included in the considered cohort in each group
n/% = number/percentage of subjects reporting the adverse event at least once
n* = number of events reported
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit
Please note the n* will only be presented for the CTRS posting with the time interval as per the secondary endpoint

Template 21 Global Summary of <grade 3> <non-serious>unsolicited signs and adverse events reported <with causal relationship with vaccination, with medically attended visit> within the 30-day (Days 1-30) post-vaccination period <Exposed Set>

	Co-Ad	Control	Total
Number of subjects with at least one unsolicited adverse event reported			
Number of doses followed by at least one unsolicited adverse event			
Number of unsolicited adverse events classified by MedDRA Preferred Term*			
Number of unsolicited adverse events reported**			

Co-Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3:HZ/su
N = number of subjects included in the considered cohort in each group
* Adverse events reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Adverse events reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Template 22 Number and percentage of subjects starting a concomitant medication during the 30- day (Days 1-30) post vaccination period by dose and overall <Exposed Set>

		<each group>				
					95% CI	
Dose	**Type**	**N**	**n**	**%**	**LL**	**UL**
Dose 1	Any					
	Any in anticipation of study vaccine reaction					
	Any chronic use					
Dose 2	Any					
	Any in anticipation of study vaccine reaction					
	Any chronic use					
Dose 3	Any					
	Any in anticipation of study vaccine reaction					
	Any chronic use					
Overall/Dose	Any					
	Any in anticipation of study vaccine reaction					
	Any chronic use					
Overall/Subject	Any					
	Any in anticipation of study vaccine reaction					
	Any chronic use					

<each group>:
Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
*For each dose: N = total number of subjects with the corresponding administered dose; n/% = number/percentage of subjects **who** took the specified type of concomitant medication at least once during the considered period*
For Overall/dose: N = number of administered doses; n/% = number/percentage of doses after which the specified type of concomitant medication was taken at least once during the considered period
For Overall/subject: N = total number of subjects with at least one administered dose; n/% = number/percentage of subjects who took the specified type of concomitant medication at least once during the considered period

Template 23 *Number of days with solicited <local, general> adverse events <during the 7 days (Days 1-7) post vaccination period following each dose and overall> <- Prevenar 13 vaccine, - HZ/su vaccine> <Exposed Set>*

			<Co-Ad group>	<Control group>
Dose	**Adverse event**	**Statistic**	**value**	**value**
<Each Dose>	<Each Adverse event>	n	xxxx	xxxx
		Mean	xx.x	xx.x
		Minimum	xx.x	xx.x
		Q1	xx.x	xx.x
		Median	xx.x	xx.x
		Q3	xx.x	xx.x
		Maximum	xx.x	xx.x
Overall/Dose	<Each Adverse event >	n	xxxx	xxxx
		Mean	xx.x	xx.x
		Minimum	xx.x	xx.x
		Q1	xx.x	xx.x
		Median	xx.x	xx.x
		Q3	xx.x	xx.x
		Maximum	xx.x	xx.x

Co-Ad group = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control group = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
n= number of doses with adverse event
Q1= 25th percentile; Q3= 75th percentile
Please note the table by vaccine type will only be done for local solicited adverse events.

Template 24 Solicited and unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term within the 30-day (Days 1-30) post-vaccination period including number of events - SAE excluded <Exposed Set>

		<each group> N =		
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n***	**n**	**%**
	At least one adverse event			
<each SOC>	<each PT term>			

<each group>:
Co-Ad group = Dose 1: Prevenar+ HZ/su, Dose 2: HZ/su
Control group = Dose 1: Prevenar, Dose 2: HZ/su, Dose 3: HZ/su
At least one adverse event = at least one adverse event experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with the administered dose
n* = number of events reported
n/% = number/percentage of subjects reporting the adverse event at least once

Template 25 Number (%) of subjects with serious adverse events from <first vaccination dose up to 30 days post last vaccination, 30 days post last vaccination up to study end, first vaccination dose up to <database freeze date(DDMMMYYYY)><study end>, including number of events reported <Exposed Set>

			<each group> N =		
Type of Event	**Primary System Organ Class**	**Preferred Term (CODE)**	**n***	**n**	**%**
SAE	At least one adverse event				
	<each SOC>	<each PT term>			
Related SAE	At least one adverse event				
	<each SOC>	<each PT term>			
Fatal SAE	At least one adverse event				
	<each SOC>	<each PT term>			
Related fatal SAE	At least one adverse event				
	<each SOC>	<each PT term>			

<each group>:
Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = number of subjects with the administered dose
n* = number of events reported
n/% = number/percentage of subjects reporting the adverse event at least once

Template 26 Number (%) of subjects reported solicited local adverse events during the 7-day (Days 1-7) post-vaccination period following each dose and across dose <Exposed Set>

				Co-Ad					Control				
							95% CI					95% CI	
Dose	**Adverse event**	**Product**	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 1	Pain	HZ/su	All										
			Grade 2 or 3										
			Grade 3										
			Medical advice										
		Prevenar	All										
			Grade 2 or 3										
			Grade 3										
			Medical advice										
	Redness (mm)	HZ/su	All										
			>50										
			>100										
			Medical advice										
		Prevenar	All										
			>50										
			>100										
			Medical advice										
	Swelling (mm)	HZ/su	All										
			>50										
			>100										
			Medical advice										
		Prevenar	All										
			>50										
			>100										
			Medical advice										
Dose 2													
Dose 3													
Across dose													

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
For each dose: N = number of subjects with the corresponding documented dose; n/% = number/percentage of subjects reporting the type of adverse event at least once following the corresponding dose
For Across dose: N = number of subjects with at least one documented dose; n/% = number/percentage of subjects reporting the adverse event at least once
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit

Template 27 Number (%) of subjects reported solicited general adverse events during the 7-day (Days 1-7) post-vaccination period following each dose and across dose <Exposed Set>

			<each group>				
						95 % CI	
Dose	**Adverse event**	**Type**	**N**	**n**	**%**	**LL**	**UL**
Dose 1	Fatigue	All					
		Grade 3					
		Related					
	Gastrointestinal symptoms	All					
		Grade 3					
		Related					
	Headache	All					
		Grade 3					
		Related					
	Myalgia	All					
		Grade 3					
		Related					
	Shivering	All					
		Grade 3					
		Related					
	Fever (Oral) (°C)	All (≥38.0)					
		>39.0					
		Related					
Dose 2	Fatigue	…					
	Gastrointestinal symptoms						
	Headache						
	Myalgia	…					
	Shivering	…					
	Fever (Oral) (°C)	…					
Across Dose		…					
		…					

<each group>:
Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
For each dose: N = number of subjects with the corresponding documented dose; n/% = number/percentage of subjects reporting the adverse event at least once following the corresponding dose
For Across dose: N = number of subjects with at least one documented dose; n/% = number/percentage of subjects reporting the adverse event at least once
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit

Template 28 Number and percentage of subjects with <anti-pneumococcal <X> antibody titres> equal to or above <cut-off> and GMT <*PPS for immunogenicity,* Exposed Set>

				<≥each serotype LLOQ>				<GMT>				
						95% CI			95% CI			
Antibody	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**	**Min**	**Max**
<anti-pneumococcal <X> antibody>	Co-Ad	PRE										
		PI(M1) or PII(M3)										
	Control	PRE or PI(M2)										
		PI(M1) or PIII(M5)										

<each group>:
Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
GMT = geometric mean antibody titre calculated on all subjects
N = **n**umber of subjects with available results
95% CI = 95% confidence interval; LL = lower limit, UL = upper limit
n/% = number/percentage of subjects with <concentration, titre> equal to or above specified value
MIN/MAX = Minimum/Maximum
PRE= Pre-vaccination at Day 1; PII(M3) = Post-vaccination dose 2 at Month 3; PI(M1) = Post-vaccination dose 1 at Month 1; PI(M2) = Post-vaccination dose 1 at Month 2; PIII(M5) = Post-vaccination dose 3 at Month 5
Please note to consider PRE and PI(M1) for both group for pneumococcal antibody. For gE antibody, PRE and PII(M3) for Co-Ad and PI(M2) and PIII(M5) for Control group.

Template 29 *Seropositivity rate and geometric mean concentration for anti-gE ELISA antibody concentration <PPS for immunogenicity, Exposed Set>*

				≥cut-off unit				GMC				
						95% CI			95% CI			
Antibody	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**	**Min**	**Max**
Anti-gE antibody	Co-Ad	PRE										
		PI(M1) or PII(M3)										
	Control	PRE or PI(M2)										
		PI(M1) or PIII(M5)										

<each group>:
Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
GMC = geometric mean antibody concentration calculated on all subjects
*N = **n**umber of subjects with available results*
95% CI = 95% confidence interval; LL = lower limit, UL = upper limit
n/% = number/percentage of subjects with concentration equal to or above specified value
MIN/MAX = Minimum/Maximum
PRE= Pre-vaccination at Day 1; PII(M3) = Post-vaccination dose 2 at Month 3; PI(M1) = Post-vaccination dose 1 at Month 1; PI(M2) = Post-vaccination dose 1 at Month 2; PIII(M5) = Post-vaccination dose 3 at Month 5
Please note to consider PRE and PI(M1) for both group for pneumococcal antibody. For gE antibody, PRE and PII(M3) for Co-Ad and PI(M2) and PIII(M5) for Control group.

Template 30 Adjusted ratios of GMCs between groups (Control group divided by Co-Ad group) for anti-gE antibody ELISA concentrations at one month post dose 2 of HZ/su vaccine <*PPS for immunogenicity,* Exposed Set>

Control				Co-Ad				Adjusted GMC ratio (Control / Co-Ad)		
		95% CI*				95% CI*			95% CI	
N	Adjusted GMC	LL	UL	N	Adjusted GMC	LL	UL	Value	LL	UL

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
Adjusted GMC = geometric mean antibody concentration adjusted for vaccine group, age and baseline concentration
N = **n**umber of subjects with both pre- and post-vaccination results available
95% CI* = 95% confidence interval for the adjusted GMC (Ancova model: adjustment for vaccine group, age and baseline concentration - pooled variance); LL = lower limit, UL = upper limit
95% CI = 95% confidence interval for the adjusted GMC ratio (Ancova model: adjustment for vaccine group, age and baseline concentration - pooled variance); LL = lower limit, UL = upper limit

Template 31 Adjusted ratios of GMTs between groups (Control group divided by Co-Ad group) for anti-pneumococcal <X> antibody titres at one month post Prevenar 13 vaccine <*PPS for immunogenicity,* Exposed Set>

	Control				Co-Ad				Adjusted GMT ratio (Control / Co-Ad)		
			95% CI*				95% CI*			95% CI	
	N	Adjusted GMT	LL	UL	N	Adjusted GMT	LL	UL	Value	LL	UL

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
Adjusted GMT = geometric mean antibody titre adjusted for vaccine group, age and baseline concentration
N = **n**umber of subjects with both pre- and post-vaccination results available
95% CI* = 95% confidence interval for the adjusted GMT (Ancova model: adjustment for vaccine group, age and baseline concentration - pooled variance); LL = lower limit, UL = upper limit
95% CI = 95% confidence interval for the adjusted GMT ratio (Ancova model: adjustment for vaccine group, age and baseline concentration - pooled variance); LL = lower limit, UL = upper limit

Template 32 Mean Geometric Increase (MGI) of anti-gE antibody ELISA concentrations from baseline to one month post dose 2 of HZ/su vaccine <*PPS for immunogenicity*, Exposed Set>

							MGI			
									95% CI	
Antibody	Group	N	Time point description	GMC	Time point description	GMC	Ratio order	Value	LL	UL
<Antibody>	Co-Ad		PII(M3)		PRE		PII(M3)/PRE			
	Control		PIII(M5)		PI(M2)		PIII(M5)/PI(M2)			

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = **n**umber of subjects with available results at the two considered time points
GMC = geometric mean antibody concentration
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE= Pre-vaccination at Day 1; PII(M3) = Post-vaccination dose 2 at Month 3 for Co-Ad group

PI(M2) = Post-vaccination dose 1 at Month 2 for Control group (considered as pre-vaccination for HZ/su in Control group)
PIII(M5) = Post-vaccination dose 3 at Month 5 for Control group (considered as post dose 2 for HZ/su in Control group)

Template 33 Descriptive statistics of fold increase from baseline to one month post dose 2 of HZ/su vaccine for anti-gE antibody ELISA concentration <*PPS for immunogenicity*, Exposed Set>

		Each Group N=		
			95% CI	
Antibody	**Parameter**	**Value**	**LL**	**UL**
Anti-gE antibody	n			
	Nmiss			
	Mean			
	SD			
	Min			
	Q1			
	Median			
	Q3			
	Max			

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = total number of subjects
n = number of subjects with available results; Nmiss = number of subjects with missing results
SD = Standard Deviation; Q1, Q3 = First and third quartiles; Min/Max = Minimum/Maximum
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit
Please note – To calculate the fold increase, result at PII(M3) compared to PRE-for Co-Ad and PIII(M5) compared to PI(M2) for Control group has to be considered

Template 34 Distribution of fold increase from baseline to one month post dose 2 of HZ/su vaccine for anti-gE antibody ELISA concentrations <*PPS for immunogenicity*, Exposed Set>

			<Each group>					<Each group>				
						95% CI					95% CI	
Antibody	**Timing**	**Fold change**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
<each antibody>	<PII(M3)>	≥2	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x	xx.x
		≥4										
		≥6										
		≥8										
		≥10										
		≥12										
		≥14										
	<PIII(M5)	>= Ratio1	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x	xx.x

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = number of subjects with available results
n/% = number/percentage of subjects with concentration within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PII(M3) = Post-vaccination dose 2 at Month 3 for Co-Ad group
PIII(M5) = Post-vaccination dose 3 at Month 5 for Control group (considered as post dose 2 for HZ/su in Control group)
Please note – To calculate the fold increase, result at PII(M3) compared to PRE-for Co-Ad and PIII(M5) compared to PI(M2) for Control group has to be considered

Template 35 Listing of potential Immune Mediated Diseases (pIMDs) reported as identified by predefined list of preferred terms and/or by investigator assessment up to end of study *by age subgroup* <Exposed Set>

Group	Sub.No.	Country	*Age strata*	Age at onset (Y)	Gender	Race	Primary System Organ Class	Preferred term	Dose	Day of onset	Causality	Serious pIMD based on Investigator?	SAE (Y/N)	Outcome	pIMD Source

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
50-59YOA = subjects aged 50-59 years; 60-69YOA = subjects aged 60-69 years; ≥70YOA = subjects aged 70 years and over

Template 36 Listing of all SAEs up to end of study *by age subgroup* <Exposed Set>

Group	Sub. No.	Gender	Country	Race	*Age strata*	Age at onset (Year)	Verbatim	Preferred term	Primary System Organ Class	MED type	Dose	Day of onset	Duration	Intensity	Causality	Outcome

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
50-59YOA = subjects aged 50-59 years; 60-69YOA = subjects aged 60-69 years; ≥70YOA = subjects aged 70 years and over

Template 37 Listing of suspected HZ cases from first administered dose up to end of study *by age subgroup*<Exposed Set>

Group	Sub. No.	*Age strata*	Previous dose	Day on-set	Duration	Preferred term	AE description	Medical advice	Medically attended visit	Intensity	Causality	Outcome

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
50-59YOA = subjects aged 50-59 years; 60-69YOA = subjects aged 60-69 years; ≥70YOA = subjects aged 70 years and over

Template 38 Listing of (S)AEs and solicited adverse events leading to study or treatment discontinuation <up to month 5><up to end of study> *by age subgroup* <Exposed Set>

Type of discontinuation: <study/treatment

Group	Subject number	*Age strata*	Gender	Country	Race	AE Description	SAE (Y/N)	Causality	Outcome	Vaccination and visit
										Vaccination: x at visit x

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
50-59YOA = subjects aged 50-59 years; 60-69YOA = subjects aged 60-69 years; ≥70YOA = subjects aged 70 years and over

Template 39 Maximum intensity of solicited <local, general> *adverse event* ongoing beyond the 7-day (Days 1-7) post-vaccination period following each dose and overall <Exposed Set>

				<each group>	<each group>
Dose	***Adverse event***	**Type**	**Time to resolution (days)**	**Value or n**	**Value or n**
<EACH DOSE>	***<Each adverse event>***	All	N	xx	xx
			n	xx	xx
			q1	xx.x	xx.x
			median	xx.x	xx.x
			q3	xx.x	xx.x
		Grade 3	N	xx	xx
			n	xx	xx
			q1	xx.x	xx.x
			median	xx.x	xx.x
			q3	xx.x	xx.x
		Grade 3*Related	N	xx	xx
			n	xx	xx
			q1	xx.x	xx.x
			median	xx.x	xx.x
			q3	xx.x	xx.x
OVERALL/DOSE	<Each adverse event>	<EACH TYPE>	N	xx	xx
			n	xx	xx
			q1	xx.x	xx.x
			median	xx.x	xx.x
			q3	xx.x	xx.x

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
Time to resolution: number of days beyond the end of the follow-up period
N = number of adverse events that were ongoing after the follow-up period
n = number of adverse events that were ongoing after the follow-up period with a complete end date
q1 = 25th percentile; q3= 75th percentile

Template 40 Number and percentage of doses reporting the occurrence of <grade 3> unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term <with causal relationship to vaccination> within the 30-day (Days 1-30) post-vaccination period <Exposed Set>

		Each group N =			
				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**
At least one adverse event					
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)				
	Teething (10043183)				
	Vomiting (10047700)				
General disorders and administration site conditions (10018065)	Pyrexia (10037660)				
Immune system disorders (10021428)	Seasonal allergy (10048908)				
Infections and infestations (10021881)	Conjunctivitis (10010741)				
	Otitis media (10033078)				
	Paronychia (10034016)				
	Tonsillitis (10044008)				
	Tonsillitis streptococcal (10044013)				
	Viral upper respiratory tract infection (10047482)				
Injury, poisoning and procedural complications (10022117)	Arthropod bite (10003399)				
	Face injury (10050392)				
	Head injury (10019196)				
Skin and subcutaneous tissue disorders (10040785)	Miliaria (10027627)				

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
At least one adverse event = at least one adverse event experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses followed by the adverse event
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Template 41 Number and percentage of subjects reporting the occurrence of <serious adverse events, potential Immune Mediated Disease> classified by MedDRA Primary System Organ Class and Preferred Term from <first vaccination up to 30 days post last vaccination, from 30 days post last vaccination dose up to end of study, from first vaccination up to study end> <,including number of events><Exposed Set>

		Co-Ad N =					Control N =				
					95% CI						95% CI
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n***	**n**	**%**	**LL**	**UL**	**n***	**n**	**%**	**LL**	**UL**
At least one adverse event											
Blood and lymphatic system disorders (10005329)	Leukocytosis (10024378)										
Cardiac disorders (10007541)	Acute myocardial infarction (10000891)										
	Atrial fibrillation (10003658)										
	Cardiac failure congestive (10007559)										
	Tachycardia (10043071)										
	Ventricular tachycardia (10047302)										

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
At least one adverse event = at least one adverse event experienced (regardless of the MedDRA Preferred Term)
N = number of subjects included in the considered cohort in each group
n/% = number/percentage of subjects reporting the adverse event at least once
n* = **n**umber of events reported
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit
Please note that n* will be used to present pIMD for CTRS posting.

Template 42 Global Summary of <serious adverse events, potential Immune Mediated Disease> <with causal relationship with vaccination> reported from <first vaccination up to 30 days post last vaccination, from 30 days post last vaccination dose up to end of study, from first vaccination up to study end> <Exposed Set>

	Co-Ad	Control	Total
Number of subjects with at least one <SAE, pIMD> reported			
Number of doses followed by at least one <SAE, pIMD>			
Number of <SAE, pIMD> classified by MedDRA Preferred Term*			
Number of <SAE, pIMD> reported**			

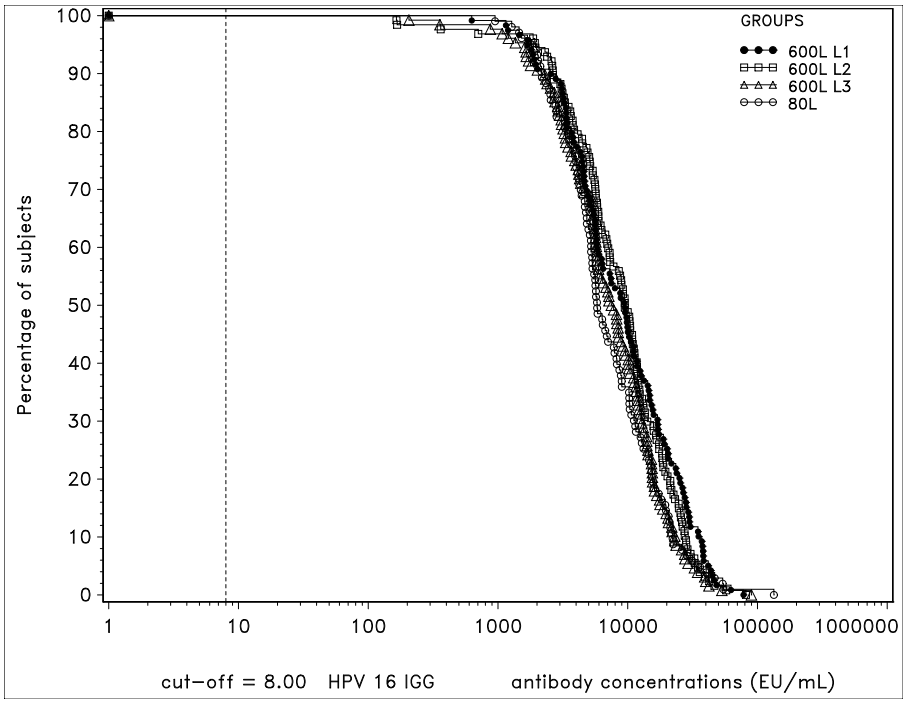
Co-Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = number of subjects included in the considered cohort in each group
* Adverse events reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Adverse events reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Template 43 Vaccine response rates for anti-gE antibody concentrations at one month post dose 2 of HZ/su vaccine *<PPS for immunogenicity,* Exposed Set>

		<Each group>				
					95% CI	
Antibody	**Pre-vaccination status**	**N**	**n**	**%**	**LL**	**UL**
<each antibody>	S-	XXXX	XXXX	XX.X	XXX.X	XXX.X
	S+	XXXX	XXXX	XX.X	XXX.X	XXX.X
	Total	XXXX	XXXX	XX.X	XXX.X	XXX.X

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
S- = seronegative subjects (antibody <concentration> < <cut off> <unit>) at pre-vaccination; S+ = seropositive subjects (antibody <concentration>≥ <cut off> <unit>) at pre-vaccination
Total = subjects either seropositive or seronegative at pre-vaccination
Vaccine response defined as :
For initially seronegative subjects, antibody concentration at post-vaccination ≥ 4 fold the cut-off for Anti-gE (4x97 mIU/ml)
For initially seropositive subjects, antibody concentration at post-vaccination ≥ 4 fold the pre-vaccination antibody concentration
N = number of subjects with both pre- and post-vaccination results available
n/% = number/percentage of responders
<95>% CI = exact <95>% confidence interval, LL = Lower Limit, UL = Upper Limit
Please note – To calculate the vaccine response, result at PII(M3) compared to PRE-for Co-Ad and PIII(M5) compared to PI(M2) for Control group has to be considered

Template 44 Reverse cumulative distribution curves for <anti-gE antibody concentration, anti-pneumococcal <X> antibody titres> in each group at baseline and <post dose 2 of HZ/su vaccine, post dose of Prevenar 13> <*PPS for immunogenicity*, Exposed Set>



Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
Note: This graph is provided as an example. The same graph will be provided in colour for each time point and each assay comparing the values of the groups
Please note to consider PRE and PI(M1) for both group for pneumococcal antibody. For gE antibody, PRE and PII(M3) for Co-Ad and PI(M2) and PIII(M5) for Control group.

Template 45 Number and percentage of subjects <with><experiencing> fatal SAEs classified by MedDRA Primary System Organ Class and Preferred Term <who died><with onset of fatal SAE> <during the period starting> <from first vaccination up to 30 days post last vaccination dose> <after 30 days post last vaccination dose up to study end><from first vaccination until the study end><during the entire study period> <Exposed Set>

		Co-Ad N =				Control N =			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one adverse event									
Blood and lymphatic system disorders (10005329)	Leukocytosis (10024378)								
Cardiac disorders (10007541)	Acute myocardial infarction (10000891)								
	Atrial fibrillation (10003658)								
	Cardiac failure congestive (10007559)								
	Tachycardia (10043071)								
	Ventricular tachycardia (10047302)								

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
At least one adverse event = at least one adverse event experienced (regardless of the MedDRA Preferred Term)
N = number of subjects included in the considered cohort in each group
n/% = number/percentage of subjects reporting the adverse event at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Template 46 Summary of subject disposition from Enrolled Set to Randomized Set

	Total N=XXX n %
Number of subjects who signed an informed consent	
Withdrawals prior to randomization	xxx xx.x
<Withdrawal reason 1>	xxx xx.x
<Withdrawal reason 2>	xxx xx.x
…	xxx xx.x
	xxx xx.x
Number of subjects included in Randomized Set	

N = number of subjects
n% = number / percentage of subjects in a given category

Template 47 Summary of subject disposition from Randomized Set to Per Protocol Set

				<Group 1> *N=XXX* *n %*	*<Group 2>* *N=XXX* *n %*	*Total* *N=XXX* *n %*
Number of subjects included in Randomized Set						
Withdrawals				xxx xx.x	xxx xx.x	xxx xx.x
<Withdrawal reason 1>				xxx xx.x	xxx xx.x	xxx xx.x
<Withdrawal reason 2>				xxx xx.x	xxx xx.x	xxx xx.x
…						
Eliminations				xxx xx.x	xxx xx.x	xxx xx.x
<Elimination reason 1				xxx xx.x	xxx xx.x	xxx xx.x
(code)>				xxx xx.x	xxx xx.x	xxx xx.x
<Elimination reason 2						
(code)>						
…				xxx xx.x	xxx xx.x	xxx xx.x
Number of subjects included in Exposed Set						
Elimination 1						
Number of subjects included in PPS for immunogenicity						

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = number of subjects
n% = number / percentage of subjects in a given category

CONFIDENTIAL

204487 (ZOSTER-059 PRI)
Statistical Analysis Plan Amendment 3

Template 48 Listing of subjects who died during the entire study period and their fatal SAEs *by age subgroup* <Enrolled Set>

Group	Sub. No.	Sex	Country	Race	*Age strata*	Age at Onset (Year)	Verbatim	Preferred term	Primary System Organ Class	MED type	Dose prior to onset of fatal SAE	Days between onset of fatal SAE and previous dose	Dose prior to death	Days between death and previous dose	SAE Duration	SAE Causality
No Group	PPD										0	-	0	-		
											0	-	0	-		
											1	xx	1	xx		
											1	xx	2	xx		
											1	xx	1	xx		
											1	xx	1	xx		

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
No Group= Enrolled not vaccinated
50-59YOA = subjects aged 50-59 years; 60-69YOA = subjects aged 60-69 years; ≥70YOA = subjects aged 70 years and over
MED = Medical Advice type (HO: hospitalisation, ER: emergency room visit, MD: medical practice visit)

Template 49 Summary of subjects by unsolicited adverse event category, with onset within 30 days of each vaccination

	<Group 1> N=XXXX				*<Group 2> N=XXXX*			
			95% CI				*95% CI*	
	n	*%*	*LL*	*UL*	*n*	*%*	*LL*	*UL*
At least one unsolicited adverse event	*xxx*	*xx.x*	*xx.x*	*xx.x*	*xxx*	*xx.x*	*xx.x*	*xx.x*
At least one grade 3 unsolicited adverse event	*xxx*	*xx.x*	*xx.x*	*xx.x*	*xxx*	*xx.x*	*xx.x*	*xx.x*
At least one related unsolicited adverse event	*xxx*	*xx.x*	*xx.x*	*xx.x*	*xxx*	*xx.x*	*xx.x*	*xx.x*
At least one grade 3 related unsolicited adverse event	*xxx*	*xx.x*	*xx.x*	*xx.x*	*xxx*	*xx.x*	*xx.x*	*xx.x*

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = number of subjects included in the considered cohort in each group
n/% = number/percentage of subjects reporting the adverse event at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Template 50 Summary of subjects by serious adverse event and potential Immune Mediated Disease categories, with onset <from first vaccination to 30 days post last vaccination, after 30 days post last vaccination until study end>

	<Group 1> N=XXXX				*<Group 2> N=XXXX*			
			95% CI				*95% CI*	
	n	*%*	*LL*	*UL*	*n*	*%*	*LL*	*UL*
At least one serious adverse event	*xxx*	*xx.x*	*xx.x*	*xx.x*	*xxx*	*xx.x*	*xx.x*	*xx.x*
At least one causally related serious adverse event	*xxx*	*xx.x*	*xx.x*	*xx.x*	*xxx*	*xx.x*	*xx.x*	*xx.x*
At least one potential Immune Mediated Disease	*xxx*	*xx.x*	*xx.x*	*xx.x*	*xxx*	*xx.x*	*xx.x*	*xx.x*
At least one causally related potential Immune Mediated Disease	*xxx*	*xx.x*	*xx.x*	*xx.x*	*xxx*	*xx.x*	*xx.x*	*xx.x*

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = number of subjects included in the considered cohort in each group
n/% = number/percentage of subjects reporting the adverse event at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

GlaxoSmithKline	**Statistical Analysis Plan**
Detailed Title:	A Phase IIIB, randomized, open-label, multicenter clinical trial to assess the immunogenicity and safety of GSK Biologicals' Herpes Zoster vaccine GSK1437173A when co-administered with *Prevenar13* in adults aged 50 years and older.
eTrack study number and Abbreviated Title	204487 (ZOSTER-059 PRI)
Scope:	All analyses planned per protocol.
Date of Statistical Analysis Plan	***Amendment 2 Final: 20 November 2019***

APP 9000058193 Statistical Analysis Plan Template V4 (Effective date: 3 June 2019)

CONFIDENTIAL

TABLE OF CONTENTS

PAGE

LIST OF TABLES

PAGE

LIST OF FIGURES

PAGE

LIST OF TEMPLATES

PAGE

LIST OF ABBREVIATIONS

AE	Adverse event
AES	***Adverse Event Screen***
ANCOVA	Analysis of Covariance
$AS01_B$:	MPL, QS21, liposome based Adjuvant System (50 μg MPL and 50 μg QS21)
BS	Blood Sampling
CDR	Clinical Data Reviewer
CI	Confidence Interval
Co-Ad	Co-administration
CRDL	Clinical Research and Development Lead
CRF	Case Report Form
CSR	Clinical Study Report
CTRS	Clinical Trial Registry Summary
ELISA	Enzyme-linked immunosorbent assay
Eli Type	Internal GSK database code for type of elimination code
EL.U/ml	ELISA unit per milliliter
EoS	End of Study
ES	Exposed Set (formally called 'Total Vaccinated Cohort')
GMC	Geometric mean antibody concentration
GMT	Geometric mean antibody titre
GSK	GlaxoSmithKline
IU/ml	International units per milliliter
LL	Lower Limit of the confidence interval
LLOQ	Lower Limit of Quantification
MedDRA	Medical Dictionary for Regulatory Activities
MGI	***Mean Geometric Increase***
MOPA	***Multiplex Opsonophagocytosis Assay***
PCD	Primary Completion Date
PD	Protocol Deviation
PDMP	Protocol Deviation Management Plan
PPS	Per-Protocol Set (formally called 'According to Protocol')
PT	***Preferred Term***

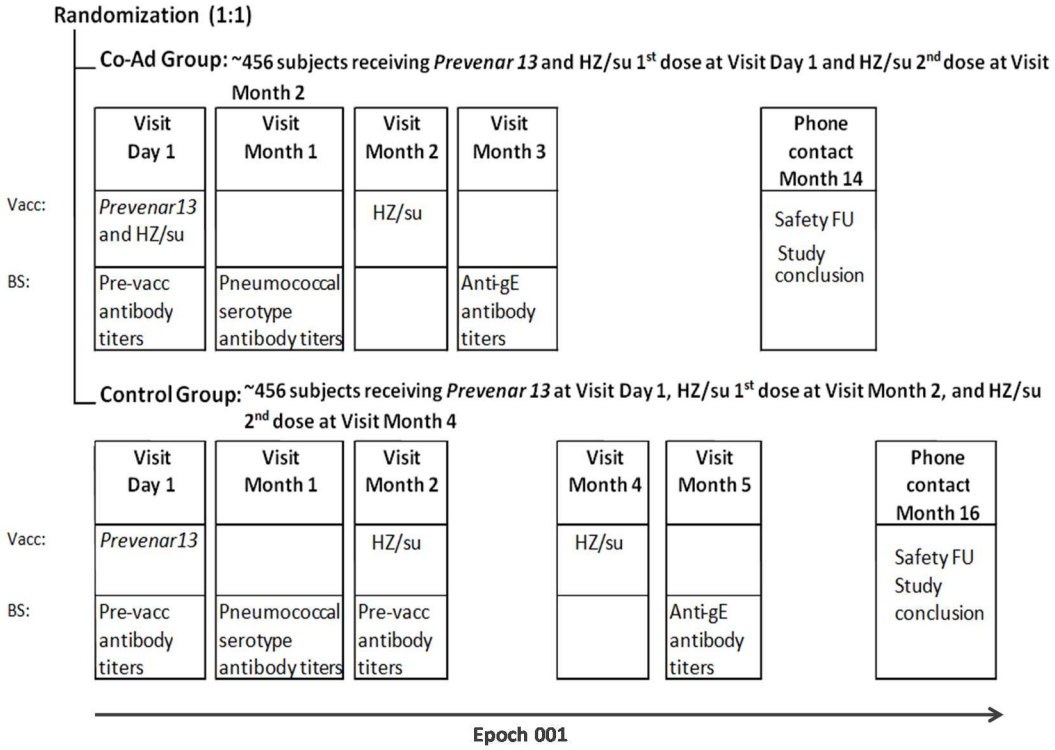
SAE	Serious adverse event
SAP	Statistical Analysis Plan
SBIR	GSK Internet Randomization System
SD	Standard Deviation
SHS	Study Headline Summary
SOC	***System Organ Class***
SUSAR	Suspected Unexpected Serious Adverse Reactions
TFL	Tables Figures and Listings
TOC	Table of Content
UL	Upper Limit of the confidence interval
ULOQ	Upper Limit of Quantification
VRR	Vaccine response rate
YOA	***Years of Age***

1. DOCUMENT HISTORY

Date	Description	Protocol Version
13 APR 2018	First Version	Amendment 2: 30 JAN 2018
11 JUN 2019	Amendment 1 Summary of changes as below: - As per new process applicable, the front page has been modified to remove the names of all the contributing author and reviewers. Also, sign-off is only required to be done by Lead Statistician - Updated LLOQ and newly calculated ULOQ for the 13 pneumococcal serotypes tested by MOPA have been added and accordingly analysis of immunogenicity section has been updated. - Consort table have been added for subject disposition. - Additional tables for fatal serious adverse events (SAEs) and grade 3 non-serious unsolicited adverse events (AEs) have been added. - The term "symptom" has been changed to "adverse event (AE)" in endpoints, table titles and content for solicited AEs, unsolicited AEs, SAEs, and potential immune mediated diseases (pIMDs). - Table 'Summary of temperature value by half degree increment reported during the 7-day (Days 1-7) post-vaccination following each dose' has been removed - Sequence of analysis has been updated - Inclusion of Enrolled and Randomized Set definition - Code 1500 in elimination codes has been removed and added under code 1070. Also, mandatory columns have been added in the elimination table under 'Elimination from PPS section.	Amendment 2: 30 JAN 2018
20-NOV-2019	***Amendment 2*** ***Summary of changes as below:*** - ***The active phase analysis has been removed as a request for a CTRS posting extension has been submitted to NIH; complete CTRS posting will be done at Last Subject Last Visit (LSLV) + 12 months rather than Primary Completion Date (PCD) +12 months as previously planned*** - ***Titles and Footnotes of selected templates have been updated following the Dry run kick-off meeting*** - ***Two new safety templates have been added (Templates 49 and 50)***	***Amendment 2: 30 JAN 2018***

2. STUDY DESIGN

Figure 1 Overview of Study Design



Vacc: vaccination; BS: blood sample; Pre-Vacc: pre-vaccination; FU: follow-up

Experimental design: Phase IIIB, open-label, randomized, controlled, multi-centric, and multi-country, with two parallel groups.

Duration of the study: The intended duration of the study per subject is approximately 14 months for subjects from the Co-Ad group and approximately 16 months for subjects from the Control group.

- Epoch 001: Primary starting at Visit Day 1 and ending with the phone contact at Month 16.

Primary completion date (PCD): Visit Month 5.

End of Study (EoS): Last testing results released of samples collected at Visit Month 3 (Co-Ad group) or at Visit Month 5 (Control group).

Study groups:

Table 1 Study groups and epochs foreseen in the study

Study groups	Number of subjects	Age	Epochs
			Epoch 001
Co-Ad	456	≥ 50 years	x
Control	456	≥ 50 years	x

Table 2 Study groups and treatment foreseen in the study

Treatment name	Vaccine/Product name	Study Groups	
		Co-Ad	Control
HZ/su	VZV gE	x	x
	AS01B	x	x
Prevenar13	*Prevenar 13*	x	x

Control: active control.

Vaccination schedule(s):

- Co-Ad Group:
  - at Visit Day 1: first dose of HZ/su and one dose of Prevenar13,
  - at Visit Month 2: second dose of HZ/su.
- Control Group:
  - at Visit Day 1: one dose of *Prevenar13*,
  - at Visit Month 2: first dose of HZ/su,
  - at Visit Month 4: second dose of HZ/su.

Treatment allocation: Subjects to be randomized in a 1:1 ratio at Visit Day 1 to either Co-Ad or Control group. Subjects in each group will be stratified by age with the following approximate distribution (not less than 25% in each age strata):

- 171 subjects in the 50-59 Years of Age (YOA) stratum,
- 171 subjects in the 60-69 YOA stratum, and
- 114 subjects in the ≥ 70 YOA stratum.

Blinding: open-label.

Table 3 Blinding of study epochs

Study Epochs	Blinding
Epoch 001	open

3. OBJECTIVES

3.1. Co-Primary objectives

To determine the vaccine response rate (VRR) to HZ/su (based on humoral immune response) one month after the second vaccine dose, when the first dose of HZ/su is co-administered with *Prevenar13* (Co-Ad group).

Criterion to be used:

The objective is met if the lower limit (LL) of the 95% CI of the VRR for anti-gE antibody concentrations in the Co-Ad group one month after the second vaccine dose is ≥60%.

If the above objective is met in the Co-Ad group, then the following objective will be evaluated:

To demonstrate non-inferiority of the humoral immune response to two doses of HZ/su at one month after the last vaccine dose, when the first dose of HZ/su is co-administered with *Prevenar13* (Co-Ad group) compared to when two doses of HZ/su are administered subsequent to *Prevenar13* (Control Group).

Criterion for non-inferiority:

One month after the last vaccine dose in each study group, the upper limit (UL) of the 95% confidence interval (CI) for the anti-gE antibodies Geometric Mean Concentration (GMC) ratio between the Control group and the Co-Ad group is <1.5.

If the above non-inferiority objective is met, then the following objective will be evaluated:

To demonstrate non-inferiority of the humoral immune response to *Prevenar13* at one month after the vaccine dose, when *Prevenar13 is* co-administered with the first HZ/su dose (Co-Ad group) compared to when *Prevenar13* is administered separately from HZ/su (Control group), for the 13 serotypes included in *Prevenar13* analyzed sequentially.

Criterion for non-inferiority:

One month after the Prevenar13 vaccine dose in each study group, the UL of the 95% CI for each individual pneumococcal conjugate serotype Geometric Mean Titer (GMT) ratio of the Control group over the Co-Ad group is <2.

For the co-primary objectives, fixed sequence testing which allows for full alpha propagation in pre-ordered hypotheses families will be used (see section 6.3.2.1).

3.2. Secondary objective

To evaluate the safety and reactogenicity following administration of HZ/su and *Prevenar13* vaccines, up to one month post last vaccination and during the whole follow-up period, in the Control group and the Co-Ad group.

4. ENDPOINTS

4.1. Primary endpoints

HZ/su immunogenicity:

- Vaccine response for anti-gE humoral immunogenicity, as determined by ELISA, in subjects from the Co-Ad group at one month post-dose 2, at Visit Month 3.
- Anti-gE antibody concentrations as determined by ELISA at one month post-dose 2, at Visit Month 3 for the Co-Ad group and Visit Month 5 for the Control group.

Pneumococcal vaccine immunogenicity:

- Anti-pneumococcal antibody titers for the 13 following serotypes as determined by MOPA at one month post-dose at Visit Month 1: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F.

The criteria used to define the VRR is given in Section 11.1.2.

4.2. Secondary endpoints

Occurrence of solicited local and general adverse events:

- Occurrence, duration and intensity of each solicited local adverse event within 7 days (Days 1 - 7) after each vaccination,
- Occurrence, duration, intensity and relationship to vaccination of each solicited general adverse event within 7 days (Days 1 - 7) after each vaccination.

Occurrence of unsolicited AEs:

- Occurrence, intensity and relationship to vaccination of unsolicited AEs within 30 days (Days 1 - 30) after each vaccination, according to the Medical Dictionary for Regulatory Activities (MedDRA) classification.

Occurrence of SAEs:

- Occurrence and relationship to vaccination of all SAEs from first vaccination at Day 1 up to 30 days post last vaccination.
- Occurrence and relationship to vaccination of all SAEs during the period starting after 30 days post last vaccination up to study end.

Occurrence of pIMDs:

- Occurrence and relationship to vaccination of any pIMDs from first vaccination at Day 1 up to 30 days post last vaccination.
- Occurrence of any pIMDs during the period starting after 30 days post last vaccination up to study end.

5. ANALYSIS SETS

5.1. Definition

5.1.1. Enrolled Set

The Enrolled Set will include all the subjects for whom valid signed informed consent form is available.

5.1.2. Randomized Set

The Randomized Set will include all the subjects for whom valid signed informed consent form is available and treatment is allocated.

5.1.3. Exposed Set (ES)*

The Exposed set (ES) will include all subjects with at least one vaccine administration documented:

- The ES for analysis of solicited adverse events will include all subjects with at least one documented administered vaccine.
- The ES for analysis of unsolicited AEs, SAEs and pIMDs will include all subjects with at least one vaccine administered.
- The ES for analysis of immunogenicity will include vaccinated subjects for whom immunogenicity data are available.

The ES analysis will be performed per treatment actually administered (at Dose 1).

5.1.4. *Per-protocol set (PPS)* for immunogenicity*

The Per-protocol set for immunogenicity will include all evaluable subjects:

- who meet all eligibility criteria,
- who comply with the procedures and intervals allowed for the analysis,
- who do not meet any of the criteria for elimination during the study,
- for whom data concerning immunogenicity endpoint measures are available.

** Note that in order to align to ICH and cDISC terminology the Total Vaccinated Cohort and the Per- Protocol cohort have been renamed Exposed Set (ES) and Per-Protocol Set (PPS) respectively.*

The intervals allowed for the inclusion in the ***PPS for immunogenicity*** are defined as follows:

	Group	Interval	Allowed interval for PPS analysis of immunogenicity
Interval between vaccinations	Co-Ad	HZ/su (Dose 1) – HZ/su (Dose 2)	49-83 Days
	Control	*Prevenar13* (Dose 1) – HZ/su (Dose 2)	>= 60 days*
	Control	HZ/su (Dose 2) – HZ/su (Dose 3)	49-83 Days
Interval between vaccination and blood sample taken	Co-Ad	*Prevenar13* (Dose 1) – Visit Month 1 for BS	28-48 Days*
	Co-Ad	HZ/su (Dose 2) – Visit Month 3 for BS	28-48 days*
	Control	*Prevenar13* (Dose 1) – Visit Month 1 for BS	28-48 Days*
	Control	HZ/su (Dose 3)– Visit Month 5 for BS	28-48 days*

BS= blood sampling taken; *please note these intervals differ from protocol amendment 2 Table 8 and 9 to increase the number of evaluable subjects while not compromising the interpretation of immunogenicity data

5.2. Criteria for eliminating data from Analysis Sets

Elimination codes are used to identify subjects to be eliminated from analysis. Detail is provided below for each set.

5.2.1. Elimination from Enrolled Set

Code 900 (invalid informed consent or fraud data) will be used for identifying subjects eliminated from Enrolled Set.

5.2.2. Elimination from Randomized Set

Code 900 (invalid informed consent or fraud data) and code 1010 (vaccine number not allocated) will be used for identifying subjects eliminated from Randomized Set.

5.2.3. Elimination from Exposed Set (ES)

Code 1030 (Study vaccine not administered at all), code 1010 (vaccine number not allocated) and code 900 (invalid informed consent or fraud data) will be used for identifying subjects eliminated from ES.

5.2.4. Elimination from Per-protocol analysis Set (PPS)

A subject will be excluded from the PPS analysis under the following conditions:

Code	Condition under which the code is used	Visit (timepoints) where the code is applicable	Applicable for analysis set
900	Invalid informed consent or fraudulent data. Subjects excluded from all stat analysis Note: Subjects receiving a code 900 should not receive any other elimination codes.	All	All
1010	Vaccine number not allocated Note: Subjects receiving a code 1010 should not receive any other elimination codes	Day 1	Randomized Set, ES, PPS
1030	Study vaccine not administered AT ALL but subject number allocated Note: Subjects receiving a code 1030 should not receive any other elimination codes	Day 1	ES, PPS
1040*	Administration of concomitant vaccine(s) forbidden in the protocol Comment: Co-Ad group: From 30 days before 1st vaccination up to Month 3 blood sampling Control group: From 30 days before 1st vaccination up to Month 5 blood sampling	Co-Ad group: Day -30 to Month 3 Control group : Day -30 to Month 5	PPS
1050	Randomization failure (subject not randomized in the correct group) Comment: To check for manual randomisation, treatment not compatible with one assigned by SBIR	Day 1	PPS
1070	– Side, site or route of study vaccine administration wrong or unknown – Administration not according to protocol for reason specified by the investigator, other than side, site and route – Wrong replacement or study vaccine administered (not compatible with the vaccine regimen associated to the treatment number) – Administered study vaccine reported as being the correct one but is not compatible with the vaccine regimen associated to the treatment number.	Co-Ad group – Day 1, Month 2 Control group – Day 1, Month 2, Month 4	PPS
1080	Vaccine has been administered (effective treatment number) despite a temperature deviation qualified by Status QA GMP NON Use	Co-Ad group – Day 1, Month 2 Control group – Day 1, Month 2, Month 4	PPS
1090	Expired vaccine administered	Co-Ad group – Day 1, Month 2 Control group – Day 1, Month 2, Month 4	PPS
2010	Protocol violation (inclusion/exclusion criteria)	Day 1	PPS
2040*	Administration of any medication forbidden by the protocol Co-Ad group: From 1st vaccination up to Month 3 blood sampling Control group : From 1st vaccination up to Month 5 blood sampling	Co-Ad group – Day 1 up to Month 3 Control group – Day 1 up to Month 5	PPS

Code	Condition under which the code is used	Visit (timepoints) where the code is applicable	Applicable for analysis set
2050*	Underlying medical condition forbidden by the protocol Co-Ad group: From 1st vaccination up to Month 3 blood sampling Control group: From 1st vaccination up to Month 5 blood sampling	Co-Ad group – Day 1 up to Month 3 Control group – Day 1 up to Month 5	PPS
2060*	Concomitant infection related to the vaccine which may influence immune response Co-Ad group: From 1st vaccination up to Month 3 blood sampling Control group: From 1st vaccination up to Month 5 blood sampling	Co-Ad group – Day 1 up to Month 3 Control group – Day 1 up to Month 5	PPS
2070*	Concomitant infection not related to the vaccine which may influence immune response Comment: Co-Ad group: From 1st vaccination up to Month 3 blood sampling Control group: From 1st vaccination up to Month 5 blood sampling	Co-Ad group – Day 1 up to Month 3 Control group – Day 1 up to Month 5	PPS
2080	Subjects did not comply with vaccination schedule (dates of vaccination not corresponding to adapted protocol intervals provided in SAP or unknown vaccination dates) Comment: Co-Ad group: DOSE 1 – DOSE 2 Control group: DOSE 1 – DOSE 2 DOSE 2 – DOSE 3	Co-Ad group: Day 1, Month 2 Control group: Day 1, Month 2, Month 4	PPS
2090	Subjects did not comply with blood sample schedule (dates of BS not corresponding to adapted protocol intervals provided in SAP or unknown BS/vaccination dates) Comment: Co-Ad group: DOSE 1 – MONTH 1 BS DOSE 2 – MONTH 3 BS Control group: DOSE 1 – MONTH 1 BS DOSE 3 – MONTH 5 BS	Co-Ad group: Month 1, Month 3 Control group: Month 1, Month 5	PPS
2100	Serological results not available post-vaccination (including lost samples, blood sample not done, unable to test, absence of parallelism). Please specify the applicable rule: ☒ elimination code if ALL are missing for a subject Comment: Co-Ad group: Check for availability of anti-gE serological result at Month 3 and for pneumococcal serological results at Month 1 Control group: Check for availability of anti-gE serological result at Month 5 and for pneumococcal serological results at Month 1	Co-Ad – Month 1, Month 3 Control – Month 1, Month 5	PPS
2120	Obvious incoherence or abnormality or error in data (incoherence between CRF and results, wrong labelling) Comment: Co-Ad group: Check for above condition on anti-gE serological result at Month 3 and on pneumococcal serological results at Month 1	Co-Ad – Month 1, Month 3 Control – Month 1, Month 5	PPS

Code	Condition under which the code is used	Visit (timepoints) where the code is applicable	Applicable for analysis set
	Control group: Check for above condition on anti-gE serological result at Month 5 and on pneumococcal serological results at Month 1		
2500	Incomplete vaccination course. Comment: The subject should receive one dose of Prevenar 13 vaccine and 2 doses of Hz/su vaccine	Co-Ad – Day 1, Month 2 Control – Day 1, Month 2, Month 4	PPS

BS = Blood sample

** Attribution of these elimination codes are responsibility of CRDL following review of individual data listings*

5.3. Important protocol deviation not leading to elimination from per-protocol analysis set

For information on important protocol deviation not leading to elimination from the PPS set, refer to the study protocol deviation and management plan (PDMP).

6. STATISTICAL ANALYSES

Note that standard data derivation rule and stat methods are described in Section 11 and will not be repeated below. All analyses will be presented by study phase when there are data for both active and follow up phases.

6.1. Demography

6.1.1. Analysis of demographics/baseline characteristics planned in the protocol

Demographic characteristics (age at first vaccination, sex, race and ethnicity) will be tabulated per treatment group.

The mean age (plus range and standard deviation [SD]) of the subjects, as a whole, and per treatment group will be calculated for ES and PPS. The distribution of subjects enrolled among the study sites will be tabulated, as a whole, and per treatment group.

The same tabulations might be performed by age strata (50-59, 60-69 and ≥70 YOA) if deemed necessary.

6.1.2. Additional considerations

- The following additional tables will be generated:
  - The number of subjects enrolled into the study as well as the number of subjects excluded from PPS analyses will be presented through two consort tables:
  - Consort table 1 - Showing the subjects disposition from Enrolled Set to Randomized Set
  - Consort table 2 – Showing the subjects disposition from Randomised Set to ***Per Protocol Set for immunogenicity***
  - Withdrawal status will be summarized by group. The numbers of withdrawn subjects will be tabulated according to the reason for withdrawal

- The following table will be generated for CTRS:
  - Percentage of Enrolled subjects by country will be tabulated by group,
  - Percentage of Enrolled subjects in the following age categories ≤64, 65-84, ≥85 will be tabulated by group.
- For computation of age, following rule need to be considered:
  - Age will be calculated as the number of years between the date of birth and the date of first vaccination.
  - To ensure that the collection of date of birth will not jeopardise the privacy of Personally Identifiable Information (PII), only a partial date of birth (MMYYYY) will be collected.
  - Therefore, the 15th of the month will be used to replace the missing date.
  - In case the month is missing, the date will be replaced by the June 30th of the year.
- Summary of important protocol deviations leading to elimination will be presented.

6.2. Exposure

6.2.1. Analysis of exposure planned in the protocol

None

6.2.2. Additional considerations

The number of doses administered will be tabulated. The number of doses administered will be tabulated by age sub-group.

6.3. Immunogenicity

6.3.1. Analysis of immunogenicity planned in the protocol

The primary analysis will be based on the ***Per-protocol set (PPS) for immunogenicity.*** A second analysis based on the Exposed set will be performed to complement the per-protocol analysis (see section 9 for changes in the planned analysis).

Immunogenicity analyses for confirmatory objectives will be performed by age stratum (50-59, 60-69 and ≥ 70 YOA) on PPS, if the number of subjects enrolled is sufficient in each stratum.

6.3.1.1. Within group assessment

The following parameters will be tabulated by vaccine group at each time point when a blood sample result is available:

- Seropositivity with exact 95% CI for all antigens
- GMC/GMT with 95% CI for all antigens
- VRR with exact 95% CI for anti-gE
- Mean Geometric Increase (MGI) with exact 95% CI for anti-gE
- Descriptive statistics (N, mean, SD, min, Q1, median, Q3, max) of Mean Geometric Increase (MGI) for anti-gE
- Distribution of the fold increase i.e. Percentage of subjects with a more than X-fold (e.g. >2, >4, >6, -fold) increase will be tabulated for anti-gE per group with 95% CI.
- Antibody titre/concentration will be displayed using reverse cumulative curves.

6.3.1.2. Between group assessment

The following between group comparison will be performed:

- For the second co-primary objective for non-inferiority of the anti-gE humoral response, at one-month post-dose 2 of HZ/su vaccine:
  - The 95% CI of the group GMCs ratio (Control divided by Co-Ad) will be computed using an ANCOVA model on the log10 transformation of the concentrations. The pre-vaccination log-transformed antibody concentrations will be included as continuous covariate and the vaccine group and age strata as fixed effects in the model.
- For the third co-primary objective for non-inferiority of the humoral response to each vaccine pneumococcal serotype (according to the pre-specified order in the protocol), one month post-dose of *Prevenar13*:
  - The 95% CI of the group MOPA GMT ratios (Control divided by Co-Ad) will be computed using an ANCOVA model on the log10 transformation of the concentrations. The pre-vaccination log-transformed antibody concentrations will be included as continuous covariate and the vaccine group and age strata as fixed effects in the model.

6.3.2. Additional considerations

The following additional points need to be considered for immunogenicity analysis:

- Percentage of subjects above the pneumococcal serotype specific LLOQ will be calculated for each serotype with exact 95% Cis.
- Immunogenicity descriptive analyses will be performed by age stratum (50-59, 60-69 and ≥ 70 YOA), if the number of subjects enrolled is sufficient in each stratum.

- Two-sided 95% CIs for Seropositivity and VRR will be computed by Clopper-Pearson method [Clopper, 1934]. The differences in percentages and the associated two-sided 95% between the groups CIs for the difference will be constructed using the method of Miettinen and Nurminen [Robert, 1998].
- The two-sided 95% CI for the mean of log-transformed titre/concentration will be first obtained assuming that log-transformed values were normally distributed with unknown variance. The 95% CI for the GMTs/GMCs/MGIs will be then obtained by exponential-transformation of the 95% CI for the mean of log-transformed titre/concentration.

6.3.2.1. Statistical considerations for confirmatory objectives

For the multiplicity adjustment, all hypotheses have been ranked into three families and one sub-family according to the following power of test:

Table 4 Power to demonstrate VRR objective and non-inferiority of the immunogenicity of HZ/su and *Prevenar13* co-administered compared to Control group

Family 1: HZ/su: VVR*(1-sided test with alpha = 2.5%)				
Endpoint	Threshold	VR assumed	Total β	Power
VRR in Co-Ad group	0.60	95%	0.001%	99.99%
Family 2: HZ/su: non-inferiority* (1-sided test with alpha = 2.5%) N=410				
Endpoint	Standard deviation	δ	Total β	Power
Anti-gE GMC ratio	0.35	1.5	0.001 %	99.99 %
Family 3: *Prevenar13*: Non-inferiority* (1-sided test with alpha = 2.5%) N=410				
Endpoint (13 vaccine pneumococcal serotypes)	Standard deviation	δ	Total β	Power
3 GMT ratio	0.660	2	0.001%	99.99%
19A GMT ratio	0.644	2	0.001%	99.99%
1 GMT ratio	0.798	2	0.029%	99.97%
18C GMT ratio	0.891	2	0.203%	99.80%
4 GMT ratio	0.906	2	0.260%	99.74%
6A GMT ratio	0.919	2	0.320%	99.68%
5 GMT ratio	0.931	2	0.383%	99.62%
19F GMT ratio	0.971	2	0.664%	99.33%
6B GMT ratio	0.995	2	0.891%	99.11%
7F GMT ratio	1.014	2	1.107%	98.89%
9V GMT ratio	1.021	2	1.194%	98.81%
14 GMT ratio	1.045	2	1.530%	98.47%
23F GMT ratio	1.094	2	2.398%	97.60%
Global β to show non-inferiority			~9%	
Global power				**~91%**

VRR: vaccine response rate; gE: Varicella Zoster Virus glycoprotein E; GMT: geometric mean titer; GMC: geometric mean concentration.
* Pass 12, alpha = 2.5%, for VRR: Exact test, for non-inferiority one-sided equivalence of means.
For gE: non-inferiority limit = 0.176 (=log10(1.5)), power under equal GMC
For each pneumococcal serotype: non-inferiority limit = 0.301 (=log10(2)), variability for each of the 13 vaccine pneumococcal serotype taken from the EMA assessment report for *Prevenar13* and multiplied by 1.1, power under equal GMT.

Fixed sequence testing which allows for full alpha propagation in pre-ordered hypotheses families will be applied in the following manner:

Family 1:

In the Co-Ad group, for anti-gE, at one month post-dose 2 of HZ/su vaccine:

- The VRR and 95% CI will be computed.

The objective is met if the LL of the 95% CI is ≥60%.

Family 2:

For anti-gE, at one month post-dose 2 of HZ/su vaccine:

- The 95% CI of the group GMCs ratio will be computed using an analysis of covariance (ANCOVA) model on the log10 transformation of the concentrations. The pre-vaccination log-transformed antibody concentrations will be included as continuous covariate and the vaccine group and age strata as fixed effects in the model.

In terms of concentrations, the Co-Ad group will be considered non-inferior to the Control group if the UL of the 95% CI for the GMC ratio of the Control group to the Co-Ad group is <1.5.

Family 3:

For each vaccine pneumococcal serotype (according to the pre-specified order), one month post-dose of *Prevenar13*:

- The 95% CI of the group MOPA GMT ratios will be computed using an analysis of covariance (ANCOVA) model on the log10 transformation of the concentrations. The pre-vaccination log-transformed antibody concentrations will be included as continuous covariate and the vaccine group and age strata as fixed effects in the model.

In terms of MOPA GMTs, the Co-Ad group will be considered non-inferior to the Control group if the UL of the 95% CI for the MOPA GMTs ratio of the Control group to the Co-Ad group is <2 for each of the 13 vaccine serotypes.

In the ANCOVA models Adjusted Least Squares (LS) means and difference of LS means between the groups will be calculated together with the 2-sided 95% CIs and back-transformed to the original units to provide GMCs and GM ratios.

6.4. Analysis of safety

6.4.1. Analysis of safety planned in the protocol

The analysis for safety will be based on the Exposed set. All safety analyses may also be performed by age strata (50-59, 60-69 and ≥70 YOA), if deemed necessary.

When appropriate, tabulations will be presented overall and by time of occurrence relative to last vaccination (e.g. using windows such as Days 1 to 7, Days 1 to 30 and more than 30 days post-vaccination).

The results for the analysis of safety will be tabulated as follows:

- The number and percentage of subjects with at least one local solicited AE, with at least one general solicited AE, and with any solicited AE during the 7-day follow-up period with exact 95% CIs after each vaccine dose and overall by vaccination group will be provided;
- The percentage of subjects reporting each individual solicited local and general AE during the solicited 7-day follow-up period will be tabulated with exact 95% CI;
- For all solicited adverse events, the same tabulation will be performed for grade 3 solicited AEs and for solicited general AEs with relationship to vaccination;
- Number of days with each individual solicited local and general AE during the solicited 7-day follow-up period;
- The proportion of subjects with at least one report of unsolicited AE (containing both serious and non-serious unsolicited AEs) classified by the MedDRA Primary System Organ Class (SOC) and Preferred Terms (PTs) and reported up to 30 days after each vaccination will be tabulated with exact 95% CI;
- The same tabulation will be performed for grade 3 unsolicited AEs and for unsolicited AEs with a relationship to vaccination reported up to 30 days after each vaccination with exact 95% CI. The proportion of AEs resulting in a medically attended visit will also be tabulated;
- Total number/percentages of doses (per dose and overall) followed by AEs will be tabulated;
- Number of subjects with pIMDs will be tabulated;
- SAEs, including fatalities and withdrawal due to AE(s) will be described in detail.

6.4.2. Additional considerations

- The following additional tables will be generated:
  - The percentage of subjects with at least one local AE (solicited and unsolicited), with at least one general AE (solicited and unsolicited) and with any AE (solicited and unsolicited) during the 7-day follow-up period will be tabulated with exact 95% CI after each vaccine dose and overall. The same computations will be done for Grade 3 AEs, for any AEs considered related to vaccination and for any Grade 3 AEs considered related to vaccination.
  - The percentage of subjects with at least one local solicited AE, with at least one general solicited AE and with any solicited AE will also be done for Grade 3 solicited AEs, for any solicited AEs considered related to vaccination and for any Grade 3 solicited AEs considered related to vaccination.
  - The percentage of subjects reporting each individual solicited local AE during the solicited 7-day follow-up period will be tabulated by study vaccine with exact 95% CI.
  - Summary of temperature value by half degree increment taken by different routes reported during the 7-day (Days 1-7) post-vaccination following each dose.
  - For fever, the number and percentage of subjects reporting fever by half degree (°C) cumulative increments during the 7-day follow-up period (Day 1-7) will be tabulated for each group after each vaccine dose and overall. Similar tabulations will be performed for Grade 3 (> 39.0°C) causally related fever.
  - List of suspected HZ cases identified during the study will be presented.
  - The number and percentage of subjects starting a concomitant medication during the 30-day post-vaccination period by dose and overall will be presented.
  - The duration of solicited local adverse events (in days), not limited to the 7-day post-vaccination period, following each dose and overall/dose. The same tabulations after Prevenar13 and HZ/su vaccinations.
  - The duration of solicited general adverse events (in days), not limited to the 7-day post-vaccination period, following each dose and overall/dose.
  - Solicited local adverse events ongoing beyond the 7-day (Days 1-7) post-vaccination period, following each dose and overall/dose. The same tabulations after Prevenar13 and HZ/su vaccinations.
  - Solicited general adverse events ongoing beyond the 7-day (Days 1-7) post-vaccination period, following each dose and overall/dose.
  - Number and percentage of subjects with at least one report of a grade 3 non-serious unsolicited AE during the 30-day (Days 0–29) follow-up period after each vaccination classified according to the MedDRA Primary SOC and PTs will be tabulated, with exact 95% CI. The same will be generated for grade 3 non-serious unsolicited AE considered related to vaccination.

- Number and percentage of subjects with fatal SAEs, classified by MedDRA Primary SOC and PTs will be presented with exact 95% CI in two ways:
- With onset of fatal SAE during the period starting from first vaccination to 30 days post last vaccination dose, after 30 days post last vaccination dose to study end and from first vaccination to study end.
- Who died during the period starting from first vaccination to 30 days post last vaccination dose, after 30 days post last vaccination dose to study end and entire study period.
- The listing of all subjects who died during the entire study period and their fatal SAEs in the Enrolled Set

6.4.2.1. Combined Solicited and Unsolicited Adverse Events

A summary of subjects with all combined solicited (regardless of their duration) and unsolicited adverse events will be provided. Solicited adverse events will be coded by MedDRA as per the following codes:

Solicited adverse event	Lower level term name	Corresponding Lower level term code
Pain	Injection site pain	10022086
Redness	Redness at injection site	10022098
Swelling	Swelling at injection site	10053425
Fatigue	Fatigue	10016256
Gastrointestinal symptoms	Gastrointestinal disorder	10017944
Headache	Headache	10019211
Myalgia	Myalgia	10028411
Shivering	Shivering	10040558
Temperature	Fever	10016558

For clintrial.gov and EudraCT posting purposes, a summary of combined solicited and unsolicited non-serious adverse events will be produced by SOC and PTs and according to occurrence of each event.

7. ANALYSIS INTERPRETATION

All co-primary objectives will be evaluated using a one-sided Type I error of 2.5% (as already justified by fixed sequential testing procedure, no alpha adjustment needed). The trial will be considered conclusive if all co-primary objectives criteria are met.

8. CONDUCT OF ANALYSES

8.1. Sequence of analyses

The analysis will be performed in the following steps:

- The final analysis on immunogenicity, reactogenicity and safety data will be performed when all data up to study end (i.e., phone contact at Month 14 for Co-Ad group and phone contact at Month 16 for Control group) will be available and cleaned. Individual data listings will also be provided.

An integrated clinical study report containing all data will be written and made available to the investigators following the final analysis.

Table 5 Analysis and disclosure plan for the planned analysis

Description	Analysis ID	Disclosure Purpose (CTRS=public posting, CSR=clinical study report, internal)	Dry run review needed (Y/N)	Reference for TFL
Final analysis	E1_01	CTRS CSR	Y	***All tables from Section 12 of the SAP Amendment 2 14OCT2019***

8.2. Statistical considerations for interim analyses

Not applicable

9. CHANGES FROM PLANNED ANALYSES

- In Protocol Amendment 2 Final (30 Jan 2018), it was specified that a second analysis for immunogenicity of the ES would be performed only if, in any study group, the percentage of enrolled subjects with serological results excluded from the PPS for immunogenicity is 5% or more. At the request of Paul Ehrlich Institute, Germany (PEI), an analysis of the ES will be performed to complement the per-protocol analysis regardless of the percentage of enrolled subjects excluded from the PPS for immunogenicity.
- Updated LLOQ values (i.e. assay cut-off values) for the pneumococcal serotypes are provided in this version of SAP (section 11.1.2). The cut-off values presented in this SAP will be used to determine seropositivity rather than those presented in Protocol Amendment 2 Final (30 Jan 2018). Analysis of immunogenicity section has been updated accordingly.
- Additional tables on presentation of grade 3 non-serious unsolicited adverse events and fatal SAEs has been added based on CBER request.
- The sequence of analysis was updated from SAP amendment 1 to accommodate a delay in the availability of immunogenicity results. ***The active phase analysis has been removed as a request for a CTRS posting extension has been submitted to NIH; complete CTRS posting will be done at Last Subject Last Visit (LSLV) + 12 months rather than Primary Completion Date (PCD) +12 months as previously planned***
- Two new cohorts – Enrolled Set and Randomized Set has been defined as required for web disclosure and SAE tables presentation.
- Analysis of demography section has been updated to add consort table and summary of important protocol deviations.

10. LIST OF FINAL REPORT TABLES, LISTINGS AND FIGURES

The TFL TOC provides the list of tables/listings and figures to be included in the study report.

The following group names will be used in the TFLs, in line with the T-domains:

Group order in tables	Group label in tables	Group definition for footnote
1	Co-Ad	Dose 1 : Prevenar 13 + HZ/su, Dose 2: HZ/su
2	Control	Dose 1 : Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su

The following sub-groups will be used in the TFL, in line with the T-domains:

Table 6 Group Definitions to be used for the sub-group analysis by age (Analysis will be included in the clinical report)

Sub-group order in tables	Sub-group label in tables	Sub-group definition for footnote
1	50-59YOA	Subjects aged 50-59 years
2	60-69YOA	Subjects aged 60-69 years
3	≥70YOA	Subjects aged 70 years and over

YOA = Year of age

Please note that for table presentation in the sub-group analysis, the sequence maintained has to be each treatment group within each age sub-group.

11. ANNEX 1 STANDARD DATA DERIVATION RULE AND STATISTICAL METHODS

11.1. Standard data derivation

11.1.1. Dose number

The study dose number is defined in reference to the number of study visits at which vaccination occurred. More specifically dose 1 refers to all vaccines administered at the first vaccination visit while dose 2 corresponds to all vaccinations administered at the second vaccination visit even if this is the first time a product is administered to the subject.

Associated dose: the associated dose for an event (AE, medication, vaccination) is the most recent study dose given before an event. In case the event takes place on the day a study dose is given, the associated dose will be that of the study dose, even if the event actually took place before vaccination. For instance, if an adverse event begins on the day of the study vaccination but prior to administration of the vaccine, it will be assigned to this dose. In case a study dose is not administered and an event occurs after the subsequent study dose (e.g. 2nd study dose), the associated dose of the event will be study dose associated to the subsequent study dose (e.g. dose 2).

The number of doses for a product is the number of times the product was administered to a subject.

The incidence per dose is the number of visits with vaccine administered at which an event was reported among all visits with vaccine administered.

11.1.2. Immunogenicity

- For a given subject and given immunogenicity measurement, missing or non-evaluable measurements will not be replaced. Therefore, an analysis will exclude subjects with missing or non-evaluable measurements.
- A seronegative subject is a subject whose antibodies concentration/titer is below the cut-off value (cut-off value is defined by the laboratory prior to the analysis).
- A seropositive subject is a subject whose antibodies concentration/titer is greater than or equal to the assay cut-off value.
- The seropositivity rate is defined as the percentage of seropositive subjects.
- The VRR for anti-gE is defined as the percentage of subjects who have at least:
  - a 4-fold increase in the anti-gE antibodies concentration as compared to the pre-vaccination anti-gE antibodies concentration, for subjects who are seropositive at baseline, or,
  - a 4-fold increase in the anti-gE antibodies concentration as compared to the anti-gE antibodies cut-off value for seropositivity, for subjects who are seronegative at baseline.
- The GMC calculations for anti-gE antibody concentration are performed by taking the anti-log of the mean of the log base 10 concentration transformations. Antibody concentrations below the cut-off of the assay will be given an arbitrary value equal to half the cut-off for the purpose of GMC/GMT calculation.
- All CI computed will be two-sided 95% CI.
- Updated LLOQ and ULOQ values for the MOPA assay are described below for each of the 13 pneumococcal serotypes:

Pneumococcal serotype	Method	Unit	LLOQ[1]	ULOQ	Laboratory
Streptococcus pneumoniae Serotype 01/37 Brugmann Hospital Ab	MOPA	1/ dilution	14	3504	University of Alabama at Birmingham
Streptococcus pneumoniae Serotype 03/1 Statens Serum Institut Ab			11	2822	
Streptococcus pneumoniae Serotype 04/2656 Brugmann Hospital Ab			40	18042	
Streptococcus pneumoniae Serotype 05 Ambrose- Statens Serum Institut Ab			15	13304	
Streptococcus pneumoniae Serotype 06A Centers for Disease Control Ab			45	15305	
Streptococcus pneumoniae Serotype 06B/DS2212/94 Centers for Disease Control Ab			29	20806	
Streptococcus pneumoniae Serotype 07F/46 Brugmann Hospital Ab			28	59809	
Streptococcus pneumoniae Serotype 09V/112 161/95 Statens Serum Institut Ab			39	28095	
Streptococcus pneumoniae Serotype 14/58 Brugmann Hospital Ab			16	47856	
Streptococcus pneumoniae Serotype 18C/4593/40 Statens Serum Institut Ab			40	13318	
Streptococcus pneumoniae Serotype 19A/DB18 Kansanterveyslaitos Folkhalsoinstitutet Ab			13	34881	
Streptococcus pneumoniae Serotype 19F/2737 Brugmann Hospital Ab			33	29352	
Streptococcus pneumoniae Serotype 23F Mac-Statens Serum Institut Ab			40	10662	

[1]LLOQ corresponds to serotype-specific assay cut-off value.

- The Geometric Mean Titres (GMTs) calculations for pneumococcal serotypes are performed by taking the anti-log of the mean of the log base 10 titre transformations. For GMT calculation for pneumococcal serotypes, antibody titres below the LLOQ of the assay will be given an arbitrary value of half the cut-off for GMT calculation. Antibody titres above the ULOQ of the assay will be given the value of ULOQ for GMT calculation.

11.1.3. Safety

For a given subject and the analysis of solicited adverse event during the 7 day follow-up period after vaccination, missing or non-evaluable measurements will not be replaced. Therefore, the analysis of the solicited adverse events based on the ES will include only vaccinated subjects with documented safety data (i.e., symptom screen completed). More specifically the following rules will be used:

- Subjects who documented the absence of a solicited adverse event after one dose will be considered not having that adverse event after that dose.
- Subjects who documented the presence of a solicited adverse event and fully or partially recorded daily measurement over the solicited period will be included in the summaries at that dose and classified according to their maximum observed daily recording over the solicited period.
- Subjects who documented the presence of a solicited adverse event after one dose without having recorded any daily measurement will be assigned to the lowest

intensity category at that dose (i.e., 38°C for fever or grade 1 for other adverse events). The subject will only be presented in the subject with adverse event experienced and not in specific grade information.

- Doses without adverse event sheets documented will be excluded.

For analysis of unsolicited AEs, such as SAEs or adverse events by MedDRA Primary SOC and PTs term, and for the analysis of concomitant medications, all vaccinated subjects will be considered. Subjects who did not report the event or the concomitant medication will be considered as subjects without the event or the concomitant medication respectively.

Associated dose: The associated dose for an event (e.g., AE, medication, vaccination,…) is the study dose given before an event. In case the event takes place on a day a study dose is given, the associated dose will be that of the study dose even if the event actually took place before. For instance, for a conc. medication started on the day of study dose 2 but before dose 2 administrations, the associated dose will be dose 2

The way the percentage of subjects will be derived will depend on the event analysed (see the following table for details). As a result, the denominator (N) will differ from one table to another.

Event	N used for deriving %	Terminology used in the tables for N
Concomitant medication	All vaccinated subjects	Number of subjects with at least one administered dose
Solicited local adverse event	All vaccinated subjects with at least one solicited local adverse event documented as either present or absent	For each dose and overall/subject: N= number of subjects with at least one documented dose For overall/dose: N= number of documented doses
Solicited general adverse event	All vaccinated subjects with at least one solicited general adverse event documented as either present or absent	For each dose and overall/subject: N= number of subjects with at least one documented dose For overall/dose: N= number of documented doses
Unsolicited adverse event from day 0 to day X	All vaccinated subjects	Number of subjects with at least one administered dose
SAE	All vaccinated subjects	Number of subjects with at least one administered dose

- The maximum intensity of local injection site redness and swelling will be scored at GSK Biologicals as follows:
  - 0 : <20 mm
  - 1 : ≥ 20 mm to ≤ 50 mm diameter
  - 2 : > 50 mm to ≤ 100 mm diameter
  - 3 : > 100 mm diameter

Fever is defined as temperature ≥ 38.0 C / 100.4 F for oral, axillary, tympanic or rectal route. The preferred route for recording temperature in this study will be oral. For the analysis, temperatures will be coded as follows:

Grade	Temperature (oral, axillary, tympanic or rectal route)
0	< 38°C
1	≥ 38°C - ≤ 38.5°C
2	> 38.5°C - ≤ 39°C
3	> 39°C

- Conversion of temperature to °C -

  The following conversion rule is used for the conversion of temperature to °C

  – Temperature in °Celsius = ((Temperature in °Fahrenheit -32) *5)/9

The result is rounded to 1 decimal digit.

11.2. Statistical Method References

Clopper CJ, Pearson ES. The use of confidence or fiducial limits illustrated in the case of binomial. *Biometrika*. 1934; 26:404-413.

Robert G. Newcombe, interval estimation for the difference between independent proportions: comparison of eleven methods, *Statist Med.* 1998; 17, 873-890.

11.3. Number of decimals displayed:

The following decimal description from the decision rules will be used for the demography, immunogenicity and safety/reactogenicity.

Display Table	Parameters	Number of decimal digits
Demographic characteristics	Mean, median age	1
Demographic characteristics	SD (age)	1
Immunogenicity	Ratio of GMT/C	2
All summaries	% of count, including LL & UL of CI	1
All summaries	% of difference, including LL & UL of CI	2

12. ANNEX 2: STUDY SPECIFIC MOCK TFL

The study specific mocks are annexed to this SAP in a separate document.

The data display, title and footnote are for illustration purpose and will be adapted to the study specificity as indicated in the TFL TOC. Note that there may be few changes between the study specific SAP mock TFL and the final TFLs as editorial/minor changes do not require a SAP amendment

12.1. List of individual data listing

Following individual data listing will be generated. ***Please refer to TFL TOC for the numbering of these Appendices.***

- Elimination codes
- Demography
- Physical examination/vital signs
- Dates of birth, Informed consent, Vaccination and blood sampling, Contact
- Reason for visit not done
- General medical history - Physical examination
- Study Conclusion
- Notes (this appendix is provided for info only and should not be used for the clinical report)
- Vaccination procedure
- Reason for not administration of vaccine
- Reason for non-eligibility
- Previous history of vaccination
- Previous history of disease
- Solicited local adverse events
- Solicited general adverse events
- Unsolicited adverse events within (30) days post-vaccination
- Unsolicited adverse events after (30) days post-vaccination
- Concomitant medications
- Concomitant vaccinations
- Immunogenicity

12.2. Template of Tables and Figures

Template 1 Number of subjects by country and center <Exposed Set>

		<Each group> N=XXXX		<Each group> N=XXXX		Total N=XXXX	
Country	**Center**	**n**	**%**	**n**	**%**	**n**	**%**
<each country>	<each center >	XXX	XX.X	XXX	XX.X	XXX	XX.X
	All	XXX	XX.X	XXX	XX.X	XXX	XX.X

<each group>:
Co_Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
n = number of subjects in a given center or country
N = total number of subjects
% = n/N x 100
Center = GSK Biologicals assigned center number

Template 2 Number of enrolled subjects by country

	<Each group> N=XXXX		<Each group> N=XXXX		Total N=XXXX	
Country	**n**	**%**	**n**	**%**	**n**	**%**
<Each country>	XXX	XX.X	XXX	XX.X	XXX	XX.X

<each group>:
Co_Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
n = number of subjects in a given country
N = total number of subjects
% = n/N x 100

Template 3 Number of enrolled subjects by age category

	<Each group> N=XXXX		<Each group> N=XXXX		Total N=XXXX	
Age category	**n**	**%**	**n**	**%**	**n**	**%**
Adults [18-64 years]	XXX	XX.X	XXX	XX.X	XXX	XX.X
From 65-84 years						
85 years and over						

<each group>:
Co_Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = number of enrolled subjects
n = number of enrolled subjects included in each group or in total for a given age category or for all age categories
% = n/N x 100

Template 4 Number of subjects by country and age category <Exposed Set>

		<Each group> N=XXXX		<Each group> N=XXXX		Total N=XXXX	
Country	**Age category**	**n**	**%**	**n**	**%**	**n**	**%**
<each country>	50-59YOA	XXX	XX.X	XXX	XX.X	XXX	XX.X
	60-69YOA						
	≥70YOA						
	All	XXX	XX.X	XXX	XX.X	XXX	XX.X

Co_Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
50-59YOA = Subjects aged 50-59 years
60-69YOA = Subjects aged 60-69 years
≥70YOA = Subjects aged 70 years and over
n = number of subjects in a given center or country
N = total number of subjects
% = n/N x 100

Template 5 Number of subjects vaccinated, completed and withdrawn with reason for withdrawal – <end of active phase, study end> <Exposed set>

	<Each group> N=XXXX	<Each group> N=XXXX	Total N=XXXX
	n	n	n
Number of subjects vaccinated	xxx	xxx	xxx
End of study status			
[EACH CATEGORY]	xxx	xxx	xxx
Reasons for withdrawal:			
[REASONS]	xxx	xxx	xxx

Co_Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
Vaccinated = number of subjects who were vaccinated in the study
Completed = number of subjects who completed <end of active phase visit, last study visit>
Withdrawn = number of subjects who did not come for the <end of active phase visit, last study visit>
Unknown = number/percentage of subjects who have not come for the <end of active phase visit, last study visit> yet

Template 6 Visit attendance <Exposed set>

		<Each group> N=XXX	
Visit	**Status**	**n**	**%**
INFORMED CONSENT	Completed		
RANDOMIZATION	Completed		
<EACH VISIT>	Attended		
	Not attended yet		
	Permanent discontinuation prior to this visit		
	Not attended		
CONCLUSION	Completed		

Co_Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = Number of subjects in each group or in total
Conclusion = date of last visit or withdrawal

Template 7 Summary of important protocol deviations leading to elimination from any analyses

Category Sub-category	<Each group> N=XXXX			Total N=XXXX		
	occ	n	%	occ	n	%
At least one important protocol deviation	xxx	xxx	xx.x	xxx	xxx	xx.x
	xxx	xxx	xx.x	xxx	xxx	xx.x
<Category 1>	xxx	xxx	xx.x	xxx	xxx	xx.x
<Sub-category 1>	xxx	xxx	xx.x	xxx	xxx	xx.x
<Sub-category 2>						
…						
	xxx	xxx	xx.x	xxx	xxx	xx.x
<Category 2>						
…						
…						

Co_Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = Total number of subjects
Occ = number of occurrences = number of important protocol deviations
n/% = number / percentage of subjects with important protocol deviations

Template 8 Percentage of subjects with serological results who were eliminated from PPS for immunogenicity

	[each group]	
Number of subjects in Exposed Set with serological results available		
Number of subjects with serological results eliminated from PPS for immunogenicity		
Percentage of subjects with serological results eliminated from PPS for immunogenicity		

Co_Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su

Template 9 Deviations from specifications for age and intervals between study visits for Co-Ad group <Exposed Set>

		Age	Dose:1-PI (M1)		Dose:1-Dose:2	Dose:2-PII (M3)		Dose:2–PHC (M14)
Group		**Protocol**	**Protocol**	**Adapted**	**Protocol**	**Protocol**	**Adapted**	**Protocol**
		from ≥ 50 years	from 30 to 42 days	from 28 to 48 days	from 49 to 83 days	from 30 to 48 days	from 28 to 48 days	from 335 to 395 days
Co-Ad	N							
	n							
	%							
	range							

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Adapted = interval used for defining PPS for immunogenicity
N = total number of subjects with available results
n/% = number / percentage of subjects with results outside of the interval
range = minimum-maximum for age and intervals
PI (M1) = Blood sample at Month 1, post-vaccination Dose 1
PII (M3) = Blood sample at Month 3, post-vaccination Dose 2
PHC (M14) = Phone Contact MONTH 14

Template 10 Deviations from specifications for age and intervals between study visits - for Control group <Exposed Set>

		Age	Dose:1-PI(M1)		Dose:1-Dose:2		Dose:2-Dose:3	Dose:3-PIII(M5)		Dose:3-PHONE CONT M16
Group		**Protocol**	**Protocol**	**Adapted**	**Protocol**	**Adapted**	**Protocol**	**Protocol**	**Adapted**	**Protocol**
		from ≥ 50 years	from 30 to 42 days	from 28 to 48 days	from 60 to 83 days	≥ 60 days	from 49 to 83 days	from 30 to 48 days	from 28 to 48 days	from 335 to 395 days
Control	N									
	n									
	%									
	range									

Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
Adapted = interval used for defining the ***PPS for immunogenicity***
N = total number of subjects with available results
n/% = number / percentage of subjects with results outside of the interval
range = minimum-maximum for age and intervals
PI(M1) = Blood sample at Month 1, post-vaccination Dose 1
PIII(M5) = Blood sample at Month 5, post-vaccination Dose 3
PHC (M16) = Phone Contact Month 16

Template 11 Summary of demographic characteristics <Exposed Set, PPS for immunogenicity>

	<Each group> N=XXXX		<Each group> N=XXXX		Total N=XXXX	
	Value or n	**%**	**Value or n**	**%**	**Value or n**	**%**
Age in Years at <timepoint>						
N with data	xxx		xxx		xxx	
Mean	xxx.x		xxx.x		xxx.x	
SD	xxx.x		xxx.x		xxx.x	
Median	xxx.x		xxx.x		xxx.x	
Minimum	xxx		xxx		xxx	
Maximum	xxx		xxx		xxx	
Gender						
<EACH GENDER>	xxx	xx.x	xxx	xx.x	xxx	xx.x
…	xxx	xx.x	xxx	xx.x	xxx	xx.x
Ethnicity						
<EACH ETHNICITY>	xxx	xx.x	xxx	xx.x	xxx	xx.x
…	xxx	xx.x	xxx	xx.x	xxx	xx.x
Geographic Ancestry						
<EACH GEOGRAPHIC ANCESTRY>	xxx	xx.x	xxx	xx.x	xxx	xx.x
…	xxx	xx.x	xxx	xx.x	xxx	xx.x
Age category						
<EACH AGE CATEGORY>	xxx	xx.x	xxx	xx.x	xxx	xx.x
Country						
<EACH COUNTRY>	xxx	xx.x	xxx	xx.x	xxx	xx.x
…	xxx	xx.x	xxx	xx.x	xxx	xx.x

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = total number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
N with data = number of subjects with documentation of the corresponding data
SD = standard deviation

Template 12 Minimum and maximum activity dates <Exposed Set>

Group	Activity number	Activity Description	Minimum date	Maximum date
Co-Ad	10	VISIT DAY 1		
	20	VISIT MONTH 1		
	30	VISIT MONTH 2		
	40	VISIT MONTH 3		
	70	PHONE CONTACT MONTH 14		
Control	10	VISIT DAY 1		
	20	VISIT MONTH 1		
	30	VISIT MONTH 2		
	50	VISIT MONTH 4		
	60	VISIT MONTH 5		
	80	PHONE CONTACT MONTH 16		

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su

Template 13 Study Population <Exposed Set>

	<Each group> N=XXXX	<Each group> N=XXXX	Total N=XXXX
Number of subjects			
Planned, N	xxx	xxx	xxx
Randomised, N <cohort name>	xxx	xxx	xxx
Completed to visit Month 3, n (%)*	***xxx (xx.x)***	***xxx (xx.x)***	***xxx (xx.x)***
Completed to visit Month 5, n (%)**	***xxx (xx.x)***	***xxx (xx.x)***	***xxx (xx.x)***
Completed to Phone contact Month 14, n (%)*	***xxx (xx.x)***	***xxx (xx.x)***	***xxx (xx.x)***
Completed to Phone contact Month 16, n (%)**	***xxx (xx.x)***	***xxx (xx.x)***	***xxx (xx.x)***
<Unknown>	xxx	xxx	xxx
Demographics			
N <cohort name>	xxx	xxx	xxx
Females:Males	xxx:xxx	xxx:xxx	xxx:xxx
Mean Age, <unit> (SD)	xxx.x (xxx.x)	xxx.x (xxx.x)	xxx.x (xxx.x)
Median Age, <unit> (minimum, maximum)	xxx (xxx,xxx)	xxx (xxx,xxx)	xxx (xxx,xxx)
<MOST FREQUENT CATEGORY OF RACE>	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
<SECOND MOST FREQUENT CATEGORY OF RACE>	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
<THIRD MOST FREQUENT CATEGORY OF RACE>	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)

<each group>:
Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = Total number of subjects
SD = Standard deviation
applicable for Co-Ad group and ** applicable for Control group

Template 14 Exposure to study vaccines <Exposed Set>

	<Each group> N=XXXX		<Each group> N=XXXX		Total N=XXXX	
Number of subjects receiving	**n**	**%**	**n**	**%**	**n**	**%**
Exactly 1 Dose						
Exactly 2 Doses						
Exactly 3 Doses						
…						
At least 1 Dose						
Total number of doses administered during the study						

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = number of subjects in each group or in total included in the considered cohort
n = number of subjects/doses in the given category
% = percentage of subjects in the given category

Template 15 Compliance in completing solicited adverse events information <Exposed Set>

		<each group>			<each group>		
DOSE	**Adverse event information**	**N**	**n**	**Compliance (%)**	**N**	**n**	**Compliance (%)**
DOSE <each dose number>	General AES						
	Local AES						
TOTAL	General AES						
	Local AES						

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N=Number of administered doses
n = number of doses with AES returned
General AES = Adverse event screens used for the collection of general solicited AEs
Local AES = Adverse event screens used for the collection of local solicited AEs
Compliance (%) = (n / N) X 100

Template 16 Incidence and nature of <grade 3, related, grade 3 related, > adverse events (<unsolicited and solicited, solicited only>) reported <during the 7-day (Days 1-7), beyond the 7-day (Days 1-7)> post-vaccination period following each dose and overall

		<Each group>					<Each group>				
					95% CI					95% CI	
Dose	**Adverse event**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 1	Any adverse event										
	General adverse events										
	Local adverse events										
Dose 2	Any adverse event										
	General adverse events										
	Local adverse events										
Dose 3	Any adverse event										
	General adverse events										
	Local adverse events										
Overall/dose	Any adverse event										
	General adverse events										
	Local adverse events										
Overall/subject	Any adverse event										
	General adverse events										
	Local adverse events										

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects presenting at least one type of adverse event
For overall/dose:
N = number of documented doses
n/% = number/percentage of doses followed by at least one type of adverse event
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Template 17 Incidence of solicited local adverse events reported during the 7-day (Days 1-7) post-vaccination period by study vaccine following each dose and overall <Exposed Set>

				Co-Ad					Control				
							95% CI					95% CI	
Dose	**Adverse event**	**Product**	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 1	Pain	HZ/su	All										
			Grade 2 or 3										
			Grade 3										
			Medical advice										
		Prevenar13	All										
			Grade 2 or 3										
			Grade 3										
			Medical advice										
	Redness (mm)	HZ/su	All										
			>50										
			>100										
			Medical advice										
		Prevenar 13	All										
			>50										
			>100										
			Medical advice										
	Swelling (mm)	HZ/su	All										
			>50										
			>100										
			Medical advice										
		Prevenar 13	All										
			>50										
			>100										
			Medical advice										
Dose 2													
Dose 3													
Overall/Dose													
Overall/Subject													

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
For each dose:
N = number of subjects with the corresponding documented dose
n/% = number/percentage of subjects reporting the type of adverse event at least once following the corresponding dose
For Overall/dose:
N = number of documented dose
n/% = number/percentage of doses followed by at least one type of adverse event
For Overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the type of adverse event at least once
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit

Template 18 Incidence of solicited general adverse events reported during the 7-day (Days 1-7) post-vaccination period following each dose and overall <Exposed Set>

			<each group>				
						95 % CI	
Dose	**Adverse event**	**Type**	**N**	**n**	**%**	**LL**	**UL**
Dose 1	Fatigue	All					
		Grade 3					
		Related					
		Grade 3*Related					
		Medical advice					
	Gastrointestinal symptoms	All					
		Grade 3					
		Related					
		Grade 3*Related					
		Medical advice					
	Headache	All					
		Grade 3					
		Related					
		Grade 3*Related					
		Medical advice					
	Myalgia	All					
		Grade 3					
		Related					
		Grade 3*Related					
		Medical advice					
	Shivering	All					
		Grade 3					
		Related					
		Grade 3*Related					
		Medical advice					
	Fever (Oral) (°C)	All (≥38.0)					
		>38.0					
		>38.5					
		>39.0					
		>39.5					
		>40.0					
		Related					
		>39.0*Related					
		Medical advice					
Dose 2		…					
Dose 3							
Overall/Dose							
Overall/Subject							

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
For each dose:
N = number of subjects with the corresponding documented dose
n/% = number/percentage of subjects reporting the adverse event at least once following the corresponding dose
For Overall/dose:
N = number of documented dose
n/% = number/percentage of doses followed by at least one type of adverse event
For Overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the type of adverse event at least once
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit

Template 19 Summary of temperature value by half degree increment taken by different routes reported during the 7-day (Days 1-7) post-vaccination following each dose <Exposed Set>

				Co-Ad					Control				
							95 % CI					95 % CI	
Dose	**Symptom**	**Route**	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 1	Temperature (°C)	Oral	≥35.0										
			>35.5										
			>36.0										
			>36.5										
			>37.0										
			>37.5										
			>38.0										
			>38.5										
			>39.0										
			>39.5										
			>40.0										
		Axillary	≥35.0										
			>35.5										
			>36.0										
			>36.5										
			>37.0										
			>37.5										
			>38.0										
			>38.5										
			>39.0										
			>39.5										
			>40.0										
Dose 2	Temperature (°C)	Oral	≥35.0										
			>35.5										
			>36.0										
			>36.5										
			>37.0										
			>37.5										
			>38.0										
			>38.5										
			>39.0										
			>39.5										
			>40.0										
Dose 3													

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
For each dose:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the temperature at least once
95%CI = Exact 95% confidence interval; LL = lower limit, UL = upper limit

Template 20 Number and percentage of subjects reporting the occurrence of <grade 3> <non-serious> unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term <with causal relationship to vaccination, with medically attended visit>, within the 30-day (Days 1-30) post-vaccination period <,including numbers of events><Exposed Set>

		Each group N =				
					95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n***	**n**	**%**	**LL**	**UL**
	At least one adverse event					
Gastrointestinal disorders (10017947)	At least one PT related to the corresponding SOC					
	Diarrhoea (10012735)					
	Teething (10043183)					
	Vomiting (10047700)					
General disorders and administration site conditions (10018065)	At least one PT related to the corresponding SOC					
	Pyrexia (10037660)					
Immune system disorders (10021428)	Seasonal allergy (10048908)					
Infections and infestations (10021881)	Conjunctivitis (10010741)					
	Otitis media (10033078)					
	Paronychia (10034016)					
	Tonsillitis (10044008)					
	Tonsillitis streptococcal (10044013)					
	Viral upper respiratory tract infection (10047482)					
Injury, poisoning and procedural complications (10022117)	Arthropod bite (10003399)					
	Face injury (10050392)					
	Head injury (10019196)					
Skin and subcutaneous tissue disorders (10040785)	Miliaria (10027627)					

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
At least one adverse event = at least one adverse event experienced (regardless of the MedDRA Preferred Term)
N = number of subjects included in the considered cohort in each group
n/% = number/percentage of subjects reporting the adverse event at least once
n* = number of events reported
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit
Please note the n* will only be presented for the CTRS posting with the time interval as per the secondary endpoint

Template 21 Global Summary of <grade 3> <non-serious>unsolicited signs and adverse events reported <with causal relationship with vaccination, with medically attended visit> within the 30-day (Days 1-30) post-vaccination period <Exposed Set>

	Co-Ad	Control	Total
Number of subjects with at least one unsolicited adverse event reported			
Number of doses followed by at least one unsolicited adverse event			
Number of unsolicited adverse events classified by MedDRA Preferred Term*			
Number of unsolicited adverse events reported**			

Co-Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3:HZ/su
* Adverse events reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Adverse events reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Template 22 Number and percentage of subjects starting a concomitant medication during the 30- day (Days 1-30) post vaccination period by dose and overall <Exposed Set>

		<each group>				
					95% CI	
Dose	**Type**	**N**	**n**	**%**	**LL**	**UL**
Dose 1	Any					
	Any in anticipation of study vaccine reaction					
	Any chronic use					
Dose 2	Any					
	Any in anticipation of study vaccine reaction					
	Any chronic use					
Dose 3	Any					
	Any in anticipation of study vaccine reaction					
	Any chronic use					
Overall/Dose	Any					
	Any in anticipation of study vaccine reaction					
	Any chronic use					
Overall/Subject	Any					
	Any in anticipation of study vaccine reaction					
	Any chronic use					

<each group>:
Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
For each dose:
N = total number of subjects with the corresponding administered dose
n/% = number/percentage of subjects ***who*** took the specified type of concomitant medication at least once during the considered period
For Overall/dose:
N = number of administered doses
n/% = number/percentage of doses after which the specified type of concomitant medication was taken at least once during the considered period
For Overall/subject:
N = total number of subjects with at least one administered dose
n/% = number/percentage of subjects who took the specified type of concomitant medication at least once during the considered period

Template 23 *Number of days with solicited <local, general> adverse events <during the 7 days (Days 1-7) post vaccination period following each dose and overall> <- Prevenar 13 vaccine, - HZ/su vaccine> <Exposed Set>*

			<Co-Ad group>	<Control group>
Dose	**Adverse event**	**Statistic**	**value**	**value**
<Each Dose>	<Each Adverse event>	n	xxxx	xxxx
		Mean	xx.x	xx.x
		Minimum	xx.x	xx.x
		Q1	xx.x	xx.x
		Median	xx.x	xx.x
		Q3	xx.x	xx.x
		Maximum	xx.x	xx.x
Overall/Dose	<Each Adverse event >	n	xxxx	xxxx
		Mean	xx.x	xx.x
		Minimum	xx.x	xx.x
		Q1	xx.x	xx.x
		Median	xx.x	xx.x
		Q3	xx.x	xx.x
		Maximum	xx.x	xx.x

Co-Ad group = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control group = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
n= number of doses with adverse event
Q1= 25th percentile
Q3= 75th percentile
Please note the table by vaccine type will only be done for local solicited adverse events.

Template 24 Solicited and unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term within the 30-day (Days 1-30) post-vaccination period including number of events - SAE excluded <Exposed Set>

		<each group> N =		
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n***	**n**	**%**
	At least one adverse event			
<each SOC>	<each PT term>			

<each group>:
Co-Ad group = Dose 1: Prevenar+ HZ/su, Dose 2: HZ/su
Control group = Dose 1: Prevenar, Dose 2: HZ/su, Dose 3: HZ/su
At least one adverse event = at least one adverse event experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with the administered dose
n* = number of events reported
n/% = number/percentage of subjects reporting the adverse event at least once

Template 25 Number (%) of subjects with serious adverse events from <first vaccination dose up to 30 days post last vaccination, 30 days post last vaccination up to study end, first vaccination dose up to <database freeze date(DDMMMYYYY)><study end>, including number of events reported <Exposed Set>

			<each group> N =		
Type of Event	**Primary System Organ Class**	**Preferred Term (CODE)**	**n***	**n**	**%**
SAE	At least one adverse event				
	<each SOC>	<each PT term>			
Related SAE	At least one adverse event				
	<each SOC>	<each PT term>			
Fatal SAE	At least one adverse event				
	<each SOC>	<each PT term>			
Related fatal SAE	At least one adverse event				
	<each SOC>	<each PT term>			

<each group>:
Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = number of subjects with the administered dose
n* = number of events reported
n/% = number/percentage of subjects reporting the adverse event at least once

Template 26 Number (%) of subjects reported solicited local adverse events during the 7-day (Days 1-7) post-vaccination period following each dose and across dose <Exposed Set>

				Co-Ad					Control				
							95% CI					95% CI	
Dose	**Adverse event**	**Product**	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 1	Pain	HZ/su	All										
			Grade 2 or 3										
			Grade 3										
			Medical advice										
		Prevenar	All										
			Grade 2 or 3										
			Grade 3										
			Medical advice										
	Redness (mm)	HZ/su	All										
			>50										
			>100										
			Medical advice										
		Prevenar	All										
			>50										
			>100										
			Medical advice										
	Swelling (mm)	HZ/su	All										
			>50										
			>100										
			Medical advice										
		Prevenar	All										
			>50										
			>100										
			Medical advice										
Dose 2													
Dose 3													
Across dose													

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
For each dose:
N = number of subjects with the corresponding documented dose
n/% = number/percentage of subjects reporting the type of adverse event at least once following the corresponding dose
For Across dose:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the adverse event at least once
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit

Template 27 Number (%) of subjects reported solicited general adverse events during the 7-day (Days 1-7) post-vaccination period following each dose and across dose <Exposed Set>

			<each group>				
						95 % CI	
Dose	**Adverse event**	**Type**	**N**	**n**	**%**	**LL**	**UL**
Dose 1	Fatigue	All					
		Grade 3					
		Related					
	Gastrointestinal symptoms	All					
		Grade 3					
		Related					
	Headache	All					
		Grade 3					
		Related					
	Myalgia	All					
		Grade 3					
		Related					
	Shivering	All					
		Grade 3					
		Related					
	Fever (Oral) (°C)	All (≥38.0)					
		>39.0					
		Related					
Dose 2	Fatigue	…					
	Gastrointestinal symptoms						
	Headache						
	Myalgia	…					
	Shivering	…					
	Fever (Oral) (°C)	…					
Across Dose		…					
		…					

<each group>:
Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
For each dose:
N = number of subjects with the corresponding documented dose
n/% = number/percentage of subjects reporting the adverse event at least once following the corresponding dose
For Across dose:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the adverse event at least once
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit

Template 28 Number and percentage of subjects with <anti-gE antibody concentration, anti-pneumococcal <X> antibody titres> equal to or above <cut-off> and <GMCs, GMT> <*PPS for immunogenicity,* Exposed Set>

				<≥cut-off unit, each serotype LLOQ>				<GMC, GMT>				
						95% CI			95% CI			
Antibody	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**	**Min**	**Max**
<Anti-gE antibody, anti-pneumococcal <X> antibody>	Co-Ad	PRE										
		PI(M1) or PII(M3)										
	Control	PRE or PI(M2)										
		PI(M1) or PIII(M5)										

<each group>:
Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
GM<C,T> = geometric mean antibody <concentration, titre> calculated on all subjects
N = Number of subjects with available results
95% CI = 95% confidence interval; LL = lower limit, UL = upper limit
n/% = number/percentage of subjects with <concentration, titre> equal to or above specified value
MIN/MAX = Minimum/Maximum
PRE= Pre-vaccination at Day 1
PII(M3) = Post-vaccination dose 2 at Month 3
PI(M1) = Post-vaccination dose 1 at Month 1
PI(M2) = Post-vaccination dose 1 at Month 2
PIII(M5) = Post-vaccination dose 3 at Month 5
Please note to consider PRE and PI(M1) for both group for pneumococcal antibody. For gE antibody, PRE and PII(M3) for Co-Ad and PI(M2) and PIII(M5) for Control group.

Template 29 Vaccine response rates for anti-gE antibody ELISA concentrations in Co-Ad group at one month post dose 2 of HZ/su vaccine – primary objective <PPS for immunogenicity, Exposed Set>

	Co-Ad				
				95% CI	
Antibody	**N**	**n**	**%**	**LL**	**UL**
Anti-gE antibody	XXXX	XXXX	XX.X	XXX.X	XXX.X

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Vaccine response defined as :
For initially seronegative subjects, antibody concentration at post-vaccination ≥ 4 fold the cut-off for Anti-gE (4x97 mIU/ml)
For initially seropositive subjects, antibody concentration at post-vaccination ≥ 4 fold the pre-vaccination antibody concentration
N = number of subjects (subjects either seropositive or seronegative at pre-vaccination) with both pre- and post-vaccination results available
n/% = number/percentage of responders
<95>% CI = exact <95>% confidence interval, LL = Lower Limit, UL = Upper Limit

Template 30 Adjusted ratios of GMCs between groups (Control group divided by Co-Ad group) for anti-gE antibody ELISA concentrations at one month post dose 2 of HZ/su vaccine <*PPS for immunogenicity,* Exposed Set>

Control				Co-Ad				Adjusted GMC ratio (Control / Co-Ad)		
		95% CI*				95% CI*			95% CI	
N	Adjusted GMC	LL	UL	N	Adjusted GMC	LL	UL	Value	LL	UL

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
Adjusted GMC = geometric mean antibody concentration adjusted for vaccine group, age and baseline concentration
N = Number of subjects with both pre- and post-vaccination results available
95% CI* = 95% confidence interval for the adjusted GMC (Ancova model: adjustment for vaccine group, age and baseline concentration - pooled variance); LL = lower limit, UL = upper limit
95% CI = 95% confidence interval for the adjusted GMC ratio (Ancova model: adjustment for vaccine group, age and baseline concentration - pooled variance); LL = lower limit, UL = upper limit

Template 31 Adjusted ratios of GMTs between groups (Control group divided by Co-Ad group) for anti-pneumococcal <X> antibody titres at one month post Prevenar 13 vaccine <*PPS for immunogenicity,* Exposed Set>

	Control				Co-Ad				Adjusted GMT ratio (Control / Co-Ad)		
			95% CI*				95% CI*			95% CI	
	N	Adjusted GMT	LL	UL	N	Adjusted GMT	LL	UL	Value	LL	UL

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
Adjusted GMT = geometric mean antibody titre adjusted for vaccine group, age and baseline concentration
N = Number of subjects with both pre- and post-vaccination results available
95% CI* = 95% confidence interval for the adjusted GMT (Ancova model: adjustment for vaccine group, age and baseline concentration - pooled variance); LL = lower limit, UL = upper limit
95% CI = 95% confidence interval for the adjusted GMT ratio (Ancova model: adjustment for vaccine group, age and baseline concentration - pooled variance); LL = lower limit, UL = upper limit

Template 32 Mean Geometric Increase (MGI) of anti-gE antibody ELISA concentrations from baseline to one month post dose 2 of HZ/su vaccine <*PPS for immunogenicity*, Exposed Set>

							MGI			
									95% CI	
Antibody	Group	N	Time point description	GMC	Time point description	GMC	Ratio order	Value	LL	UL
<Antibody>	Co-Ad		PII(M3)		PRE		PII(M3)/PRE			
	Control		PIII(M5)		PI(M2)		PIII(M5)/PI(M2)			

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = Number of subjects with available results at the two considered time points
GMC = geometric mean antibody concentration
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE= Pre-vaccination at Day 1
PII(M3) = Post-vaccination dose 2 at Month 3 for Co-Ad group
PI(M2) = Post-vaccination dose 1 at Month 2 for Control group (considered as pre-vaccination for HZ/su in Control group)
PIII(M5) = Post-vaccination dose 3 at Month 5 for Control group (considered as post dose 2 for HZ/su in Control group)

Template 33 Descriptive statistics of fold increase from baseline to one month post dose 2 of HZ/su vaccine for anti-gE antibody ELISA concentration <*PPS for immunogenicity*, Exposed Set>

		Each Group N=		
			95% CI	
Antibody	**Parameter**	**Value**	**LL**	**UL**
Anti-gE antibody	n			
	Nmiss			
	Mean			
	SD			
	Min			
	Q1			
	Median			
	Q3			
	Max			

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = total number of subjects
n = number of subjects with available results
Nmiss = number of subjects with missing results
SD = Standard Deviation
Q1, Q3 = First and third quartiles
Min/Max = Minimum/Maximum
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit
Please note – To calculate the fold increase, result at PII(M3) compared to PRE-for Co-Ad and PIII(M5) compared to PI(M2) for Control group has to be considered

Template 34 Distribution of fold increase from baseline to one month post dose 2 of HZ/su vaccine for anti-gE antibody ELISA concentrations <*PPS for immunogenicity*, Exposed Set>

			<Each group>					<Each group>				
						95% CI					95% CI	
Antibody	**Timing**	**Fold change**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
<each antibody>	<PII(M3)>	≥2	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x	xx.x
		≥4										
		≥6										
		≥8										
		≥10										
		≥12										
		≥14										
	<PIII(M5)	>= Ratio1	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x	xx.x

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = number of subjects with available results
n/% = number/percentage of subjects with concentration within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PII(M3) = Post-vaccination dose 2 at Month 3 for Co-Ad group
PIII(M5) = Post-vaccination dose 3 at Month 5 for Control group (considered as post dose 2 for HZ/su in Control group)
Please note – To calculate the fold increase, result at PII(M3) compared to PRE-for Co-Ad and PIII(M5) compared to PI(M2) for Control group has to be considered

Template 35 Listing of potential Immune Mediated Diseases (pIMDs) reported as identified by predefined list of preferred terms and/or by investigator assessment up to end of study <Exposed Set>

Group	Patient ID	Country	Age at onset (Y)	Gender	Race	Primary System Organ Class	Preferred term	Dose	Day of onset	Relation	Serious pIMD based on Investigator?	SAE (Y/N)	Outcome	pIMD Source

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su

Template 36 Listing of all SAEs up to end of study <Exposed Set>

Group	Sub. No.	Sex	Country	Race	Age at onset (Year)	Verbatim	Preferred term	Primary System Organ Class	MED type	Dose	Day of onset	Duration	Intensity	Causality	Outcome

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su

Template 37 Listing of suspected HZ cases from first administered dose up to end of study <Exposed Set>

Group	Sub. No.	Previous dose	Day on-set	Duration	Preferred term	AE description	Medical advice	Medically attended visit	Intensity	Causality	Outcome

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su

Template 38 Listing of (S)AEs and solicited adverse events leading to study or treatment discontinuation <up to month 5><up to end of study> <Exposed Set>

Type of discontinuation: <study/treatment

Group	Subject number	Gender	Country	Race	AE Description	SAE (Y/N)	Causality	Outcome	Vaccination and visit
									Vaccination: x at visit x

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su

Template 39 Maximum intensity of solicited <local, general> *adverse event* ongoing beyond the 7-day (Days 1-7) post-vaccination period following each dose and overall <Exposed Set>

				<each group>	<each group>
Dose	***Adverse event***	**Type**	**Time to resolution (days)**	**Value or n**	**Value or n**
<EACH DOSE>	***<Each adverse event>***	All	N	xx	xx
			n	xx	xx
			q1	xx.x	xx.x
			median	xx.x	xx.x
			q3	xx.x	xx.x
		Grade 3	N	xx	xx
			n	xx	xx
			q1	xx.x	xx.x
			median	xx.x	xx.x
			q3	xx.x	xx.x
		Grade 3*Related	N	xx	xx
			n	xx	xx
			q1	xx.x	xx.x
			median	xx.x	xx.x
			q3	xx.x	xx.x
OVERALL/DOSE	<Each adverse event>	<EACH TYPE>	N	xx	xx
			n	xx	xx
			q1	xx.x	xx.x
			median	xx.x	xx.x
			q3	xx.x	xx.x

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
Time to resolution: number of days beyond the end of the follow-up period
N = number of adverse events that were ongoing after the follow-up period
n = number of adverse events that were ongoing after the follow-up period with a complete end date
q1 = 25th percentile
q3= 75th percentile

Template 40 Number and percentage of doses reporting the occurrence of <grade 3> unsolicited adverse events classified by MedDRA Primary System Organ Class and Preferred Term <with causal relationship to vaccination> within the 30-day (Days 1-30) post-vaccination period <Exposed Set>

		Each group N =			
				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**
At least one adverse event					
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)				
	Teething (10043183)				
	Vomiting (10047700)				
General disorders and administration site conditions (10018065)	Pyrexia (10037660)				
Immune system disorders (10021428)	Seasonal allergy (10048908)				
Infections and infestations (10021881)	Conjunctivitis (10010741)				
	Otitis media (10033078)				
	Paronychia (10034016)				
	Tonsillitis (10044008)				
	Tonsillitis streptococcal (10044013)				
	Viral upper respiratory tract infection (10047482)				
Injury, poisoning and procedural complications (10022117)	Arthropod bite (10003399)				
	Face injury (10050392)				
	Head injury (10019196)				
Skin and subcutaneous tissue disorders (10040785)	Miliaria (10027627)				

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
At least one adverse event = at least one adverse event experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses followed by the adverse event
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Template 41 Number and percentage of subjects reporting the occurrence of <serious adverse events, potential Immune Mediated Disease> classified by MedDRA Primary System Organ Class and Preferred Term from <first vaccination up to 30 days post last vaccination, from 30 days post last vaccination dose up to end of study, from first vaccination up to study end> <,including number of events><Exposed Set>

		Co-Ad N =					Control N =				
					95% CI						95% CI
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n***	**n**	**%**	**LL**	**UL**	**n***	**n**	**%**	**LL**	**UL**
At least one adverse event											
Blood and lymphatic system disorders (10005329)	Leukocytosis (10024378)										
Cardiac disorders (10007541)	Acute myocardial infarction (10000891)										
	Atrial fibrillation (10003658)										
	Cardiac failure congestive (10007559)										
	Tachycardia (10043071)										
	Ventricular tachycardia (10047302)										

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
At least one adverse event = at least one adverse event experienced (regardless of the MedDRA Preferred Term)
N = number of subjects included in the considered cohort in each group
n/% = number/percentage of subjects reporting the adverse event at least once
n* = Number of events reported
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit
Please note that n* will be used to present pIMD for CTRS posting.

Template 42 Global Summary of <serious adverse events, potential Immune Mediated Disease> <with causal relationship with vaccination> reported from <first vaccination up to 30 days post last vaccination, from 30 days post last vaccination dose up to end of study, from first vaccination up to study end> <Exposed Set>

	Co-Ad	Control	Total
Number of subjects with at least one <SAE, pIMD> reported			
Number of doses followed by at least one <SAE, pIMD>			
Number of <SAE, pIMD> classified by MedDRA Preferred Term*			
Number of <SAE, pIMD> reported**			

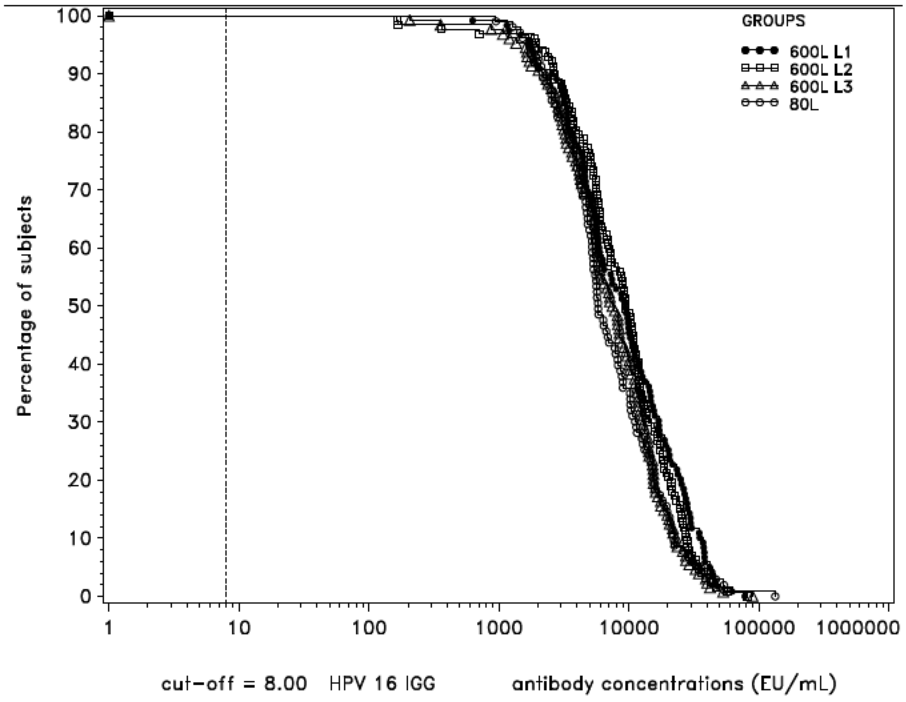
Co-Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
* Adverse events reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Adverse events reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Template 43 Vaccine response rates for anti-gE antibody concentrations at one month post dose 2 of HZ/su vaccine <*PPS for immunogenicity*, Exposed Set>

		<Each group>				
					95% CI	
Antibody	**Pre-vaccination status**	**N**	**n**	**%**	**LL**	**UL**
<each antibody>	S-	XXXX	XXXX	XX.X	XXX.X	XXX.X
	S+	XXXX	XXXX	XX.X	XXX.X	XXX.X
	Total	XXXX	XXXX	XX.X	XXX.X	XXX.X

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
S- = seronegative subjects (antibody <concentration> < <cut off> <unit>) at pre-vaccination
S+ = seropositive subjects (antibody <concentration>≥ <cut off> <unit>) at pre-vaccination
Total = subjects either seropositive or seronegative at pre-vaccination
Vaccine response defined as :
For initially seronegative subjects, antibody concentration at post-vaccination ≥ 4 fold the cut-off for Anti-gE (4x97 mIU/ml)
For initially seropositive subjects, antibody concentration at post-vaccination ≥ 4 fold the pre-vaccination antibody concentration
N = number of subjects with both pre- and post-vaccination results available
n/% = number/percentage of responders
<95>% CI = exact <95>% confidence interval, LL = Lower Limit, UL = Upper Limit
Please note – To calculate the vaccine response, result at PII(M3) compared to PRE-for Co-Ad and PIII(M5) compared to PI(M2) for Control group has to be considered

Template 44 Reverse cumulative distribution curves for <anti-gE antibody concentration, anti-pneumococcal <X> antibody titres> in each group at baseline and <post dose 2 of HZ/su vaccine, post dose of Prevenar 13> <*PPS for immunogenicity*, Exposed Set>



Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
Note: This graph is provided as an example. The same graph will be provided in colour for each time point and each assay comparing the values of the groups
Please note to consider PRE and PI(M1) for both group for pneumococcal antibody. For gE antibody, PRE and PII(M3) for Co-Ad and PI(M2) and PIII(M5) for Control group.

Template 45 Number and percentage of subjects <with><experiencing> fatal SAEs classified by MedDRA Primary System Organ Class and Preferred Term <who died><with onset of fatal SAE> <during the period starting> <from first vaccination up to 30 days post last vaccination dose> <after 30 days post last vaccination dose up to study end><from first vaccination until the study end><during the entire study period> <Exposed Set>

		Co-Ad N =				Control N =			
				95% CI				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
At least one adverse event									
Blood and lymphatic system disorders (10005329)	Leukocytosis (10024378)								
Cardiac disorders (10007541)	Acute myocardial infarction (10000891)								
	Atrial fibrillation (10003658)								
	Cardiac failure congestive (10007559)								
	Tachycardia (10043071)								
	Ventricular tachycardia (10047302)								

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
At least one adverse event = at least one adverse event experienced (regardless of the MedDRA Preferred Term)
N = number of subjects included in the considered cohort in each group
n/% = number/percentage of subjects reporting the adverse event at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Template 46 Summary of subject disposition from Enrolled Set to Randomized Set

	Total N=XXX n %	
Number of subjects who signed an informed consent		
Withdrawals prior to randomization	xxx	xx.x
<Withdrawal reason 1>	xxx	xx.x
<Withdrawal reason 2>	xxx	xx.x
…	xxx	xx.x
	xxx	xx.x
Number of subjects included in Randomized Set		

N = Number of subjects
n% = Number / Percentage of subjects in a given category

Template 47 Summary of subject disposition from Randomized Set to Per Protocol Set

				<Group 1> *N=XXX* *n %*	*<Group 2>* *N=XXX* *n %*	*Total* *N=XXX* *n %*
Number of subjects included in Randomized Set						
Withdrawals				xxx xx.x	xxx xx.x	xxx xx.x
<Withdrawal reason 1>				xxx xx.x	xxx xx.x	xxx xx.x
<Withdrawal reason 2>				xxx xx.x	xxx xx.x	xxx xx.x
…						
Eliminations				xxx xx.x	xxx xx.x	xxx xx.x
<Elimination reason 1 (code)>				xxx xx.x	xxx xx.x	xxx xx.x
<Elimination reason 2 (code)>				xxx xx.x	xxx xx.x	xxx xx.x
…						
Number of subjects included in Exposed Set						
Elimination 1						
Number of subjects included in PPS for immunogenicity						

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = Number of subjects
n% = Number / Percentage of subjects in a given category

Template 48 Listing of subjects who died during the entire study period and their fatal SAEs <Enrolled Set>

Group	Sub. No.	Sex	Country	Race	Age at Onset (Year)	Verbatim	Preferred term	Primary System Organ Class	MED type	Dose prior to onset of fatal SAE	Days between onset of fatal SAE and previous dose	Dose prior to death	Days between death and previous dose	SAE Duration	SAE Causality
No Group	PPD									0	-	0	-		
										0	-	0	-		
										1	xx	1	xx		
										1	xx	2	xx		
										1	xx	1	xx		
										1	xx	1	xx		

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
No Group= Enrolled not vaccinated
MED = Medical Advice type (HO: hospitalisation, ER: emergency room visit, MD: medical practice visit)

Template 49 Summary of subjects by unsolicited adverse event category, with onset within 30 days of each vaccination

	<Group 1> N=XXXX				*<Group 2> N=XXXX*			
			95% CI				*95% CI*	
	n	*%*	*LL*	*UL*	*n*	*%*	*LL*	*UL*
At least one unsolicited adverse event	*xxx*	*xx.x*	*xx.x*	*xx.x*	*xxx*	*xx.x*	*xx.x*	*xx.x*
At least one grade 3 unsolicited adverse event	*xxx*	*xx.x*	*xx.x*	*xx.x*	*xxx*	*xx.x*	*xx.x*	*xx.x*
At least one related unsolicited adverse event	*xxx*	*xx.x*	*xx.x*	*xx.x*	*xxx*	*xx.x*	*xx.x*	*xx.x*
At least one grade 3 related unsolicited adverse event	*xxx*	*xx.x*	*xx.x*	*xx.x*	*xxx*	*xx.x*	*xx.x*	*xx.x*

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = number of subjects included in the considered cohort in each group
n/% = number/percentage of subjects reporting the adverse event at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Template 50 Summary of subjects by serious adverse event and potential Immune Mediated Disease categories, with onset <from first vaccination to 30 days post last vaccination, after 30 days post last vaccination until study end>

	<Group 1> N=XXXX				*<Group 2> N=XXXX*			
			95% CI				*95% CI*	
	n	*%*	*LL*	*UL*	*n*	*%*	*LL*	*UL*
At least one serious adverse event	*xxx*	*xx.x*	*xx.x*	*xx.x*	*xxx*	*xx.x*	*xx.x*	*xx.x*
At least one causally related serious adverse event	*xxx*	*xx.x*	*xx.x*	*xx.x*	*xxx*	*xx.x*	*xx.x*	*xx.x*
At least one potential Immune Mediated Disease	*xxx*	*xx.x*	*xx.x*	*xx.x*	*xxx*	*xx.x*	*xx.x*	*xx.x*
At least one causally related potential Immune Mediated Disease	*xxx*	*xx.x*	*xx.x*	*xx.x*	*xxx*	*xx.x*	*xx.x*	*xx.x*

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = number of subjects included in the considered cohort in each group
n/% = number/percentage of subjects reporting the adverse event at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

GlaxoSmithKline	**Statistical Analysis Plan**
Detailed Title:	A Phase IIIB, randomized, open-label, multicenter clinical trial to assess the immunogenicity and safety of GSK Biologicals' Herpes Zoster vaccine GSK1437173A when co-administered with *Prevenar13* in adults aged 50 years and older.
eTrack study number and Abbreviated Title	204487 (ZOSTER-059 PRI)
Scope:	All analyses planned per protocol.
Date of Statistical Analysis Plan	Amendment 1 Final : 11 June 2019

APP 9000058193 Statistical Analysis Plan Template V4 (Effective date: 3 June 2019)

TABLE OF CONTENTS

PAGE

LIST OF TABLES

PAGE

LIST OF FIGURES

PAGE

LIST OF TEMPLATES

PAGE

LIST OF ABBREVIATIONS

AE	Adverse event
AES	***Adverse Event Screen***
ANCOVA	Analysis of Covariance
$AS01_B$:	MPL, QS21, liposome based Adjuvant System (50 μg MPL and 50 μg QS21)
BS	Blood Sampling
CDR	Clinical Data Reviewer
CI	Confidence Interval
Co-Ad	Co-administration
CRDL	Clinical Research and Development Lead
CRF	Case Report Form
CSR	Clinical Study Report
CTRS	Clinical Trial Registry Summary
ELISA	Enzyme-linked immunosorbent assay
Eli Type	Internal GSK database code for type of elimination code
EL.U/ml	ELISA unit per milliliter
EoS	End of Study
ES	Exposed Set (formally called 'Total Vaccinated Cohort')
GMC	Geometric mean antibody concentration
GMT	Geometric mean antibody titre
GSK	GlaxoSmithKline
IU/ml	International units per milliliter
LL	Lower Limit of the confidence interval
LLOQ	Lower Limit of Quantification
MedDRA	Medical Dictionary for Regulatory Activities
MGI	***Mean Geometric Increase***
MOPA	***Multiplex Opsonophagocytosis Assay***
PCD	Primary Completion Date
PD	Protocol Deviation
PDMP	Protocol Deviation Management Plan
PPS	Per-Protocol Set (formally called 'According to Protocol')
PT	***Preferred Term***

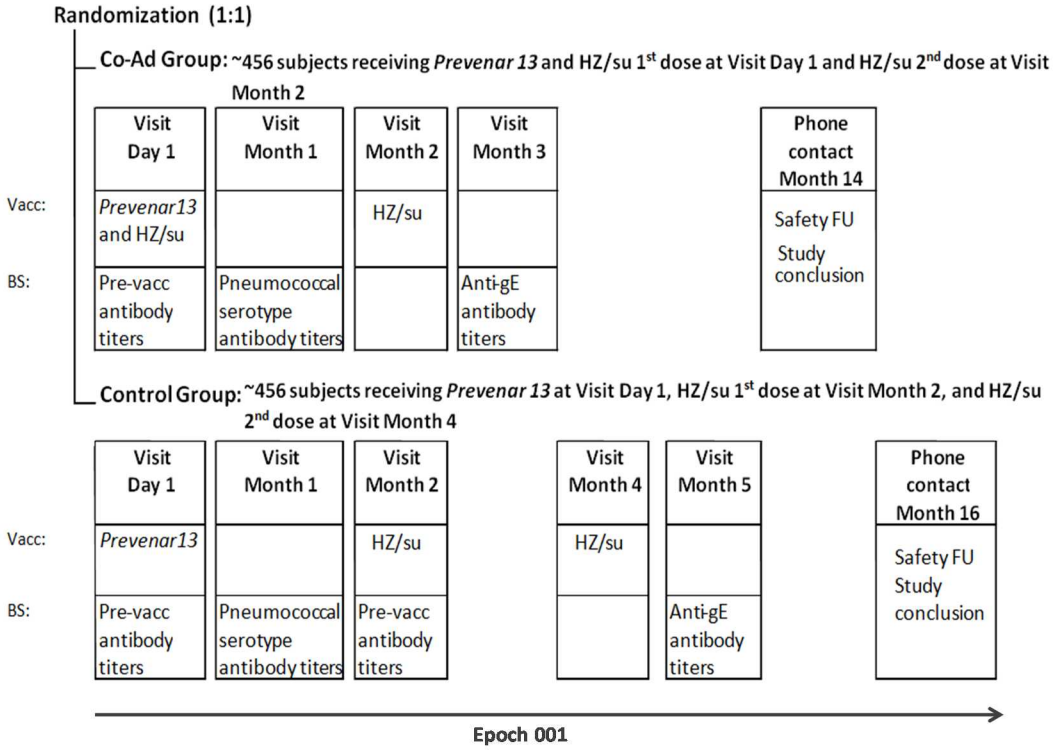
SAE	Serious adverse event
SAP	Statistical Analysis Plan
SBIR	GSK Internet Randomization System
SD	Standard Deviation
SHS	Study Headline Summary
SOC	***System Organ Class***
SUSAR	Suspected Unexpected Serious Adverse Reactions
TFL	Tables Figures and Listings
TOC	Table of Content
UL	Upper Limit of the confidence interval
ULOQ	Upper Limit of Quantification
VRR	Vaccine response rate
YOA	***Years of Age***

1. DOCUMENT HISTORY

Date	Description	Protocol Version
13 APR 2018	First Version	Amendment 2: 30 JAN 2018
11 JUN 2019	***Amendment 1*** ***Summary of changes as below:*** - ***As per new process applicable, the front page has been modified to remove the names of all the contributing author and reviewers. Also, sign-off is only required to be done by Lead Statistician*** - ***Updated LLOQ and newly calculated ULOQ for the 13 pneumococcal serotypes tested by MOPA have been added and accordingly analysis of immunogenicity section has been updated.*** - ***Consort table have been added for subject disposition.*** - ***Additional tables for fatal serious adverse events (SAEs) and grade 3 non-serious unsolicited adverse events (AEs) have been added.*** - ***The term "symptom" has been changed to "adverse event (AE)" in endpoints, table titles and content for solicited AEs, unsolicited AEs, SAEs, and potential immune mediated diseases (pIMDs).*** - ***Table 'Summary of temperature value by half degree increment reported during the 7-day (Days 1-7) post-vaccination following each dose' has been removed*** - ***Sequence of analysis has been updated*** - ***Inclusion of Enrolled and Randomized Set definition*** - ***Code 1500 in elimination codes has been removed and added under code 1070. Also, mandatory columns have been added in the elimination table under 'Elimination from PPS section.***	***Amendment 2: 30 JAN 2018***

2. STUDY DESIGN

Figure 1 Overview of Study Design



Vacc: vaccination; BS: blood sample; Pre-Vacc: pre-vaccination; FU: follow-up

Experimental design: Phase IIIB, open-label, randomized, controlled, multi-centric, and multi-country, with two parallel groups.

Duration of the study: The intended duration of the study per subject is approximately 14 months for subjects from the Co-Ad group and approximately 16 months for subjects from the Control group.

- Epoch 001: Primary starting at Visit Day 1 and ending with the phone contact at Month 16.

Primary completion date (PCD): Visit Month 5.

End of Study (EoS): Last testing results released of samples collected at Visit Month 3 (Co-Ad group) or at Visit Month 5 (Control group).

Study groups:

Table 1 Study groups and epochs foreseen in the study

Study groups	Number of subjects	Age	Epochs
			Epoch 001
Co-Ad	456	≥ 50 years	x
Control	456	≥ 50 years	x

Table 2 Study groups and treatment foreseen in the study

Treatment name	Vaccine/Product name	Study Groups	
		Co-Ad	Control
HZ/su	VZV gE	x	x
	AS01B	x	x
Prevenar13	*Prevenar 13*	x	x

Control: active control.

Vaccination schedule(s):

- Co-Ad Group:
  - at Visit Day 1: first dose of HZ/su and one dose of Prevenar13,
  - at Visit Month 2: second dose of HZ/su.
- Control Group:
  - at Visit Day 1: one dose of *Prevenar13*,
  - at Visit Month 2: first dose of HZ/su,
  - at Visit Month 4: second dose of HZ/su.

Treatment allocation: Subjects to be randomized in a 1:1 ratio at Visit Day 1 to either Co-Ad or Control group. Subjects in each group will be stratified by age with the following approximate distribution (not less than 25% in each age strata):

- 171 subjects in the 50-59 Years of Age (YOA) stratum,
- 171 subjects in the 60-69 YOA stratum, and
- 114 subjects in the ≥ 70 YOA stratum.

Blinding: open-label.

Table 3 Blinding of study epochs

Study Epochs	Blinding
Epoch 001	open

3. OBJECTIVES

3.1. Co-Primary objectives

To determine the vaccine response rate (VRR) to HZ/su (based on humoral immune response) one month after the second vaccine dose, when the first dose of HZ/su is co-administered with *Prevenar13* (Co-Ad group).

Criterion to be used:

The objective is met if the lower limit (LL) of the 95% CI of the VRR for anti-gE antibody concentrations in the Co-Ad group one month after the second vaccine dose is ≥60%.

If the above objective is met in the Co-Ad group, then the following objective will be evaluated:

To demonstrate non-inferiority of the humoral immune response to two doses of HZ/su at one month after the last vaccine dose, when the first dose of HZ/su is co-administered with *Prevenar13* (Co-Ad group) compared to when two doses of HZ/su are administered subsequent to *Prevenar13* (Control Group).

Criterion for non-inferiority:

One month after the last vaccine dose in each study group, the upper limit (UL) of the 95% confidence interval (CI) for the anti-gE antibodies Geometric Mean Concentration (GMC) ratio between the Control group and the Co-Ad group is <1.5.

If the above non-inferiority objective is met, then the following objective will be evaluated:

To demonstrate non-inferiority of the humoral immune response to *Prevenar13* at one month after the vaccine dose, when *Prevenar13 is* co-administered with the first HZ/su dose (Co-Ad group) compared to when *Prevenar13* is administered separately from HZ/su (Control group), for the 13 serotypes included in *Prevenar13* analyzed sequentially.

Criterion for non-inferiority:

One month after the Prevenar13 vaccine dose in each study group, the UL of the 95% CI for each individual pneumococcal conjugate serotype Geometric Mean Titer (GMT) ratio of the Control group over the Co-Ad group is <2.

For the co-primary objectives, fixed sequence testing which allows for full alpha propagation in pre-ordered hypotheses families will be used (see section 6.3.2.1).

3.2. Secondary objective

To evaluate the safety and reactogenicity following administration of HZ/su and *Prevenar13* vaccines, up to one month post last vaccination and during the whole follow-up period, in the Control group and the Co-Ad group.

4. ENDPOINTS

4.1. Primary endpoints

HZ/su immunogenicity:

- Vaccine response for anti-gE humoral immunogenicity, as determined by ELISA, in subjects from the Co-Ad group at one month post-dose 2, at Visit Month 3.
- Anti-gE antibody concentrations as determined by ELISA at one month post-dose 2, at Visit Month 3 for the Co-Ad group and Visit Month 5 for the Control group.

Pneumococcal vaccine immunogenicity:

- Anti-pneumococcal antibody titers for the 13 following serotypes as determined by MOPA at one month post-dose at Visit Month 1: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F.

The criteria used to define the VRR is given in Section 11.1.2.

4.2. Secondary endpoints

Occurrence of solicited local and general ***adverse events***:

- Occurrence, duration and intensity of each solicited local ***adverse event*** within 7 days (Days 1 - 7) after each vaccination,
- Occurrence, duration, intensity and relationship to vaccination of each solicited general ***adverse event*** within 7 days (Days 1 - 7) after each vaccination.

Occurrence of unsolicited AEs:

- Occurrence, intensity and relationship to vaccination of unsolicited AEs within 30 days (Days 1 - 30) after each vaccination, according to the Medical Dictionary for Regulatory Activities (MedDRA) classification.

Occurrence of SAEs:

- Occurrence and relationship to vaccination of all SAEs from first vaccination at Day 1 up to 30 days post last vaccination.
- Occurrence and relationship to vaccination of all SAEs during the period starting after 30 days post last vaccination up to study end.

Occurrence of pIMDs:

- Occurrence and relationship to vaccination of any pIMDs from first vaccination at Day 1 up to 30 days post last vaccination.
- Occurrence of any pIMDs during the period starting after 30 days post last vaccination up to study end.

5. ANALYSIS SETS

5.1. Definition

5.1.1. Enrolled Set

The enrolled set will include all the subjects for whom valid signed informed consent form is available.

5.1.2. Randomized Set

The randomized set will include all the subjects for whom valid signed informed consent form is available and treatment is allocated.

5.1.3. Exposed Set (ES)*

The Exposed set (ES) will include all subjects with at least one vaccine administration documented:

- The ES for analysis of solicited adverse events will include all subjects with at least one documented administered vaccine.
- The ES for analysis of unsolicited AEs, SAEs and pIMDs will include all subjects with at least one vaccine administered.
- The ES for analysis of immunogenicity will include vaccinated subjects for whom immunogenicity data are available.

The ES analysis will be performed per treatment actually administered (at Dose 1).

5.1.4. Per-protocol set (PPS)* for analysis of immunogenicity

The Per-protocol set for analysis of immunogenicity will include all evaluable subjects:

- who meet all eligibility criteria,
- who comply with the procedures and intervals allowed for the analysis,
- who do not meet any of the criteria for elimination during the study,
- for whom data concerning immunogenicity endpoint measures are available.

** Note that in order to align to ICH and cDISC terminology the Total Vaccinated Cohort and the Per- Protocol cohort have been renamed Exposed Set (ES) and Per-Protocol Set (PPS) respectively.*

The intervals allowed for the inclusion in the PPS for analysis of immunogenicity are defined as follows:

	Group	Interval	Allowed interval for PPS analysis of immunogenicity
Interval between vaccinations	Co-Ad	HZ/su (Dose 1) – HZ/su (Dose 2)	49-83 Days
	Control	*Prevenar13* (Dose 1) – HZ/su (Dose 2)	>= 60 days*
	Control	HZ/su (Dose 2) – HZ/su (Dose 3)	49-83 Days
Interval between vaccination and blood sample taken	Co-Ad	*Prevenar13* (Dose 1) – Visit Month 1 for BS	28-48 Days*
	Co-Ad	HZ/su (Dose 2) – Visit Month 3 for BS	28-48 days*
	Control	*Prevenar13* (Dose 1) – Visit Month 1 for BS	28-48 Days*
	Control	HZ/su (Dose 3)– Visit Month 5 for BS	28-48 days*

BS= blood sampling taken; ***please note these intervals differ from protocol amendment 2 Table 8 and 9 to increase the number of evaluable subjects while not compromising the interpretation of immunogenicity data***

5.2. Criteria for eliminating data from Analysis Sets

Elimination codes are used to identify subjects to be eliminated from analysis. Detail is provided below for each set.

5.2.1. Elimination from Enrolled Set

Code 900 (invalid informed consent or fraud data) will be used for identifying subjects eliminated from Enrolled Set.

5.2.2. Elimination from Randomized Set

Code 900 (invalid informed consent or fraud data) and code 1010 (vaccine number not allocated) will be used for identifying subjects eliminated from Randomized Set.

5.2.3. Elimination from Exposed Set (ES)

Code 1030 (Study vaccine not administered at all), ***code 1010 (vaccine number not allocated)*** and code 900 (invalid informed consent or fraud data) will be used for identifying subjects eliminated from ES.

5.2.4. Elimination from Per-protocol analysis Set (PPS)

A subject will be excluded from the PPS analysis under the following conditions:

Code	Condition under which the code is used	*Visit (timepoints) where the code is applicable*	*Applicable for analysis set*
900	Invalid informed consent or fraudulent data. Subjects excluded from all stat analysis *Note: Subjects receiving a code 900 should not receive any other elimination codes.*	All	All
1010	***Vaccine number not allocated*** ***Note: Subjects receiving a code 1010 should not receive any other elimination codes***	***Day 1***	***Randomized Set, ES, PPS***
1030	Study vaccine not administered AT ALL but subject number allocated *Note: Subjects receiving a code 1030 should not receive any other elimination codes*	*Day 1*	*ES, PPS*
1040*	Administration of concomitant vaccine(s) forbidden in the protocol ***Comment:*** ***Co-Ad group: From 30 days before 1st vaccination up to Month 3 blood sampling*** ***Control group: From 30 days before 1st vaccination up to Month 5 blood sampling***	***Co-Ad group: Day -30 to Month 3*** ***Control group : Day -30 to Month 5***	***PPS***
1050	Randomization failure (subject not randomized in the correct group) *Comment: To check for manual randomisation, treatment not compatible with one assigned by SBIR*	***Day 1***	***PPS***
1070	– Side, site or route of study vaccine administration wrong or unknown – Administration not according to protocol for reason specified by the investigator, other than side, site and route – Wrong replacement or study vaccine administered (not compatible with the vaccine regimen associated to the treatment number) – Administered study vaccine reported as being the correct one but is not compatible with the vaccine regimen associated to the treatment number.	***Co-Ad group – Day 1, Month 2*** ***Control group – Day 1, Month 2, Month 4***	***PPS***
1080	Vaccine has been administered (effective treatment number) despite a temperature deviation qualified by Status QA GMP NON Use	***Co-Ad group – Day 1, Month 2*** ***Control group – Day 1, Month 2, Month 4***	***PPS***
1090	Expired vaccine administered	***Co-Ad group – Day 1, Month 2*** ***Control group – Day 1, Month 2, Month 4***	***PPS***
2010	Protocol violation (inclusion/exclusion criteria)	***Day 1***	***PPS***
2040*	Administration of any medication forbidden by the protocol ***Co-Ad group: From 1st vaccination up to Month 3 blood sampling*** ***Control group : From 1st vaccination up to Month 5 blood sampling***	***Co-Ad group – Day 1 up to Month 3*** ***Control group – Day 1 up to Month 5***	***PPS***

Code	Condition under which the code is used	*Visit (timepoints) where the code is applicable*	*Applicable for analysis set*
2050*	Underlying medical condition forbidden by the protocol ***Co-Ad group: From 1st vaccination up to Month 3 blood sampling*** ***Control group: From 1st vaccination up to Month 5 blood sampling***	***Co-Ad group – Day 1 up to Month 3*** ***Control group – Day 1 up to Month 5***	***PPS***
2060*	Concomitant infection related to the vaccine which may influence immune response ***Co-Ad group: From 1st vaccination up to Month 3 blood sampling*** ***Control group: From 1st vaccination up to Month 5 blood sampling***	***Co-Ad group – Day 1 up to Month 3*** ***Control group – Day 1 up to Month 5***	***PPS***
2070*	Concomitant infection not related to the vaccine which may influence immune response ***Comment:*** ***Co-Ad group: From 1st vaccination up to Month 3 blood sampling*** ***Control group: From 1st vaccination up to Month 5 blood sampling***	***Co-Ad group – Day 1 up to Month 3*** ***Control group – Day 1 up to Month 5***	***PPS***
2080	Subjects did not comply with vaccination schedule (dates of vaccination not corresponding to adapted protocol intervals provided in SAP or unknown vaccination dates) *Comment:* *Co-Ad group: DOSE 1 – DOSE 2* *Control group: DOSE 1 – DOSE 2* *DOSE 2 – DOSE 3*	***Co-Ad group: Day 1, Month 2*** ***Control group: Day 1, Month 2, Month 4***	***PPS***
2090	Subjects did not comply with blood sample schedule (dates of BS not corresponding to adapted protocol intervals provided in SAP or unknown BS/vaccination dates) *Comment:* *Co-Ad group: DOSE 1 – MONTH 1 BS* *DOSE 2 – MONTH 3 BS* *Control group: DOSE 1 – MONTH 1 BS* *DOSE 3 – MONTH 5 BS*	***Co-Ad group: Month 1, Month 3*** ***Control group: Month 1, Month 5***	***PPS***
2100	Serological results not available post-vaccination (including lost samples, blood sample not done, unable to test, absence of parallelism). Please specify the applicable rule: ☒ **elimination code if ALL are missing for a subject** ***Comment:*** ***Co-Ad group: Check for availability of anti-gE serological result at Month 3 and for pneumococcal serological results at Month 1*** ***Control group: Check for availability of anti-gE serological result at Month 5 and for pneumococcal serological results at Month 1***	***Co-Ad – Month 1, Month 3*** ***Control – Month 1, Month 5***	***PPS***
2120	Obvious incoherence or abnormality or error in data (incoherence between CRF and results, wrong labelling) *Comment:* *Co-Ad group: Check for above condition on anti-gE serological result at Month 3 and on pneumococcal serological results at Month 1*	***Co-Ad – Month 1, Month 3*** ***Control – Month 1, Month 5***	***PPS***

Code	Condition under which the code is used	*Visit (timepoints) where the code is applicable*	*Applicable for analysis set*
	Control group: Check for above condition on anti-gE serological result at Month 5 and on pneumococcal serological results at Month 1		
2500	Incomplete vaccination course. *Comment: The subject should receive one dose of Prevenar 13 vaccine and 2 doses of Hz/su vaccine*	***Co-Ad – Day 1, Month 2*** ***Control – Day 1, Month 2, Month 4***	***PPS***

BS = Blood sample

** Attribution of these elimination codes are responsibility of CRDL following review of individual data listings*

5.3. Important protocol deviation not leading to elimination from per-protocol analysis set

For information on important protocol deviation not leading to elimination from the PPS set, refer to the study protocol deviation and management plan (PDMP).

6. STATISTICAL ANALYSES

Note that standard data derivation rule and stat methods are described in Section 11 and will not be repeated below. All analyses will be presented by study phase when there are data for both active and follow up phases.

6.1. Demography

6.1.1. Analysis of demographics/baseline characteristics planned in the protocol

Demographic characteristics (age ***at first vaccination***, sex, race and ethnicity) will be tabulated per treatment group.

The mean age (plus range and standard deviation [SD]) of the subjects, as a whole, and per treatment group will be calculated for ***ES and PPS***. The distribution of subjects enrolled among the study sites will be tabulated, as a whole, and per treatment group.

The same tabulations might be performed by age strata (50-59, 60-69 and ≥70 YOA) if deemed necessary.

6.1.2. Additional considerations

- The following additional tables will be generated:
  - The number of subjects enrolled into the study as well as the number of subjects excluded from PPS analyses ***will be presented through two consort tables:***
  - ***Consort table 1 - Showing the subjects disposition from Enrolled Set to Randomized Set***
  - ***Consort table 2 – Showing the subjects disposition from Randomised Set to Per Protocol Set***

  - Withdrawal status will be summarized by group. The numbers of withdrawn subjects will be tabulated according to the reason for withdrawal

- The following table will be generated for CTRS:
  - Percentage of Enrolled subjects by country will be tabulated by group,
  - Percentage of Enrolled subjects in the following age categories ≤64, 65-84, ≥85 will be tabulated by group.
- For computation of age, following rule need to be considered:
  - Age will be calculated as the number of years between the date of birth and the date of first vaccination.
  - To ensure that the collection of date of birth will not jeopardise the privacy of Personally Identifiable Information (PII), only a partial date of birth (MMYYYY) will be collected.
  - Therefore, the 15th of the month will be used to replace the missing date.
  - In case the month is missing, the date will be replaced by the June 30th of the year.
- ***Summary of important protocol deviations leading to elimination will be presented.***

6.2. Exposure

6.2.1. Analysis of exposure planned in the protocol

None

6.2.2. Additional considerations

The number of doses administered will be tabulated. The number of doses administered will be tabulated by age sub-group.

6.3. Immunogenicity

6.3.1. Analysis of immunogenicity planned in the protocol

The primary analysis will be based on the per-protocol set for analysis of immunogenicity. A second analysis based on the Exposed set will be performed to complement the per-protocol analysis (see section 9 for changes in the planned analysis).

Immunogenicity analyses for confirmatory objectives will be performed by age stratum (50-59, 60-69 and ≥ 70 YOA) on PPS, if the number of subjects enrolled is sufficient in each stratum.

6.3.1.1. Within group assessment

The following parameters will be tabulated by vaccine group at each time point when a blood sample result is available:

- Seropositivity with exact 95% CI for all antigens
- GMC/GMT with 95% CI for all antigens
- VRR with exact 95% CI for anti-gE
- Mean Geometric Increase (MGI) with exact 95% CI for anti-gE
- Descriptive statistics (N, mean, SD, min, Q1, median, Q3, max) of Mean Geometric Increase (MGI) for anti-gE
- Distribution of the fold increase i.e. Percentage of subjects with a more than X-fold (e.g. >2, >4, >6, -fold) increase will be tabulated for anti-gE per group with 95% CI.
- Antibody titre/concentration will be displayed using reverse cumulative curves.

6.3.1.2. Between group assessment

The following between group comparison will be performed:

- For the second co-primary objective for non-inferiority of the anti-gE humoral response, at one-month post-dose 2 of HZ/su vaccine:
  - The 95% CI of the group GMCs ratio (Control divided by Co-Ad) will be computed using an ANCOVA model on the log10 transformation of the concentrations. The pre-vaccination log-transformed antibody concentrations will be included as continuous covariate and the vaccine group and age strata as fixed effects in the model.
- For the third co-primary objective for non-inferiority of the humoral response to each vaccine pneumococcal serotype (according to the pre-specified order in the protocol), one month post-dose of *Prevenar13*:
  - The 95% CI of the group MOPA GMT ratios (Control divided by Co-Ad) will be computed using an ANCOVA model on the log10 transformation of the concentrations. The pre-vaccination log-transformed antibody concentrations will be included as continuous covariate and the vaccine group and age strata as fixed effects in the model.

6.3.2. Additional considerations

The following additional points need to be considered for immunogenicity analysis:

- ***Percentage of subjects above the pneumococcal serotype specific LLOQ will be calculated for each serotype with exact 95% Cis.***
- Immunogenicity descriptive analyses will be performed by age stratum (50-59, 60-69 and ≥ 70 YOA), if the number of subjects enrolled is sufficient in each stratum.

- Two-sided 95% CIs for Seropositivity and VRR will be computed by Clopper-Pearson method [Clopper, 1934]. The differences in percentages and the associated two-sided 95% between the groups CIs for the difference will be constructed using the method of Miettinen and Nurminen [Robert, 1998].
- The two-sided 95% CI for the mean of log-transformed titre/concentration will be first obtained assuming that log-transformed values were normally distributed with unknown variance. The 95% CI for the GMTs/GMCs/MGIs will be then obtained by exponential-transformation of the 95% CI for the mean of log-transformed titre/concentration.

6.3.2.1. Statistical considerations for confirmatory objectives

For the multiplicity adjustment, all hypotheses have been ranked into three families and one sub-family according to the following power of test:

Table 4 Power to demonstrate VRR objective and non-inferiority of the immunogenicity of HZ/su and *Prevenar13* co-administered compared to Control group

Family 1: HZ/su: VVR*(1-sided test with alpha = 2.5%)				
Endpoint	Threshold	VR assumed	Total β	Power
VRR in Co-Ad group	0.60	95%	0.001%	99.99%
Family 2: HZ/su: non-inferiority* (1-sided test with alpha = 2.5%) N=410				
Endpoint	Standard deviation	δ	Total β	Power
Anti-gE GMC ratio	0.35	1.5	0.001 %	99.99 %
Family 3: *Prevenar13*: Non-inferiority* (1-sided test with alpha = 2.5%) N=410				
Endpoint (13 vaccine pneumococcal serotypes)	Standard deviation	δ	Total β	Power
3 GMT ratio	0.660	2	0.001%	99.99%
19A GMT ratio	0.644	2	0.001%	99.99%
1 GMT ratio	0.798	2	0.029%	99.97%
18C GMT ratio	0.891	2	0.203%	99.80%
4 GMT ratio	0.906	2	0.260%	99.74%
6A GMT ratio	0.919	2	0.320%	99.68%
5 GMT ratio	0.931	2	0.383%	99.62%
19F GMT ratio	0.971	2	0.664%	99.33%
6B GMT ratio	0.995	2	0.891%	99.11%
7F GMT ratio	1.014	2	1.107%	98.89%
9V GMT ratio	1.021	2	1.194%	98.81%
14 GMT ratio	1.045	2	1.530%	98.47%
23F GMT ratio	1.094	2	2.398%	97.60%
Global β to show non-inferiority			~9%	
Global power				**~91%**

VRR: vaccine response rate; gE: Varicella Zoster Virus glycoprotein E; GMT: geometric mean titer; GMC: geometric mean concentration.

* Pass 12, alpha = 2.5%, for VRR: Exact test, for non-inferiority one-sided equivalence of means.

For gE: non-inferiority limit = 0.176 (=log10(1.5)), power under equal GMC

For each pneumococcal serotype: non-inferiority limit = 0.301 (=log10(2)), variability for each of the 13 vaccine pneumococcal serotype taken from the EMA assessment report for *Prevenar13* and multiplied by 1.1, power under equal GMT.

Fixed sequence testing which allows for full alpha propagation in pre-ordered hypotheses families will be applied in the following manner:

Family 1:

In the Co-Ad group, for anti-gE, at one month post-dose 2 of HZ/su vaccine:

- The VRR and 95% CI will be computed.

The objective is met if the LL of the 95% CI is ≥60%.

Family 2:

For anti-gE, at one month post-dose 2 of HZ/su vaccine:

- The 95% CI of the group GMCs ratio will be computed using an analysis of covariance (ANCOVA) model on the log10 transformation of the concentrations. The pre-vaccination log-transformed antibody concentrations will be included as continuous covariate and the vaccine group and age strata as fixed effects in the model.

In terms of concentrations, the Co-Ad group will be considered non-inferior to the Control group if the UL of the 95% CI for the GMC ratio of the Control group to the Co-Ad group is <1.5.

Family 3:

For each vaccine pneumococcal serotype (according to the pre-specified order), one month post-dose of *Prevenar13*:

- The 95% CI of the group MOPA GMT ratios will be computed using an analysis of covariance (ANCOVA) model on the log10 transformation of the concentrations. The pre-vaccination log-transformed antibody concentrations will be included as continuous covariate and the vaccine group and age strata as fixed effects in the model.

In terms of MOPA GMTs, the Co-Ad group will be considered non-inferior to the Control group if the UL of the 95% CI for the MOPA GMTs ratio of the Control group to the Co-Ad group is <2 for each of the 13 vaccine serotypes.

In the ANCOVA models Adjusted Least Squares (LS) means and difference of LS means between the groups will be calculated together with the 2-sided 95% CIs and back-transformed to the original units to provide GMCs and GM ratios.

6.4. Analysis of safety

6.4.1. Analysis of safety planned in the protocol

The analysis for safety will be based on the Exposed set. All safety analyses may also be performed by age strata (50-59, 60-69 and ≥70 YOA), if deemed necessary.

When appropriate, tabulations will be presented overall and by time of occurrence relative to last vaccination (e.g. using windows such as Days 1 to 7, Days 1 to 30 and more than 30 days post-vaccination).

The results for the analysis of safety will be tabulated as follows:

- The number and percentage of subjects with at least one local solicited AE, with at least one general solicited AE, and with any solicited AE during the 7-day follow-up period with exact 95% CIs after each vaccine dose and overall by vaccination group will be provided;
- The percentage of subjects reporting each individual solicited local and general AE during the solicited 7-day follow-up period will be tabulated with exact 95% CI;
- For all solicited adverse events, the same tabulation will be performed for grade 3 solicited AEs and for solicited general AEs with relationship to vaccination;
- Number of days with each individual solicited local and general AE during the solicited 7-day follow-up period;
- The proportion of subjects with at least one report of unsolicited AE ***(containing both serious and non-serious unsolicited AEs)*** classified by the MedDRA ***Primary System Organ Class (SOC) and Preferred Terms (PTs)*** and reported up to 30 days after each vaccination will be tabulated with exact 95% CI;
- The same tabulation will be performed for grade 3 unsolicited AEs and for unsolicited AEs with a relationship to vaccination ***reported up to 30 days after each vaccination with exact 95% CI.*** The proportion of AEs resulting in a medically attended visit will also be tabulated;
- Total number/percentages of doses (per dose and overall) followed by AEs will be tabulated;
- Number of subjects with pIMDs will be tabulated;
- SAEs, including fatalities and withdrawal due to AE(s) will be described in detail.

6.4.2. Additional considerations

- The following additional tables will be generated:
  - The percentage of subjects with at least one local AE (solicited and unsolicited), with at least one general AE (solicited and unsolicited) and with any AE (solicited and unsolicited) during the 7-day follow-up period will be tabulated with exact 95% CI after each vaccine dose and overall. The same computations will be done for Grade 3 AEs, for any AEs considered related to vaccination and for any Grade 3 AEs considered related to vaccination.
  - The percentage of subjects with at least one local solicited AE, with at least one general solicited AE and with any solicited AE will also be done for Grade 3 solicited AEs, for any solicited AEs considered related to vaccination and for any Grade 3 solicited AEs considered related to vaccination.
  - ***The percentage of subjects reporting each individual solicited local AE during the solicited 7-day follow-up period will be tabulated by study vaccine with exact 95% CI.***

- Summary of temperature value by half degree increment taken by different routes reported during the 7-day (Days 1-7) post-vaccination following each dose.
- For fever, the number and percentage of subjects reporting fever by half degree (°C) cumulative increments during the 7-day follow-up period (Day 1-7) will be tabulated for each group after each vaccine dose and overall. Similar tabulations will be performed for Grade 3 (> 39.0°C) causally related fever.
- List of suspected HZ cases identified during the study will be presented.
- The number and percentage of subjects starting a concomitant medication during the 30-day post-vaccination period by dose and overall will be presented.
- The duration of solicited local adverse events (in days), not limited to the 7-day post-vaccination period, following each dose and overall/dose. The same tabulations after Prevenar13 and HZ/su vaccinations.
- The duration of solicited general adverse events (in days), not limited to the 7-day post-vaccination period, following each dose and overall/dose.
- Solicited local adverse events ongoing beyond the 7-day (Days 1-7) post-vaccination period, following each dose and overall/dose. The same tabulations after Prevenar13 and HZ/su vaccinations.
- Solicited general adverse events ongoing beyond the 7-day (Days 1-7) post-vaccination period, following each dose and overall/dose.
- ***Number and percentage of subjects with at least one report of a grade 3 non-serious unsolicited AE during the 30-day (Days 0–29) follow-up period after each vaccination classified according to the MedDRA Primary SOC and PTs will be tabulated, with exact 95% CI. The same will be generated for grade 3 non-serious unsolicited AE considered related to vaccination.***
- ***Number and percentage of subjects with fatal SAEs, classified by MedDRA Primary SOC and PTs will be presented with exact 95% CI in two ways:***
- ***With onset of fatal SAE during the period starting from first vaccination to 30 days post last vaccination dose, after 30 days post last vaccination dose to study end and from first vaccination to study end.***
- ***Who died during the period starting from first vaccination to 30 days post last vaccination dose, after 30 days post last vaccination dose to study end and entire study period.***
- ***The listing of all subjects who died during the entire study period and their fatal SAEs in the Enrolled Set***

6.4.2.1. Combined Solicited and Unsolicited Adverse Events

A summary of subjects with all combined solicited (regardless of their duration) and unsolicited adverse events will be provided. Solicited adverse events will be coded by MedDRA as per the following codes:

Solicited adverse event	Lower level term name	Corresponding Lower level term code
Pain	Injection site pain	10022086
Redness	Redness at injection site	10022098
Swelling	Swelling at injection site	10053425
Fatigue	Fatigue	10016256
Gastrointestinal symptoms	Gastrointestinal disorder	10017944
Headache	Headache	10019211
Myalgia	Myalgia	10028411
Shivering	Shivering	10040558
Temperature	Fever	10016558

For clintrial.gov and EudraCT posting purposes, a summary of combined solicited and unsolicited non-serious adverse events will be produced by SOC and PTs and according to occurrence of each event.

7. ANALYSIS INTERPRETATION

All co-primary objectives will be evaluated using a one-sided Type I error of 2.5% (as already justified by fixed sequential testing procedure, no alpha adjustment needed). The trial will be considered conclusive if all co-primary objectives criteria are met.

8. CONDUCT OF ANALYSES

8.1. Sequence of analyses

The analysis will be performed in the following steps:

- ***An active phase analysis for public disclosure of demography and safety/reactogenicity result will be performed on available data as clean as possible at the end of active phase.***
- ***The final analysis on immunogenicity, reactogenicity and*** safety data will be performed when all data up to study end (i.e., phone contact at Month 14 for Co-Ad group and phone contact at Month 16 for Control group) will be available and cleaned. ***Individual data listings will also be provided.***

An integrated clinical study report containing all data will be written and made available to the investigators following the final analysis.

Table 5 Analysis and disclosure plan for the planned analysis

Description	Analysis ID	Disclosure Purpose (CTRS=public posting, CSR=clinical study report, internal)	Dry run review needed (Y/N)	Reference for TFL
End of Active phase – posting	***E1_02***	***CTRS***	***Y***	***See in TFL TOC where POSTING=YES***
Final analysis	E1_01	CTRS CSR	Y	***All tables from Section 12 of the SAP Amendment 1 03JUN2018***

8.2. Statistical considerations for interim analyses

Not applicable

9. CHANGES FROM PLANNED ANALYSES

- In Protocol Amendment 2 Final (30 Jan 2018), it was specified that a second analysis for immunogenicity of the ES would be performed only if, in any study group, the percentage of enrolled subjects with serological results excluded from the PPS for immunogenicity is 5% or more. At the request of Paul Ehrlich Institute, Germany (PEI), an analysis of the ES will be performed to complement the per-protocol analysis regardless of the percentage of enrolled subjects excluded from the PPS for immunogenicity.
- ***Updated LLOQ values (i.e. assay cut-off values) for the pneumococcal serotypes are provided in this version of SAP (section 11.1.2). The cut-off values presented in this SAP will be used to determine seropositivity rather than those presented in Protocol Amendment 2 Final (30 Jan 2018). Analysis of immunogenicity section has been updated accordingly.***
- ***Additional tables on presentation of grade 3 non-serious unsolicited adverse events and fatal SAEs has been added based on CBER request.***
- ***The sequence of analysis was updated to accommodate a delay in the availability of immunogenicity results.***
- ***Two new cohorts – Enrolled Set and Randomized Set has been defined as required for web disclosure and SAE tables presentation.***
- ***Analysis of demography section has been updated to add consort table and summary of important protocol deviations.***

10. LIST OF FINAL REPORT TABLES, LISTINGS AND FIGURES

The TFL TOC provides the list of tables/listings and figures to be included in the study report.

The following group names will be used in the TFLs, in line with the T-domains:

Group order in tables	Group label in tables	Group definition for footnote
1	Co-Ad	Dose 1 : Prevenar 13 + HZ/su, Dose 2: HZ/su
2	Control	Dose 1 : Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su

The following sub-groups will be used in the TFL, in line with the T-domains:

Table 6 Group Definitions to be used for the sub-group analysis by age (Analysis will be included in the clinical report)

Sub-group order in tables	Sub-group label in tables	Sub-group definition for footnote
1	50-59YOA	Subjects aged 50-59 years
2	60-69YOA	Subjects aged 60-69 years
3	≥70YOA	Subjects aged 70 years and over

YOA = Year of age

Please note that for table presentation in the sub-group analysis, the sequence maintained has to be each treatment group within each age sub-group.

11. ANNEX 1 STANDARD DATA DERIVATION RULE AND STATISTICAL METHODS

11.1. Standard data derivation

11.1.1. Dose number

The study dose number is defined in reference to the number of study visits at which vaccination occurred. More specifically dose 1 refers to all vaccines administered at the first vaccination visit while dose 2 corresponds to all vaccinations administered at the second vaccination visit even if this is the first time a product is administered to the subject.

Associated dose: the associated dose for an event (AE, medication, vaccination) is the most recent study dose given before an event. In case the event takes place on the day a study dose is given, the associated dose will be that of the study dose, even if the event actually took place before vaccination. For instance, if an adverse event begins on the day of the study vaccination but prior to administration of the vaccine, it will be assigned to this dose. In case a study dose is not administered and an event occurs after the

subsequent study dose (e.g. 2nd study dose), the associated dose of the event will be study dose associated to the subsequent study dose (e.g. dose 2).

The number of doses for a product is the number of times the product was administered to a subject.

The incidence per dose is the number of visits with vaccine administered at which an event was reported among all visits with vaccine administered.

11.1.2. Immunogenicity

- For a given subject and given immunogenicity measurement, missing or non-evaluable measurements will not be replaced. Therefore, an analysis will exclude subjects with missing or non-evaluable measurements.
- A seronegative subject is a subject whose antibodies concentration/titer is below the cut-off value (cut-off value is defined by the laboratory prior to the analysis).
- A seropositive subject is a subject whose antibodies concentration/titer is greater than or equal to the assay cut-off value.
- The seropositivity rate is defined as the percentage of seropositive subjects.
- The VRR for anti-gE is defined as the percentage of subjects who have at least:
  - a 4-fold increase in the anti-gE antibodies concentration as compared to the pre-vaccination anti-gE antibodies concentration, for subjects who are seropositive at baseline, or,
  - a 4-fold increase in the anti-gE antibodies concentration as compared to the anti-gE antibodies cut-off value for seropositivity, for subjects who are seronegative at baseline.
- The GMC calculations for anti-gE antibody concentration are performed by taking the anti-log of the mean of the log base 10 concentration transformations. Antibody concentrations below the cut-off of the assay will be given an arbitrary value equal to half the cut-off for the purpose of GMC/GMT calculation.
- All CI computed will be two-sided 95% CI.

- ***Updated LLOQ and ULOQ values for the MOPA assay are described below for each of the 13 pneumococcal serotypes:***

Pneumococcal serotype	Method	Unit	LLOQ[1]	ULOQ	Laboratory
Streptococcus pneumoniae Serotype 01/37 Brugmann Hospital Ab	MOPA	1/ dilution	14	3504	University of Alabama at Birmingham
Streptococcus pneumoniae Serotype 03/1 Statens Serum Institut Ab			11	2822	
Streptococcus pneumoniae Serotype 04/2656 Brugmann Hospital Ab			40	18042	
Streptococcus pneumoniae Serotype 05 Ambrose- Statens Serum Institut Ab			15	13304	
Streptococcus pneumoniae Serotype 06A Centers for Disease Control Ab			45	15305	
Streptococcus pneumoniae Serotype 06B/DS2212/94 Centers for Disease Control Ab			29	20806	
Streptococcus pneumoniae Serotype 07F/46 Brugmann Hospital Ab			28	59809	
Streptococcus pneumoniae Serotype 09V/112 161/95 Statens Serum Institut Ab			39	28095	
Streptococcus pneumoniae Serotype 14/58 Brugmann Hospital Ab			16	47856	
Streptococcus pneumoniae Serotype 18C/4593/40 Statens Serum Institut Ab			40	13318	
Streptococcus pneumoniae Serotype 19A/DB18 Kansanterveyslaitos Folkhalsoinstitutet Ab			13	34881	
Streptococcus pneumoniae Serotype 19F/2737 Brugmann Hospital Ab			33	29352	
Streptococcus pneumoniae Serotype 23F Mac-Statens Serum Institut Ab			40	10662	

[1]LLOQ corresponds to serotype-specific assay cut-off value.

- ***The Geometric Mean Titres (GMTs) calculations for pneumococcal serotypes are performed by taking the anti-log of the mean of the log base 10 titre transformations. For GMT calculation for pneumococcal serotypes, antibody titres below the LLOQ of the assay will be given an arbitrary value of half the cut-off for GMT calculation. Antibody titres above the ULOQ of the assay will be given the value of ULOQ for GMT calculation.***

11.1.3. Safety

For a given subject and the analysis of solicited ***adverse event*** during the 7 day follow-up period after vaccination, missing or non-evaluable measurements will not be replaced. Therefore, the analysis of the solicited ***adverse events*** based on the ES will include only vaccinated subjects with documented safety data (i.e., symptom screen completed). More specifically the following rules will be used:

- Subjects who documented the absence of a solicited ***adverse event*** after one dose will be considered not having that ***adverse event*** after that dose.
- Subjects who documented the presence of a solicited ***adverse event*** and fully or partially recorded daily measurement over the solicited period will be included in the

summaries at that dose and classified according to their maximum observed daily recording over the solicited period.

- Subjects who documented the presence of a solicited ***adverse event*** after one dose without having recorded any daily measurement will be assigned to the lowest intensity category at that dose (i.e., 38°C for fever or grade 1 for other adverse events). The subject will only be presented in the subject with ***adverse event*** experienced and not in specific grade information.
- Doses without ***adverse event*** sheets documented will be excluded.

For analysis of unsolicited AEs, such as SAEs or adverse events by MedDRA Primary SOC and PTs term, and for the analysis of concomitant medications, all vaccinated subjects will be considered. Subjects who did not report the event or the concomitant medication will be considered as subjects without the event or the concomitant medication respectively.

Associated dose: The associated dose for an event (e.g., AE, medication, vaccination,…) is the study dose given before an event. In case the event takes place on a day a study dose is given, the associated dose will be that of the study dose even if the event actually took place before. For instance, for a conc. medication started on the day of study dose 2 but before dose 2 administrations, the associated dose will be dose 2

The way the percentage of subjects will be derived will depend on the event analysed (see the following table for details). As a result, the denominator (N) will differ from one table to another.

Event	N used for deriving %	Terminology used in the tables for N
Concomitant medication	All vaccinated subjects	Number of subjects with at least one administered dose
Solicited local ***adverse event***	All vaccinated subjects with at least one solicited local ***adverse event*** documented as either present or absent	For each dose and overall/subject: N= number of subjects with at least one documented dose For overall/dose: N= number of documented doses
Solicited general ***adverse event***	All vaccinated subjects with at least one solicited general ***adverse event*** documented as either present or absent	For each dose and overall/subject: N= number of subjects with at least one documented dose For overall/dose: N= number of documented doses
Unsolicited ***adverse event*** from day 0 to day X	All vaccinated subjects	Number of subjects with at least one administered dose
SAE	All vaccinated subjects	Number of subjects with at least one administered dose

- The maximum intensity of local injection site redness and swelling will be scored at GSK Biologicals as follows:
  - 0 : <20 mm
  - 1 : ≥ 20 mm to ≤ 50 mm diameter
  - 2 : > 50 mm to ≤ 100 mm diameter
  - 3 : > 100 mm diameter

Fever is defined as temperature ≥ 38.0 C / 100.4 F for oral, axillary, tympanic or rectal route. The preferred route for recording temperature in this study will be oral. For the analysis, temperatures will be coded as follows:

Grade	Temperature (oral, axillary, tympanic or rectal route)
0	< 38°C
1	≥ 38°C - ≤ 38.5°C
2	> 38.5°C - ≤ 39°C
3	> 39°C

- Conversion of temperature to °C -

  The following conversion rule is used for the conversion of temperature to °C

  - Temperature in °Celsius = ((Temperature in °Fahrenheit -32) *5)/9

The result is rounded to 1 decimal digit.

11.2. Statistical Method References

Clopper CJ, Pearson ES. The use of confidence or fiducial limits illustrated in the case of binomial. *Biometrika*. 1934; 26:404-413.

Robert G. Newcombe, interval estimation for the difference between independent proportions: comparison of eleven methods, *Statist Med.* 1998; 17, 873-890.

11.3. Number of decimals displayed:

The following decimal description from the decision rules will be used for the demography, immunogenicity and safety/reactogenicity.

Display Table	Parameters	Number of decimal digits
Demographic characteristics	Mean, median age	1
Demographic characteristics	SD (age)	1
Immunogenicity	Ratio of GMT/C	2
All summaries	% of count, including LL & UL of CI	1
All summaries	% of difference, including LL & UL of CI	2

12. ANNEX 2: STUDY SPECIFIC MOCK TFL

The study specific mocks are annexed to this SAP in a separate document.

The data display, title and footnote are for illustration purpose and will be adapted to the study specificity as indicated in the TFL TOC. Note that there may be few changes between the study specific SAP mock TFL and the final TFLs as editorial/minor changes do not require a SAP amendment

12.1. List of individual data listing

Following individual data listing will be generated

Appendix Table I.A - Elimination codes

Appendix Table I.B – Demography

Appendix Table IBii - Physical examination/vital signs

Appendix Table I.Ci - Dates of birth, Informed consent, Vaccination and blood sampling, Contact

Appendix Table I.Cii - Reason for visit not done

Appendix Table I.D - General medical history - Physical examination

Appendix Table I.Ei – Study Conclusion

Appendix Table I.F – Notes (this appendix is provided for info only and should not be used for the clinical report)

Appendix Table I.G / I.H - Vaccination procedure

Appendix Table I.I - Reason for not administration of vaccine

Appendix Table I.J - Reason for non-eligibility

Appendix Table I.Ki – Previous history of vaccination

Appendix Table I.Kii – Previous history of disease

Appendix Table II.Ai - Solicited local adverse events

Appendix Table II.B - Solicited general adverse events

Appendix Table II.Ci - Unsolicited adverse events within (30) days post-vaccination

Appendix Table II.Cii - Unsolicited adverse events after (30) days post-vaccination

Appendix Table II.Di - Concomitant medications

Appendix Table II.Dii - Concomitant vaccinations

Appendix Table III.A – Immunogenicity

12.2. Template of Tables and Figures

Template 1 Number of subjects by country and center <Exposed Set>

		<Each group> N=XXXX		<Each group> N=XXXX		Total N=XXXX	
Country	**Center**	**n**	**%**	**n**	**%**	**n**	**%**
<each country>	<each center >	XXX	XX.X	XXX	XX.X	XXX	XX.X
	All	XXX	XX.X	XXX	XX.X	XXX	XX.X

<each group>:
Co_Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
n = number of subjects in a given center or country
N = total number of subjects
% = n/N x 100
Center = GSK Biologicals assigned center number

Template 2 Number of enrolled subjects by country

	<Each group> N=XXXX		<Each group> N=XXXX		Total N=XXXX	
Country	**n**	**%**	**n**	**%**	**n**	**%**
<Each country>	XXX	XX.X	XXX	XX.X	XXX	XX.X

<each group>:
Co_Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
n = number of subjects in a given country
N = total number of subjects
% = n/N x 100

Template 3 Number of enrolled subjects by age category

	<Each group> N=XXXX		<Each group> N=XXXX		Total N=XXXX	
Age category	**n**	**%**	**n**	**%**	**n**	**%**
Adults [18-64 years]	XXX	XX.X	XXX	XX.X	XXX	XX.X
From 65-84 years						
85 years and over						

<each group>:
Co_Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = number of enrolled subjects
n = number of enrolled subjects included in each group or in total for a given age category or for all age categories
% = n/N x 100

Template 4 Number of subjects by country and age category <Exposed Set>

		<Each group> N=XXXX		<Each group> N=XXXX		Total N=XXXX	
Country	**Age category**	**n**	**%**	**n**	**%**	**n**	**%**
<each country>	50-59YOA	XXX	XX.X	XXX	XX.X	XXX	XX.X
	60-69YOA						
	≥70YOA						
	All	XXX	XX.X	XXX	XX.X	XXX	XX.X

Co_Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
50-59YOA = Subjects aged 50-59 years
60-69YOA = Subjects aged 60-69 years
≥70YOA = Subjects aged 70 years and over
n = number of subjects in a given center or country
N = total number of subjects
% = n/N x 100

Template 5 Number of subjects vaccinated, completed and withdrawn with reason for withdrawal – <end of active phase, study end> <Exposed set>

	<Each group> N=XXXX	<Each group> N=XXXX	Total N=XXXX
	n	**n**	**n**
Number of subjects vaccinated	xxx	xxx	xxx
End of study status			
[EACH CATEGORY]	xxx	xxx	xxx
Reasons for withdrawal:			
[REASONS]	xxx	xxx	xxx

Co_Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
Vaccinated = number of subjects who were vaccinated in the study
Completed = number of subjects who completed <end of active phase visit, last study visit>
Withdrawn = number of subjects who did not come for the <end of active phase visit, last study visit>
Unknown = number/percentage of subjects who have not come for the <end of active phase visit, last study visit> yet

Template 6 Visit attendance <Exposed set>

		<Each group> N=XXX	
Visit	**Status**	**n**	**%**
INFORMED CONSENT	Completed		
RANDOMIZATION	Completed		
<EACH VISIT>	Attended		
	Not attended yet		
	Permanent discontinuation prior to this visit		
	Not attended		
CONCLUSION	Completed		

Co_Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = Number of subjects in each group or in total
Conclusion = date of last visit or withdrawal

Template 7 Summary of important protocol deviations leading to elimination from any analyses

Category Sub-category		<Each group> N=XXXX			Total N=XXXX		
		occ	n	%	occ	n	%
At least one important protocol deviation		**xxx**	**xxx**	**xx.x**	**xxx**	**xxx**	**xx.x**
		xxx	**xxx**	**xx.x**	**xxx**	**xxx**	**xx.x**
<Category 1>		**xxx**	**xxx**	**xx.x**	**xxx**	**xxx**	**xx.x**
<Sub-category 1>		**xxx**	**xxx**	**xx.x**	**xxx**	**xxx**	**xx.x**
<Sub-category 2>							
…							
		xxx	**xxx**	**xx.x**	**xxx**	**xxx**	**xx.x**
<Category 2>							
…							
…							

Co_Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = Total number of subjects
Occ = number of occurrences = number of important protocol deviations
n/% = number / percentage of subjects with important protocol deviations

Template 8 Percentage of subjects with serological results who were eliminated from PPS for immunogenicity

	[each group]	
Number of subjects in Exposed Set with serological results available		
Number of subjects with serological results eliminated from PPS for immunogenicity		
Percentage of subjects with serological results eliminated from PPS for immunogenicity		

Co_Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su

Template 9 Deviations from specifications for age and intervals between study visits for Co-Ad group <Exposed Set, PPS for immunogenicity>

		Age	Dose:1-PI (M1)		Dose:1-Dose:2	Dose:2-PII (M3)		Dose:2–PHC (M14)
Group		**Protocol**	**Protocol**	**Adapted**	**Protocol**	**Protocol**	**Adapted**	**Protocol**
		from ≥ 50 years	from 30 to 42 days	from 28 to 48 days	from 49 to 83 days	from 30 to 48 days	from 28 to 48 days	from 335 to 395 days
Co-Ad	N							
	n							
	%							
	range							

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Adapted = interval used for defining PPS for immunogenicity
N = total number of subjects with available results
n/% = number / percentage of subjects with results outside of the interval
range = minimum-maximum for age and intervals
PI (M1) = Blood sample at Month 1, post-vaccination Dose 1

PII (M3) = Blood sample at Month 3, post-vaccination Dose 2
PHC (M14) = Phone Contact MONTH 14
Note that the exact age is unknown since only the month and year of birthdate are recorded. Accordingly the age estimated using the middle of the month may be inexact by one month

Template 10 Deviations from specifications for age and intervals between study visits - for Control group <Exposed Set, PPS for immunogenicity>

		Age	Dose:1-PI(M1)		Dose:1-Dose:2		Dose:2-Dose:3	Dose:3-PIII(M5)		Dose:3-PHONE CONT M16
Group		**Protocol**	**Protocol**	**Adapted**	**Protocol**	**Adapted**	**Protocol**	**Protocol**	**Adapted**	**Protocol**
		from ≥ 50 years	from 30 to 42 days	from 28 to 48 days	from 60 to 83 days	≥ 60 days	from 49 to 83 days	from 30 to 48 days	from 28 to 48 days	from 335 to 395 days
Control	N									
	n									
	%									
	range									

Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
Adapted = interval used for defining the ATP cohorts for immunogenicity
N = total number of subjects with available results
n/% = number / percentage of subjects with results outside of the interval
range = minimum-maximum for age and intervals
PI(M1) = Blood sample at Month 1, post-vaccination Dose 1
PIII(M5) = Blood sample at Month 5, post-vaccination Dose 3
PHC (M16) = Phone Contact Month 16

Template 11 Summary of demographic characteristics <Exposed Set, PPS for immunogenicity>

	<Each group> N=XXXX		<Each group> N=XXXX		Total N=XXXX	
	Value or n	**%**	**Value or n**	**%**	**Value or n**	**%**
Age in Years at <timepoint>						
N with data	xxx		xxx		xxx	
Mean	xxx.x		xxx.x		xxx.x	
SD	xxx.x		xxx.x		xxx.x	
Median	xxx.x		xxx.x		xxx.x	
Minimum	xxx		xxx		xxx	
Maximum	xxx		xxx		xxx	
Gender						
<EACH GENDER>	xxx	xx.x	xxx	xx.x	xxx	xx.x
…	xxx	xx.x	xxx	xx.x	xxx	xx.x
Ethnicity						
<EACH ETHNICITY>	xxx	xx.x	xxx	xx.x	xxx	xx.x
…	xxx	xx.x	xxx	xx.x	xxx	xx.x
Geographic Ancestry						
<EACH GEOGRAPHIC ANCESTRY>	xxx	xx.x	xxx	xx.x	xxx	xx.x
…	xxx	xx.x	xxx	xx.x	xxx	xx.x
Age category						
<EACH AGE CATEGORY>	xxx	xx.x	xxx	xx.x	xxx	xx.x
Country						
<EACH COUNTRY>	xxx	xx.x	xxx	xx.x	xxx	xx.x
…	xxx	xx.x	xxx	xx.x	xxx	xx.x

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su

Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = total number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
N with data = number of subjects with documentation of the corresponding data
SD = standard deviation

Template 12 Minimum and maximum activity dates <Exposed Set>

Group	Activity number	Activity Description	Minimum date	Maximum date
Co-Ad	10	VISIT DAY 1		
	20	VISIT MONTH 1		
	30	VISIT MONTH 2		
	40	VISIT MONTH 3		
	70	PHONE CONTACT MONTH 14		
Control	10	VISIT DAY 1		
	20	VISIT MONTH 1		
	30	VISIT MONTH 2		
	50	VISIT MONTH 4		
	60	VISIT MONTH 5		
	80	PHONE CONTACT MONTH 16		

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su

Template 13 Study Population <Exposed Set>

	<Each group> N=XXXX	<Each group> N=XXXX	Total N=XXXX
Number of subjects			
Planned, N	xxx	xxx	xxx
Randomised, N <cohort name>	xxx	xxx	xxx
Completed, n (%)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
<Unknown>	xxx	xxx	xxx
Demographics			
N <cohort name>	xxx	xxx	xxx
Females:Males	xxx:xxx	xxx:xxx	xxx:xxx
Mean Age, <unit> (SD)	xxx.x (xxx.x)	xxx.x (xxx.x)	xxx.x (xxx.x)
Median Age, <unit> (minimum, maximum)	xxx (xxx,xxx)	xxx (xxx,xxx)	xxx (xxx,xxx)
<MOST FREQUENT CATEGORY OF RACE>	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
<SECOND MOST FREQUENT CATEGORY OF RACE>	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
<THIRD MOST FREQUENT CATEGORY OF RACE>	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)

<each group>:
Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = Total number of subjects
SD = Standard deviation

Template 14 Exposure to study vaccines <Exposed Set>

	<Each group> N=XXXX		<Each group> N=XXXX		Total N=XXXX	
Number of subjects receiving	**n**	**%**	**n**	**%**	**n**	**%**
Exactly 1 Dose						
Exactly 2 Doses						
Exactly 3 Doses						
…						
At least 1 Dose						
Total number of doses administered during the study						

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = number of subjects in each group or in total included in the considered cohort
n = number of subjects/doses in the given category
% = percentage of subjects in the given category

Template 15 Compliance in completing *solicited adverse events* information <Exposed Set>

		<each group>			<each group>		
DOSE	***Adverse event* information**	**N**	**n**	**Compliance (%)**	**N**	**n**	**Compliance (%)**
DOSE <each dose number>	***General AES***						
	Local AES						
TOTAL	***General AES***						
	Local AES						

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N=Number of administered doses
n = number of doses with AES returned
General AES = Adverse event screens used for the collection of general solicited AEs
Local AES = Adverse event screens used for the collection of local solicited AEs
Compliance (%) = (n / N) X 100

Template 16 Incidence and nature of <grade 3, related, grade 3 related, > adverse events (<unsolicited and solicited, solicited only>) reported <during the 7-day (Days 1-7), beyond the 7-day (Days 1-7)> post-vaccination period following each dose and overall

		<Each group>					<Each group>				
					95% CI					95% CI	
Dose	***Adverse event***	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 1	***Any adverse event***										
	General adverse events										
	Local adverse events										
Dose 2	***Any adverse event***										
	General adverse events										
	Local adverse events										
Dose 3	***Any adverse event***										
	General adverse events										
	Local adverse events										
Overall/dose	***Any adverse event***										
	General adverse events										
	Local adverse events										
Overall/subject	***Any adverse event***										
	General adverse events										
	Local adverse events										

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects presenting at least one type of ***adverse event***
For overall/dose:
N = number of documented doses
n/% = number/percentage of doses followed by at least one type of ***adverse event***
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Template 17 Incidence of solicited local *adverse events* reported during the 7-day (Days 1-7) post-vaccination period by study vaccine following each dose and overall <Exposed Set>

				Co-Ad					Control				
							95% CI					95% CI	
Dose	***Adverse event***	**Product**	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 1	Pain	HZ/su	All										
			Grade 2 or 3										
			Grade 3										
			Medical advice										
		Prevenar13	All										
			Grade 2 or 3										
			Grade 3										
			Medical advice										
	Redness (mm)	HZ/su	All										
			>50										
			>100										
			Medical advice										
		Prevenar 13	All										
			>50										
			>100										
			Medical advice										
	Swelling (mm)	HZ/su	All										
			>50										
			>100										
			Medical advice										
		Prevenar 13	All										
			>50										
			>100										
			Medical advice										
Dose 2													
Dose 3													
Overall/Dose													
Overall/Subject													

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
For each dose:
N = number of subjects with the corresponding documented dose
n/% = number/percentage of subjects reporting the type of ***adverse event*** at least once following the corresponding dose
For Overall/dose:
N = number of documented dose
n/% = number/percentage of doses followed by at least one type of ***adverse event***
For Overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the type of ***adverse event*** at least once
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit

Template 18 Incidence of solicited general *adverse events* reported during the 7-day (Days 1-7) post-vaccination period following each dose and overall <Exposed Set>

			<each group>				
						95 % CI	
Dose	**Adverse event**	**Type**	**N**	**n**	**%**	**LL**	**UL**
Dose 1	Fatigue	All					
		Grade 3					
		Related					
		Grade 3*Related					
		Medical advice					
	Gastrointestinal symptoms	All					
		Grade 3					
		Related					
		Grade 3*Related					
		Medical advice					
	Headache	All					
		Grade 3					
		Related					
		Grade 3*Related					
		Medical advice					
	Myalgia	All					
		Grade 3					
		Related					
		Grade 3*Related					
		Medical advice					
	Shivering	All					
		Grade 3					
		Related					
		Grade 3*Related					
		Medical advice					
	Fever (Oral) (°C)	All (≥38.0)					
		>38.0					
		>38.5					
		>39.0					
		>39.5					
		>40.0					
		Related					
		>39.0*Related					
		Medical advice					
Dose 2		…					
Dose 3							
Overall/Dose							
Overall/Subject							

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
For each dose:
N = number of subjects with the corresponding documented dose
n/% = number/percentage of subjects reporting the ***adverse event*** at least once following the corresponding dose
For Overall/dose:
N = number of documented dose
n/% = number/percentage of doses followed by at least one type of ***adverse event***
For Overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the type of ***adverse event*** at least once
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit

Template 19 Summary of temperature value by half degree increment taken by different routes reported during the 7-day (Days 1-7) post-vaccination following each dose <Exposed Set>

				Co-Ad					Control				
							95 % CI					95 % CI	
Dose	**Symptom**	**Route**	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 1	Temperature (°C)	Oral	≥35.0										
			>35.5										
			>36.0										
			>36.5										
			>37.0										
			>37.5										
			>38.0										
			>38.5										
			>39.0										
			>39.5										
			>40.0										
		Axillary	≥35.0										
			>35.5										
			>36.0										
			>36.5										
			>37.0										
			>37.5										
			>38.0										
			>38.5										
			>39.0										
			>39.5										
			>40.0										
Dose 2	Temperature (°C)	Oral	≥35.0										
			>35.5										
			>36.0										
			>36.5										
			>37.0										
			>37.5										
			>38.0										
			>38.5										
			>39.0										
			>39.5										
			>40.0										
Dose 3													

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
For each dose:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the ***adverse event*** at least once
95%CI = Exact 95% confidence interval; LL = lower limit, UL = upper limit
=Temperature is defined on oral, axillary, tympanic or rectal

Template 20 *Number and percentage* of subjects reporting the occurrence of <grade 3> <*non-serious*> unsolicited *adverse events* classified by MedDRA Primary System Organ Class and Preferred Term <with causal relationship to vaccination, with medically attended visit>, within the 30-day (Days 1-30) post-vaccination period <,*including numbers of events*><Exposed Set>

		Each group N =				
					95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n***	**n**	**%**	**LL**	**UL**
	At least one adverse event					
Gastrointestinal disorders (10017947)	***At least one PT related to the corresponding SOC***					
	Diarrhoea (10012735)					
	Teething (10043183)					
	Vomiting (10047700)					
General disorders and administration site conditions (10018065)	***At least one PT related to the corresponding SOC***					
	Pyrexia (10037660)					
Immune system disorders (10021428)	Seasonal allergy (10048908)					
Infections and infestations (10021881)	Conjunctivitis (10010741)					
	Otitis media (10033078)					
	Paronychia (10034016)					
	Tonsillitis (10044008)					
	Tonsillitis streptococcal (10044013)					
	Viral upper respiratory tract infection (10047482)					
Injury, poisoning and procedural complications (10022117)	Arthropod bite (10003399)					
	Face injury (10050392)					
	Head injury (10019196)					
Skin and subcutaneous tissue disorders (10040785)	Miliaria (10027627)					

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
At least one ***adverse event*** = at least one ***adverse event*** experienced (regardless of the MedDRA Preferred Term)
N = number of subjects included in the considered cohort in each group
n/% = number/percentage of subjects reporting the ***adverse event*** at least once
n* = number of events reported
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit
Please note the n* will only be presented for the CTRS posting with the time interval as per the secondary endpoint

Template 21 Global Summary of <grade 3> <non-serious>unsolicited signs and *adverse events* reported <with causal relationship with vaccination, with medically attended visit> within the 30-day (Days 1-30) post-vaccination period <Exposed Set>

	Co-Ad	Control	Total
Number of subjects with at least one unsolicited ***adverse event*** reported			
Number of doses followed by at least one unsolicited ***adverse event***			
Number of unsolicited ***adverse event***s classified by MedDRA Preferred Term*			
Number of unsolicited ***adverse events*** reported**			

Co-Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3:HZ/su
* ***Adverse events*** reported by a subject after a given dose and classified by the same Preferred Term are counted once
** ***Adverse events*** reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Template 22 Number and percentage of subjects starting a concomitant medication during the 30- day (Days 1-30) post vaccination period by dose and overall <Exposed Set>

		<each group>				
					95% CI	
Dose	**Type**	**N**	**n**	**%**	**LL**	**UL**
Dose 1	Any					
	Any in anticipation of study vaccine reaction					
	Any chronic use					
Dose 2	Any					
	Any in anticipation of study vaccine reaction					
	Any chronic use					
Dose 3	Any					
	Any in anticipation of study vaccine reaction					
	Any chronic use					
Overall/Dose	Any					
	Any in anticipation of study vaccine reaction					
	Any chronic use					
Overall/Subject	Any					
	Any in anticipation of study vaccine reaction					
	Any chronic use					

<each group>:
Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
For each dose:
N = total number of subjects with the corresponding administered dose
n/% = number/percentage of subjects took the specified type of concomitant medication at least once during the considered period
For Overall/dose:
N = number of administered doses
n/% = number/percentage of doses after which the specified type of concomitant medication was taken at least once during the considered period

For Overall/subject:
N = total number of subjects with at least one administered dose
n/% = number/percentage of subjects who took the specified type of concomitant medication at least once during the considered period

Template 23 Number of days with <local, general> solicited *adverse events* <during the 7 days (Days 1-7), beyond the 7-days (Days 1-7) of> post vaccination period following each dose and overall <- Prevenar 13 vaccine, - HZ/su vaccine> <Exposed Set>

			<Co-Ad group>	<Control group>
Dose	**Adverse event**	**Statistic**	**value**	**value**
<Each Dose>	<Each Adverse event>	n	xxxx	xxxx
		Mean	xx.x	xx.x
		Minimum	xx.x	xx.x
		Q1	xx.x	xx.x
		Median	xx.x	xx.x
		Q3	xx.x	xx.x
		Maximum	xx.x	xx.x
Overall/Dose	<Each Adverse event >	n	xxxx	xxxx
		Mean	xx.x	xx.x
		Minimum	xx.x	xx.x
		Q1	xx.x	xx.x
		Median	xx.x	xx.x
		Q3	xx.x	xx.x
		Maximum	xx.x	xx.x

Co-Ad group = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control group = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = number of doses with ***adverse event***
Q1= 25th percentile
Q3= 75th percentile
Please note the table by vaccine type will only be done for local solicited adverse events.

Template 24 Solicited and unsolicited *adverse events* classified by MedDRA Primary System Organ Class and Preferred Term within the 30-day (Days 1-30) post-vaccination period including number of events - SAE excluded <Exposed Set>

		<each group> N =		
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n***	**n**	**%**
	At least one adverse event			
<each SOC>	<each PT term>			

<each group>:
Co-Ad group = Dose 1: Prevenar+ HZ/su, Dose 2: HZ/su
Control group = Dose 1: Prevenar, Dose 2: HZ/su, Dose 3: HZ/su
At least one adverse event = at least one adverse event experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with the administered dose
n* = number of events reported
n/% = number/percentage of subjects reporting the adverse event at least once

Template 25 Number (%) of subjects with serious adverse events from <first vaccination dose up to 30 days post last vaccination, 30 days post last vaccination up to study end, first vaccination dose up to <database freeze date(DDMMMYYYY)><study end>, including number of events reported <Exposed Set>

			<each group> N =		
Type of Event	**Primary System Organ Class**	**Preferred Term (CODE)**	**n***	**n**	**%**
SAE	At least one ***adverse event***				
	<each SOC>	<each PT term>			
Related SAE	At least one ***adverse event***				
	<each SOC>	<each PT term>			
Fatal SAE	At least one ***adverse event***				
	<each SOC>	<each PT term>			
Related fatal SAE	At least one ***adverse event***				
	<each SOC>	<each PT term>			

<each group>:
Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = number of subjects with the administered dose
n* = number of events reported
n/% = number/percentage of subjects reporting the ***adverse event*** at least once

Template 26 Number (%) of subjects reported solicited local *adverse events* during the 7-day (Days 1-7) post-vaccination period following each dose and across dose <Exposed Set>

				Co-Ad					Control				
							95% CI					95% CI	
Dose	***Adverse event***	**Product**	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 1	Pain	HZ/su	All										
			Grade 2 or 3										
			Grade 3										
			Medical advice										
		Prevenar	All										
			Grade 2 or 3										
			Grade 3										
			Medical advice										
	Redness (mm)	HZ/su	All										
			>50										
			>100										
			Medical advice										
		Prevenar	All										
			>50										
			>100										
			Medical advice										
	Swelling (mm)	HZ/su	All										
			>50										
			>100										
			Medical advice										
		Prevenar	All										
			>50										
			>100										
			Medical advice										
Dose 2													
Dose 3													
Across dose													

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
For each dose:
N = number of subjects with the corresponding documented dose
n/% = number/percentage of subjects reporting the type of ***adverse event*** at least once following the corresponding dose
For Across dose:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the adverse event at least once
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit

Template 27 Number (%) of subjects reported solicited general *adverse events* during the 7-day (Days 1-7) post-vaccination period following each dose and across dose <Exposed Set>

			<each group>				
						95 % CI	
Dose	***Adverse event***	**Type**	**N**	**n**	**%**	**LL**	**UL**
Dose 1	Fatigue	All					
		Grade 3					
		Related					
	Gastrointestinal symptoms	All					
		Grade 3					
		Related					
	Headache	All					
		Grade 3					
		Related					
	Myalgia	All					
		Grade 3					
		Related					
	Shivering	All					
		Grade 3					
		Related					
	Fever (Oral) (°C)	All (≥38.0)					
		>39.0					
		Related					
Dose 2	Fatigue	…					
	Gastrointestinal symptoms						
	Headache						
	Myalgia	…					
	Shivering	…					
	Fever (Oral) (°C)	…					
Across Dose		…					
		…					

<each group>:
Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
For each dose:
N = number of subjects with the corresponding documented dose
n/% = number/percentage of subjects reporting the ***adverse event*** at least once following the corresponding dose
For Across dose:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the adverse event at least once
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit

Template 28 Number and percentage of subjects with <anti-gE antibody concentration, anti-pneumococcal <X> antibody titres> equal to or above <cut-off> and <GMCs, GMT> <PPS for analysis of immunogenicity, Exposed Set>

				<≥cut-off unit, each serotype LLOQ>				<GMC, GMT>				
						95% CI			95% CI			
Antibody	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**	**Min**	**Max**
<Anti-gE antibody, anti-pneumococcal <X> antibody titres>	Co-Ad	PRE										
		PI(M1) or PII(M3)										
	Control	PRE or PI(M2)										
		PI(M1) or PIII(M5)										

<each group>:
Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
GM<C,T> = geometric mean antibody <concentration, titre> calculated on all subjects
N = Number of subjects with available results
95% CI = 95% confidence interval; LL = lower limit, UL = upper limit
n/% = number/percentage of subjects with <concentration, titre> equal to or above specified value
MIN/MAX = Minimum/Maximum
PRE= Pre-vaccination at Day 1
PII(M3) = Post-vaccination dose 2 at Month 3
PI(M1) = Post-vaccination dose 1 at Month 1
PI(M2) = Post-vaccination dose 1 at Month 2
PIII(M5) = Post-vaccination dose 3 at Month 5
Please note to consider PRE and PI(M1) for both group for pneumococcal antibody. For gE antibody, PRE and PII(M3) for Co-Ad and PI(M2) and PIII(M5) for Control group.

Template 29 Vaccine response rates for anti-gE antibody ELISA concentrations in Co-Ad group at one month post dose 2 of HZ/su vaccine – primary objective <PPS for analysis of immunogenicity, Exposed Set>

	Co-Ad				
				95% CI	
Antibody	**N**	**n**	**%**	**LL**	**UL**
Anti-gE antibody	XXXX	XXXX	XX.X	XXX.X	XXX.X

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Total = subjects either seropositive or seronegative at pre-vaccination
Vaccine response defined as:
Vaccine response defined as :
For initially seronegative subjects, antibody concentration at post-vaccination ≥ 4 fold the cut-off for Anti-gE (4x97 mIU/ml)
For initially seropositive subjects, antibody concentration at post-vaccination ≥ 4 fold the pre-vaccination antibody concentration
N = number of subjects with both pre- and post-vaccination results available
n/% = number/percentage of responders
<95>% CI = exact <95>% confidence interval, LL = Lower Limit, UL = Upper Limit

Template 30 Adjusted ratios of GMCs between groups (Control group divided by Co-Ad group) for anti-gE antibody ELISA concentrations at one month post dose 2 of HZ/su vaccine <PPS for analysis of immunogenicity, Exposed Set>

Control				Co-Ad				Adjusted GMC ratio (Control / Co-Ad)		
		95% CI*				95% CI*			95% CI	
N	Adjusted GMC	LL	UL	N	Adjusted GMC	LL	UL	Value	LL	UL

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
Adjusted GMC = geometric mean antibody concentration adjusted for vaccine group, age and baseline concentration
N = Number of subjects with both pre- and post-vaccination results available
95% CI* = 95% confidence interval for the adjusted GMC (Ancova model: adjustment for vaccine group, age and baseline concentration - pooled variance); LL = lower limit, UL = upper limit
95% CI = 95% confidence interval for the adjusted GMC ratio (Ancova model: adjustment for vaccine group, age and baseline concentration - pooled variance); LL = lower limit, UL = upper limit

Template 31 Adjusted ratios of GMTs between groups (Control group divided by Co-Ad group) for anti-pneumococcal <X> antibody titres at one month post Prevenar 13 vaccine <PPS for analysis of immunogenicity, Exposed Set>

	Control				Co-Ad				Adjusted GMT ratio (Control / Co-Ad)		
			95% CI*				95% CI*			95% CI	
	N	Adjusted GMT	LL	UL	N	Adjusted GMT	LL	UL	Value	LL	UL

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
Adjusted GMT = geometric mean antibody titre adjusted for vaccine group, age and baseline concentration
N = Number of subjects with both pre- and post-vaccination results available
95% CI* = 95% confidence interval for the adjusted GMT (Ancova model: adjustment for vaccine group, age and baseline concentration - pooled variance); LL = lower limit, UL = upper limit
95% CI = 95% confidence interval for the adjusted GMT ratio (Ancova model: adjustment for vaccine group, age and baseline concentration - pooled variance); LL = lower limit, UL = upper limit

Template 32 Mean Geometric Increase (MGI) of anti-gE antibody ELISA concentrations from baseline to one month post dose 2 of HZ/su vaccine <PPS for analysis of immunogenicity, Exposed Set>

							MGI			
									95% CI	
Antibody	Group	N	Time point description	GMC	Time point description	GMC	Ratio order	Value	LL	UL
<Antibody>	Co-Ad		PII(M3)		PRE		PII(M3)/PRE			
	Control		PIII(M5)		PI(M2)		PIII(M5)/PI(M2)			

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = Number of subjects with available results at the two considered time points
MGI = Geometric mean of the within -subject ratios of the post-vaccination reciprocal anti-gE concentration to the Day 1 reciprocal anti-gE concentration
GMC = geometric mean antibody concentration
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit

PRE= Pre-vaccination at Day 1
PII(M3) = Post-vaccination dose 2 at Month 3 for Co-Ad group
PI(M2) = Post-vaccination dose 1 at Month 2 for Control group (considered as pre-vaccination for HZ/su in Control group)
PIII(M5) = Post-vaccination dose 3 at Month 5 for Control group (considered as post dose 2 for HZ/su in Control group)

Template 33 Descriptive statistics of fold increase from baseline to one month post dose 2 of HZ/su vaccine for anti-gE antibody ELISA concentration <PPS for analysis of immunogenicity, Exposed Set>

			Each Group N=		
				95% CI	
Parameters		**Parameter**	**Value**	**LL**	**UL**
Anti-gE antibody		n			
		Nmiss			
		Mean			
		SD			
		Min			
		Q1			
		Median			
		Q3			
		Max			

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = number of subjects with available results
Nmiss = number of subjects with missing results
SD = Standard Deviation
Q1, Q3 = First and third quartiles
Min/Max = Minimum/Maximum
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit
Please note – To calculate the fold increase, result at PII(M3) compared to PRE-for Co-Ad and PIII(M5) compared to PI(M2) for Control group has to be considered

Template 34 Distribution of fold increase from baseline to one month post dose 2 of HZ/su vaccine for anti-gE antibody ELISA concentrations <PPS for analysis of immunogenicity, Exposed Set>

			<Each group>					<Each group>				
						95% CI					95% CI	
Antibody	**Timing**	**Fold change**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
<each antibody>	<PII(M3)>	≥2	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x	xx.x
		≥4										
		≥6										
		≥8										
		≥10										
		≥12										
		≥14										
	<PIII(M5)	>= Ratio1	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x	xx.x

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = number of subjects with available results
n/% = number/percentage of subjects with concentration within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PII(M3) = Post-vaccination dose 2 at Month 3 for Co-Ad group
PIII(M5) = Post-vaccination dose 3 at Month 5 for Control group (considered as post dose 2 for HZ/su in Control group)
Please note – To calculate the fold increase, result at PII(M3) compared to PRE-for Co-Ad and PIII(M5) compared to PI(M2) for Control group has to be considered

Template 35 Listing of potential Immune Mediated Diseases (pIMDs) reported as identified by predefined list of preferred terms and/or by investigator assessment up to end of study <Exposed Set>

Group	Patient ID	Country	Age at onset (Y)	Gender	Race	Primary System Organ Class	Preferred term	Dose	Day of onset	Relation	Serious pIMD based on Investigator?	SAE (Y/N)	Outcome	pIMD Source

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su

Template 36 Listing of all SAEs up to end of study <Exposed Set>

Group	Sub. No.	Sex	Country	Race	Age at onset (Year)	Verbatim	Preferred term	Primary System Organ Class	MED type	Dose	Day of onset	Duration	Intensity	Causality	Outcome

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su

Template 37 Listing of suspected HZ cases from first administered dose up to end of study <Exposed Set>

Group	Sub. No.	Previous dose	Day on-set	Duration	Preferred term	AE description	Medical advice	Medically attended visit	Intensity	Causality	Outcome

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su

Template 38 Listing of (S)AEs and solicited adverse events leading to study or treatment discontinuation <up to month 5><up to end of study> <Exposed Set>

Type of discontinuation: <study/treatment

Group	Subject number	Gender	Country	Race	AE Description	SAE (Y/N)	Causality	Outcome	Vaccination and visit
									Vaccination: x at visit x

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su

Template 39 Maximum intensity of solicited <local, general> *adverse event* ongoing beyond the 7-day (Days 1-7) post-vaccination period following each dose and overall <Exposed Set>

				<each group>	<each group>
Dose	***Adverse event***	**Type**	**Time to resolution (days)**	**Value or n**	**Value or n**
<EACH DOSE>	***<Each adverse event>***	All	N	xx	xx
			n	xx	xx
			q1	xx.x	xx.x
			median	xx.x	xx.x
			q3	xx.x	xx.x
		Grade 3	N	xx	xx
			n	xx	xx
			q1	xx.x	xx.x
			median	xx.x	xx.x
			q3	xx.x	xx.x
		Grade 3*Related	N	xx	xx
			n	xx	xx
			q1	xx.x	xx.x
			median	xx.x	xx.x
			q3	xx.x	xx.x
OVERALL/DOSE	<Each adverse event>	<EACH TYPE>	N	xx	xx
			n	xx	xx
			q1	xx.x	xx.x
			median	xx.x	xx.x
			q3	xx.x	xx.x

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
Time to resolution: number of days beyond the end of the follow-up period
N = number of ***adverse events*** that were ongoing after the follow-up period
n = number of ***adverse events*** that were ongoing after the follow-up period with a complete end date
q1 = 25th percentile
q3= 75th percentile

Template 40 *Number and* percentage of doses reporting the occurrence of <grade 3> unsolicited *adverse events* classified by MedDRA Primary System Organ Class and Preferred Term <with causal relationship to vaccination> within the 30-day (Days 1-30) post-vaccination period <Exposed Set>

		Each group N =			
				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**
At least one ***adverse event***					
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)				
	Teething (10043183)				
	Vomiting (10047700)				
General disorders and administration site conditions (10018065)	Pyrexia (10037660)				
Immune system disorders (10021428)	Seasonal allergy (10048908)				
Infections and infestations (10021881)	Conjunctivitis (10010741)				
	Otitis media (10033078)				
	Paronychia (10034016)				
	Tonsillitis (10044008)				
	Tonsillitis streptococcal (10044013)				
	Viral upper respiratory tract infection (10047482)				
Injury, poisoning and procedural complications (10022117)	Arthropod bite (10003399)				
	Face injury (10050392)				
	Head injury (10019196)				
Skin and subcutaneous tissue disorders (10040785)	Miliaria (10027627)				

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
At least one ***adverse event*** = at least one ***adverse event*** experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses followed by the **adverse event**
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Template 41 *Number and* percentage of subjects reporting the occurrence of <serious adverse events, potential Immune Mediated Disease> classified by MedDRA Primary System Organ Class and Preferred Term from <first vaccination up to 30 days post last vaccination, from 30 days post last vaccination dose up to end of study, from first vaccination up to study end> <,including number of events><Exposed Set>

		Co-Ad N =					Control N =				
					95% CI						95% CI
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n***	**n**	**%**	**LL**	**UL**	**n***	**n**	**%**	**LL**	**UL**
At least one ***adverse event***											
Blood and lymphatic system disorders (10005329)	Leukocytosis (10024378)										
Cardiac disorders (10007541)	Acute myocardial infarction (10000891)										
	Atrial fibrillation (10003658)										
	Cardiac failure congestive (10007559)										
	Tachycardia (10043071)										
	Ventricular tachycardia (10047302)										

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
At least one ***adverse event*** = at least one ***adverse event*** experienced (regardless of the MedDRA Preferred Term)
N = number of subjects included in the considered cohort in each group
n/% = number/percentage of subjects reporting the ***adverse event*** at least once
n* = Number of events reported
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit
Please note that n* will be used to present pIMD for CTRS posting.

Template 42 Global Summary of <serious adverse events, potential Immune Mediated Disease> <with causal relationship with vaccination> reported from <first vaccination up to 30 days post last vaccination, from 30 days post last vaccination dose up to end of study, from first vaccination up to study end> <Exposed Set>

	Co-Ad	Control	Total
Number of subjects with at least one <SAE, pIMD> reported			
Number of doses followed by at least one <SAE, pIMD>			
Number of <SAE, pIMD> classified by MedDRA Preferred Term*			
Number of <SAE, pIMD> reported**			

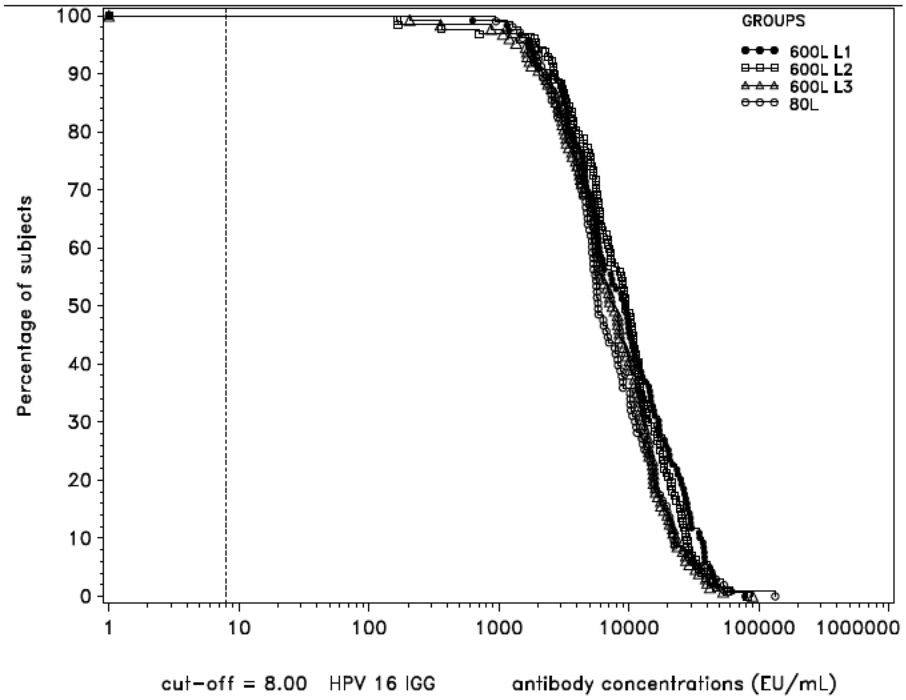
Co-Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
* ***Adverse events*** reported by a subject after a given dose and classified by the same Preferred Term are counted once
** ***Adverse events*** reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Template 43 Vaccine response rates for anti-gE antibody concentrations at one month post dose 2 of HZ/su vaccine <PPS for analysis of immunogenicity, Exposed Set>

		<Each group>				
					95% CI	
Antibody Timing	**Pre-vaccination status**	**N**	**n**	**%**	**LL**	**UL**
<each antibody>	S-	XXXX	XXXX	XX.X	XXX.X	XXX.X
	S+	XXXX	XXXX	XX.X	XXX.X	XXX.X
	Total	XXXX	XXXX	XX.X	XXX.X	XXX.X

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
S- = seronegative subjects (antibody <concentration> < <cut off> <unit>) at pre-vaccination
S+ = seropositive subjects (antibody <concentration>≥ <cut off> <unit>) at pre-vaccination
Total = subjects either seropositive or seronegative at pre-vaccination
Vaccine response defined as:
Vaccine response defined as :
For initially seronegative subjects, antibody concentration at post-vaccination ≥ 4 fold the cut-off for Anti-gE (4x97 mIU/ml)
For initially seropositive subjects, antibody concentration at post-vaccination ≥ 4 fold the pre-vaccination antibody concentration
N = number of subjects with both pre- and post-vaccination results available
n/% = number/percentage of responders
<95>% CI = exact <95>% confidence interval, LL = Lower Limit, UL = Upper Limit
Please note – To calculate the vaccine response, result at PII(M3) compared to PRE-for Co-Ad and PIII(M5) compared to PI(M2) for Control group has to be considered

Template 44 Reverse cumulative distribution curves for <anti-gE antibody concentration, anti-pneumococcal <X> antibody titres> in each group at baseline and <post dose 2 of HZ/su vaccine, post dose of Prevenar 13> <PPS for analysis of immunogenicity, Exposed Set>



Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
Note: This graph is provided as an example. The same graph will be provided in colour for each time point and each assay comparing the values of the groups
Please note to consider PRE and PI(M1) for both group for pneumococcal antibody. For gE antibody, PRE and PII(M3) for Co-Ad and PI(M2) and PIII(M5) for Control group.

Template 45 Number and percentage of subjects <with><experiencing> fatal SAEs classified by MedDRA Primary System Organ Class and Preferred Term <who died><with onset of fatal SAE> <during the period starting> <from first vaccination up to 30 days post last vaccination dose> <after 30 days post last vaccination dose up to study end><from first vaccination until the study end><during the entire study period> <Exposed Set>

		Co-Ad N =				*Control N =*			
				95% CI					*95% CI*
Primary System Organ Class (CODE)	*Preferred Term (CODE)*	*n*	*%*	*LL*	*UL*	*n*	*%*	*LL*	*UL*
At least one adverse event									
Blood and lymphatic system disorders (10005329)	*Leukocytosis (10024378)*								
Cardiac disorders (10007541)	*Acute myocardial infarction (10000891)*								
	Atrial fibrillation (10003658)								
	Cardiac failure congestive (10007559)								
	Tachycardia (10043071)								
	Ventricular tachycardia (10047302)								

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
At least one adverse event = at least one adverse event experienced (regardless of the MedDRA Preferred Term)
N = number of subjects included in the considered cohort in each group
n/% = number/percentage of subjects reporting the adverse event at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Template 46 Summary of subject disposition from enrolled set to randomized set

	Total N=XXX	
	n	*%*
Number of subjects who signed an informed consent		
Withdrawals prior to randomization	***xxx***	***xx.x***
<Withdrawal reason 1>	***xxx***	***xx.x***
<Withdrawal reason 2>	***xxx***	***xx.x***
…	***xxx***	***xx.x***
	xxx	***xx.x***
Number of subjects included in randomized set		

N = Number of subjects
n = number of subjects enrolled by center
% = n / Number of subjects with available results x 100

Template 47 Summary of subject disposition from Randomised Set to Per Protocol Set

				<Group 1> *N=XXX* *n %*	*<Group 2>* *N=XXX* *n %*	*Total* *N=XXX* *n %*
NUMBER OF SUBJECTS INCLUDED IN RANDOMISED SET						
Withdrawals				***xxx xx.x***	***xxx xx.x***	***xxx xx.x***
<Withdrawal reason 1>				***xxx xx.x***	***xxx xx.x***	***xxx xx.x***
<Withdrawal reason 2>				***xxx xx.x***	***xxx xx.x***	***xxx xx.x***
…						
Eliminations				***xxx xx.x***	***xxx xx.x***	***xxx xx.x***
<Elimination reason 1 (code)>				***xxx xx.x***	***xxx xx.x***	***xxx xx.x***
<Elimination reason 2 (code)>				***xxx xx.x***	***xxx xx.x***	***xxx xx.x***
…				***xxx xx.x***	***xxx xx.x***	***xxx xx.x***
NUMBER OF SUBJECTS INCLUDED IN EXPOSED SET						
Elimination 1						
NUMBER OF SUBJECTS INCLUDED IN PER PROTOCOL SET						

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = Number of subjects
n = number of subjects enrolled by center
% = n / Number of subjects with available results x 100

Template 48 Listing of subjects who died during the entire study period and their fatal SAEs <Enrolled Set>

Group	Sub. No.	Sex	Country	Race	Age at Onset (Year)	Verbatim	Preferred term	Primary System Organ Class	MED type	Dose prior to onset of fatal SAE	Days between onset of fatal SAE and previous dose	Dose prior to death	Days between death and previous dose	SAE Duration	SAE Causality
No Group	PPD									0	-	0	-		
										0	-	0	-		
										1	xx	1	xx		
										1	xx	2	xx		
										1	xx	1	xx		
										1	xx	1	xx		

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
No Group= Enrolled not vaccinated
MED = Medical Advice type (HO: hospitalisation, ER: emergency room visit, MD: medical practice visit)

CONFIDENTIAL

GlaxoSmithKline	**Statistical Analysis Plan**
Detailed Title:	A Phase IIIB, randomized, open-label, multicenter clinical trial to assess the immunogenicity and safety of GSK Biologicals' Herpes Zoster vaccine GSK1437173A when co-administered with *Prevenar13* in adults aged 50 years and older.
eTrack study number and Abbreviated Title	204487 (ZOSTER-059 PRI) Statistical Analysis Plan – Final
Scope:	All analyses planned per protocol.
Date of Statistical Analysis Plan	Final: 13-APR-2018
Co-ordinating author:	PPD (Study Statistician), PPD (Project Statistician)
Reviewed by:	PPD (Clinical and Epidemiology Project Lead) PPD (Clinical and Research Development Lead) PPD (Clinical and Epidemiology Scientist) PPD (Lead statistician) PPD (Lead statistical analyst) PPD (Scientific writer) PPD (Regulatory Affair) PPD (SERM Expert Scientist) PPD (Medical Affairs) PPD (Public disclosure representative) PPD (Public disclosure representative) PPD (Lead Scientific writer)
Approved by:	PPD (Clinical and Epidemiology Project Lead) PPD (Clinical and Research Development Lead) PPD (Lead statistician) PPD (Scientific writer) PPD (Lead stat Analyst)

APP 9000058193 Statistical Analysis Plan Template (Effective date: 14 April 2017)

TABLE OF CONTENTS

PAGE

LIST OF TABLES

PAGE

LIST OF FIGURES

PAGE

LIST OF TEMPLATES

PAGE

LIST OF ABBREVIATIONS

AE	Adverse event
ANCOVA	Analysis of Covariance
$AS01_B$:	MPL, QS21, liposome based Adjuvant System (50 μg MPL and 50 μg QS21)
CDR	Clinical Data Reviewer
CI	Confidence Interval
Co-Ad:	Co-administration
CRDL	Clinical Research and Development Lead
CRF	Case Report Form
CSR	Clinical Study Report
CTRS	Clinical Trial Registry Summary
EL.U/ml	ELISA unit per milliliter
Eli Type	Internal GSK database code for type of elimination code
ELISA	Enzyme-linked immunosorbent assay
EoS:	End of Study
ES	Exposed Set (formally called 'Total Vaccinated Cohort')
FAS	Full Analysis Set
GMC	Geometric mean antibody concentration
GMT	Geometric mean antibody titer
GSK	GlaxoSmithKline
IU/ml	International units per milliliter
LL	Lower Limit of the confidence interval
MedDRA	Medical Dictionary for Regulatory Activities
N.A.	Not Applicable
PCD	Primary Completion Date
PD	Protocol Deviation
PPS	Per Protocol Set (formally called 'According to Protocol')
SAE	Serious adverse event
SAP	Statistical Analysis Plan
SBIR	GSK Biological's Internet Randomization System
SD	Standard Deviation
SHS	Study Headline Summary

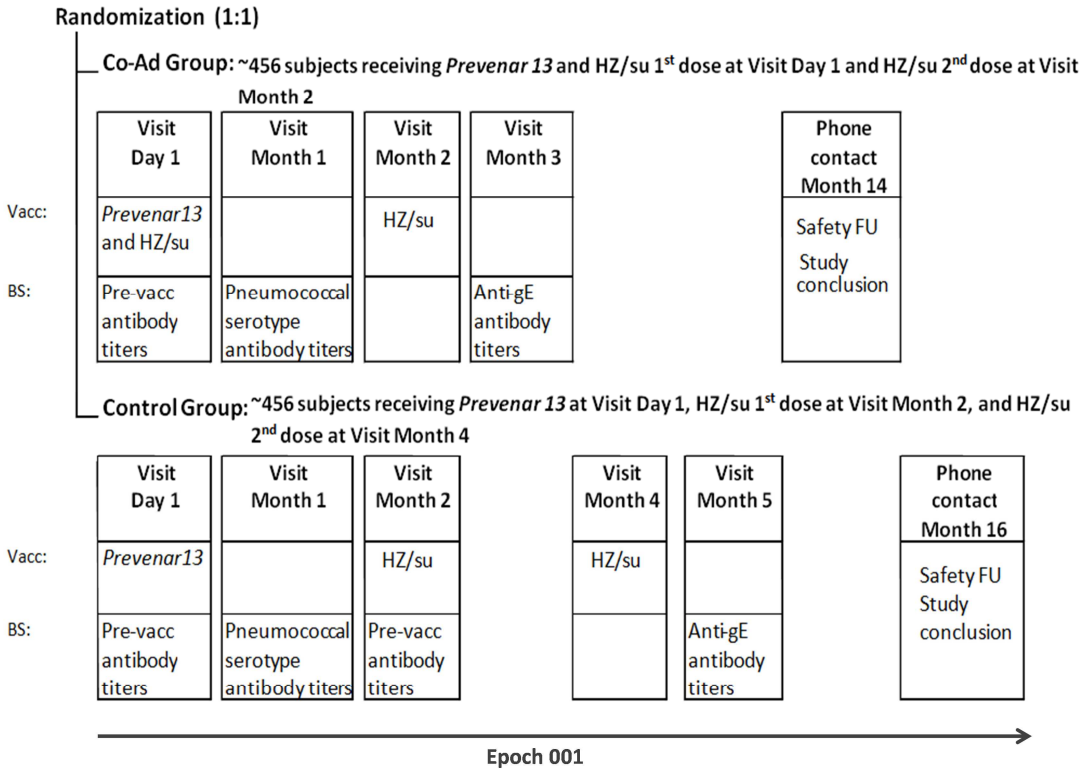
SR	Study Report
SUSAR	Suspected Unexpected Serious Adverse Reactions
TFL	Tables Figures and Listings
TOC	Table of Content
UL	Upper Limit of the confidence interval
VRR	Vaccine response rate
WBR	Web-based Randomization

1. DOCUMENT HISTORY

Date	Description	Protocol Version
13-APR-2018	First Version	Amendment 2: 30-JAN-2018

2. STUDY DESIGN

Figure 1 Overview of Study Design



Vacc: vaccination; BS: blood sample; Pre-Vacc: pre-vaccination; FU: follow-up

Experimental design: Phase IIIB, open-label, randomized, controlled, multi-centric, and multi-country, with two parallel groups.

Duration of the study: The intended duration of the study per subject is approximately 14 months for subjects from the Co-Ad group and approximately 16 months for subjects from the Control group.

- Epoch 001: Primary starting at Visit Day 1 and ending with the phone contact at Month 16.

Primary completion date (PCD): Visit Month 5.

End of Study (EoS): Last testing results released of samples collected at Visit Month 3 (Co-Ad group) or at Visit Month 5 (Control group).

Study groups:

Table 1 Study groups and epochs foreseen in the study

Study groups	Number of subjects	Age	Epochs
			Epoch 001
Co-Ad	456	≥ 50 years	x
Control	456	≥ 50 years	x

Table 2 Study groups and treatment foreseen in the study

Treatment name	Vaccine/Product name	Study Groups	
		Co-Ad	Control
HZ/su	VZV gE	x	x
	AS01B	x	x
Prevenar13	*Prevenar 13*	x	x

Control: active control.

Vaccination schedule(s):

Co-Ad Group:

- at Visit Day 1: first dose of HZ/su and one dose of Prevenar13,
- at Visit Month 2: second dose of HZ/su.

Control Group:

- at Visit Day 1: one dose of Prevenar13,
- at Visit Month 2: first dose of HZ/su,
- at Visit Month 4: second dose of HZ/su.

Treatment allocation: Subjects to be randomized in a 1:1 ratio at Visit Day 1 to either Co-Ad or Control group. Subjects in each group will be stratified by age with the following approximate distribution (not less than 25% in each age strata):

- 171 subjects in the 50-59 YOA stratum,
- 171 subjects in the 60-69 YOA stratum, and
- 114 subjects in the ≥ 70 YOA stratum.

Blinding: open-label.

Table 3 Blinding of study epochs

Study Epochs	Blinding
Epoch 001	open

3. OBJECTIVES

3.1. Co-Primary objectives

To determine the vaccine response rate (VRR) to HZ/su (based on humoral immune response) one month after the second vaccine dose, when the first dose of HZ/su is co-administered with *Prevenar13* (Co-Ad group).

Criterion to be used:

The objective is met if the lower limit (LL) of the 95% CI of the VRR for anti-gE antibody concentrations in the Co-Ad group one month after the second vaccine dose is ≥60%.

If the above objective is met in the Co-Ad group, then the following objective will be evaluated:

To demonstrate non-inferiority of the humoral immune response to two doses of HZ/su at one month after the last vaccine dose, when the first dose of HZ/su is co-administered with *Prevenar13* (Co-Ad group) compared to when two doses of HZ/su are administered subsequent to *Prevenar13* (Control Group).

Criterion for non-inferiority:

One month after the last vaccine dose in each study group, the upper limit (UL) of the 95% confidence interval (CI) for the anti-gE antibodies Geometric Mean Concentration (GMC) ratio between the Control group and the Co-Ad group is <1.5.

If the above non-inferiority objective is met, then the following objective will be evaluated:

To demonstrate non-inferiority of the humoral immune response to *Prevenar13* at one month after the vaccine dose, when *Prevenar13 is* co-administered with the first HZ/su dose (Co-Ad group) compared to when *Prevenar13* is administered separately from HZ/su (Control group), for the 13 serotypes included in *Prevenar13* analyzed sequentially.

Criterion for non-inferiority:

One month after the Prevenar13 vaccine dose in each study group, the UL of the 95% CI for each individual pneumococcal conjugate serotype Geometric Mean Titer (GMT) ratio of the Control group over the Co-Ad group is <2.

For the co-primary objectives, fixed sequence testing which allows for full alpha propagation in pre-ordered hypotheses families will be used (see section 6.3.2.1).

3.2. Secondary objective

To evaluate the safety and reactogenicity following administration of HZ/su and *Prevenar13 vaccines*, up to one month post last vaccination and during the whole follow-up period, in the Control group and the Co-Ad group.

4. ENDPOINTS

4.1. Primary endpoints

HZ/su immunogenicity:

- Vaccine response for anti-gE humoral immunogenicity, as determined by ELISA, in subjects from the Co-Ad group at one month post-dose 2, at Visit Month 3.
- Anti-gE antibody concentrations as determined by ELISA at one month post-dose 2, at Visit Month 3 for the Co-Ad group and Visit Month 5 for the Control group.

Pneumococcal vaccine immunogenicity:

- Anti-pneumococcal antibody titers for the 13 following serotypes as determined by MOPA at one month post-dose at Visit Month 1: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F.

The criteria used to define the VRR is given in Section 11.1.2.

4.2. Secondary endpoints

Occurrence of solicited local and general symptoms:

- Occurrence, duration and intensity of each solicited local symptom within 7 days (Days 1 - 7) after each vaccination,
- Occurrence, duration, intensity and relationship to vaccination of each solicited general symptom within 7 days (Days 1 - 7) after each vaccination.

Occurrence of unsolicited AEs:

- Occurrence, intensity and relationship to vaccination of unsolicited AEs within 30 days (Days 1 - 30) after each vaccination, according to the Medical Dictionary for Regulatory Activities (MedDRA) classification.

Occurrence of SAEs:

- Occurrence and relationship to vaccination of all SAEs from first vaccination at Day 1 up to 30 days post last vaccination.
- Occurrence and relationship to vaccination of all SAEs during the period starting after 30 days post last vaccination up to study end.

Occurrence of pIMDs:

- Occurrence and relationship to vaccination of any pIMDs from first vaccination at Day 1 up to 30 days post last vaccination.
- Occurrence of any pIMDs during the period starting after 30 days post last vaccination up to study end.

5. ANALYSIS SETS

5.1. Definition

5.1.1. Exposed Set (ES)*

The Exposed set (ES) will include all subjects with at least one vaccine administration documented:

- The ES for analysis of solicited symptoms will include all subjects with at least one documented administered vaccine.
- The ES for analysis of unsolicited AEs, SAEs and pIMDs will include all subjects with at least one vaccine administered.
- The ES for analysis of immunogenicity will include vaccinated subjects for whom immunogenicity data are available.

The ES analysis will be performed per treatment actually administered (at Dose 1).

5.1.2. Per-protocol set (PPS)* for analysis of immunogenicity

The Per-protocol set for analysis of immunogenicity will include all evaluable subjects:

- who meet all eligibility criteria,
- who comply with the procedures and intervals allowed for the analysis,
- who do not meet any of the criteria for elimination during the study,
- for whom data concerning immunogenicity endpoint measures are available.

* *Note that in order to align to ICH and cDISC terminology the Total Vaccinated Cohort and the Per- Protocol cohort have been renamed Exposed Set (ES) and Per-Protocol Set (PPS) respectively*.

The intervals allowed for the inclusion in the PPS for analysis of immunogenicity are defined as follow

	Group	Interval	Allowed interval for PPS analysis of immunogenicity
Interval between vaccinations	Co-Ad	HZ/su (Dose 1) – HZ/su (Dose 2)	49-83 Days
	Control	Prevenar13 (Dose 1) – HZ/su (Dose 2)	>= 60 days
	Control	HZ/su (Dose 2) – HZ/su (Dose 3)	49-83 Days
Interval between vaccination and blood sample taken	Co-Ad	Prevenar13 (Dose 1) – Visit Month 1 for BS	28-48 Days
	Co-Ad	HZ/su (Dose 2) – Visit Month 3 for BS	28-48 days
	Control	Prevenar13 (Dose 1) – Visit Month 1 for BS	28-48 Days
	Control	HZ/su (Dose 3)– Visit Month 5 for BS	28-48 days

BS= blood sampling taken

5.2. Criteria for eliminating data from Analysis Sets

Elimination codes are used to identify subjects to be eliminated from analysis. Detail is provided below for each set.

5.2.1. Elimination from Exposed Set (ES)

Code 1030 (Study vaccine not administered at all) and code 900 (invalid informed consent or fraud data) will be used for identifying subjects eliminated from ES

5.2.2. Elimination from Per-protocol analysis Set (PPS)

A subject will be excluded from the PPS analysis under the following conditions

Code	Condition under which the code is used
900	Invalid informed consent or fraud data. Subjects excluded from all stat analysis *Note: Subjects receiving a code 900 should not receive any other elimination codes.*
1030	Study vaccine not administered AT ALL but subject number allocated *Note: Subjects receiving a code 1030 should not receive any other elimination codes*
1040*	Administration of concomitant vaccine(s) forbidden in the protocol *Comment :- Up to 30 days post last dose at Visit Month 3 for co-ad group and up to 30 days post last dose at Visit Month 5 for control group.*
1050	Randomization failure (subject not randomized in the correct group) *Comment: To check for manual randomisation, treatment not compatible with one assigned by SBIR*
1070	- Side, site or route of study vaccine administration wrong or unknown - Administration not according to protocol for reason specified by the investigator, other than side, site and route - Wrong replacement or study vaccine administered (not compatible with the vaccine regimen associated to the treatment number) - Administered study vaccine reported as being the correct one but is not compatible with the vaccine regimen associated to the treatment number.
1080	Vaccine has been administered (effective treatment number) despite a temperature deviation qualified by Status QA GMP NON Use
1090	Expired vaccine administered
1500	Wrong replacement or study vaccine administered (not compatible with the vaccine regimen associated to the treatment number).
2010	Protocol violation (inclusion/exclusion criteria)
2040*	Administration of any medication forbidden by the protocol *Comment: - Up to 30 days post last dose at Visit Month 3 for co-ad group and up to 30 days post last dose at Visit Month 5 for control group*
2050*	Underlying medical condition forbidden by the protocol *Comment: - Up to 30 days post last dose at Visit Month 3 for co-ad group and up to 30 days post last dose at Visit Month 5 for control group*
2060*	Concomitant infection related to the vaccine which may influence immune response *Comment: Up to 30 days post last dose at Visit Month 3 for co-ad group and up to 30 days post last dose at Visit Month 5 for control group*

Code	Condition under which the code is used
2070*	Concomitant infection not related to the vaccine which may influence immune response *Comment: Up to 30 days post last dose at Visit Month 3 for co-ad group and up to 30 days post last dose at Visit Month 5 for control group*
2080	Subjects did not comply with vaccination schedule (dates of vaccination not corresponding to protocol intervals or unknown vaccination dates) Comments: Co-Ad group: DOSE 1 – DOSE 2 Control group: DOSE 1 – DOSE 2 DOSE 2 – DOSE 3
2090	Subjects did not comply with blood sample schedule (dates of BS not corresponding to adapted protocol intervals or unknown BS/vaccination dates) Comments: Co-Ad group: DOSE 1 – MONTH 1 BS DOSE 2 – MONTH 3 BS Control group: DOSE 1 – MONTH 1 BS DOSE 3 – MONTH 5 BS
2100	Serological results not available post-vaccination (including lost samples, blood sample not done, unable to test, absence of parallelism). Please specify the applicable rule: ☒ elimination code if **ALL** are missing Comment: Co-Ad group: Check for availability of anti-gE serological result at Month 3 and for pneumococcal serotype at Month 1 Control group: Check for availability of anti-gE serological result at Month 5 and for pneumococcal serotype at Month 1
2120	Obvious incoherence or abnormality or error in data (incoherence between CRF and results, wrong labelling) Comment: Co-Ad group: Check for above condition on anti-gE serological result at Month 3 and on pneumococcal serotype at Month 1 Control group: Check for above condition on anti-gE serological result at Month 5 and on pneumococcal serotype at Month 1
2500	Incomplete vaccination course. *Comment: The subject should receive one dose of Prevenar 13 vaccine and 2 doses of Hz/su vaccine*

BS = Blood sample

** Attribution of these elimcodes are responsibility of CRDL following review of individual data listings*

5.3. Important protocol deviation not leading to elimination from per-protocol analysis set

For information on important protocol deviation not leading to elimination from the PPS set, refer to the study protocol deviation and management plan (PDMP).

6. STATISTICAL ANALYSES

Note that standard data derivation rule and stat methods are described in annex 1 and will not be repeated below. All analyses will be presented by study phase when there are data for both active and follow up phases.

6.1. Demography

6.1.1. Analysis of demographics/baseline characteristics planned in the protocol

Demographic characteristics (age, sex, race and ethnicity) will be tabulated per treatment group.

The mean age (plus range and standard deviation [SD]) of the enrolled subjects, as a whole, and per treatment group will be calculated. The distribution of subjects enrolled among the study sites will be tabulated as a whole and per treatment group.

The same tabulations might be performed by age strata (50-59, 60-69 and ≥70 YOA) if deemed necessary.

6.1.2. Additional considerations

- Following additional tables will be generated: -
  - The number of subjects enrolled into the study as well as the number of subjects excluded from PPS analyses will be tabulated.
  - Withdrawal status will be summarized by group. The numbers of withdrawn subjects will be tabulated according to the reason for withdrawal
- The following table will be performed for CTRS:
  - Percentage of Enrolled subjects by country will be tabulated by group,
  - Percentage of Enrolled subjects in the following age categories ≤64, 65-84, ≥85 will be tabulated by group.
- For computation of age, following rule need to be considered:-
  - Age will be calculated as the number of years between the date of birth and the date of first vaccination.

- To ensure that the collection of date of birth will not jeopardise the privacy of Personally Identifiable Information (PII), only a partial date of birth (MMYYYY) will be collected.
- Therefore, the 15th of the month will be used to replace the missing date.
- In case the month is missing, the date will be replaced by the June 30th of the year. Analysis of demography will be based on exposed set.

6.2. Exposure

6.2.1. Analysis of exposure planned in the protocol

The number of doses administered will be tabulated.

6.2.2. Additional considerations

None

6.3. Immunogenicity

6.3.1. Analysis of immunogenicity planned in the protocol

The primary analysis will be based on the per-protocol set for analysis of immunogenicity. A second analysis based on the Exposed set will be performed to complement the per-protocol analysis (see section 9 for changes in the planned analysis).

Immunogenicity analyses for confirmatory objectives will be performed by age stratum (50-59, 60-69 and ≥ 70 YOA) on PPS, if the number of subjects enrolled is sufficient in each stratum.

6.3.1.1. Within group assessment

The following parameters will be tabulated by vaccine group at each time point when a blood sample result is available:

- Seropositivity with exact 95% CI for all antigens
- GMC/GMT with 95% CI for all antigens
- VRR with exact 95% CI for anti-gE
- Mean Geometric Increase (MGI) with exact 95% CI for anti-gE
- Descriptive statistics (N, mean, SD, min, Q1, median, Q3, max) of Mean Geometric Increase (MGI) for anti-gE
- Distribution of the fold increase i.e. Percentage of subjects with a more than X-fold (e.g. >2, >4, >6, -fold) increase will be tabulated for anti-gE per group with 95%CI.
- Antibody titre/concentration will be displayed using reverse cumulative curves.

6.3.1.2. Between group assessment

Following between group comparison will be performed: -

- For the second primary objective for anti-gE, at one month post-dose 2 of HZ/su vaccine:
  - The 95% CI of the group GMCs ratio (Control divided by Co-Ad) will be computed using an analysis of covariance (ANCOVA) model on the log10 transformation of the concentrations. The pre-vaccination log-transformed antibody concentrations will be included as continuous covariate and the vaccine group and age strata as fixed effects in the model.
- For third primary objective for each vaccine pneumococcal serotype (according to the pre-specified order in the protocol), one month post-dose of pneumococcal vaccine:
  - The 95% CI of the group MOPA GMT ratios (Control divided by Co-Ad) will be computed using an analysis of covariance (ANCOVA) model on the log10 transformation of the concentrations. The pre-vaccination log-transformed antibody concentrations will be included as continuous covariate and the vaccine group and age strata as fixed effects in the model.

6.3.2. Additional considerations

Following additional points need to be considered for immunogenicity analysis:-

- Immunogenicity descriptive analyses will be performed by age stratum (50-59, 60-69 and ≥ 70 YOA), if the number of subjects enrolled is sufficient in each stratum.
- Two-sided 95% confidence intervals (CIs) for Seropositivity and VRR will be computed by Clopper-Pearson method [Clopper, 1934]. The differences in percentages and the associated two-sided 95% between the groups CIs for the difference will be constructed using the method of Miettinen and Nurminen [Robert, 1998].
- The two-sided 95% CI for the mean of log-transformed titre/concentration will be first obtained assuming that log-transformed values were normally distributed with unknown variance. The 95% CI for the GMTs/GMCs/MGIs will be then obtained by exponential-transformation of the 95% CI for the mean of log-transformed titre/concentration.

6.3.2.1. Statistical considerations for confirmatory objectives

For the multiplicity adjustment, all hypotheses have been ranked into three families and one sub-family according to the following power of test:

Table 4 Power to demonstrate VRR objective and non-inferiority of the immunogenicity of HZ/su and Prevenar13 co-administered compared to Control group

Family 1: HZ/su: VVR*(1-sided test with alpha = 2.5%)				
Endpoint	Threshold	VR assumed	Total β	Power
VRR in Co-Ad group	0.60	95%	0.001%	99.99%
***Family 2: HZ/su*: non-inferiority* (1-sided test with alpha = 2.5%) N=410**				
Endpoint	Standard deviation	δ	Total β	Power
Anti-gE GMC ratio	0.35	1.5	0.001 %	99.99 %
***Family 3: Prevenar13*: Non-inferiority* (1-sided test with alpha = 2.5%) N=410**				
Endpoint (13 vaccine pneumococcal serotypes)	Standard deviation	δ	Total β	Power
3 GMT ratio	0.660	2	0.001%	99.99%
19A GMT ratio	0.644	2	0.001%	99.99%
1 GMT ratio	0.798	2	0.029%	99.97%
18C GMT ratio	0.891	2	0.203%	99.80%
4 GMT ratio	0.906	2	0.260%	99.74%
6A GMT ratio	0.919	2	0.320%	99.68%
5 GMT ratio	0.931	2	0.383%	99.62%
19F GMT ratio	0.971	2	0.664%	99.33%
6B GMT ratio	0.995	2	0.891%	99.11%
7F GMT ratio	1.014	2	1.107%	98.89%
9V GMT ratio	1.021	2	1.194%	98.81%
14 GMT ratio	1.045	2	1.530%	98.47%
23F GMT ratio	1.094	2	2.398%	97.60%
Global β to show non-inferiority			~9%	
Global power				**~91%**

VRR: vaccine response rate; gE: Varicella Zoster Virus glycoprotein E; GMT: geometric mean titer; GMC: geometric mean concentration.
* Pass 12, alpha = 2.5%, for VRR: Exact test, for non-inferiority one-sided equivalence of means.
For gE: non-inferiority limit = 0.176 (=log10(1.5)), power under equal GMC
For each pneumococcal serotype: non-inferiority limit = 0.301 (=log10(2)), variability for each of the 13 vaccine pneumococcal serotype taken from the EMA assessment report for *Prevenar13* and multiplied by 1.1, power under equal GMT.

Fixed sequence testing which allows for full alpha propagation in pre-ordered hypotheses families will be applied in the following manner:

Family 1:

In the Co-Ad group, for anti-gE, at one month post-dose 2 of HZ/su vaccine:

- The VRR and 95% CI will be computed.

The objective is met if the LL of the 95% CI is ≥60%.

Family 2:

For anti-gE, at one month post-dose 2 of HZ/su vaccine:

- The 95% CI of the group GMCs ratio will be computed using an analysis of covariance (ANCOVA) model on the log10 transformation of the concentrations. The pre-vaccination log-transformed antibody concentrations will be included as continuous covariate and the vaccine group and age strata as fixed effects in the model.

In terms of concentrations, the Co-Ad group will be considered non-inferior to the Control group if the UL of the 95% CI for the GMC ratio of the Control group to the Co-Ad group is <1.5.

Family 3:

For each vaccine pneumococcal serotype (according to the pre specified order), one month post-dose of pneumococcal vaccine:

- The 95% CI of the group MOPA GMT ratios will be computed using an analysis of covariance (ANCOVA) model on the log10 transformation of the concentrations. The pre-vaccination log-transformed antibody concentrations will be included as continuous covariate and the vaccine group and age strata as fixed effects in the model.

In terms of MOPA GMTs, the Co-Ad group will be considered non-inferior to the Control group if the UL of the 95% CI for the MOPA GMTs ratio of the Control group to the Co-Ad group is <2 for each of the 13 vaccine serotypes.

In the ANCOVA models Adjusted Least Squares (LS) means and difference of LS means between the groups will be calculated together with the 2-sided 95% CIs and back-transformed to the original units to provide GMCs and GM ratios.

6.4. Analysis of safety

6.4.1. Analysis of safety planned in the protocol

The analysis for safety will be based on the Exposed set. All safety analyses may also be performed by age strata (50-59, 60-69 and ≥70 YOA), if the number of subjects enrolled is sufficient in each stratum

When appropriate, tabulations will be presented overall and by time of occurrence relative to last vaccination (e.g. using windows such as Days 1 to 7, Days 1 to 30 and more than 30 days post-vaccination).

The results for the analysis of safety will be tabulated as follows:

- The number and percentage of subjects with at least one local solicited AE, with at least one general solicited AE, and with any solicited AE during the 7-day follow-up

period with exact 95% CIs after each vaccine dose and overall by vaccination group will be provided;

- The percentage of subjects reporting each individual solicited local and general AE during the solicited 7-day follow-up period will be tabulated with exact 95% CI;
- For all solicited symptoms, the same tabulation will be performed for grade 3 solicited AEs and for solicited general AEs with relationship to vaccination;
- Number of days with each individual solicited local and general AE during the solicited 7-day follow-up period;
- The proportion of subjects with at least one report of unsolicited AE classified by the MedDRA preferred term and reported up to 30 days after each vaccination will be tabulated with exact 95% CI;
- The same tabulation will be performed for grade 3 unsolicited AEs and for unsolicited AEs with a relationship to vaccination. The proportion of AEs resulting in a medically attended visit will also be tabulated;
- Total number/percentages of doses (per dose and overall) followed by AEs will be tabulated;
- Number of subjects with pIMDs will be tabulated;
- SAEs, including fatalities and withdrawal due to AE(s) will be described in detail.

6.4.2. Additional considerations

- Following additional tables will be generated:-
  - The percentage of subjects with at least one local AE (solicited and unsolicited), with at least one general AE (solicited and unsolicited) and with any AE during the 7-day follow-up period will be tabulated with exact 95% confidence interval (CI) after each vaccine dose and overall. The same computations will be done for Grade 3 AEs, for any AEs considered related to vaccination and for any Grade 3 AEs considered related to vaccination.
  - The percentage of subjects with at least one local solicited AE, with at least one general solicited AE and with any AE will also be done for Grade 3 AEs, for any AEs considered related to vaccination and for any Grade 3 AEs considered related to vaccination.
  - Summary of temperature value by half degree increment reported during the 7-day (Days 1-7) post-vaccination following each dose.
  - Summary of temperature value by half degree increment taken by different routes reported during the 7-day (Days 1-7) post-vaccination following each dose
  - For fever, the number and percentage of subjects reporting fever by half degree (°C) cumulative increments during the 7-day follow-up period (Day 1-7) will be tabulated for each group after each vaccine dose and overall. Similar tabulations will be performed for Grade 3 (> 39.0°C) causally related fever.
  - List of suspected HZ cases identified during the study will be presented

- The number and percentage of subjects starting a concomitant medication during the 30-day post-vaccination period by dose and overall will be presented
- The duration of solicited local symptoms (in days), not limited to the 7-day post-vaccination period, following each dose and overall/dose. The same tabulations after Prevenar13 and HZ/su vaccinations.
- The duration of solicited general symptoms (in days), not limited to the 7-day post-vaccination period, following each dose and overall/dose.
- Solicited local symptoms ongoing beyond the 7-day (Days 1-7) post-vaccination period, following each dose and overall/dose. The same tabulations after Prevenar13 and HZ/su vaccinations.
- Solicited general symptoms ongoing beyond the 7-day (Days 1-7) post-vaccination period, following each dose and overall/dose

6.4.2.1. Combined Solicited and Unsolicited Adverse Events

A summary of subjects with all combined solicited (regardless of their duration) and unsolicited adverse events will be provided. Solicited adverse events will be coded by MedDRA as per the following codes

Solicited symptom	Lower level term name	Corresponding Lower level term code
Pain	Injection site pain	10022086
Redness	Redness at injection site	10022098
Swelling	Swelling at injection site	10053425
Fatigue	Fatigue	10016256
Gastrointestinal symptoms	Gastrointestinal disorder	10017944
Headache	Headache	10019211
Myalgia	Myalgia	10028411
Shivering	Shivering	10040558
Temperature	Fever	10016558

For clintrial.gov and EudraCT posting purposes, a summary of combined solicited and unsolicited non-serious adverse events will be produced by System Organ Class and preferred terms and according to occurrence of each event.

7. ANALYSIS INTERPRETATION

All co-primary objectives will be evaluated using a one-sided Type I error of 2.5% (as already justified by fixed sequential testing procedure, no alpha adjustment needed). The trial will be considered conclusive if all co-primary objectives criteria are met.

8. CONDUCT OF ANALYSES

8.1. Sequence of analyses

The analysis will be performed in the following steps:

- Analysis of the co-primary immunogenicity objectives will be performed at the end of the active phase on data as clean as possible. A confirmatory re-analysis will be done at the end of the study using the final database. In addition, analyses of secondary objectives will also be performed at the end of the active phase.
- Analyses on safety data will be performed when all data up to study end (i.e., phone contact at Month 14 for Co-Ad group and phone contact at Month 16 for Control group) will be available and cleaned.

An integrated clinical study report containing all data will be written and made available to the investigators.

Table 5 Analysis and disclosure plan for the planned analysis

Description	Analysis ID	Disclosure Purpose (CTRS=public posting, SR=study report, internal)	Dry run review needed (Y/N)	*Study Headline Summary (SHS)*requiring expedited communication to upper management (Yes/No)	Reference for TFL
End of Active phase	E1_02	CTRS	Y	Y	See in TFL TOC where POSTING=YES
Final analysis	E1_01	CTRS CSR	Y	Y	All tables from Annex 2 of the SAP13 APR2018

8.2. Statistical considerations for interim analyses

Not applicable

9. CHANGES FROM PLANNED ANALYSES

In protocol, it was specified that the second analysis for immunogenicity on Exposed set will be performed only if, in any study group, the percentage of enrolled subjects with serological results excluded from the per-protocol set for analysis of immunogenicity is 5% or more. At Paul Ehrlich Institute, Germany (PEI) request, a ES analysis will be performed to complement the per-protocol analysis.

10. LIST OF FINAL REPORT TABLES, LISTINGS AND FIGURES

The TFL TOC provides the list of tables/listings and figures to be included in the study report.

The following group names will be used in the TFLs, in line with the T-domains:

Group order in tables	Group label in tables	Group definition for footnote
1	Co-Ad	Dose 1 : Prevenar 13 + HZ/su, Dose 2: HZ/su
2	Control	Dose 1 : Prevenar 13, Dose 2: HZ/su, Dose 3:HZ/su

The following sub-group will be used in the TFL, in line with the T-domain

Group Definitions to be used for the sub-group analysis by age (Analysis will be included in the clinical report)

Sub-group order in tables	Sub-group label in tables	Sub-group definition for footnote
1	50-59YOA	Subjects aged 50-59 years
2	60-69YOA	Subjects aged 60-69 years
3	≥70YOA	Subjects aged 70 years and over

YOA = Year of age

Please note that for table presentation in the sub-group analysis, the sequence maintained has to be each treatment group within each age sub-group.

11. ANNEX 1 STANDARD DATA DERIVATION RULE AND STATISTICAL METHODS

11.1. Standard data derivation

11.1.1. Dose number

The study dose number is defined in reference to the number of study visits at which vaccination occurred. More specifically dose 1 refers to all vaccines administered at the first vaccination visit while dose 2 corresponds to all vaccinations administered at the second vaccination visit even if this is the first time a product is administered to the subject.

Associated dose: the associated dose for an event (AE, medication, vaccination) is the most recent study dose given before an event. In case the event takes place on the day a study dose is given, the associated dose will be that of the study dose, even if the event

actually took place before vaccination. For instance, if an adverse event begins on the day of the study vaccination but prior to administration of the vaccine, it will be assigned to this dose. In case a study dose is not administered and an event occurs after the subsequent study dose (e.g. 2nd study dose), the associated dose of the event will be study dose associated to the subsequent study dose (e.g. dose 2).

The number of doses for a product is the number of times the product was administered to a subject.

The incidence per dose is the number of visits with vaccine administered at which an event was reported among all visits with vaccine administered.

11.1.2. Immunogenicity

- For a given subject and given immunogenicity measurement, missing or non-evaluable measurements will not be replaced. Therefore, an analysis will exclude subjects with missing or non-evaluable measurements.

- A seronegative subject is a subject whose antibodies concentration/titer is below the cut-off value (cut-off value is defined by the laboratory prior to the analysis).
- A seropositive subject is a subject whose antibodies concentration/titer is greater than or equal to the assay cut-off value.
- The seropositivity rate is defined as the percentage of seropositive subjects.
- The VRR for anti-gE is defined as the percentage of subjects who have at least:
    - a 4-fold increase in the anti-gE antibodies concentration as compared to the pre-vaccination anti-gE antibodies concentration, for subjects who are seropositive at baseline, or,
    - a 4-fold increase in the anti-gE antibodies concentration as compared to the anti-gE antibodies cut-off value for seropositivity, for subjects who are seronegative at baseline.
- The GMC/GMT calculations are performed by taking the anti-log of the mean of the log concentration transformations. Antibody concentrations below the cut-off of the assay will be given an arbitrary value equal to half the cut-off for the purpose of GMC/GMT calculation.
- All CI computed will be two-sided 95% CI.

11.1.3. Safety

For a given subject and the analysis of solicited symptoms during the 7 day follow-up period after vaccination, missing or non-evaluable measurements will not be replaced. Therefore, the analysis of the solicited symptoms based on the ES will include only vaccinated subjects with documented safety data (i.e., symptom screen completed). More specifically the following rules will be used:

- Subjects who documented the absence of a solicited symptom after one dose will be considered not having that symptom after that dose.
- Subjects who documented the presence of a solicited symptom and fully or partially recorded daily measurement over the solicited period will be included in the summaries at that dose and classified according to their maximum observed daily recording over the solicited period.
- Subjects who documented the presence of a solicited symptom after one dose without having recorded any daily measurement will be assigned to the lowest intensity category at that dose (i.e., 38°C for fever or grade 1 for other symptoms). The subject will only be presented in the subject with symptom experienced and not in specific grade information.
- Doses without symptom sheets documented will be excluded.

For analysis of unsolicited adverse events, such as serious adverse events or adverse events by primary MedDRA term, and for the analysis of concomitant medications, all vaccinated subjects will be considered. Subjects who did not report the event or the concomitant medication will be considered as subjects without the event or the concomitant medication respectively.

Associated dose: The associated dose for an event (e.g., AE, medication, vaccination,…) is the study dose given before an event. In case the event takes place on a day a study dose is given, the associated dose will be that of the study dose even if the event actually took place before. For instance, for a conc. medication started on the day of study dose 2 but before dose 2 administrations, the associated dose will be dose 2

The way the percentage of subjects will be derived will depend on the event analysed (see the following table for details). As a result, the denominator (N) will differ from one table to another.

Event	N used for deriving %	Terminology used in the tables for N
Concomitant medication	All vaccinated subjects	Number of subjects with at least one administered dose
Solicited local symptom	All vaccinated subjects with at least one solicited general symptom documented as either present or absent	For each dose and overall/subject: N= number of subjects with at least one documented dose For overall/dose: N= number of documented doses
Solicited general symptom	All vaccinated subjects with at least one solicited local symptom documented as either present or absent	For each dose and overall/subject: N= number of subjects with at least one documented dose For overall/dose: N= number of documented doses
Unsolicited symptom from day 0 to day X	All vaccinated subjects	Number of subjects with at least one administered dose
SAE	All vaccinated subjects	Number of subjects with at least one administered dose

- The maximum intensity of local injection site redness and swelling will be scored at GSK Biologicals as follows:
  - 0 : <20 mm
  - 1 : ≥ 20 mm to ≤ 50 mm diameter
  - 2 : > 50 mm to ≤ 100 mm diameter
  - 3 : > 100 mm diameter

Fever is defined as temperature ≥ 38.0 C / 100.4 F for oral, axillary, tympanic or rectal route. The preferred route for recording temperature in this study will be oral. For the analysis, temperatures will be coded as follows:

Grade	Temperature (oral, axillary, tympanic or rectal route)
0	< 38°C
1	≥ 38°C - ≤ 38.5°C
2	> 38.5°C - ≤ 39°C
3	> 39°C

- Conversion of temperature to °C -

  The following conversion rule is used for the conversion of temperature to °C
  - Temperature in °Celsius = ((Temperature in °Fahrenheit -32) *5)/9

The result is rounded to 1 decimal digit.

11.2. Statistical Method References

Clopper CJ, Pearson ES. The use of confidence or fiducial limits illustrated in the case of binomial. *Biometrika*. 1934; 26:404-413.

Robert G. Newcombe, interval estimation for the difference between independent proportions: comparison of eleven methods, *Statist Med.* 1998; 17, 873-890.

11.3. Number of decimals displayed:

The following decimal description from the decision rules will be used for the demography, immunogenicity and safety/reactogenicity.

Display Table	Parameters	Number of decimal digits
Demographic characteristics	Mean, median age	1
Demographic characteristics	SD (age)	1
Immunogenicity	Ratio of GMT/C	2
All summaries	% of count, including LL & UL of CI	1
All summaries	% of difference, including LL & UL of CI	2

12. ANNEX 2: STUDY SPECIFIC MOCK TFL

The study specific mocks are annexed to this SAP in a separate document.

The data display, title and footnote are for illustration purpose and will be adapted to the study specificity as indicated in the TFL TOC. Note that there may be few changes between the study specific SAP mock TFL and the final TFLs as editorial/minor changes do not require a SAP amendment

12.1. List of individual data listing

Following individual data listing will be generated

Appendix Table I.A - Elimination codes
Appendix Table I.B – Demography
Appendix Table IBii - Physical examination/vital signs
Appendix Table I.Ci - Dates of birth, Informed consent, Vaccination and blood sampling, Contact
Appendix Table I.Cii - Reason for visit not done
Appendix Table I.D - General medical history - Physical examination
Appendix Table I.Ei – Study Conclusion
Appendix Table I.F – Notes (this appendix is provided for info only and should not be used for the clinical report)
Appendix Table I.G / I.H - Vaccination procedure
Appendix Table I.I - Reason for not administration of vaccine
Appendix Table I.J - Reason for non-eligibility
Appendix Table I.Ki – Previous history of vaccination
Appendix Table I.Kii – Previous history of disease
Appendix Table II.Ai - Solicited local adverse events
Appendix Table II.B - Solicited general adverse events
Appendix Table II.Ci - Unsolicited adverse events within (30) days post-vaccination
Appendix Table II.Cii - Unsolicited adverse events after (30) days post-vaccination
Appendix Table II.Di - Concomitant medications
Appendix Table II.Dii - Concomitant vaccinations
Appendix Table III.A – Immunogenicity

12.2. Template of Tables and Figures

Template 1 Number of subjects by country and center <Exposed Set>

		<Each group> N=XXXX		<Each group> N=XXXX		Total N=XXXX	
Country	**Center**	**n**	**%**	**n**	**%**	**n**	**%**
<each country>	<each center >	XXX	XX.X	XXX	XX.X	XXX	XX.X
	All	XXX	XX.X	XXX	XX.X	XXX	XX.X

<each group>:
Co_Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3:HZ/su
n = number of subjects in a given center or country
N = total number of subjects
% = n/N x 100
Center = GSK Biologicals assigned center number

Template 2 Number of enrolled subjects by country

	<Each group> N=XXXX		<Each group> N=XXXX		Total N=XXXX	
Country	**n**	**%**	**n**	**%**	**n**	**%**
<Each country>	XXX	XX.X	XXX	XX.X	XXX	XX.X

<each group>:
Co_Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3:HZ/su
n = number of subjects in a given center or country
N = total number of subjects
% = n/N x 100

Template 3 Number of enrolled subjects by age category

	<Each group> N=XXXX		<Each group> N=XXXX		Total N=XXXX	
Age category	**n**	**%**	**n**	**%**	**n**	**%**
Adults [18-64 years]	XXX	XX.X	XXX	XX.X	XXX	XX.X
From 65-84 years						
85 years and over						

<each group>:
Co_Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3:HZ/su
N = number of enrolled subjects
n = number of enrolled subjects included in each group or in total for a given age category or for all age categories
% = n/N x 100

Template 4 Number of subjects by country and age category <Exposed Set>

		<Each group> N=XXXX		<Each group> N=XXXX		Total N=XXXX	
Country	**Age category**	**n**	**%**	**n**	**%**	**n**	**%**
<each country>	50-59YOA	XXX	XX.X	XXX	XX.X	XXX	XX.X
	60-69YOA						
	≥70YOA						
	All	XXX	XX.X	XXX	XX.X	XXX	XX.X

Co_Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3:HZ/su
50-59YOA = Subjects aged 50-59 years
60-69YOA = Subjects aged 60-69 years
≥70YOA = Subjects aged 70 years and over
n = number of subjects in a given center or country
N = total number of subjects
% = n/N x 100

Template 5 Number of subjects vaccinated, completed and withdrawn with reason for withdrawal – <end of active phase, study end> <Exposed set>

	<Each group> N=XXXX	<Each group> N=XXXX	Total N=XXXX
	n	**n**	**n**
Number of subjects vaccinated	xxx	xxx	xxx
End of study status			
[EACH CATEGORY]	xxx	xxx	xxx
Reasons for withdrawal:			
[REASONS]	xxx	xxx	xxx

Co_Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3:HZ/su
Vaccinated = number of subjects who were vaccinated in the study
Completed = number of subjects who completed last study visit
Withdrawn = number of subjects who did not come for the last study visit

Template 6 Visit attendance <Exposed set>

		<Each group> N=XXX	
Visit	**Status**	**n**	**%**
INFORMED CONSENT	Completed		
RANDOMIZATION	Completed		
<EACH VISIT>	Attended		
	Not attended yet		
	Permanent discontinuation prior to this visit		
	Not attended		
CONCLUSION	Completed		

Co_Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3:HZ/su
N = Number of subjects in each group or in total
Conclusion = date of last visit or withdrawal

Template 7 List of subjects withdrawn from vaccination with reason for withdrawal

Group	Sub. number	Dose	Decision	Reason	comment
Co-Ad					
Control					

Co_Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3:HZ/su

Template 8 Number of subjects enrolled into the study as well as the number excluded from PPS analyses of immunogenicity with reasons for exclusion

	Total			[each group]	
Title	**n**	**s**	**%**	**n**	**s**
Total enrolled Set					
Subjects eliminated from stat analyses (code 900)					
Study vaccine dose not administrated but subject number allocated (code 1030)					
Exposed Set					
<each reason for elimination from PPS immuno (code)>					
PPS for immunogenicity					

Co_Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3:HZ/su
Note: Subjects may have more than one elimination code assigned
n = number of subjects with the elimination code assigned excluding subjects who have been assigned a lower elimination code number
s = number of subjects with the elimination code assigned
% = percentage of subjects in the considered PPS relative to Total Exposed Set

Template 9 Percentage of subjects with serological results who were eliminated from PPS for immunogenicity

	[each group]	
Number of subjects in Total Exposed Set with serological results available		
Number of subjects with serological results eliminated from PPS for immunogenicity		
Percentage of subjects with serological results eliminated from PPS for immunogenicity		

Co_Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3:HZ/su

Template 10 Deviations from specifications for age and intervals between study visits for Co-Ad group <Exposed Set, PPS for immunogenicity>

		Age	Dose:1-PI (M1)		Dose:1-Dose:2	Dose:2-PII (M3)		Dose:2–PHC (M14)
Group		**Protocol**	**Protocol**	**Protocol**	**Protocol**	**Protocol**	**Adapted**	**Protocol**
		from ≥ 50 years	from 30 to 42 days	from 28 to 48 days	from 49 to 83 days	from 30 to 48 days	from 28 to 48 days	from 335 to 395 days
Co-Ad	N							
	n							
	%							
	range							

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Adapted = interval used for defining PPS for immunogenicity
N = total number of subjects with available results
n/% = number / percentage of subjects with results outside of the interval
range = minimum-maximum for age and intervals
PI (M1) = Blood sample at Month 1, post-vaccination Dose 1
PII (M3) = Blood sample at Month 3, post-vaccination Dose 2
PHC (M14) = Phone Contact MONTH 14
Note that the exact age is unknown since only the month and year of birthdate are recorded. Accordingly the age estimated using the middle of the month may be inexact by one month

Template 11 Deviations from specifications for age and intervals between study visits - for Control group <Exposed Set, PPS for immunogenicity>

		Age	Dose:1-PI(M1)		Dose:1-Dose:2		Dose:2-Dose:3	Dose:3-PIII(M5)		Dose:3-PHONE CONT M16
Group		**Protocol**	**Protocol**	**Adapted**	**Protocol**	**Adapted**	**Protocol**	**Protocol**	**Adapted**	**Protocol**
		from ≥ 50 years	from 30 to 42 days	from 28 to 48 days	from 60 to 83 days	≥ 60 days	from 49 to 83 days	from 30 to 48 days	from 28 to 48 days	from 335 to 395 days
Control	N									
	n									
	%									
	range									

Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
Adapted = interval used for defining the ATP cohorts for immunogenicity
N = total number of subjects with available results
n/% = number / percentage of subjects with results outside of the interval
range = minimum-maximum for age and intervals
PI(M1) = Blood sample at Month 1, post-vaccination Dose 1
PIII(M5) = Blood sample at Month 5, post-vaccination Dose 3
PHC (M16) = Phone Contact Month 16

Template 12 Summary of demographic characteristics <Exposed Set, PPS for immunogenicity>

	<Each group> N=XXXX		<Each group> N=XXXX		Total N=XXXX	
	Value or n	**%**	**Value or n**	**%**	**Value or n**	**%**
Age in Years at <timepoint>						
N with data	xxx		xxx		xxx	
Mean	xxx.x		xxx.x		xxx.x	
SD	xxx.x		xxx.x		xxx.x	
Median	xxx.x		xxx.x		xxx.x	
Minimum	xxx		xxx		xxx	
Maximum	xxx		xxx		xxx	
Gender						
<EACH GENDER>	xxx	xx.x	xxx	xx.x	xxx	xx.x
…	xxx	xx.x	xxx	xx.x	xxx	xx.x
Ethnicity						
<EACH ETHNICITY>	xxx	xx.x	xxx	xx.x	xxx	xx.x
…	xxx	xx.x	xxx	xx.x	xxx	xx.x
Geographic Ancestry						
<EACH GEOGRAPHIC ANCESTRY>	xxx	xx.x	xxx	xx.x	xxx	xx.x
…	xxx	xx.x	xxx	xx.x	xxx	xx.x
Age category						
<EACH AGE CATEGORY>	xxx	xx.x	xxx	xx.x	xxx	xx.x
Country						
<EACH COUNTRY>	xxx	xx.x	xxx	xx.x	xxx	xx.x
…	xxx	xx.x	xxx	xx.x	xxx	xx.x

<each group>:
Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = total number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
N with data = number of subjects with documentation of the corresponding data
SD = standard deviation

Template 13 Minimum and maximum activity dates <Exposed Set>

Group	Activity number	Activity Description	Minimum date	Maximum date
Co-Ad	10	VISIT DAY 1		
	20	VISIT MONTH 1		
	30	VISIT MONTH 2		
	40	VISIT MONTH 3		
	70	PHONE CONTACT MONTH 14		
Control	10	VISIT DAY 1		
	20	VISIT MONTH 1		
	30	VISIT MONTH 2		
	50	VISIT MONTH 4		
	60	VISIT MONTH 5		
	80	PHONE CONTACT MONTH 16		

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su

Template 14 Study Population <Exposed Set>

	<Each group> N=XXXX	<Each group> N=XXXX	Total N=XXXX
Number of subjects			
Planned, N	xxx	xxx	xxx
Randomised, N <cohort name>	xxx	xxx	xxx
Completed, n (%)	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
<Unknown>	xxx	xxx	xxx
Demographics			
N <cohort name>	xxx	xxx	xxx
Females:Males	xxx:xxx	xxx:xxx	xxx:xxx
Mean Age, <unit> (SD)	xxx.x (xxx.x)	xxx.x (xxx.x)	xxx.x (xxx.x)
Median Age, <unit> (minimum, maximum)	xxx (xxx,xxx)	xxx (xxx,xxx)	xxx (xxx,xxx)
<MOST FREQUENT CATEGORY OF RACE>	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
<SECOND MOST FREQUENT CATEGORY OF RACE>	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)
<THIRD MOST FREQUENT CATEGORY OF RACE>	xxx (xx.x)	xxx (xx.x)	xxx (xx.x)

<each group>:
Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = Total number of subjects
SD = Standard deviation

Template 15 Exposure to study vaccines <Exposed Set>

	<Each group> N=XXXX		<Each group> N=XXXX		Total N=XXXX	
Number of subjects receiving	**n**	**%**	**n**	**%**	**n**	**%**
Exactly 1 Dose						
Exactly 2 Doses						
Exactly 3 Doses						
...						
At least 1 Dose						
Total number of doses administered during the study						

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = number of subjects in each group or in total included in the considered cohort
n = number of subjects/doses in the given category
% = percentage of subjects in the given category

Template 16 Compliance in completing solicited symptoms information <Exposed Set>

		<each group>			<each group>		
DOSE	**Symptom information**	**N**	**n**	**Compliance (%)**	**N**	**n**	**Compliance (%)**
DOSE <each dose number>	General SS						
	Local SS						
TOTAL	General SS						
	Local SS						

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N=Number of administered doses
n = number of doses with SS returned
General SS = Symptom screens used for the collection of general solicited AEs
Local SS = Symptom screens used for the collection of local solicited AEs
Compliance (%) = (n / N) X 100

Template 17 Incidence and nature of <grade 3, related, grade 3 related, > symptoms (<unsolicited and solicited, solicited only>) reported <during the 7-day (Days 1-7), beyond the 7-day (Days 1-7)> post-vaccination period following each dose and overall

		<Each group>					<Each group>				
					95% CI					95% CI	
Dose	**Symptoms**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 1	Any symptom										
	General symptoms										
	Local symptoms										
Dose 2	Any symptom										
	General symptoms										
	Local symptoms										
Dose 3	Any symptom										
	General symptoms										
	Local symptoms										
Overall/dose	Any symptom										
	General symptoms										
	Local symptoms										
Overall/subject	Any symptom										
	General symptoms										
	Local symptoms										

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
For each dose and overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects presenting at least one type of symptom for overall/dose:
N = number of documented doses
n/% = number/percentage of doses followed by at least one type of symptom
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Template 18 Incidence of solicited local symptoms reported during the 7-day (Days 1-7) post-vaccination period by study vaccine following each dose and overall <Exposed Set>

				Co-Ad					Control				
							95% CI					95% CI	
Dose	**Symptom**	**Product**	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 1	Pain	HZ/su	All										
			Grade 2 or 3										
			Grade 3										
			Medical advice										
		Prevenar13	All										
			Grade 2 or 3										
			Grade 3										
			Medical advice										
	Redness (mm)	HZ/su	All										
			>50										
			>100										
			Medical advice										
		Prevenar 13	All										
			>50										
			>100										
			Medical advice										
	Swelling (mm)	HZ/su	All										
			>50										
			>100										
			Medical advice										
		Prevenar 13	All										
			>50										
			>100										
			Medical advice										
Dose 2													
Dose 3													
Overall/Dose													
Overall/Subject													

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
For each dose:
N = number of subjects with the corresponding documented dose
n/% = number/percentage of subjects reporting the type of symptom at least once following the corresponding dose
For Overall/dose:
N = number of documented dose
n/% = number/percentage of doses followed by at least one type of symptom
For Overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the type of symptom at least once
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit

Template 19 Incidence of solicited general symptoms reported during the 7-day (Days 1-7) post-vaccination period following each dose and overall <Exposed Set>

			<each group>				
						95 % CI	
Dose	**Symptom**	**Type**	**N**	**n**	**%**	**LL**	**UL**
Dose 1	Fatigue	All					
		Grade 3					
		Related					
		Grade 3*Related					
		Medical advice					
	Gastrointestinal symptoms	All					
		Grade 3					
		Related					
		Grade 3*Related					
		Medical advice					
	Haeadache	All					
		Grade 3					
		Related					
		Grade 3*Related					
		Medical advice					
	Myalgia	All					
		Grade 3					
		Related					
		Grade 3*Related					
		Medical advice					
	Shivering	All					
		Grade 3					
		Related					
		Grade 3*Related					
		Medical advice					
	Fever (Oral) (°C)	All (≥38.0)					
		>38.0					
		>38.5					
		>39.0					
		>39.5					
		>40.0					
		Related					
		>39.0*Related					
		Medical advice					
Dose 2		…					
Dose 3							
Overall/Dose							
Overall/Subject							

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
For each dose:
N = number of subjects with the corresponding documented dose
n/% = number/percentage of subjects reporting the symptom at least once following the corresponding dose
For Overall/dose:
N = number of documented dose
n/% = number/percentage of doses followed by at least one type of symptom
For Overall/subject:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the type of symptom at least once

95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit

Template 20 Summary of temperature value by half degree increment reported during the 7-day (Days 1-7) post-vaccination following each dose <Exposed Set>

			Co-Ad					Control				
						95 % CI					95 % CI	
Dose	**Symptom**	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 1	Temperature/(*) (°C)	All										
		≥35.0										
		>35.5										
		>36.0										
		>36.5										
		>37.0										
		>37.5										
		>38.0										
		>38.5										
		>39.0										
		>39.5										
		>40.0										
Dose 2	Temperature/(*) (°C)	All										
		≥35.0										
		>35.5										
		>36.0										
		>36.5										
		>37.0										
		>37.5										
		>38.0										
		>38.5										
		>39.0										
		>39.5										
		>40.0										
Dose 3												

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
For each dose:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the symptom at least once
95%CI = Exact 95% confidence interval; LL = lower limit, UL = upper limit
*=Temperature is defined on oral, axillary or tympanic

Template 21 Percentage of subjects reporting the occurrence of <grade 3> unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term <with causal relationship to vaccination, with medically attended visit>, within the 30-day (Days 1-30) post-vaccination period <Exposed Set>

		Each group N =				
					95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n***	**n**	**%**	**LL**	**UL**
At least one symptom						
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)					
	Teething (10043183)					
	Vomiting (10047700)					
General disorders and administration site conditions (10018065)	Pyrexia (10037660)					
Immune system disorders (10021428)	Seasonal allergy (10048908)					
Infections and infestations (10021881)	Conjunctivitis (10010741)					
	Otitis media (10033078)					
	Paronychia (10034016)					
	Tonsillitis (10044008)					
	Tonsillitis streptococcal (10044013)					
	Viral upper respiratory tract infection (10047482)					
Injury, poisoning and procedural complications (10022117)	Arthropod bite (10003399)					
	Face injury (10050392)					
	Head injury (10019196)					
Skin and subcutaneous tissue disorders (10040785)	Miliaria (10027627)					

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects included in the considered cohort in each group
n/% = number/percentage of subjects reporting the symptom at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit
Please note the n* will only be presented for the CTRS posting with the time interval as per the secondary endpoint

Template 22 Global Summary of <grade 3> unsolicited signs and symptoms reported <with causal relationship with vaccination, with medically attended visit> within the 30-day (Days 1-30) post-vaccination period <Exposed Set>

	Co-Ad	Control	Total
Number of subjects with at least one unsolicited symptom reported			
Number of doses followed by at least one unsolicited symptom			
Number of unsolicited symptoms classified by MedDRA Preferred Term*			
Number of unsolicited symptoms reported**			

Co-Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3:HZ/su
* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Template 23 Number and percentage of subjects starting a concomitant medication during the 30- day (Days 1-30) post vaccination period by dose and overall <Exposed Set>

		<each group>				
					95% CI	
Dose	**Type**	**N**	**n**	**%**	**LL**	**UL**
Dose 1	Any					
	Any in anticipation of study vaccine reaction					
	Any chronic use					
Dose 2	Any					
	Any in anticipation of study vaccine reaction					
	Any chronic use					
Dose 3	Any					
	Any in anticipation of study vaccine reaction					
	Any chronic use					
Overall/Dose	Any					
	Any in anticipation of study vaccine reaction					
	Any chronic use					
Overall/Subject	Any					
	Any in anticipation of study vaccine reaction					
	Any chronic use					

<each group>:
Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
For each dose:
N = total number of subjects with the corresponding administered dose
n/% = number/percentage of subjects took the specified type of concomitant medication at least once during the considered period
For Overall/dose:
N = number of administered doses
n/% = number/percentage of doses after which the specified type of concomitant medication was taken at least once during the considered period
For Overall/subject:
N = total number of subjects with at least one administered dose
n/% = number/percentage of subjects who took the specified type of concomitant medication at least once during the considered period

Template 24 Number of days with <local, general> solicited symptoms <during the 7 days (Days 1-7), beyond the 7-days (Days 1-7) of> post vaccination period following each dose and overall <- Prevenar 13 vaccine, - HZ/su vaccine> <Exposed Set>

			<Co-Ad group>	<Control group>
Dose	**Symptom**	**Statistic**	**value**	**value**
<Each Dose>	<Each Symptoms>	n	xxxx	xxxx
		Mean	xx.x	xx.x
		Minimum	xx.x	xx.x
		Q1	xx.x	xx.x
		Median	xx.x	xx.x
		Q3	xx.x	xx.x
		Maximum	xx.x	xx.x
Overall/Dose	<Each Symptoms>	n	xxxx	xxxx
		Mean	xx.x	xx.x
		Minimum	xx.x	xx.x
		Q1	xx.x	xx.x
		Median	xx.x	xx.x
		Q3	xx.x	xx.x
		Maximum	xx.x	xx.x

Co-Ad group = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control group = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = number of doses with symptom
Q1= 25th percentile
Q3= 75th percentile

Please note the table by vaccine will only be done for local symptom and not for general symptom

Template 25 Solicited and unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term within the 30-day (Days 1-30) post-vaccination period including number of events - SAE excluded <Exposed Set>

		<each group> N =		
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n***	**n**	**%**
At least one symptom				
<each SOC>	<each PT term>			

<each group>:
Co-Ad group = Dose 1: Prevenar+ HZ/su, Dose 2: HZ/su
Control group = Dose 1: Prevenar, Dose 2: HZ/su, Dose 3: HZ/su
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with the administered dose
n* = number of events reported
n/% = number/percentage of subjects reporting the symptom at least once

Template 26 Number (%) of subjects with <serious adverse events from <first vaccination dose up to 30 days post last vaccination, 30 days post last vaccination up to study end, first vaccination dose up to study end>, including number of events reported <Exposed Set>

			<each group> N =		
Type of Event	**Primary System Organ Class**	**Preferred Term (CODE)**	**n***	**n**	**%**
SAE	At least one symptom				
	<each SOC>	<each PT term>			
Related SAE	At least one symptom				
	<each SOC>	<each PT term>			
Fatal SAE	At least one symptom				
	<each SOC>	<each PT term>			
Related fatal SAE	At least one symptom				
	<each SOC>	<each PT term>			

<each group>:
Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = number of subjects with the administered dose
n* = number of events reported
n/% = number/percentage of subjects reporting the symptom at least once

Template 27 Number (%) of subjects reported solicited local symptoms during the 7-day (Days 1-7) post-vaccination period following each dose and across dose <Exposed Set>

				Co-Ad					Control				
							95% CI					95% CI	
Dose	**Symptom**	**Product**	**Type**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Dose 1	Pain	HZ/su	All										
			Grade 2 or 3										
			Grade 3										
			Medical advice										
		Prevenar	All										
			Grade 2 or 3										
			Grade 3										
			Medical advice										
	Redness (mm)	HZ/su	All										
			>50										
			>100										
			Medical advice										
		Prevenar	All										
			>50										
			>100										
			Medical advice										
	Swelling (mm)	HZ/su	All										
			>50										
			>100										
			Medical advice										
		Prevenar	All										
			>50										
			>100										
			Medical advice										
Dose 2													
Dose 3													
Overall/Dose													
Overall/Subject													

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
For each dose:
N = number of subjects with the corresponding documented dose
n/% = number/percentage of subjects reporting the type of symptom at least once following the corresponding dose
For Across dose:
N = number of documented doses
n/% = number/percentage of doses followed by at least one type of symptom
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit

Template 28 Number (%) of subjects reported solicited general symptoms during the 7-day (Days 1-7) post-vaccination period following each dose and across dose <Exposed Set>

			<each group>				
						95 % CI	
Dose	**Symptom**	**Type**	**N**	**n**	**%**	**LL**	**UL**
Dose 1	Fatigue	All					
		Grade 3					
		Related					
	Gastrointestinal symptoms	All					
		Grade 3					
		Related					
	Headache	All					
		Grade 3					
		Related					
	Myalgia	All					
		Grade 3					
		Related					
	Shivering	All					
		Grade 3					
		Related					
	Fever (Oral) (°C)	All (≥38.0)					
		>39.0					
		Related					
Dose 2	Fatigue	…					
	Gastrointestinal symptoms						
	Headache						
	Myalgia	…					
	Shivering	…					
	Fever (Oral) (°C)	…					
Across Dose		…					
		…					

<each group>:
Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
For each dose:
N = number of subjects with the corresponding documented dose
n/% = number/percentage of subjects reporting the symptom at least once following the corresponding dose
For Across dose:
N = number of documented doses
n/% = number/percentage of doses followed by at least one type of symptom
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit

Template 29 Number and percentage of subjects with <anti-gE antibody concentration, anti-pneumococcal <X> antibody titres> equal to or above <cut-off> and <GMCs, GMT> <PPS for analysis of immunogenicity, Exposed Set>

				≥cut-off unit				<GMC, GMT>				
						95% CI			95% CI			
Antibody	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**	**Min**	**Max**
<Anti-gE antibody, anti-pneumococcal <X> antibody titres>	Co-Ad	PRE										
		PI(M1) or PII(M3)										
	Control	PRE or PI(M2)										
		PI(M1) or PIII(M5)										

<each group>:
Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
GM<C,T> = geometric mean antibody <concentration, titre> calculated on all subjects
N = Number of subjects with available results
95% CI = 95% confidence interval; LL = lower limit, UL = upper limit
n/% = number/percentage of subjects with <concentration, titre> equal to or above specified value
MIN/MAX = Minimum/Maximum
PRE= Pre-vaccination at Day 1
PII(M3) = Post-vaccination dose 2 at Month 3
PI(M1) = Post-vaccination dose 1 at Month 1
PI(M2) = Post-vaccination dose 1 at Month 2
PIII(M5) = Post-vaccination dose 3 at Month 5
Please note to consider PRE and PI(M1) for both group for pneumococcal antibody. For gE antibody, PRE and PII(M3) for Co-Ad and PI(M2) and PIII(M5) for Control group.

Template 30 Vaccine response rates for anti-gE antibody ELISA concentrations in Co-Ad group at one month post dose 2 of HZ/su vaccine – primary objective <PPS for analysis of immunogenicity, Exposed Set>

	Co-Ad				
				95% CI	
Antibody	**N**	**n**	**%**	**LL**	**UL**
Anti-gE antibody	XXXX	XXXX	XX.X	XXX.X	XXX.X

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Total = subjects either seropositive or seronegative at pre-vaccination
Vaccine response defined as:
Vaccine response defined as :
For initially seronegative subjects, antibody concentration at post-vaccination ≥ 4 fold the cut-off for Anti-gE (4x97 mIU/ml)
For initially seropositive subjects, antibody concentration at post-vaccination ≥ 4 fold the pre-vaccination antibody concentration
N = number of subjects with both pre- and post-vaccination results available
n/% = number/percentage of responders
<95>% CI = exact <95>% confidence interval, LL = Lower Limit, UL = Upper Limit

Template 31 Adjusted ratios of GMCs between groups (Control group divided by Co-Ad group) for anti-gE antibody ELISA concentrations at one month post dose 2 of HZ/su vaccine <PPS for analysis of immunogenicity, Exposed Set>

Control				Co-Ad				Adjusted GMC ratio (Control / Co-Ad)		
		95% CI*				95% CI*			95% CI	
N	**Adjusted GMC**	**LL**	**UL**	**N**	**Adjusted GMC**	**LL**	**UL**	**Value**	**LL**	**UL**

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
Adjusted GMC = geometric mean antibody concentration adjusted for vaccine group, age and baseline concentration
N = Number of subjects with both pre- and post-vaccination results available
95% CI* = 95% confidence interval for the adjusted GMC (Ancova model: adjustment for vaccine group, age and baseline concentration - pooled variance); LL = lower limit, UL = upper limit
95% CI = 95% confidence interval for the adjusted GMC ratio (Ancova model: adjustment for vaccine group, age and baseline concentration - pooled variance); LL = lower limit, UL = upper limit

Template 32 Adjusted ratios of GMTs between groups (Control group divided by Co-Ad group) for anti-pneumococcal <X> antibody titres at one month post Prevenar 13 vaccine <PPS for analysis of immunogenicity, Exposed Set>

	Control				Co-Ad				Adjusted GMT ratio (Control / Co-Ad)		
			95% CI*				95% CI*			95% CI	
	N	Adjusted GMT	LL	UL	N	Adjusted GMT	LL	UL	Value	LL	UL

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
Adjusted GMT = geometric mean antibody titre adjusted for vaccine group, age and baseline concentration
N = Number of subjects with both pre- and post-vaccination results available
95% CI* = 95% confidence interval for the adjusted GMT (Ancova model: adjustment for vaccine group, age and baseline concentration - pooled variance); LL = lower limit, UL = upper limit
95% CI = 95% confidence interval for the adjusted GMT ratio (Ancova model: adjustment for vaccine group, age and baseline concentration - pooled variance); LL = lower limit, UL = upper limit

Template 33 Mean Geometric Increase (MGI) of anti-gE antibody ELISA concentrations from baseline to one month post dose 2 of HZ/su vaccine <PPS for analysis of immunogenicity, Exposed Set>

							MGI			
									95% CI	
Antibody	Group	N	Time point description	GMC	Time point description	GMC	Ratio order	Value	LL	UL
<Antibody>	Co-Ad		PII(M3)		PRE		PII(M3)/PRE			
	Control		PIII(M5)		PI(M2)		PIII(M5)/PI(M2)			

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = Number of subjects with available results at the two considered time points
MGI = Geometric mean of the within -subject ratios of the post-vaccination reciprocal anti-gE concentration to the Day 1 reciprocal anti-gE concentration
GMC = geometric mean antibody concentration
95% CI = 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE= Pre-vaccination at Day 1
PII(M3) = Post-vaccination dose 2 at Month 3 for Co-Ad group
PI(M2) = Post-vaccination dose 1 at Month 2 for Control group (considered as pre for HZ/su in Control group)
PIII(M5) = Post-vaccination dose 3 at Month 5 for Control group (considered as post dose 2 for HZ/su in Control group)

Template 34 Descriptive statistics of fold increase from baseline to one month post dose 2 of HZ/su vaccine for anti-gE antibody ELISA concentration <PPS for analysis of immunogenicity, Exposed Set>

		Each Group N=		
			95% CI	
Parameters	**Parameter**	**Value**	**LL**	**UL**
Anti-gE antibody	n			
	nmiss			
	Mean			
	SD			
	Min			
	Q1			
	Median			
	Q3			
	Max			

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = number of subjects with available results
Nmiss = number of subjects with missing results
SD = Standard Deviation
Q1, Q3 = First and third quartiles
Min/Max = Minimum/Maximum
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit
Please note – To calculate the fold increase, result at PII(M3) compared to PRE-for Co-Ad and PIII(M5) compared to PI(M2) for Control group has to be considered

Template 35 Distribution of fold increase from baseline to one month post dose 2 of HZ/su vaccine for anti-gE antibody ELISA concentrations <PPS for analysis of immunogenicity, Exposed Set>

			<Each group>					<Each group>				
						95% CI						95% CI
Antibody	**Timing**	**Fold change**	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
<each antibody>	<PII(M3)>	≥2	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x	xx.x
		≥4										
		≥6										
		≥8										
		≥10										
		≥12										
		≥14										
	<PIII(M5)	>= Ratio1	xx	xx	xx.x	xx.x	xx.x	xx	xx	xx.x	xx.x	xx.x

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
N = number of subjects with available results
n/% = number/percentage of subjects with concentration within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
PII(M3) = Post-vaccination dose 2 at Month 3 for Co-Ad group
PIII(M5) = Post-vaccination dose 3 at Month 5 for Control group (considered as post dose 2 for HZ/su in Control group)
Please note – To calculate the fold increase, result at PII(M3) compared to PRE-for Co-Ad and PIII(M5) compared to PI(M2) for Control group has to be considered

Template 36 Listing of potential Immune Mediated Diseases (pIMDs) reported as identified by predefined list of preferred terms and/or by investigator assessment up to end of study <Exposed Set>

Group	Patient ID	Country	Age at onset (Y)	Gender	Race	Primary System Organ Class	Preferred term	Dose	Day of onset	Relation	Serious pIMD based on Investigator?	SAE (Y/N)	Outcome	pIMD Source

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su

Template 37 Listing of all SAEs up to end of study <Exposed Set>

Group	Sub. No.	Sex	Country	Race	Age at onset (Year)	Verbatim	Preferred term	Primary System Organ Class	MED type	Dose	Day of onset	Duration	Intensity	Causality	Outcome

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su

Template 38 Listing of suspected HZ cases from first administered dose up to end of study <Exposed Set>

Group	Sub. No.	Previous dose	Day on-set	Duration	Preferred term	AE description	Medical advice	Medically attended visit	Intensity	Causality	Outcome

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su

Template 39 Listing of dropouts due to AEs, SAEs and solicited symptoms up to end of study <Exposed Set>

Group	Study-Subject No.	Country	Gender	Race	AE Description	SAE	Causality	Outcome	Type of discontinuation

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su

Template 40 Maximum intensity of solicited <local, general> symptoms ongoing beyond the 7-day (Days 1-7) post-vaccination period following each dose and overall <Exposed Set>

				<each group>	<each group>
Dose	Symptom	Type	Time to resolution (days)	Value or n	Value or n
<EACH DOSE>	<Each symptom>	All	N	xx	xx
			n	xx	xx
			q1	xx.x	xx.x
			median	xx.x	xx.x
			q3	xx.x	xx.x
		Grade 3	N	xx	xx
			n	xx	xx
			q1	xx.x	xx.x
			median	xx.x	xx.x
			q3	xx.x	xx.x
		Grade 3*Related	N	xx	xx
			n	xx	xx
			q1	xx.x	xx.x
			median	xx.x	xx.x
			q3	xx.x	xx.x
OVERALL/DOSE	<Each symptom>	<EACH TYPE>	N	xx	xx
			n	xx	xx
			q1	xx.x	xx.x
			median	xx.x	xx.x
			q3	xx.x	xx.x

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
Time to resolution: number of days beyond the end of the follow-up period
N = number of symptoms that were ongoing after the follow-up period
n = number of symptoms that were ongoing after the follow-up period with a complete end date
q1 = 25th percentile
q3= 75th percentile

Template 41 Percentage of doses reporting the occurrence of <grade 3> unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term <with causal relationship to vaccination> within the 30-day (Days 1-30) post-vaccination period <Exposed Set>

		Each group N =			
				95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n**	**%**	**LL**	**UL**
At least one symptom					
Gastrointestinal disorders (10017947)	Diarrhoea (10012735)				
	Teething (10043183)				
	Vomiting (10047700)				
General disorders and administration site conditions (10018065)	Pyrexia (10037660)				
Immune system disorders (10021428)	Seasonal allergy (10048908)				
Infections and infestations (10021881)	Conjunctivitis (10010741)				
	Otitis media (10033078)				
	Paronychia (10034016)				
	Tonsillitis (10044008)				
	Tonsillitis streptococcal (10044013)				
	Viral upper respiratory tract infection (10047482)				
Injury, poisoning and procedural complications (10022117)	Arthropod bite (10003399)				
	Face injury (10050392)				
	Head injury (10019196)				
Skin and subcutaneous tissue disorders (10040785)	Miliaria (10027627)				

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses followed by the symptom
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Template 42 Percentage of subjects reporting the occurrence of <serious adverse events, potential Immune Mediated Disease> classified by MedDRA Primary System Organ Class and Preferred Term from <first vaccination up to 30 days post last vaccination, from 30 days post last vaccination dose up to end of study, from first vaccination up to study end> <Exposed Set>

		Co-Ad N =					Control N =				
					95% CI					95% CI	
Primary System Organ Class (CODE)	**Preferred Term (CODE)**	**n***	**n**	**%**	**LL**	**UL**	**n***	**n**	**%**	**LL**	**UL**
At least one symptom											
Blood and lymphatic system disorders (10005329)	Leukocytosis (10024378)										
Cardiac disorders (10007541)	Acute myocardial infarction (10000891)										
	Atrial fibrillation (10003658)										
	Cardiac failure congestive (10007559)										
	Tachycardia (10043071)										
	Ventricular tachycardia (10047302)										

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects included in the considered cohort in each group
n/% = number/percentage of subjects reporting the symptom at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit
Please note that n* will be used to present pIMD for CTRS posting.

Template 43 Summary of temperature value by half degree increment taken by different routes reported during the 7-day (Days 1-7) post-vaccination following each dose <Exposed Set>

				Co-Ad					Control				
							95 % CI					95 % CI	
Dose	Symptom	Route	Type	N	n	%	LL	UL	N	n	%	LL	UL
Dose 1	Temperature (°C)	Oral	≥35.0										
			>35.5										
			>36.0										
			>36.5										
			>37.0										
			>37.5										
			>38.0										
			>38.5										
			>39.0										
			>39.5										
			>40.0										
		Axillary	≥35.0										
			>35.5										
			>36.0										
			>36.5										
			>37.0										
			>37.5										
			>38.0										
			>38.5										
			>39.0										
			>39.5										
			>40.0										
Dose 2	Temperature (°C)	Oral	≥35.0										
			>35.5										
			>36.0										
			>36.5										
			>37.0										
			>37.5										
			>38.0										
			>38.5										
			>39.0										
			>39.5										
			>40.0										
Dose 3													

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
For each dose:
N = number of subjects with at least one documented dose
n/% = number/percentage of subjects reporting the symptom at least once
95%CI = Exact 95% confidence interval; LL = lower limit, UL = upper limit
*=Temperature is defined on oral, axillary or tympanic

Template 44 Global Summary of <serious adverse events, potential Immune Mediated Disease> <with causal relationship with vaccination> reported from <first vaccination up to 30 days post last vaccination, from 30 days post last vaccination dose up to end of study, from first vaccination up to study end> <Exposed Set>

	Co-Ad	Control	Total
Number of subjects with at least one <SAE, pIMD> reported			
Number of doses followed by at least one <SAE, pIMD>			
Number of <SAE, pIMD> classified by MedDRA Preferred Term*			
Number of <SAE, pIMD> reported**			

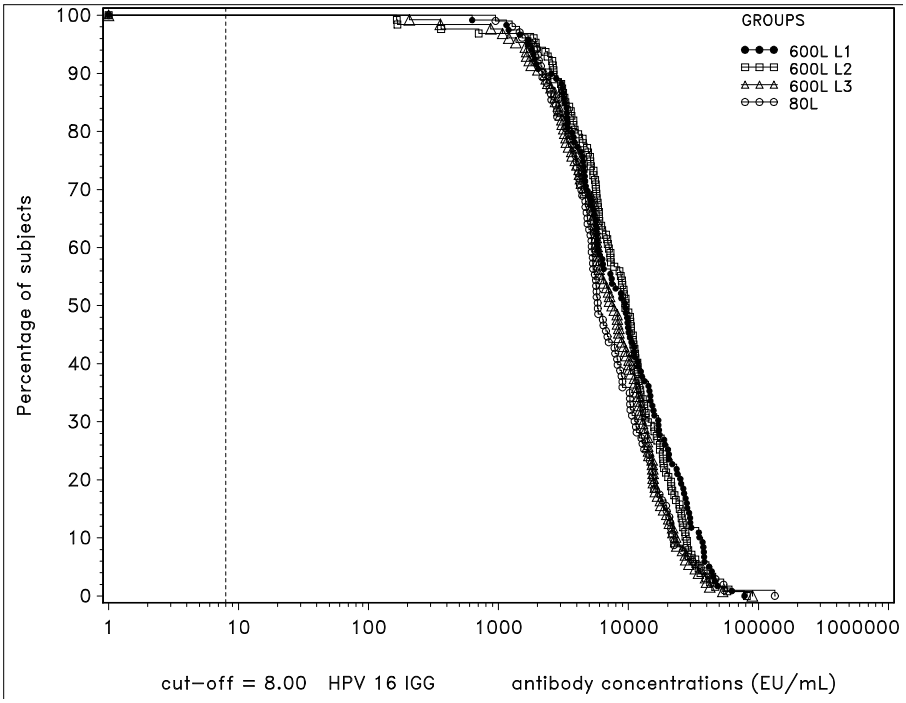
Co-Ad = Dose 1: Prevenar 13 + HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3:HZ/su
* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
** Symptoms reported by a subject after a given dose and classified by the same Preferred Term and the same start date of the event, are counted once

Template 45 Vaccine response rates for anti-gE antibody concentrations at one month post dose 2 of HZ/su vaccine <PPS for analysis of immunogenicity, Exposed Set>

		<Each group>				
					95% CI	
Antibody Timing	**Pre-vaccination status**	**N**	**n**	**%**	**LL**	**UL**
<each antibody>	S-	XXXX	XXXX	XX.X	XXX.X	XXX.X
	S+	XXXX	XXXX	XX.X	XXX.X	XXX.X
	Total	XXXX	XXXX	XX.X	XXX.X	XXX.X

Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
S- = seronegative subjects (antibody <concentration> < <cut off> <unit>) at pre-vaccination
S+ = seropositive subjects (antibody <concentration>≥ <cut off> <unit>) at pre-vaccination
Total = subjects either seropositive or seronegative at pre-vaccination
Vaccine response defined as:
Vaccine response defined as :
For initially seronegative subjects, antibody concentration at post-vaccination ≥ 4 fold the cut-off for Anti-gE (4x97 mIU/ml)
For initially seropositive subjects, antibody concentration at post-vaccination ≥ 4 fold the pre-vaccination antibody concentration
N = number of subjects with both pre- and post-vaccination results available
n/% = number/percentage of responders
<95>% CI = exact <95>% confidence interval, LL = Lower Limit, UL = Upper Limit
Please note – To calculate the vaccine response, result at PII(M3) compared to PRE-for Co-Ad and PIII(M5) compared to PI(M2) for Control group has to be considered

Template 46 Reverse cumulative distribution curves for <anti-gE antibody concentration, anti-pneumococcal <X> antibody titres> in each group at baseline and <post dose 2 of HZ/su vaccine, post dose of Prevenar 13> <PPS for analysis of immunogenicity, Exposed Set>



Co-Ad = Dose 1: Prevenar 13+ HZ/su, Dose 2: HZ/su
Control = Dose 1: Prevenar 13, Dose 2: HZ/su, Dose 3: HZ/su
Note: This graph is provided as an example. The same graph will be provided in colour for each time point and each assay comparing the values of the groups
Please note to consider PRE and PI(M1) for both group for pneumococcal antibody. For gE antibody, PRE and PII(M3) for Co-Ad and PI(M2) and PIII(M5) for Control group.