Statistical Analysis Plan

Study ID: 217212

Official Title of Study: A phase II, observer-blind, randomized, controlled study to evaluate the immunogenicity and safety of a varicella vaccine at various potencies compared with Varivax, as a first dose, administered in healthy children in their second year of life.

NCT number: NCT05084508

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STATISTICAL ANALYSIS PLAN

217212 (VNS 20-006)

A phase II, observer-blind, randomized, controlled study to evaluate the immunogenicity and safety of a varicella vaccine at various potencies compared with *Varivax*, as a first dose, administered in healthy children in their second year of life.

AUTHOR: PPD

VERSION NUMBER AND DATE: V7.0, 24JUN2024

STATISTICAL ANALYSIS PLAN SIGNATURE PAGE

Statistical Analysis Plan V7.0 (Dated 24JUN2024) for Protocol 217212 (VNS 20-006).

	Name	Signature	Date (DDMMYYYY)
Author:	PPD	PPD	
Position:	Statistical Scientist		
Company:	IQVIA		

Upon review of this document, the undersigned approves this version of the Statistical Analysis Plan, authorizing that the content is acceptable for the reporting of this study.

	Name	Signature	Date (DDMMYYYY)
Approved By:	PPD	PPD	
Position:	Lead Statistician		
Company:	GlaxoSmithKline Biologicals SA		

MODIFICATION HISTORY

Unique Identifier for this Version	Date of the Document Version	Author	Significant Changes from Previous Authorized Version
1.0	30JUL2021	PPD	Not Applicable – First Version
2.0	28OCT2021	PPD	Update following protocol amendment 1 dated 8th October 2021, CBER feedback and to complete the analysis specification: • Update reference to protocol amendment 1 • New study visit at Day 15 and safety call at Day 2-3 • SRT to be monthly rather than frequently • Update prior medication definition to include all medications started before first dose of study treatment • Ensure consistency on missing data • Varicella-like rash now includes injection site varicella-like rash • Clarified solicited and unsolicited adverse events analysis • Include intensity grades for fever and updated grades for varicella-like rash
3.0	25NOV2021	PPD	Update following protocol amendment 2 dated 15th November 2021: • Include general rash (not varicella-like), drowsiness, irritability and loss of appetite as solicited events

4.0	09JUN2022	PPD	Include countries other than the US. *Prevnar 13* not administered in all countries. Include new analysis split by country, duration of solicited events and ongoing solicited events post the solicited period.
5.0	27SEP2022	PPD	Update following the Spanish protocol amendment – adding a co-administered meningococcal vaccine visit at Day 15 for Spain. Update algorithm in appendix 2 to be consistent with section 15.
6.0	04MAR2024	PPD	Reverted update made for the Spanish protocol amendment in SAP version 5. Added derivation for age. Added country as fixed effect to all models. Updated the MedDRA version number and Preferred Terms for Drowsiness and Loss of appetite. Updated Preferred Terms for unsolicited adverse events that are synonymous with solicited adverse events. Added details for handling duplicate solicited adverse events. Explained handling of solicited events recorded beyond the end of the solicited periods. Added definition of immediate unsolicited AEs.
7.0	24JUN2024	PPD	Added Section 18.1.1.1 eCOA Compliance.

TABLE OF CONTENTS

1. LIST OF ABBREVATIONS

AE	Adverse Event
ANOVA	Analysis of variance
ATC	Anatomical Therapeutic Chemical
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence Interval
COVID-19	Coronavirus disease 2019
CSR	Clinical Study Report
eCOA	Electronic Diary
eCRF	Electronic Case Report Form
ENR	Enrolled Set
ES	Exposed Set
gE	Glycoprotein E
GCP	Good Clinical Practice
GMC	Geometric Mean Concentration
IDMC	Independent Data Monitoring Committee
LAR	Legally Acceptable Representative
LL	Lower Limit
LLOQ	Lower Limit Of Quantification
MedDRA	Medical Dictionary for Regulatory Activities

MMR	Measles, mumps, and rubella vaccine
PD	Protocol Deviation
PDMP	Protocol Deviations Management Plan
PPS	Per Protocol Set
PT	Preferred Term
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SOC	System Organ Class
SRT	Safety Review Team
TEAE	Treatment Emergent Adverse Event
VNS	Varicella vaccine (investigational vaccine)
VV	Varicella vaccine (comparator)

2. INTRODUCTION

This document describes the rules and conventions to be used in the presentation and analysis of immunogenicity and safety at final analyses for Protocol 217212 (VNS 20-006). It describes the data to be summarized and analyzed, including specifics of the statistical analyses to be performed.
This Statistical Analysis Plan (SAP) is based on protocol amendment 3 dated 18th May 2022.

3. STUDY OBJECTIVES

3.1. PRIMARY OBJECTIVE

The primary objective is

- To evaluate the immune response of VNS vaccine (formulated with different potencies) and VV vaccine in terms of geometric mean concentration at Day 43

3.2. SECONDARY OBJECTIVES

The secondary objectives are

- To evaluate the immune response of VNS vaccine (formulated with different potencies) and VV vaccine in terms of seroresponse rate* at Day 43
- To evaluate safety and reactogenicity following administration of VNS and VV vaccines

3.3. ENDPOINTS

The primary endpoint is

- Anti-VZV gE antibody concentration at Day 43

The secondary endpoints are

- Seroresponse to gE at Day 43
- Solicited events
    - Percentage of participants reporting each solicited administration site event in terms of injection site redness, pain and swelling within 4 days (Day 1 to Day 4)

post-dose of VNS vaccine or VV vaccine
    - Percentage of participants reporting each solicited systemic event in terms of fever, varicella-like rash+ and general rash (not varicella-like) within 43 days (Day 1 to Day 43) post-dose of study interventions at Day 1**
    - Percentage of participants reporting each solicited systemic event in terms of drowsiness, loss of appetite and irritability within 15 days (Day 1 to Day 15) post-dose of study interventions at Day 1**
- Unsolicited Adverse Events (AEs)***
    - Percentage of participants reporting unsolicited AEs within 43 days (Day 1 to Day 43) post-dose of study interventions at Day 1**
- Serious Adverse Events (SAEs)
    - Percentage of participants reporting SAEs post-dose of study interventions at Day 1** up to the end of study

* Seroresponse rate is defined as the percentage of participants for whom post-dose of the study interventions (Day 43), the anti-VZV gE antibody concentration is ≥300 mIU/mL.
** Study interventions = VNS vaccine (investigational vaccine); VV vaccine (Varivax, comparator vaccine); MMR (*M-M-R II* or *M-M-RVaxPro*), *Havrix* and *Prevnar 13* (if applicable) vaccines (co-administered vaccines) at Day 1.
*** Unsolicited AEs include non-serious and serious AEs
+ Includes injection site varicella-like rash

4. STUDY DESIGN

4.1. GENERAL DESCRIPTION

This will be a phase II, observer-blind, randomized, multicenter controlled study with 5 parallel intervention groups of healthy children aged 12 to 15 months at the time of intervention. Participants will be randomized to receive a single dose of an investigational varicella vaccine (3 groups of 200 participants each receiving one of the 3 different vaccine potencies [a low, a medium, and a high potency of the VNS vaccine, respectively]) or a single dose of a comparator licensed varicella vaccine (2 groups of 100 participants each receiving one of the 2 different lots

of the VV vaccine, which will be pooled for all analyses).

The rationale of this study is to demonstrate the immunogenicity of the investigational VNS vaccine at 3 potencies compared with commercially available Merck's varicella vaccine, Varivax (hereafter designated as VV vaccine). In addition to assessing the immunogenicity of both varicella vaccines, this study intends to also generate safety data in the participants. All participants in the US will be co-administered with a measles, mumps and rubella vaccine (MMR vaccine), a hepatitis A vaccine (*Havrix*), and a 13-valent pneumococcal conjugate vaccine (*Prevnar 13*). Participants outside of the US will be co-administered with MMR, *Havrix* and in some countries, with *Prevnar 13*. Outside the US, *Prevnar 13* will only be administered in countries where pneumococcal conjugate is recommended at 12-15 months as per national immunization schedule. If *Prevnar 13* is to be administered, participants are required to have previously received the primary series of pneumococcal conjugate vaccine in their first year of life with last dose at least 60 days prior to study entry. There will be 3 in-person study visits, at Day 1 (intervention), when the participants receive study intervention, at Day 15 (either in-person or virtually, for review of post-vaccination safety data) and Day 43, as well as 1 safety call and 1 safety follow-up contact, at Day 2-3 and Day 181, respectively.

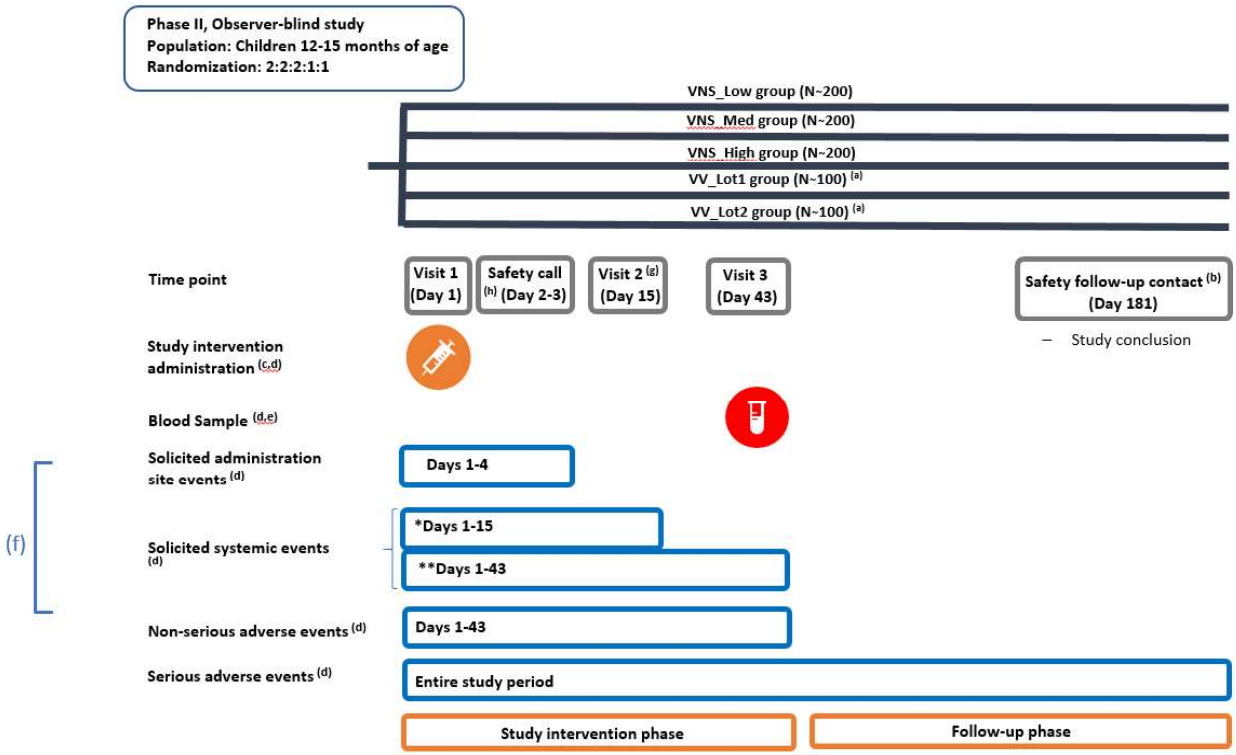
Healthy children aged 12 to 15 months will be enrolled in this study according to the inclusion and exclusion criteria (see protocol Section 5.0). Approximately 800 participants will be randomly assigned to the 5 study groups in a 2:2:2:1:1 ratio prior to intervention to provide approximately 200 enrolled participants per each VNS group and 100 enrolled participants per each VV group (VV Lot 1 and VV lot 2). Approximately 90% of the enrolled participants are expected to be included in the Per Protocol Set (PPS) and evaluated for immunogenicity.

Study intervention Groups

Intervention groups	Number of participants	Age (Min-max)	Study interventions
VNS_Low	200	12-15 months	VNS_Low vaccine, MMR*, *Havrix*, *Prevnar 13***
VNS_Med	200	12-15 months	VNS_Med vaccine, MMR*, *Havrix*, *Prevnar 13***
VNS_High	200	12-15 months	VNS_High vaccine, MMR*, *Havrix*, *Prevnar 13***
VV_Lot 1	100	12-15 months	VV vaccine (Varivax Lot 1), MMR*, *Havrix*, *Prevnar 13***
VV_Lot 2	100	12-15 months	VV vaccine (Varivax Lot 2), MMR*, *Havrix*, *Prevnar 13***

*** *M-M-R II* or *M-M-RVax Pro*, depending on the country. ** *Prevnar 13* will only be administered to participants enrolled in the US and in countries where pneumococcal conjugate vaccine is recommended at 12-15 months as per national immunization schedule.**

Figure A: Study Schema



VNS_Low, VNS_Med, and VNS_High vaccine = VNS vaccine in low, medium, and high potency; VV_Lot 1 and VV_Lot 2 = VV vaccine in 2 lots

[a] VV_Lot 1 and VV_Lot 2 groups will be analyzed as pooled groups

[b] Contact (by telephone call or any other convenient procedure) for the safety follow-up will take place 6 months post-dose of study interventions

[c] Study interventions: VNS vaccine (investigational vaccine) or VV vaccine (*Varivax*, comparator vaccine); MMR (*M-M-R II or M-M-RVaxPro)*, *Havrix*, and *Prevnar 13* if applicable (co-administered vaccines) will be administered at Day 1. Note: *Prevnar 13* will only be administered to participants enrolled in the US and in countries where pneumococcal conjugate vaccine is recommended at 12-15 months as per national immunization schedule.

[d] Recording in the electronic Case Report Form

[e] Blood sampling for anti-varicella zoster virus enzyme-linked immunosorbent assay
[f] Independent Data Monitoring Committee review details are provided in protocol Section 8.2.3
[g] Visit 2 (Day 15) for review of post-vaccination safety data may be a virtual visit.
[h] Safety call to remind completion of the electronic Diary/smartphone application and address any potential early post-vaccination safety concerns.
*Drowsiness, loss of appetite, irritability
**Fever, varicella-like rash (including injections site varicella-like rash) and general rash (not varicella like)

4.2. SCHEDULE OF EVENTS

Schedule of events can be found in Section 1.3 of the protocol.

4.3. CHANGES TO ANALYSIS FROM PROTOCOL

- No changes

5. PLANNED ANALYSES

The following analyses will be performed for this study:

- Analyses for Independent Data Monitoring Committee (IDMC) meetings
- Analyses for Safety Review Team (SRT) review
- Interim Analysis
- Final Analysis

5.1. INDEPENDENT DATA MONITORING COMMITTEE (IDMC)

An IDMC SAP, describing the methodology and the presentation of, and access to, results will be provided by IQVIA as a separate document.

An IDMC will provide safety oversight during the active vaccination period, through unblinded review of the cumulative safety data.

An enrollment pause is foreseen for the first IDMC review after 200 participants (approximately 50 participants in each group, considering pooled VV groups) are enrolled and vaccinated. The analysis will take place once all 200 participants have returned for their Day 43 visit (Visit 3) or have withdrawn from the study, within the allowed interval for the visit. A positive outcome of the IDMC review will be a pre-requisite for the continuation of the study. A subsequent IDMC review meeting is planned during the study, after Day 43 safety follow-up of 400 participants is completed. No enrolment pause is foreseen after this.

5.2. SRT REVIEW

The SRT is responsible for ongoing safety monitoring. Monthly SRT reviews will occur up to the enrollment and vaccination of the first 200 participants through their Day 43 follow-up, to monitor cumulative, blinded safety data (including serious and non-serious AEs). The blinded safety data review by the SRT may trigger an emergency ad-hoc IDMC review before the 200 participants are enrolled and vaccinated.

5.3. INTERIM ANALYSIS

One interim analysis will take place for this study. A statistical analysis including safety and final immunogenicity data for all participants up to Day 43 timepoint is planned, the results of which will be based on the unblinded intervention groups. All analyses are descriptive and therefore no statistical adjustment for interim analyses is required.

5.4. FINAL ANALYSIS

All final, planned analyses identified in this SAP will be performed by IQVIA Biostatistics following Sponsor Authorization of this Statistical Analysis Plan, Database Lock, Sponsor Authorization of Analysis Sets and Unblinding of intervention group.

This SAP is focused/limited to planned interim and final analyses. Outputs required for the final analyses will be flagged in the TFL mock shells document.

6. ANALYSIS SETS

Agreement and authorization of participants included/excluded from each analysis set will be conducted prior to the database lock.

6.1. PROCESS FOR ANALYSIS SET ASSIGNMENT

- Definitions for analysis sets are provided below.
- Prior to database lock, a transfer of raw data from the electronic Case Report Form (eCRF) will occur, and participants will be assigned to analysis sets in accordance with the definitions in this SAP and the available data at that time. However, the protocol deviations will be monitored continuously throughout the study.
- Listings presenting participants excluded from each preliminary analysis set and reasons for exclusion will be prepared for sponsor review ahead of database lock in order to allow appropriate related data queries to be issued.
- Listings presenting participants excluded from each final analysis set and reasons for exclusion will be prepared for sponsor review ahead of unblinding for a final review and approval. However, for deviations that can only be assessed after unblinding such as vaccination errors these will be reviewed after unblinding.
- A Data Review meeting will be held to confirm analysis set assignment for each participant and any changes will be recorded. Changes will be implemented, and an updated analysis set assignment will be approved by the sponsor.
- Sponsor authorization of the analysis sets will be necessary to unblind the data after database lock. Once approved, the study will be unblinded, analysis sets will be finalized including additional eliminations requiring unblinding, and the database will be locked.
- After database lock, the final analysis sets will be derived using the final study data, i.e., clinical database (eCRF), external vendor data (immunogenicity results), protocol deviations

log and blinded data report.

6.2. ENROLLED SET [ENR]

All eligible participants who received a study intervention or were randomized. Note that as per Good Clinical Practice (GCP) enrolled participants' parent(s)/ legally acceptable representative (LAR) should have completed the informed consent process and participants should be eligible before initiating any study procedure.

6.3. EXPOSED SET [ES]

All participants who received a study intervention. Analysis per group is based on the varicella intervention administered.

6.4. PER PROTOCOL SET [PPS]

All eligible participants who received all study interventions as per protocol, were not unblinded, had immunogenicity results post-dose, complied with blood draw intervals (refer to Table 3 of the protocol), without intercurrent medical conditions that may interfere with immunogenicity and without prohibited concomitant medication/vaccination*.

*Intercurrent medical conditions that may lead to elimination from the PPS are defined as confirmed immunodeficiency condition, or development of varicella or herpes zoster in the interval between study intervention administration at Day 1 and the collection of the blood specimen for immunogenicity at Visit 3.

7. GENERAL CONSIDERATIONS

Data will be summarized descriptively (frequency and percentage for categorical data and mean, standard deviation [SD] and range for continuous data, unless specified otherwise). In summary

tables for categorical data for which categories are defined on the eCRF, all categories will be presented as specified, even if the participant count within that category is zero.

In all the summary tables intervention VV lot 1 and VV lot 2 will be analyzed as pooled lots.

Unless otherwise specified, all data collected during the trial will be presented in listings for the ENR.

7.1. REFERENCE START DATE AND STUDY DAY

Study Day will be calculated from the reference start date and will be used to show start/stop day of assessments and events.

Reference start date is defined as the day of the dose of study vaccination at day 1 and will appear in every listing where an assessment date or event date appears.

If the date of the event is on or after the date of vaccination at Day 1 then:
Study Day = (date of event – date of vaccination at Day 1) + 1.

If the date of the event is prior to the date of vaccination at Day 1 then:
Study Day = (date of event – date of vaccination at Day 1).

In the situation where the event date is partial or missing, Study Day, and any corresponding durations will appear partial or missing in the listings.

7.2. BASELINE

Unless otherwise specified, baseline is defined as the last non-missing measurement taken prior to reference start date (including unscheduled assessments). In the case where the last non-missing measurement and the reference start date coincide, that measurement will be considered pre-baseline.

7.3. RETESTS, UNSCHEDULED VISITS AND EARLY TERMINATION DATA

In general, for by-visit summaries, data recorded at the nominal visit will be presented. Unscheduled measurements will not be included in by-visit summaries.

Listings will include all scheduled, and early termination discontinuation data.

7.4. WINDOWING CONVENTIONS

Allowed time window for each visit will performed as mentioned in "Schedule of Activities", section 1.3 of protocol.

Intervals between Study Visits

Interval	Planned visit interval	Allowed interval range
Visit 1 → Safety call	1 to 2 days	1 to 3 days
Visit 1 → Visit 2	14 days	14 to 19 days
Visit 1 → Visit 3	42 days	35 to 56 days
Visit 1 → Safety follow-up contact	180 days	180 to 201 days

Window convention

Assigned Study Day	Visit label as per protocol	Visit assigned
Day 1	Visit 1	Visit 1 (Day 1)
Day 2 to 3 (Day 1 + 1 to 3 days)	Safety Call	Safety Call (Day 2 – 3)
Day 15 (Day 1 + 14 to 19 days)	Visit 2	Visit 2 (Day 15)
Day 43 (Day 1 + 35 to 56 days)	Visit 3	Visit 3 (Day 43)
Day 181 (Day 1 + 180 to 201 days)	Safety Follow-up contact	Safety Follow-up (Day 181)

7.5. STATISTICAL TESTS

The default significant level will be (5%); 2-sided confidence intervals (CIs) will be 95%, unless otherwise specified in the description of the analyses.

7.6. COMMON CALCULATIONS

Geometric Mean Concentration (GMC):

Distributions of antibodies are generally skewed to the right (Nauta, 2010). Therefore, prior to any statistical analysis that assumes normally distributed observations, antibody titers or concentrations will be log10-transformed. GMCs and their 95% CI are computed by exponentiating (base 10) the least squares mean and 95% CI of the log10 titers.

The GMC will be calculated using the following formula:

$$10^{\left(\frac{\sum_{i=1}^{n}\log 10(t_i)}{n}\right)}$$

Where $t_1, t_2, \ldots, t_n$ are n observed immunogenicity concentrations.

Concentration below assay cut-off (i.e., <lower limit of quantification or < LLOQ) will be replaced by half the assay cut-off (LLOQ/2) for the purpose of GMC computation.

Seroresponse rate:

Defined as the percentage of participants for whom the post-dose anti-VZV gE antibody concentration (Day 43) is ≥ 300 mIU/mL.

7.7. SOFTWARE VERSION

All analyses will be conducted using SAS version 9.4 or higher.

8. STATISTICAL CONSIDERATIONS

8.1. ADJUSTMENTS FOR COVARIATES AND FACTORS TO BE INCLUDED IN ANALYSES

The following factors will be used in the analyses. For details, refer to section 17.1 and 17.2. The model will include all groups and country as fixed categorical effects in the Analysis of Variance (ANOVA) model.

For the interim analysis an ANCOVA model on log-transformed anti-VZV gE with VNS dose level will be used as covariable in addition to the indicator of investigational vaccine. Likewise, seroresponse will be analyzed using a logistic regression with the same covariable. The dose effect will be constrained to be positive. Country will be included as a fixed effect to both models.

8.2. MULTICENTER STUDIES

This study will be conducted by multiple investigators at multiple centers. The participants will be randomised to one of the 5 groups (refer to 0 in section 4.1) which will be performed in a 2:2:2:1:1 ratio prior to intervention to provide approximately 200 enrolled participants per each VNS group and 100 enrolled participants per each VV group (VV Lot 1 and VV lot 2).

8.3. MISSING DATA

Missing data (missing, incomplete or partial dates, AE measurement (including missing AE severity and relationship), prior and concomitant medications and death date) will be handled as per APPENDIX 2 of this analysis plan.

Missing immunogenicity data will not be imputed. Concentration below assay cut-off (i.e., lower limit of quantification or < LLOQ) will be replaced by half the assay cut-off (LLOQ/2) for the purpose of GMC computation**.**

9. OUTPUT PRESENTATIONS

APPENDIX 1 shows conventions for presentation of data in outputs.

The templates provided with this SAP describe the presentations for this study and therefore the format and content of the summary tables, figures, and listings to be provided by IQVIA Biostatistics. Statistical output numbering will follow 'ICH E3 Structure and Content of Clinical Study Reports'.

10. DISPOSITION AND WITHDRAWALS

All participants who are enrolled in the study (those who received a study intervention at Day 1 or were randomized) will be accounted for in this study.

10.1. DISPOSITION

Participant disposition, withdrawals, and reasons for exclusion from each analysis set, including inclusion as well as exclusion criteria will be presented for the ENR. Specifically, the number of participants, vaccinated, completed the study, discontinuing the study and the reason for discontinuation will be summarized by study group for the ENR. Additionally, the number of participants returning for each visit for the ES will be presented.

A listing of the disposition for all participants with early withdrawal or discontinuation due to having Coronavirus Disease 2019 (COVID-19) or COVID-19 related issues information will be provided.

10.2. PROTOCOL DEVIATIONS

Protocol deviations (PDs) will be collected in a PD log, as detailed in the Protocol Deviations Management Plan (PDMP). All PDs will be assessed as either important or non-important. PDs will be reviewed by the sponsor, and their status confirmed by the time that all data are cleaned for the Final Analysis. A summary table presenting the number and percentage of participants with important PDs (i.e., those PDs associated to elimination from PPS) will be presented for participants in the ES. A listing of all PDs including an indicator of those excluded from the PPS and an indicator of COVID causality will be provided.

10.2.1. PROTOCOL DEVIATIONS RELATED TO STUDY CONDUCT

A PD is any non-compliance with the clinical trial protocol, GCP, or protocol deviation guidelines requirements. The non-compliance may be either on the part of the participant, the site PI, the study site staff or the sponsor.

10.2.2. PROTOCOL DEVIATIONS RELATED TO IMMUNOGENICITY ANALYSIS

Changes to the procedures or events, which may impact the quality of the immunogenicity data, will be considered significant PDs and will be described within the Clinical Study Report (CSR).

This includes any circumstances that could alter the evaluation of the immunogenicity results such as sample processing errors that lead to inaccurate immunogenicity results, and/or inaccurate dosing which could exclude them from the PPS. In addition, participants may also be eliminated from the PPS based on usage of certain concomitant medications or vaccines as described in Section 5.2.2 of the Protocol.

11. DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

Demographic data and other baseline characteristics will be presented for ES and PPS. The following demographic and other baseline characteristics will be reported for this study:

- Age (months) – at the time of first vaccination
- Sex
- Race (as per CDISC categories)
- Ethnicity

Age at time of first vaccination will be derived as the number of complete months between date of birth and date of vaccination. If date of vaccination is missing (the participant was not vaccinated), then date of informed consent will be used.

Descriptive statistics (mean, median, standard deviation and range) will be presented for continuous variables and frequency counts and percentages for categorical variables.

Age category (preterm newborn infants (gestational age < 37 weeks), newborn (0-27 days), infant and toddlers (28 days – 23 months), children (2-11 years), adolescents (12-17 years), adults (18-64 years), 65-84 years and >=85 years) will be summarized by study group where participants are enrolled.

The number of participants enrolled at each country will be summarized by study group.

No statistical testing will be carried out for demographic or other baseline characteristics.

12. COVID-19 INFECTION ASSESSMENT AND DIAGNOSIS

The COVID-19 infection assessment and diagnosis data including assessment, symptom, diagnosis, visit impact and study impact data will be listed for the ENR and captured on the "COVID-19" page of the eCRF.

13. GENERAL MEDICAL/VACCINATION HISTORY AND EXAMINATIONS

Medical/Vaccination History information will be presented for the ENR.

- Medical History will be coded using Medical Dictionary for Regulatory Activities (MedDRA) central coding dictionary, Version 26.1 or higher.
- Data captured on the "Medical History" page of the eCRF will be presented by System Organ Class (SOC) and Preferred Term (PT). Medical occurrences that begin before the start of study intervention but after obtaining informed consent will be recorded on the Medical History/Current Medical Conditions section of the eCRF, not the AE section.
- Vaccine history will be checked for each participant with the participant's parent/LAR (protocol-specific vaccines including PCV).

A listing of medical/vaccination history data will be provided.

14. PRIOR, CONCOMITANT AND CO-ADMINISTERED VACCINATIONS

Prior, concomitant and co-administered vaccination will be coded with the current version of the GSK drug dictionary.

- Prior vaccinations are vaccinations per protocol given to participants prior to the dosing of study intervention at Day 1 and are recorded on the eCRF.
- MMR, *Havrix*, and *Prevnar 13* are co-administered with both VNS and VV in this study as

study interventions.

- Concomitant vaccinations are defined as any vaccine that the participant is receiving as of the time of enrolment or receives during the study (other than study interventions) as recorded on the “Concomitant Vaccination” page of the eCRF.

In addition, if a concomitant vaccination may help explain an AE/SAE, the cause of the AE/SAE or the treatment of an AE/SAE, this information will be recorded under the “Concomitant Medications/Vaccinations Entry" section of the “Expedited Adverse Events (Serious adverse event)” page of the eCRF.

Data will be presented in table summaries for co-administered MMR, *Havrix*, and *Prevnar 13* vaccines, for the ES and in listings for all prior/concomitant and co-administered vaccines.

15. MEDICATIONS

The percentage of participants who started medications after study vaccination will be presented by intervention group for the ES. Medications will be presented by Anatomical Therapeutic Chemical (ATC) classification and preferred drug name and by intervention group.

See APPENDIX 2 for handling of partial dates for medications, in the case where it is not possible to define a medication as prior or concomitant, the medication will be classified by the worst case; i.e., concomitant.

- ‘Prior’ medications are medications which started prior to the dose of study vaccination at Day 1.
- ‘Concomitant’ medications are medications which started on or after the day of the administration of study vaccination at Day 1.

Further details are in Section 6.8 of the Protocol. Concomitant medications which started from Day 1 to Visit 3 blood sample will be presented in table summaries (Any, antipyretic action) and in listings for all medications.

16. STUDY VACCINATION EXPOSURE

Exposure to study vaccine will be presented for the ES. The date and time of study vaccine administration will be taken from the eCRF "Exposure-VNS vaccine/VV vaccine" form. Similarly, the date and time of co-administered vaccines will be taken from the eCRF "Exposure MMR/*Havrix*/*Prevnar 13*" form. For dosing instructions and route, refer to Table 7 of the Protocol amendment 3 dated 18 May 2022.

Data will also be presented in listings.

17. IMMUNOGENICITY OUTCOMES

17.1. PRIMARY IMMUNOGENICITY

17.1.1. PRIMARY IMMUNOGENICITY VARIABLE(S) AND DERIVATION(S)

The primary objective is to evaluate the immune response of VNS vaccine (formulated with different potencies) and VV vaccine in terms of GMC at Day 43. For the derivation of GMC refer to section 7.6.

17.1.2. MISSING DATA METHODS FOR PRIMARY IMMUNOGENICITY VARIABLE

Missing data will not be replaced.

17.1.3. PRIMARY ANALYSIS OF PRIMARY IMMUNOGENICITY VARIABLE

The primary immunogenicity endpoint GMCs of anti-VZV gE antibody concentration at Day 43 will be summarized by vaccine group with their 95% CI derived considering log10-transformed antibody concentrations are normally distributed with unknown variance. Anti-VZV gE antibody concentration will be graphically presented by reverse cumulative curves per vaccine group. The concentration below the assay cut-off will be assigned to half the cut-off for the purpose of GMC

computation. This will be based on the PPS and the ES. The analysis will also be done split by country.

An adjusted GMC and GMC ratio with 2-sided 95% CI for intervention group which is derived from an ANOVA model on log10 transformed concentration will be tabulated for anti-VZV gE antibody concentration. The model based on the data from all groups will include intervention group as a fixed effect and will be based on the PPS.

The GMC ratio will be estimated along with its corresponding 2-sided 95% CI by exponentiating the least-squares means for the difference.
For the interim analyses, an ANCOVA model on log-transformed anti-VZV gE with VNS dose level will be used as covariable in addition to the indicator of investigational vaccine.

17.2. SECONDARY IMMUNOGENICITY

17.2.1. SECONDARY IMMUNOGENICITY VARIABLE & DERIVATION

The secondary objective is to evaluate the immune response of VNS vaccine (formulated with different potencies) and VV vaccine in terms of seroresponse rate* at Day 43 and will be based on the PPS and ES.
* Seroresponse rate is defined as the percentage of participants for whom the post-dose anti-VZV gE antibody concentration (Day 43) is ≥ 300 mIU/mL.

17.2.2. MISSING DATA METHODS FOR SECONDARY IMMUNOGENICITY VARIABLE

Missing data will not be replaced. Please refer to section 8.3 for more details

17.2.3. ANALYSIS OF SECONDARY IMMUNOGENICITY VARIABLE

The percentage of participants with a seroresponse will be summarized by intervention groups and corresponding 2-sided 95% exact CI will be reported based on Clopper and Pearson method.

The analysis will also be done split by country.

The number and percentage of participants with a seroresponse at Day 43 and 2-sided 95% CI on group difference in the seroresponse rate (VV pooled group-VNS group [different potencies – Low, Med, High]) will be computed based on Miettinen and Nurminen method [Miettinen, 1985].
For interim analyses, seroresponse will be analyzed using a logistic regression with VNS dose level used as a covariable. The dose effect will be constrained to be positive.

18. SAFETY OUTCOMES

All outputs for safety outcomes will be based on the ES.

There will be no statistical comparisons between the treatment groups for safety data.

Secondary Safety Endpoints:

- Solicited events
  - Percentage of participants reporting each solicited administration site event in terms of injection site redness, pain and swelling within 4 days (Day 1 to Day 4) post-dose of VNS vaccine or VV vaccine
  - Percentage of participants reporting each solicited systemic event in terms of fever, varicella-like rash (including injection site varicella-like rash) and general rash (not varicella-like) within 43 days (Day 1 to Day 43) post-dose of study interventions at Day 1
  - Percentage of participants reporting each solicited systemic event in terms of drowsiness, loss of appetite and irritability within 15 days (Day 1 to Day 15) post-dose of study interventions at Day 1

- Unsolicited adverse events
  - Percentage of participants reporting unsolicited AEs within 43 days (Day 1 to Day

43) post-dose of study interventions at Day 1

- Serious adverse events
  - Percentage of participants reporting SAEs post-dose of study interventions at Day 1 up to the end of study

18.1. ADVERSE EVENTS

AEs will be coded using MedDRA central coding dictionary, Version 26.1 or higher. Adverse events will be described using frequency and percentage.

AEs will be grouped by SOC and PT and summarized by intervention at time of onset of the AE. The summary tables will present the number and percentage of total participants and number of events, by SOC and by PT for each intervention group.

For the summaries of AEs, participants who experience the same AE (in terms of the MedDRA SOC and PT) more than once will only be counted once for that event in the number of participants but all occurrences of the same event will be counted in the number of events.

See APPENDIX 2 for handling of partial dates for AEs. In the case where it is not possible to define an AE as pre-treatment or treatment-emergent (TEAE) due to missing or partial dates, the AE will be classified by the worst case; i.e., TEAE. TEAE are defined as AEs which commence on or after the time of the vaccine administration through to the study end. All AE summaries will be restricted to TEAEs only.

Listings of all AEs and SAEs leading to discontinuation of study will be provided.

18.1.1. SOLICITED ADVERSE EVENTS

Solicited events are recorded in electronic diaries. Duplicate entries are defined as records with identical participant ID, category, object of the observation, date and time of collection, result or

finding in original units and evaluator. In case of duplicate records, the first record will be kept for analysis. The first record is determined by sequence number assigned in the SDTM dataset.

In the event the electronic diary was started later than the day of vaccination, it remained open to record solicited events beyond the end of the solicited periods. Data beyond the solicited period will remain in the datasets but will not be used in the statistical analysis, since the solicited period is based on Study Day for the statistical analyses, see section 7.1.

For each study group and each solicited event, the incidence rates (frequencies and percentages) of vaccinated participants with solicited administration site events, systemic events (drowsiness, loss of appetite and irritability) and systemic events (fever, varicella-like rash (including injection site varicella-like rash) and general rash) collected within 4 days (Day 1 to Day 4), within 15 days (Day 1 to Day 15) and within 43 days (Day 1 to Day 43) respectively will be summarized (percentage of vaccinated participants with each of any, grade 2 or 3, related, grade 3 leading to medical attention). The completeness defined as the percentage of vaccinated participants who documented presence/absence of each event as well as the daily prevalence of each symptom among vaccinated participants who documented presence /absence of the event on that day will be provided. These will also be summarized for each country.

The duration of each solicited event, in days, will be summarized using descriptive statistics (n, mean, standard deviation, median and range) for each study group. The duration will be calculated from the first date that the symptom was reported up to the last date the symptom was reported ignoring any dates when the symptom was absent or was not recorded: Last date symptom recorded – first date symptom recorded + 1
The number of solicited events still ongoing at the end of the solicited period will be summarized by study group by maximum intensity (any, grade 2-3 and grade 3).

Solicited administration site events	**Solicited systemic events**
Pain at Injection Site	Fever

Solicited administration site events	Solicited systemic events
Redness at Injection Site Swelling at Injection Site	Varicella-like rash (including injection site varicella-like rash) General rash (not varicella-like) Drowsiness Loss of appetite Irritability

Intensity Scales for Solicited Events in Toddlers (12 to 15 Months of Age) will be assessed as follows:

Adverse Event	MedDRA Preferred Term	Intensity Grade	Parameter
Pain at Injection Site	Administration site pain (10058049)	0	None
		1	Mild: Minor reaction to touch
		2	Moderate: Cries/protests on touch
		3	Severe: Cries when limb is moved/spontaneously painful
Redness at Injection Site	Administration site erythema (10074796)	0	None
		1	> 0 - ≤ 5 mm
		2	> 5 - ≤ 20 mm
		3	> 20 mm
Swelling at Injection Site	Administration site swelling (10075107)	0	None
		1	> 0 - ≤ 5 mm
		2	> 5 - ≤ 20 mm

Adverse Event	MedDRA Preferred Term	Intensity Grade	Parameter
		3	> 20 mm
Fever*	Pyrexia (10037660)	0	<38.0°C (100.4°F)
		1	≥ 38.0°C (≥ 100.4°F) - ≤ 39.0°C (≥ 102.2°F)
		2	> 39.0°C (≥ 102.2°F) - ≤ 39.5°C (≥ 103.1°F)
		3	> 39.5°C (≥ 103.1°F)
Varicella-like rash (including injection site varicella-like rash)	Rash vesicular (10052566)	0	None
		1	1-25 lesions
		2	26-50 lesions
		3	≥51 lesions
General rash (not varicella-like)	General rash (10049201)	0	None
		1	Mild: Rash which is easily tolerated by the child, causing minimal discomfort and not interfering with everyday activities
		2	Moderate: Rash which is sufficiently discomforting to interfere with normal everyday activities
		3	Severe: Rash which prevents normal, everyday activities (in a young child, such an AE would, for example, prevent attendance at school/day care and would cause the parent(s)/LAR(s) to seek medical advice)
Drowsiness	Lowest level term: Drowsiness (10013649)	0	Behaviour as usual
		1	Mild: Drowsiness easily tolerated
		2	Moderate: Drowsiness that interferes with normal activity

Adverse Event	MedDRA Preferred Term	Intensity Grade	Parameter
	PT: Somnolence (10041349)	3	Severe: Drowsiness that prevents normal activity
Loss of appetite	Decreased appetite (10061428)	0	Appetite as usual
		1	Mild: Eating less than usual/ no effect on normal activity
		2	Moderate: Eating less than usual/ interferes with normal activity
		3	Severe: Not eating at all
Irritability	Irritability (10022998)	0	Behavior as usual
		1	Mild: Crying more than usual/no effect on normal activity
		2	Moderate: Crying more than usual/ interferes with normal activity
		3	Severe: Crying that cannot be comforted/ prevents normal activity

* Temperature will be analyzed in 0.5°C increments from ≥ 38.0°C (≥ 100.4°F)

The number and percentage of participants per study intervention reporting unsolicited adverse events with MedDRA preferred terms that are synonymous with solicited adverse events, and starting after the end of each solicited period, will be summarized by severity (mild, moderate or severe). If a participant experiences an event on more than one occasion, the maximum intensity will be reported. The following table shows the corresponding MedDRA preferred terms or higher level terms that will be selected from the unsolicited adverse events for this analysis.

Unsolicited adverse events that are synonymous with solicited adverse events

Solicited Adverse Event	MedDRA PT/HLT
Pain at injection site	Administration site pain (PT)
Redness at injection site	Administration site erythema (PT)
Swelling at injection site	Administration site swelling (PT)
Drowsiness	Somnolence (PT)
Loss of appetite	Decreased appetite (PT)
Fever	Pyrexia (PT)
Irritability	Irritability (PT)
Rash (all types combined)	Rashes, eruptions and exanthems NEC (HLT)

18.1.1.1. eCOA Compliance

Overall electronic diary (eCOA) compliance (across all eCOAs and all participants) for the study is calculated as:

$$\frac{Total\ number\ of\ complete\ eCOAs}{(Expected\ number\ of\ complete\ eCOAs\ per\ participant\ \times\ Total\ number\ of\ particpants)}$$

Where the expected number of complete eCOAs per participant is defined as 43, the number of days in which the eCOA is expected to be completed. This definition will also apply to participants who discontinue the study early.

An eCOA is considered complete if there is no missing data within the assessment. Solicited

event data reported by the investigator will not contribute to eCOA compliance.

A participant is considered to be compliant with their eCOA if at least 80% of their eCOA are complete, i.e, a participant is compliant if they meet the following criteria:

$$\frac{Total\ number\ of\ complete\ eCOAs}{Expected\ number\ of\ complete\ eCOAs} \times 100\ \geq 80\%$$

The overall compliance, and the number of participants who are 0 - <50% compliant, 50 - <80% compliant and ≥80% compliant with eCOA assessments will be summarized for the Final Analysis.

18.1.2. UNSOLICITED AES, INCLUDING SAES

For each study group, the incidence rates (frequencies and percentages) of participants/events with unsolicited AEs (any, related, grade 3, leading to medical advice and related grade 3 respectively), including serious AE, occurring within 43-days (Days 1-43) post-dose of study interventions at Day 1 will be presented by SOC and PT. The incidence rates of participants/events with any unsolicited AEs will be summarized by country.

18.1.2.1. Relationship to Study Vaccination

Causality, as indicated by the Investigator is classed as "related" and "not related" to VNS/VV or MMR or *Havrix* or *Prevnar 13*. A "related" AE is defined as an AE with a relationship to study intervention as "related". If a participant reports the same AE more than once within that SOC/ PT, the AE with the worst-case relationship to study intervention will be used in the corresponding relationship summaries for each vaccination group.

18.1.3. UNSOLICITED AES, EXCLUDING SAES

For each study group, the incidence rates (frequencies and percentages) of participants/events with unsolicited AEs, excluding serious AE, occurring within 43-days (Days 1-43) post-dose of

study interventions at Day 1 will be presented by SOC and PT.

Immediate unsolicited AE is defined as an unsolicited AE that occurred within 30 minutes of vaccination. The immediate unsolicited AE flag is derived as follows: If the AE does not occur on the day of vaccination the flag is set to 'N'. Otherwise, if the AE occurs on the day of vaccination but happened before the vaccination then the flag is also set to 'N'. Otherwise, if the AE occurs on the day of vaccination and AE DATETIME minus Vaccination DATETIME is <= 30 minutes then set the flag to 'Y'. Otherwise, if the AE occurs on the day of vaccination and did not happen before the vaccination but either the time of vaccination or time of the AE is missing, then flag is set to 'U'. If the time of the AE is set to "00:00", then it will be assumed to be unknown and will be handled as missing. Immediate unsolicited AEs will be flagged in the listings.

18.1.4. SERIOUS AEs

For each study group, the incidence rates (frequencies and percentages) of participants with SAE occurring post-dose of study interventions at Day 1 will be presented by SOC and PT. Similar tabulation will be done for SAE with causal relationship to vaccination as assessed by the investigator; for fatal SAE and for causally related fatal SAE. Serious AEs will be recorded on the "Expedited Adverse Events" page of the eCRF. The incidence rates of participants with serious AEs will be summarized by country.

Listings of AEs and SAEs leading to discontinuation of study will be provided.

19. DATA NOT SUMMARIZED OR PRESENTED

The other variables and/or domains not summarized or presented are:

- Physical examination

These domains and/or variables will not be summarized or presented, but will be available in the

clinical study database, SDTM and/or ADaM datasets.

20. REFERENCES

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

Miettinen O., Nurminen M. Comparative analysis of 2 rates. Statistics in Medicine 1985; 4(2):213-26

Nauta J. Statistics in Clinical Vaccine Trials. 2010. Heidelberg: Springer.

APPENDIX 1. PROGRAMMING CONVENTIONS FOR OUTPUTS

IQVIA OUTPUT CONVENTIONS

Outputs will be presented according to the following IQVIA Output Conventions

Document Headers
All TFL is to include the following header:

GSK Vaccines Vaccine: *VNS and VV* Study 217212 (VNS 20-006) - *DELIVERY DESIGNATION*

where delivery designation is the name of the current delivery, e.g., DRY-RUN, FINAL ANALYSIS REPORT, etc

DATES & TIMES

Depending on data available, dates and times will take the form yyyy-mm-dd Thh:mm:ss.

SPELLING FORMAT

English US

PRESENTATION OF INTERVENTION GROUPS

For outputs, intervention groups will be represented as follows and in the given order:

Intervention Group	For Tables and Graphs	For Listings
VNS_Low	VNS Low	VNS Low
VNS_Med	VNS Med	VNS Med

Intervention Group	For Tables and Graphs	For Listings
VNS_High	VNS High	VNS High
VV_Lot1	VV	VV Lot1
VV_Lot2		VV Lot2

PRESENTATION OF VISITS

For outputs, visits will be represented as follows and in that order:

Short Name	Long Name
Visit 1	Visit 1 (Day 1)
Visit 2	Visit 2 (Day 15)
Visit 3	Visit 3 (Day 43)
Safety Follow-up	Safety Follow-up (Day 181)

LISTINGS

All listings will be ordered by the following (unless otherwise indicated in the template):

- Randomized intervention group (or intervention received if it's a safety output), first by active dose [by ascending dose group] and then control,
- Center-participant ID,
- Date (where applicable).

DECIMAL PLACES

Decimal places for categorical data

- For percentages one decimal will be displayed.
- Differences in percentages and their corresponding confidence limits will be displayed with one more decimal than the maximum number used to display the individual percentages, for example the difference between two percentages displayed with one decimal will be displayed with two decimals.

Decimal places for Demographic and baseline characteristics will be as follows:

- The mean, median, and standard deviation for continuous baseline characteristics (age) will be presented with one decimal.

Serological Summary Statistics:

- The number of decimals used when displaying geometric mean concentrations (GMC) and their confidence limits is shown in the following table:

GMC value	**Number of decimals**
<0.1	3
>=0.1 and <10	2
>=10 and <1000	1
>=1000	0

When multiple categories of GMC values are present in the same table, the number of decimals displayed should match that of the smallest category (i.e., the one with the higher number of decimals). For example, if GMC values of <0.1 appear in the same table as values of >=0.1 and <10 3 decimals should be displayed for both.

GMC ratios and their confidence limits will be displayed with 2 decimals regardless of the actual values.

APPENDIX 2. PARTIAL DATE CONVENTIONS

Imputed dates will NOT be presented in the listings.

When partially completed dates (i.e., with missing day or month) are used in calculations, the following standard rules will be applied:

- A missing day will be replaced by 15
- A missing day and month will be replaced by June 30th.

The following exceptions apply:

- Adverse event start dates with missing day:
  - If the event starts in the same month as the study intervention, the contents of AE.AESTRTPT (the flag indicating if the event occurred before or after vaccination) will be used to complete the date. If 'after vaccination' is selected, the imputed start date will match study dose given during that month. If 'before vaccination' is selected, the imputed date will be one day before the study intervention given during that month.
- Adverse event start dates with missing day and month:
  - If the event starts in the same year as study intervention, the contents of AE.AESTRTPT (the flag indicating if the event occurred before or after vaccination) will be used to complete the date. If 'after vaccination' is selected, the imputed start date will match the study intervention given during that year. If 'before vaccination' is selected, the imputed date will be one day before the) study intervention given during that year.

All other cases of incomplete AE or concomitant medication/vaccination start date will follow the standard rules above.

ALGORITHM FOR PRIOR / CONCOMITANT MEDICATIONS:

START DATE	STOP DATE	ACTION
Known	Known	If start date < study med start date, assign as prior If start date >= study med start date and start date <= Day 43, assign as concomitant
	Partial	Impute stop date as latest possible date (i.e., last day of month if day unknown or 31st December if day and month are unknown), then: If start date < study med start date, assign as prior If start date >= study med start date and start date <= Day 43, assign as concomitant
	Missing	If stop date is missing could never be assumed a prior medication If start date <= end of intervention, assign as concomitant
Partial	Known	Impute start date as earliest possible date (i.e., first day of month if day unknown or 1st January if day and month are unknown), then: If start date < study med start date, assign as prior If start date >= study med start date and start date <= Day 43, assign as concomitant

START DATE	STOP DATE	ACTION
	Partial	Impute start date as earliest possible date (i.e., first day of month if day unknown or 1st January if day and month are unknown) and impute stop date as latest possible date (i.e., last day of month if day unknown or 31st December if day and month are unknown), then: If stop date < study med start date, assign as prior If stop date >= study med start date and start date <= end of intervention, assign as concomitant
	Missing	Impute start date as earliest possible date (i.e., first day of month if day unknown or 1st January if day and month are unknown), then: If stop date is missing could never be assumed a prior medication If start date <= end of intervention, assign as concomitant
Missing	Known	If stop date < study med start date, assign as prior
	Partial	Impute stop date as latest possible date (i.e., last day of month if day unknown or 31st December if day and month are unknown), then: If stop date < study med start date, assign as prior
	Missing	Assign as concomitant

DocuSign

Certificate Of Completion

Envelope Id: PPD
Status: Completed
Subject: Complete with Docusign: GSK_217212(VNS 20-006)_ZZA47662_SAP_Final_v7.0_24Jun2024.docx
Project Code (Enter 0 for non-billable projects): ZZA47662
IQVIA ID (Login ID): PPD
Business Unit:
DSSR
Source Envelope:
Document Pages: 46
Signatures: 2
Envelope Originator:
Certificate Pages: 5
Initials: 0
PPD
AutoNav: Enabled
One IMS Way
EnvelopeId Stamping: Disabled
Plymouth Meeting, 19462
Time Zone: (UTC-08:00) Pacific Time (US & Canada)
PPD
IP Address: PPD

Record Tracking

Status: Original
6/24/2024 8:51:50 AM
Holder: PPD
Location: DocuSign

Signer Events	Signature	Timestamp
PPD Security Level: Email, Account Authentication (Required)	PPD Signature Adoption: Drawn on Device Signature ID: PPD Using IP Address: PPD With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	Sent: 6/24/2024 8:55:54 AM Viewed: 6/24/2024 9:04:33 AM Signed: 6/24/2024 9:05:03 AM
Electronic Record and Signature Disclosure: Accepted: 11/13/2020 12:14:20 AM ID: PPD		
PPD Security Level: Email, Account Authentication (Required)	PPD Signature Adoption: Pre-selected Style Signature ID: PPD Using IP Address: PPD With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	Sent: 6/24/2024 8:55:55 AM Viewed: 6/24/2024 9:13:02 AM Signed: 6/24/2024 9:13:36 AM
Electronic Record and Signature Disclosure: Accepted: 12/21/2021 1:15:11 AM ID: PPD		

In Person Signer Events	Signature	Timestamp

Editor Delivery Events	Status	Timestamp

Agent Delivery Events	Status	Timestamp

Intermediary Delivery Events	Status	Timestamp

Certified Delivery Events	Status	Timestamp

Carbon Copy Events	Status	Timestamp

Witness Events	Signature	Timestamp

Notary Events	Signature	Timestamp

Envelope Summary Events	Status	Timestamps
Envelope Sent	Hashed/Encrypted	6/24/2024 8:55:55 AM
Certified Delivered	Security Checked	6/24/2024 9:13:02 AM
Signing Complete	Security Checked	6/24/2024 9:13:36 AM
Completed	Security Checked	6/24/2024 9:13:36 AM

Payment Events	Status	Timestamps

Electronic Record and Signature Disclosure

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PDF Reader:	Acrobat® or similar software may be required to view and print PDF files
Screen Resolution:	1024 x 768 Recommended
Enabled Security Settings:	Allow per session cookies
Mobile Signing:	• Apple iOS 7.0 or above • Android 4.0 or above

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