Protocol C3671032

A PHASE 3, RANDOMIZED, DOUBLE-BLINDED, PLACEBO-CONTROLLED TRIAL TO EVALUATE THE SAFETY, TOLERABILITY, AND IMMUNOGENICITY OF RESPIRATORY SYNCYTIAL VIRUS (RSV) PREFUSION F SUBUNIT VACCINE IN PREGNANT PARTICIPANTS LIVING WITH HIV AND THEIR INFANTS

Statistical Analysis Plan (SAP)

Version: 2

Date: **21-Nov-2024**

TABLE OF CONTENTS

LIST OF TABLES

APPENDICES

1. VERSION HISTORY

Table 1. Summary of Changes

Version/ Date	Associated Protocol Amendment	Rationale	Specific Changes
1 26 Feb 2024	Original 23 Aug 2023	N/A	N/A
2 21-Nov-2024	Original 23 Aug 2023	Describe sensitivity analysis planned as corrective action for Quality Event	Section 6.1.1.1: repeated analysis of reactogenicity data excluding affected participants.

2. INTRODUCTION

This SAP provides the detailed methodology for summary and statistical analyses of the data collected in Study C3671032. A brief description of the study design and study objectives is given below. Subsequent sections describe analysis populations and give the definitions of the endpoints, followed by details of statistical reporting. A list of tables, listings, and figures; mockup shells; and programming rules are prepared separately based on the methods described in this document.

2.1. Modifications to the Analysis Plan Described in the Protocol

This document may modify the plans outlined in the protocol; however, any major modifications of the primary endpoint definition or its analysis will also be reflected in a protocol amendment.

A secondary endpoint (seroresponse immunogenicity) was added for the maternal participant group. The details are described in this SAP.

2.2. Study Objectives, Endpoints, and Estimands

Type	Objectives	Endpoints	Estimands
Maternal – Primary (Safety)	To describe the safety profile of RSVpreF in maternal participants living with HIV.	• Prespecified local reactions (pain at the injection site, redness, and swelling) • Prespecified systemic events (fever, nausea, diarrhea, vomiting, headache, fatigue, muscle pain, and joint pain) • AEs • AESIs • SAEs	In maternal participants living with HIV receiving 1 dose of the study intervention, the proportion of the following safety events reported: • Prespecified local reactions within 7 days after vaccination • Prespecified systemic events within 7 days after vaccination • AEs from the time of vaccination through 1 month after vaccination • AESIs throughout the study • SAEs throughout the study

Type	Objectives	Endpoints	Estimands
Maternal – Secondary (Immunogenicity)	To describe the immune responses elicited by RSVpreF in maternal participants living with HIV.	• RSV A and RSV B serum NTs	In maternal participants in compliance with the key protocol criteria (evaluable immunogenicity population): • GMT of NTs for RSV A and RSV B at each blood-sampling visit • GMFR of NTs for RSV A and RSV B from before vaccination to the postvaccination blood-sampling visit
Maternal – Exploratory (Immunogenicity)	To descriptively compare the immune responses elicited by RSVpreF between pregnant participants living with HIV from this study and pregnant participants without HIV from Study C3671008.	• RSV A and RSV B serum NTs	
Infant – Primary (Safety)	To describe the safety profile of RSVpreF.	• Specific birth outcomes • AEs from birth through 1 month of age • SAEs and NDCMCs from birth through 6 months of age	In infant participants born to maternal participants living with HIV receiving 1 dose of the study intervention, the percentage of participants with each safety endpoint
Infant – Exploratory (Immunogenicity)	To evaluate RSV serum NTs elicited by RSVpreF and transferred transplacentally.	• RSV A and RSV B serum NTs measured at birth	

2.2.1. Primary Estimand(s)

2.2.1.1. Safety Estimand – Maternal Participants

The safety primary estimand for maternal participants is defined by the following attributes:

Population: Maternal participants living with HIV receiving 1 dose of the study intervention.

Endpoints:

- Prespecified local reactions within 7 days after vaccination.
- Prespecified systemic events within 7 days after vaccination.

- AEs from the time of vaccination through 1 month after vaccination.
- AESIs throughout the study.
- SAEs throughout the study.

Treatment condition: The RSVpreF group or placebo group according to the study intervention administered.

Intercurrent events: There are no intercurrent events to be considered. All data collected after discontinuation or major protocol deviation would be included. Missing e-diary data will not be imputed. Missing AE dates and missing AE intensity data will be handled according to Pfizer safety rules.

Population-level summary: The percentage of maternal participants reporting local reactions, systemic events, AEs, AESIs, and SAEs in each group.

2.2.1.2. Safety Estimand – Infant Participants

The safety primary estimand for infant participants is defined by the following attributes:

Population: Infant participants born to maternal participants living with HIV receiving 1 dose of the study intervention.

Endpoints:

- Specific birth outcomes.
- AEs from birth through 1 month of age.
- SAEs and NDCMCs from birth through 6 months of age.

Treatment condition: The RSVpreF group or placebo group according to the study intervention administered.

Intercurrent events: There are no intercurrent events to be considered. All data collected after discontinuation or major protocol deviation would be included. Missing AE dates and missing AE intensity data will be handled according to Pfizer safety rules.

Population-level summary: The percentage of infant participants with specific birth outcomes, and the percentages for whom AEs, SAEs, and NDCMCs are reported in each group.

2.2.2. Secondary Estimand(s)

2.2.2.1. Immunogenicity Estimand – Maternal Participants

The immunogenicity secondary estimand for maternal participants is defined by the following attributes:

Population: Maternal participants living with HIV in compliance with the key protocol criteria (evaluable immunogenicity population).

Endpoints: RSV A and RSV B serum NTs.

Treatment condition: The randomized RSVpreF group or placebo group.

Intercurrent events: The following intercurrent events could impact the interpretation or the measurement of the immune response:

- The participant's having major protocol violations (eg, receiving a prohibited vaccine or treatment) that may alter the immune response and subsequently impact the vaccine protection.

The immunogenicity data after intercurrent events will be excluded (hypothetical strategy). The intercurrent events will be determined by clinical review of major protocol violations.

Missing serology results will not be imputed, as MCAR is assumed.

Population-level summary:

- The immune response, estimated by the GMFR from baseline in RSV A and RSV B serum NTs.
- GMR, estimated by the ratio of the GMTs for RSV A and RSV B serum NTs of the RSVpreF group to the placebo group.
- Seroresponse rates by vaccine group, defined as a ≥4-fold rise in serum NTs at delivery compared to baseline; or ≥4 times the LLOQ if the baseline titer is below the LLOQ.

2.3. Study Design

This is a Phase 3, multicenter, randomized, double-blinded, placebo-controlled study in which pregnant participants ≤49 years of age living with HIV will receive 1 dose of RSVpreF or placebo. Approximately 330 pregnant participants living with HIV will be assigned to either the RSVpreF or placebo group. Assessments will include descriptions of safety, tolerability, and immunogenicity in maternal participants, as well as safety and characteristics of transplacentally transferred antibodies in their infants.

Study-eligible, pregnant participants living with HIV providing informed consent will be referred to as "maternal participants" and will receive a single dose of RSVpreF or placebo (1:1 randomization). Follow-up for maternal participants will continue through pregnancy and until 6 months after delivery. Assessments will include evaluations of safety, tolerability, and immunogenicity of the vaccine in maternal participants.

Pregnant participants will participate in the study from enrollment during their pregnancy through approximately 6 months after delivery of their infants. The total duration will be up to approximately 10 months, depending on the participant's GA at the time of vaccination, and when the infant is actually born.

All eligible infant participants born to enrolled maternal participants will participate in the study from the time of birth and will be followed for up to 6 months after birth.

To assess immunogenicity, all maternal participants will have blood drawn at baseline (prior to vaccination) and at delivery. All infant participants will have cord blood collected at birth. Immune responses elicited by RSVpreF in maternal and infant participants in this study will be analyzed and will also be compared to immune responses elicited by RSVpreF in participants in the C3671008 study, in which RSVpreF efficacy was demonstrated.

3. ENDPOINTS AND BASELINE VARIABLES: DEFINITIONS AND CONVENTIONS

3.1. Primary Endpoint(s)

3.1.1. Safety Endpoints – Maternal Participants

- Local reactions (pain at the injection site, redness, and swelling) within 7 days after vaccination.
- Systemic events (fever, nausea, diarrhea, vomiting, headache, fatigue, muscle pain, and joint pain) within 7 days after vaccination.
- AEs from the time of vaccination through 1 month after vaccination.
- AESIs throughout the study.
- SAEs throughout the study.

3.1.1.1. Local Reactions and Systemic Events

The local reactions, including pain at the injection site, redness, and swelling, and the systemic events, including fever, nausea, diarrhea, vomiting, headache, fatigue, muscle pain, and joint pain, are reported in the e-diary and the PARREACT CRF page from Day 1 through Day 7 after vaccination, where Day 1 is the day of vaccination. For any missing response in the e-diary (including no e-diary data), participants will be asked by the investigator at the site visit to recall any reactogenicity via the PARREACT CRF page.

This section describes derivations with details for the assessment of reactogenicity data: severity level, duration, and onset day.

Severity

Redness and swelling will be measured by the maternal participant and recorded in measuring device units in the e-diary (range: 1 to 21). **Note:** An entry in the e-diary of 21 will be used to denote measurements ≥21. Measurements will be categorized during analysis as mild, moderate, or severe, based on the grading scale in Table 2. Measuring device units can be converted to centimeters according to the following scale: 1 measuring device unit = 0.5 cm. Pain at the injection site will be assessed by the participant as absent, mild, moderate, or severe according to the grading scale in Table 2.

Only an investigator or a qualified designee is able to classify a maternal participant's local reaction as Grade 4, after clinical evaluation of the maternal participant, documentation from another medically qualified source (eg, emergency room or hospital record), or contact with the maternal participant. If a maternal participant experiences a Grade 4 local reaction, the investigator must immediately notify the sponsor. Grade 4 local reactions will be collected on the CRF.

If a local reaction persists beyond the end of the 7-day e-diary follow-up period, the maternal participant or the participant's parent(s)/legal guardian (if a minor) will be requested to report that information and/or any new events that develop to the investigator or the study staff. The investigational site staff will continue to contact the maternal participant to assess and record the information until resolution. The investigator will enter this additional information in the maternal participant's source notes and CRF.

Table 2. Grading Scale for Local Reactions

	Mild Grade 1	Moderate Grade 2	Severe Grade 3	Grade 4[a]
Redness	>2.0 cm to 5.0 cm (5 to 10 measuring device units)	>5.0 cm to 10.0 cm (11 to 20 measuring device units)	>10 cm (>20 measuring device units)	Necrosis or exfoliative dermatitis
Swelling	>2.0 cm to 5.0 cm (5 to 10 measuring device units)	>5.0 cm to 10.0 cm (11 to 20 measuring device units)	>10 cm (>20 measuring device units)	Necrosis
Pain (at the injection site)	Does not interfere with activity	Interferes with activity	Prevents daily activity	Emergency room visit or hospitalization for severe pain at the injection site

a. Only an investigator or qualified designee is able to classify a maternal participant's local reaction as Grade 4, after clinical evaluation of the maternal participant, documentation from another medically qualified source (eg, emergency room or hospital record), or contact with the maternal participant or the participant's parent(s)/legal guardian (if a minor). Grade 4 local reactions will be collected on the CRF and assessed by the investigator or qualified designee.

Systemic events will be assessed by the maternal participant according to the grading scale in Table 3.

Only an investigator or qualified designee is able to classify a maternal participant's systemic event as Grade 4, after clinical evaluation of the maternal participant, documentation from another medically qualified source (eg, emergency room or hospital record), or contact with the maternal participant. If a maternal participant experiences a Grade 4 systemic event, the investigator must immediately notify the sponsor. Grade 4 systemic events will be collected on the CRF.

Further, if a systemic event persists beyond the end of the 7-day e-diary follow-up period, the maternal participant or the participant's parent(s)/legal guardian (if a minor) will be requested to report that information and/or any new events that develop to the investigator or the study staff. The investigational site staff will continue to call or visit the maternal participant to assess and record the information until resolution, as per local practice. The investigator will enter this additional information in the maternal participant's source notes and CRF.

Table 3. Grading Scale for Systemic Events

	Mild Grade 1	**Moderate Grade 2**	**Severe Grade 3**	**Grade 4[a]**
Fatigue (= tiredness in diaries)	Does not interfere with activity	Some interference with activity	Prevents daily routine activity	Emergency room visit or hospitalization for severe fatigue
Headache	Does not interfere with activity	Some interference with activity	Prevents daily routine activity	Emergency room visit or hospitalization for severe headache
Vomiting	1 to 2 times in 24 hours	>2 times in 24 hours	Requires IV hydration	Emergency room visit or hospitalization for severe vomiting
Nausea	Does not interfere with activity	Some interference with activity	Prevents daily routine activity	Emergency room visit or hospitalization for severe nausea
Diarrhea	2 to 3 loose stools in 24 hours	4 to 5 loose stools in 24 hours	6 or more loose stools in 24 hours	Emergency room visit or hospitalization for severe diarrhea

Table 3. Grading Scale for Systemic Events

	Mild Grade 1	Moderate Grade 2	Severe Grade 3	Grade 4[a]
Muscle pain	Does not interfere with activity	Some interference with activity	Prevents daily routine activity	Emergency room visit or hospitalization for severe muscle pain
Joint pain	Does not interfere with activity	Some interference with activity	Prevents daily routine activity	Emergency room visit or hospitalization for severe joint pain

a. Only an investigator or qualified designee is able to classify a maternal participant's systemic event as Grade 4, after clinical evaluation of the maternal participant, documentation from another medically qualified source (eg, emergency room or hospital record), or contact with the maternal participant or the participant's parent(s)/legal guardian (if a minor). Grade 4 systemic events will be collected on the CRF and assessed by the investigator or qualified designee.

Fever is defined as an oral temperature of ≥38.0°C (≥100.4°F). The highest temperature for each day will be recorded in the e-diary, where possible.

In the event of a fever on the last day the e-diary was completed, temperature will be measured daily until fever has resolved (1 day of temperature <38.0°C [<100.4°F]) in order to collect a stop date in the CRF.

Only an investigator or qualified designee is able to classify a maternal participant's fever as Grade 4, after clinical evaluation of the maternal participant, documentation from another medically qualified source (eg, emergency room or hospital record), or contact with the maternal participant or the participant's parent(s)/legal guardian (if a minor). Grade 4 fevers will be collected on the CRF and assessed by the investigator.

Temperature will be measured and recorded to 1 decimal place and then categorized during analysis as mild, moderate, or severe, based on the intensity grading scale provided in Table 4. Temperatures recorded in degrees Fahrenheit will be programmatically converted to degrees Celsius first for reporting.

Table 4. Ranges for Fever

	Mild Grade 1	Moderate Grade 2	Severe Grade 3	Grade 4[a]
Fever	≥38.0°C to 38.4°C	>38.4°C to 38.9°C	>38.9°C to 40.0°C	>40.0°C

a. Only an investigator or qualified designee is able to classify a maternal participant's fever as Grade 4, after clinical evaluation of the maternal participant, documentation from another medically qualified source (eg, emergency room or hospital record), or contact with the maternal participant or the participant's parent(s)/legal guardian (if a minor). Grade 4 fevers will be collected on the CRF and assessed by the investigator or qualified designee.

Maximum Severity

The maximum severity (highest grading) of each local reaction within 7 days after vaccination will be derived. The maximum severity will be derived as follows:

= "Missing," if values are missing for all days from Day 1 through Day 7.

= 0, if all reactions are reported as "no" or a combination of missing and "no" for all days from Day 1 through Day 7.

= *highest grade* (maximum severity) within 7 days after vaccination if the answer is not "no" for at least 1 day.

Maximum severity for systemic event after vaccination is derived similarly to maximum severity for each local reaction after vaccination.

If the local reaction/systemic event is captured in more than 1 data source, eg, the e-diary and the PARREACT CRF page, the highest grade across all sources will be used in the summary.

Maximum severity for any local reaction and any systemic event will be derived in a similar way to the individual local reactions and systemic events, respectively, except that the maximum severity level will be the maximum severity for any local reaction or any systemic event reported during the collection period.

Duration (First to Last Day Reported)

The duration (days) of each local reaction or systemic event will be calculated as the number of days from the start of the first reported reaction or event to the resolution of the last reported reaction or event, inclusive, after vaccination. For a reaction or event collected in the e-diary, the resolution day is defined as the last day on which the reaction or event is recorded in the e-diary if the reaction or event lasted 7 days or less, or defined as the day on which the reaction or event ended if it continued beyond Day 7 (the latter will be collected on the CRF) after vaccination. For a reaction or event collected with the CRF, the event end date will be considered the resolution date.

For a reaction or event collected in multiple sources, the earliest start date and the latest end date will be used in calculating duration. If there is no known resolution/end date, the duration will be reported as "unknown" or "missing."

Onset Day

The onset day of each local reaction or systemic event will be derived. Onset day is defined as the first day of reporting a reaction or event of any severity after vaccination. Change in severity during the event does not impact the originally determined onset day. For a reaction or event collected in multiple sources, the earliest date of reporting the reaction will be used in calculating the onset day.

3.1.1.2. Adverse Events

AEs will be categorized according to MedDRA terms.

In this study, for maternal participants, the investigator and site staff will ensure the active elicitation and collection of safety events as detailed below:

- The active collection period for nonserious AEs begins once informed consent has been provided and continues through a minimum of 28 calendar days after vaccination.
- The active collection period for AESIs and SAEs begins once informed consent has been provided and continues until the maternal participant completes the study.
- AEs occurring up to 48 hours after blood draws that are related to study procedures must be reported in the CRF.
- For participants who are screen failures, the active collection period ends when screen failure status is determined. If the participant withdraws from the study and also withdraws consent for the collection of future information, the active collection period ends when consent is withdrawn.
- During the active collection period, both nonserious AEs and SAEs are recorded on the CRF and will be categorized according to the current version of MedDRA at the time of reporting.
- The active collection period for AESIs is from the signing of the ICD until the end of the study for maternal participants. An AESI is to be recorded as an AE or SAE on the CRF. The AESI flag is captured in the CRF.

AESIs for maternal participants:

- Preterm delivery (delivery at <37 0/7 weeks' gestation).
- Diagnosis of Guillain-Barre syndrome.
- Diagnosis of acute polyneuropathy without an underlying etiology.
- Hypertensive disorders of pregnancy.
- Atrial fibrillation.

A 3-tier approach will be used to summarize AEs. Under this approach, AEs are classified into 1 of 3 tiers. Different analyses will be performed for different tiers.

- Tier 1 events: These are prespecified events of clinical importance and are identified in a list in the product's safety review plan. The AESIs are considered Tier 1 events for RSVpreF and will be analyzed for the entire study period.

- Tier 2 events: These are events that are not Tier 1 but are "relatively common." A MedDRA PT is defined as a Tier 2 event if there are 4 or more participants with the AE term in at least 1 vaccine group.
- Tier 3 events: These are events that are neither Tier 1 nor Tier 2.
- Additional supportive safety endpoints include related AEs, severe AEs, and immediate AEs (within the first 30 minutes after vaccination).

3.1.2. Safety Endpoints – Infant Participants

- Specific birth outcomes.
- AEs from birth through 1 month of age.
- SAEs and NDCMCs from birth through 6 months of age.

3.1.2.1. Specific Birth Outcomes

The infant birth outcome information will be collected, including the infant's birth data (eg, birth weight), GA, and Apgar score. The percentage of infant participants with specific birth outcomes (Appendix 2) will be provided.

3.1.2.2. Adverse Events

AEs will be categorized according to MedDRA terms. Reporting AEs in infant participants is similar to reporting AEs in maternal participants. The percentage of infant participants having AEs from birth through 1 month of age and the percentage of infant participants having SAEs and NDCMCs from birth through 6 months of age will be provided.

For the infant participant, the time period for actively eliciting and collecting safety events is detailed below:

- The active collection period for nonserious AEs begins at birth and continues through and including a minimum of 28 calendar days after birth.
- The active collection period for AESIs, NDCMCs, and SAEs begins at birth and continues through the last study visit.
- AEs occurring up to 48 hours after blood draws that are related to study procedures must be reported in the CRF.

AESIs for infant participants:

- Preterm birth (born at <37 0/7 weeks' gestation).
- Birth weight 1001 to 2500 g.

- Developmental delay.*

The following AESIs are to be reported as SAEs:

- Extremely preterm birth (born at <28 0/7 weeks' gestation).
- Extremely low birth weight (≤1000 g).

Events identified as both an AESI and an NDCMC should be reported as an AESI in the CRF.

*Developmental delay is to be assessed by a study staff member with clinical expertise using local guidelines for standard of care.

An NDCMC is defined as a disease or medical condition, not previously identified, that is expected to be persistent or otherwise long-lasting in its effects (eg, asthma).

3.2. Secondary Endpoint(s)

3.2.1. Immunogenicity Endpoints – Maternal Participants

- GMT of NTs for RSV A and RSV B at each blood-sampling visit.
- GMFR of NTs for RSV A and RSV B from before vaccination to the postvaccination blood-sampling visit.
- Seroresponse rate, defined as a ≥4-fold rise in serum NTs at delivery compared to baseline; or ≥4 times the LLOQ if the baseline titer is below the LLOQ.

3.3. Other Safety Endpoint(s)

3.3.1. Physical Examination, Including Vital Signs

3.3.1.1. Maternal Participants

A targeted physical examination will be performed on the same day or within 7 days before the vaccination visit and will note any clinically significant abnormalities within the following body systems: 1) Mandatory: general appearance; heart; lungs; abdomen; 2) Discretionary: skin; head, eyes, ears, nose, and throat; musculoskeletal; extremities; neurological; and lymph nodes. Significant medical, surgical, and obstetric history, and abnormal observations from the physical and obstetric examination, will be documented and recorded in the CRF.

Vital signs, including sitting systolic and diastolic blood pressure, heart rate, and body temperature, will be measured at the vaccination visit and recorded in the CRF.

3.3.1.2. Infant Participants

The physical examination will be performed within 72 hours after birth, if not performed as part of standard of care, and will include any clinically significant abnormalities within the following body systems: general appearance; skin; head, eyes, ears, nose, and throat; heart; lungs; abdomen; musculoskeletal; extremities; genitourinary, neurological; and lymph nodes.

A targeted physical examination will be performed at all scheduled in-clinic visits noting any clinically significant abnormalities in the site source documents. Newly identified abnormal findings must be recorded on source documents and, if considered clinically significant in the judgment of the investigator/examiner, on the AE page of the CRF.

Length, head circumference, and weight will also be measured and recorded.

Temperature, heart rate, and respiratory rate will be obtained as part of vital sign assessments.

3.3.2. Obstetric Examination and Pregnancy Outcomes

Obstetric history will be collected at screening. Obstetric examination findings will be collected at the vaccination visit. The assessments will include, but not be limited to, number of pregnancies, cesarean deliveries, spontaneous abortions, ectopic pregnancies, number of preterm deliveries, GA at vaccination, and fetal movement.

Vital signs, including sitting systolic and diastolic blood pressure, heart rate, and body temperature, will be measured at the vaccination visit and recorded in the CRF.

The following information regarding a participant's pregnancy outcome will be collected at delivery: date of delivery, location of delivery (medical facility, home, other), mode of delivery (vaginal, cesarean), cesarean delivery type (elective, semielective, emergency), delivery complications (yes, no), number of births, outcome at delivery (live delivery, stillbirth, induced/elective abortion, unknown), gross visual inspection of the aborted fetus/stillbirth (not done, no observed abnormalities, observed abnormalities), and fetal pathology performed (yes, no).

3.3.3. Birth Outcomes

Infant outcome at birth will be collected at the delivery visit and includes the following: GA (weeks, days); Apgar score at 1, 5, and 10 minutes; and infant outcome (normal, congenital malformation/anomaly, other neonatal problem, or unknown).

3.4. Exploratory/Tertiary Endpoint(s)

3.4.1. Immunogenicity Endpoints – Maternal Participants

- GMR of NTs for RSV A and RSV B at delivery from maternal participants living with HIV in this study compared to non–HIV-infected maternal participants from Study C3671008, estimated from an ANCOVA model (see Section 6.4.1).

3.4.2. Immunogenicity Endpoints – Infant Participants

- GMT of the RSV A and RSV B serum NTs at birth.

- GMR of NTs for RSV A and RSV B at birth from infant participants living with HIV in this study compared to non–HIV-infected infant participants from Study C3671008, estimated from an ANCOVA model (see Section 6.4.3).

3.5. Baseline and Other Variables

3.5.1. Baseline – Maternal Participants

Day 1 is defined as the day of vaccination for the maternal participants. Day 1 is considered the baseline visit for the maternal immunogenicity assessments. Day 1 is the start of the reporting period for local reactions/systemic events.

The demographic variables are age, sex, racial designation (Black/African American, American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, White, not reported or unknown), and ethnicity (Hispanic/Latino, non-Hispanic/non-Latino, and not reported).

For reporting of race, where more than 1 category is selected for race, the participant will be counted under the category "multiracial" for analysis.

Medical history will be categorized according to the current version of MedDRA at the time of reporting.

3.5.2. Baseline – Infant Participants

Day 1 is defined as the day of birth (Visit 1) for the infant participants.

Day 1 is considered the baseline visit for the following assessments in infant participants: immunogenicity (cord blood sample collected at birth), physical examination, and vital signs.

4. ANALYSIS SETS (POPULATIONS FOR ANALYSIS)

Analysis populations are defined for the statistical analysis of safety and immunogenicity results in the table below. For the specified criteria in each population definition that are not associated with unblinded or sensitive information (vaccination randomized or actually received, immunogenicity results, etc), available data for all participants will be assessed to determine if participants meet the criteria for inclusion in each analysis population prior to unblinding and releasing the database.

Population	Description
Enrolled	All participants who sign the ICD.
Randomized	All participants who are assigned a randomization number in the IRT system.
Evaluable immunogenicity – maternal	All maternal participants who are eligible, receive the study intervention to which they were randomized, have blood drawn for assay testing within the specified time frame, have valid and determinate assay results for the proposed analysis, and have no major protocol violations.
Evaluable immunogenicity – infant	All infant participants who are eligible, are born to the maternal participants who received the study intervention to which they were randomized, have blood drawn for assay testing within the specified time frame, have valid and determinate assay results for the proposed analysis, and have no major protocol violations.
mITT – maternal	All randomized participants who receive the study intervention and have at least 1 valid and determinate assay result after vaccination.
mITT – infant	All infant participants who are born to vaccinated maternal participants and have at least 1 valid and determinate assay result for the proposed analysis.
Safety – maternal	All randomized participants who receive at least 1 dose of the study intervention.
Safety – infant	All infant participants who are born to vaccinated maternal participants.

For determination of the evaluable immunogenicity population(s), major protocol violations will be determined by clinical review. A major protocol violation is a protocol violation that, in the opinion of the sponsor clinician, would materially affect assessment of immunogenicity, eg, a participant's receipt of a prohibited vaccine or medication that might affect immune response or a vaccination error with suspected decrease in potency of the vaccine. The sponsor clinician will identify those participants with a protocol violation prior to unblinding of the study.

5. GENERAL METHODOLOGY AND CONVENTIONS

5.1. Hypotheses and Decision Rules

There are no statistical hypotheses for this descriptive study.

5.2. General Methods

Descriptive summary statistics will be provided for all endpoints. Unless otherwise explicitly stated, descriptive statistics for continuous variables are n, mean, median, standard deviation, minimum, and maximum. Descriptive statistics for categorical variables are the percentage (%) and the n (the numerator) and N (the denominator) used in the calculation of the percentage.

All data will be presented separately for maternal and infant participants. The only exception is the combined analysis of maternal-to-infant placental transfer ratio (infant/mother) of RSV A and RSV B serum NTs.

5.2.1. Analyses for Binary Endpoints

Descriptive statistics for categorical variables are the percentage (%), the numerator (n) and the denominator (N) used in the percentage calculation, and the 2-sided 95% CIs where applicable.

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

For the between-group difference, the 2-sided 95% CI will be calculated using the Miettinen and Nurminen method.[2]

Three-Tier Approach for AE Summary

A 3-tier approach will be used to summarize AEs. For both Tier 1 (AESIs) and Tier 2 events, the 95% CIs for the difference in percentage of participants reporting the events between the RSVpreF and placebo groups will be calculated using the Miettinen and Nurminen method. In addition, for Tier 1 events, the Farrington-Manning p-values will be presented for the difference in percentage of participants reporting the events between the RSVpreF and placebo groups.

5.2.2. Analyses for Continuous Endpoints

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

5.2.2.1. Geometric Mean Titers

The GMT for each vaccine group will be calculated as the mean of the logarithmically transformed assay results and then exponentiating the mean. The 2-sided 95% CI will be obtained by exponentiating the limits of the CI for the mean of the logarithmically transformed assay results based on the t distribution.

5.2.2.2. Geometric Mean Ratio

The GMR will be calculated as the difference in the means of logarithmically transformed assay results between 2 vaccine groups and exponentiating the difference. The 2-sided 95% CI will be obtained by exponentiating the limits of the CI for the mean difference of the logarithmically transformed assay results based on the t distribution.

5.2.2.3. Geometric Mean Fold Rise

The GMFR for each vaccine group is defined as the geometric mean of the fold rises in the assay results from the specified time points. Only data from participants with nonmissing assay results at both time points will be included in the GMFR calculation.

GMFR will be calculated as the mean difference of logarithmically transformed assay results (postvaccination blood-sample visit – before vaccination) and exponentiating the mean difference. The 2-sided 95% CI will be obtained by exponentiating the limits of the CI for the mean difference of the logarithmically transformed assay results based on the t distribution.

5.2.2.4. Reverse Cumulative Distribution Curves

Empirical RCDCs for RSV A and RSV B serum NTs will be plotted as a step function of the proportion of participants with the assay results equal to or exceeding a specified value over the full range of the observed assay results. Data points will be joined by a step function with the line first going down and then to the right to the next assay value.

5.3. Methods to Manage Missing Data

5.3.1. Safety Data

Standard algorithms on handling missing AE dates and missing AE severity will be applied as described in Pfizer's Vaccine Statistics Rulebook.

5.3.1.1. Reactogenicity Data

For derived variables based on reactogenicity data, if any day of the 7-day e-diary or the PARREACT CRF page is available, the "any day (Day 1 to 7)" data will be considered nonmissing.

The reactogenicity data are collected in the e-diary, which allows participants to enter data later if for some reason they miss an earlier opportunity to do so. Additionally, for any e-diary entries that are out of the window to reenter the information in the e-diary recollection period, the data will be collected on-site via the PARREACT CRF page. Therefore, it is expected that very few e-diary entries would be missing.

5.3.2. Immunogenicity Data

For GMT analysis, a titer reported as < LLOQ will be converted to a value of ½ LLOQ. The LLOQs applicable for each assay will be included in the final release assay data.

For calculating a fold rise, < LLOQ will be converted to ½ LLOQ for a numerator, and < LLOQ will be converted to LLOQ for a denominator when only 1 of either the numerator or denominator is < LLOQ. If both the numerator and denominator are < LLOQ, then both will be converted in the same way.

Values that are designated as serum QNS, designated as indeterminate results, or recorded as "not done" will be set to "missing." No imputation will be done for these missing values.

6. ANALYSES AND SUMMARIES

6.1. Primary Endpoint(s)

6.1.1. Safety Endpoints – Maternal Participants

6.1.1.1. Local Reactions and Systemic Events

- Estimand strategy: Treatment policy.
- Analysis set(s): Safety – maternal (Section 4).
- Analysis time point(s): Day 1 through Day 7 after vaccination.
- Statistical method(s): Descriptive summary statistics.
- Method of handling intercurrent events (Section 2.2.1.1) and missing values (Section 5.3.1.1): There are no intercurrent events to be considered. All data collected after discontinuation or major protocol deviation will be included. Missing data will not be imputed.
- Descriptive statistics including the proportion (%), the numerator (n) and the denominator (N) used in the proportion calculation, and the 95% CI for percentage using the Clopper-Pearson method will be presented for each vaccine group.
    - Presence or absence of any local reaction or systemic event on each day (Days 1 to 7) after vaccination.
    - Presence or absence of any local reaction or systemic event on "any day (Day 1 to 7)" after vaccination.
    - Maximum severity of each local reaction or systemic event on "any day (Day 1 to 7)" after vaccination.
    - Maximum severity of any local reaction or systemic event on "any day (Day 1 to 7)" after vaccination.

- For each group, n, mean, median, minimum, and maximum will be presented by vaccine group for the following variables for each local reaction and each systemic event:
    - Duration of each local reaction or systemic event after vaccination.
    - Onset day of each local reaction or systemic event after vaccination.
- Bar charts with the proportions of participants for each and any local reaction and each and any systemic event throughout the 7 days will be plotted for each vaccine group. The bars will be divided into severity categories to highlight the proportions of participants by maximum severity.
- At one site, #1011, a study co-ordinator was found to have entered e-diary data on behalf of some study participants. It was not possible to verify these data had been collected accurately, and therefore summaries of local and systemic reactogenicity will be repeated excluding the affected participants subjects. The issue is confined to e-diary data so other summaries of safety data are unaffected.

6.1.1.2. Adverse Events

- Estimand strategy: Treatment policy.
- Analysis set(s): Safety – maternal (Section 4).
- Analysis time point(s): From the time of vaccination through 1 month after vaccination.
- Statistical method(s): Descriptive summary statistics for Tier 3 events; difference and 95% CI between the RSVpreF group and the placebo group for Tier 1 and Tier 2 events.
- Method of handling intercurrent events (Section 2.2.1.1) and missing values (Section 5.3.1): There are no intercurrent events to be considered. All data collected after discontinuation or major protocol deviation will be included. Missing AE dates and missing AE intensity will be handled according to Pfizer safety rules.
- For each group, the number of participants with AEs within 1 month (28 days) after vaccination (n), percentage, and 95% CI will be presented for any AE, each SOC, and each PT within each SOC, by vaccine group. For AEs classified as Tier 2 events, the difference in proportions and associated 2-sided 95% CI between the RSVpreF group and placebo group will be presented in the summary tables.
- To support the assessment of AEs, the following AEs will be summarized with the same analysis population for each vaccine group:
    - Immediate AEs.
    - Related AEs.

- Severe AEs.

Nonserious AEs that were collected before vaccination or more than 1 month after vaccination (outside of the reporting period) will be included in the AE listings. A separate summary of AEs before vaccination will be provided.

6.1.1.3. AESIs Throughout the Study

- Estimand strategy: Treatment policy.
- Population: Safety – maternal (Section 4).
- Statistical method/test: Difference and 95% CI between the RSVpreF group and the placebo group.
- Method of handling intercurrent events (Section 2.2.1.1) and missing values (Section 5.3.1): There are no intercurrent events to be considered. All data collected after discontinuation or major protocol deviation will be included. Missing AE dates and missing AE intensity will be handled according to Pfizer safety rules.
- For each group, the number of participants with AESIs throughout the study (n), percentage, and 95% CI will be presented for any event, each SOC, and each PT within each SOC, by vaccine group. For AESIs, the difference in proportions and associated 2-sided 95% CI between the RSVpreF group and placebo group will be presented in the summary table. In addition, the Farrington-Manning p-values will also be presented for the difference between groups.
- A listing of AESIs will be generated.

6.1.1.4. SAEs Throughout the Study

- Estimand strategy: Treatment policy.
- Population: Safety – maternal (Section 4).
- Statistical method/test: Descriptive summary statistics.
- Method of handling intercurrent events (Section 2.2.1.1) and missing values (Section 5.3.1): There are no intercurrent events to be considered. All data collected after discontinuation or major protocol deviation will be included. Missing AE dates and missing AE intensity will be handled according to Pfizer safety rules.
- For each group, the number of participants with SAEs throughout the study (n), percentage, and 95% CI will be presented for any event, each SOC, and each PT within each SOC, by vaccine group.

- To support the assessment of SAEs, the following SAEs will be summarized with the same analysis population for each vaccine group:
  - Related SAEs.
  - Severe SAEs.

6.1.2. Safety Endpoints – Infant Participants

6.1.2.1. Specific Birth Outcomes

- Estimand strategy: Treatment policy.
- Population: Safety – infant (Section 4).
- Statistical method/test: Descriptive summary statistics.
- Method of handling intercurrent events (Section 2.2.1.2) and missing values (Section 5.3.1): There are no intercurrent events to be considered. All data collected after discontinuation or major protocol deviation will be included. Missing AE dates and missing AE intensity will be handled according to Pfizer safety rules.
- For each group, the number and proportion of participants with each specific birth outcome (Appendix 2) will be presented by vaccine group. In addition, the difference in proportions and associated 2-sided 95% CI between the RSVpreF group and placebo group will be presented.

6.1.2.2. AEs From Birth Through 1 Month of Age

- Estimand strategy: Treatment policy.
- Population: Safety – infant (Section 4).
- Statistical method/test: Descriptive summary statistics for Tier 3 events; difference and 95% CI between the RSVpreF group and placebo group for Tier 2 events. No Tier 1 events are identified.
- Method of handling intercurrent events (Section 2.2.1.2) and missing values (Section 5.3.1): There are no intercurrent events to be considered. All data collected after discontinuation or major protocol deviation will be included. Missing AE dates and missing AE intensity will be handled according to Pfizer safety rules.
- For each group, the number and proportion of participants with AEs from birth through 1 month of age will be presented for any AE, each SOC, and each PT within each SOC, by vaccine group. For AEs classified as Tier 2 events, the difference in proportions and associated 2-sided 95% CI between the RSVpreF group and placebo group will be presented.

6.1.2.3. SAEs and NDCMC From Birth Through 6 Months of Age

- Estimand strategy: Treatment policy.
- Population: Safety – infant (Section 4).
- Statistical method/test: Descriptive summary statistics.
- Method of handling intercurrent events (Section 2.2.1.2) and missing values (Section 5.3.1): There are no intercurrent events to be considered. All data collected after discontinuation or major protocol deviation will be included. Missing AE dates and missing AE intensity will be handled according to Pfizer safety rules.
- For each group, the number of participants with SAEs and NDCMCs from birth through 6 months of age (n), percentage, and 95% CI will be presented (in separate outputs) for any event, each SOC, and each PT within each SOC, by vaccine group.

6.1.2.4. AESIs Through 6 Months of Age

- Estimand strategy: Treatment policy.
- Population: Safety – infant (Section 4).
- Statistical method/test: Descriptive summary statistics.
- Method of handling intercurrent events (Section 2.2.1.2) and missing values (Section 5.3.1): There are no intercurrent events to be considered. All data collected after discontinuation or major protocol deviation will be included. Missing AE dates and missing AE intensity will be handled according to Pfizer safety rules.
- For each group, the number of participants with AESIs from birth through 6 months of age (n), percentage, and 95% CI will be presented for any event, each SOC, and each PT within each SOC, by vaccine group. For AESIs, the difference in proportions and associated 2-sided 95% CI between the RSVpreF group and placebo group will be presented in the summary table. In addition, the Farrington-Manning p-values will also be presented for the difference between groups.
- A listing of AESIs will be generated.

6.2. Secondary Endpoint(s)

6.2.1. Immunogenicity Endpoint – Maternal Participants

6.2.1.1. Main Analysis

- Estimand strategy: Hypothetical.
- Population: Evaluable immunogenicity – maternal (Section 4).

- Method of handling intercurrent events (Section 2.2.2.1) and missing values (Section 5.3.2): The immunogenicity data after intercurrent events will be excluded. Missing serology results will not be imputed, as MCAR is assumed.

- Statistical method/test: Descriptive summary

    - GMTs of RSV A and RSV B serum NTs will be summarized for each vaccine group, along with associated 2-sided 95% CIs.

    - GMRs, the ratio of the GMTs for RSV A and RSV B serum NTs of the RSVpreF group to the placebo group, before vaccination and at the postvaccination blood-sampling visit will be calculated, along with associated 2-sided 95% CIs.

    - GMFRs and associated 2-sided 95% CIs will be provided for RSV A and RSV B serum NTs from before vaccination to the postvaccination blood-sampling visit for each vaccine group.

    - Empirical RCDCs for RSV A and RSV B serum NTs for the prespecified time points and vaccine groups will be generated.

All of the above descriptive summaries are also applied to RSV A/B serum NTs.

    - Seroresponse rates by vaccine group, defined as a ≥4-fold rise in RSV A and RSV B serum NTs at delivery compared to baseline; or ≥4 times the LLOQ if the baseline titer is below the LLOQ.

6.2.1.2. Sensitivity/Supplementary Analysis

The main analysis will also be performed based on the mITT population. This analysis will be performed only if there is enough difference (eg, ~10%) between the evaluable immunogenicity population and the mITT population.

6.3. Other Safety Summaries and Analyses Endpoint(s)

6.3.1. Adverse Events

It should be recognized that most studies are not designed to reliably demonstrate a causal relationship between the use of a pharmaceutical product and an AE or a group of AEs. As such, safety analysis is generally considered as an exploratory analysis and its purpose is to generate hypotheses for further investigation. The 3-tier approach facilitates this exploratory analysis. There will be no adjustment for multiple comparison in the analyses.

Analyses and summaries of primary AE endpoints using the 3-tier approach are described in detail in Section 6.1.1 and Section 6.1.2.

Listings of participants reporting any AE and immediate AEs, and listings of all reported AEs, will be generated. In addition, nonserious AEs that were collected before vaccination or more than 1 month after vaccination (outside of the reporting period) will be included in the AE listings. A separate summary of AEs before vaccination will be provided.

6.3.2. Reactogenicity

Analysis and summaries of primary reactogenicity endpoints are described in Section 6.1.1.1.

In addition, participant data listings will be provided for all reactogenicity data (separate for local reactions and systemic events) as well as a listing for maternal participants experiencing severe redness or swelling.

6.3.3. Physical Examination, Including Vital Signs

Descriptive summaries (counts and percentages) and listings based on the safety populations (maternal and infant) might be provided in accordance with Pfizer reporting standards. All summaries and listings for these data will be generated separately for maternal and infant participants.

6.3.4. Obstetric Examination and Pregnancy Outcome

Descriptive summaries and data listings will be generated for the obstetric examination findings and pregnancy outcomes. The summaries and listings for these data will be generated only for maternal participants.

6.3.5. Birth Outcomes

Descriptive summaries and data listings will be generated for the birth outcomes. The summaries and listings for these data will be generated only for infant participants. In addition to the information collected in the CRF, the following groups will also be presented for the GA at birth: ≥24 to <28 weeks, ≥28 to <34 weeks, ≥34 to <37 weeks, ≥37 to <42 weeks, and ≥42 weeks.

6.4. Exploratory/Tertiary Endpoint(s)

6.4.1. Immunogenicity Endpoint – Maternal Participants

- Estimand strategy: Hypothetical.
- Population: Evaluable immunogenicity – maternal (Section 4).
- Method of handling intercurrent events and missing values is similar to Section 6.2.1: The immunogenicity data after intercurrent events will be excluded. Missing serology results will not be imputed, as MCAR is assumed.
- Statistical method/test: Comparison between maternal participants living with HIV in this study and non–HIV-infected maternal participants from Study C3671008.
    - The comparison will be based on participants with the same geographic locations from Study C3671008.
    - The GMR will be estimated from an ANCOVA model, including adjustment for time from vaccination to delivery, and may include other covariates.

- The GMRs at delivery after vaccination will be provided along with associated 2-sided 95% CIs.

6.4.2. Immunogenicity Endpoint – Infant Participants

- Estimand strategy: Hypothetical.
- Population: Evaluable immunogenicity – infant (Section 4).
- Method of handling intercurrent events and missing values in infant participants is similar to maternal participants in Section 2.2.2.1: The immunogenicity data after intercurrent events will be excluded. Missing serology results will not be imputed, as MCAR is assumed.
- Statistical method/test: Descriptive summary statistics.
  - GMT of the RSV A and RSV B serum NTs at birth, by vaccine group.
  - GMR, estimated by the ratio of the GMTs for RSV A and RSV B serum NTs of the RSVpreF group to the placebo group.
  - Geometric means of the transplacental transfer ratio and associated 2-sided 95% CIs will be provided for RSV A, RSV B, and combined RSV A/B serum NTs. For each mother-infant dyad, the transfer ratio will be calculated as the ratio of the infant's RSV serum NT at birth to the mother's RSV serum NT at delivery. Group geometric means and CIs are calculated in the same way as for similar endpoints using the fold rise calculated above.

All of the above descriptive summaries are also applied to RSV A/B serum NTs.

6.4.3. Immunogenicity Endpoint – Infant Participants

- Estimand strategy: Hypothetical.
- Population: Evaluable immunogenicity – infant (Section 4).
- Method of handling intercurrent events and missing values is similar to Section 6.2.1: The immunogenicity data after intercurrent events will be excluded. Missing serology results will not be imputed, as MCAR is assumed.
- Statistical method/test: Comparison between infant participants living with HIV in this study and non–HIV-infected infant participants from Study C3671008.
  - The comparison will be based on participants with the same geographic locations from Study C3671008.

- The GMR will be estimated from an ANCOVA model, including adjustment for time from maternal vaccination to delivery, and may include other covariates.
- The GMRs at birth will be provided along with associated 2-sided 95% CIs.

6.5. Subset Analyses

The immunogenicity endpoints for maternal and infant participants (except for the ones that will be compared with Study C3671008) will be analyzed by GA-at-vaccination groups for RSV A, RSV B, and RSV A/B serum NTs.

6.6. Baseline and Other Summaries and Analyses

6.6.1. Baseline Summaries

6.6.1.1. Maternal Participants

Descriptive summary statistics for demographic characteristics (age at vaccination, sex, race, ethnicity, and GA at vaccination), medical history, and obstetric history will be generated, by vaccine group and overall, based on the maternal safety population.

Participant data listings for demography and baseline characteristics data will also be generated.

6.6.1.2. Infant Participants

Descriptive summary statistics for demographic characteristics will be generated by vaccine group, based on the infant safety population.

Participant data listings for demography and other infant data will also be generated.

6.6.2. Study Conduct and Participant Disposition

The number and proportion of randomized participants will be included in the participant disposition summary. In addition, participants who completed the delivery visit, those who withdrew before delivery, along with the reasons for withdrawal, those who completed the 6-month postdelivery visit, and those who withdrew before the 6-month postdelivery visit, along with the reasons for withdrawal, will be tabulated by vaccine group, separately, for maternal and infant participants. The reasons for withdrawal will be those as specified in the database. This will be created only for infants.

Participant disposition tables will be generated separately for maternal and infant participants.

Participants excluded from the evaluable immunogenicity (maternal and infant) and mITT immunogenicity (maternal and infant) populations will also be summarized with reasons for exclusion. These summaries will be generated separately for maternal and infant participants.

The numbers and percentage of participants who were randomized, were vaccinated, and had blood drawn within the protocol-specified time frame, and outside the specified window, will be tabulated by vaccine group. These summaries will be generated separately for maternal and infant participants.

The numbers and proportions of participants with e-diary data not transmitted, transmitted by day (Days 1 to 7), and transmitted on "all days" will be summarized by vaccine group. These summaries will be generated only for maternal participants.

Data listings for participants who withdrew during the study will be generated. In addition, data listings for participants excluded from different populations will be generated separately. These listings will be generated separately for maternal and infant participants.

The important protocol deviations listings will be generated separately for maternal and infant participants.

6.6.3. Concomitant Medications and Nondrug Treatments

Nonstudy vaccines and medications taken during pregnancy or during the study will be categorized according to the WHO Drug Dictionary and summarized in accordance with the sponsor reporting standards. These will be generated (if needed) separately for maternal and infant participants.

7. INTERIM ANALYSES

7.1. Introduction

No formal interim analysis will be conducted for this study. The analysis will be performed after all participants completed the study and when all the data are available.

The study will use an independent EDMC, which is composed of external members. The EDMC will monitor the safety of the participants in the study.

7.2. Interim Analyses and Summaries

Not applicable.

8. REFERENCES

1. Newcombe RG. Two-sided confidence intervals for the single proportion: comparison of seven methods. Stat Med. 1998;17(8):857-72.

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

Appendix 1. List of Abbreviations

Abbreviation	Term
AE	adverse event
AESI	adverse event of special interest
ANCOVA	analysis of covariance
Apgar	appearance, pulse, grimace, activity, and respiration
CI	confidence interval
CRF	case report form
e-diary	electronic diary
EDMC	external data monitoring committee
GA	gestational age
GMFR	geometric mean fold rise
GMR	geometric mean ratio
GMT	geometric mean titer
HIV	human immunodeficiency virus
ICD	informed consent document
IRT	interactive response technology
IV	intravenous
LLOQ	lower limit of quantitation
MCAR	missing completely at random
MedDRA	Medical Dictionary for Regulatory Activities
mITT	modified intent-to-treat
N/A	not applicable
NDCMC	newly diagnosed chronic medical condition
NT	neutralizing titer
PARREACT	participant-reported reactogenicity
PT	preferred term
QNS	quantity not sufficient
RCDC	reverse cumulative distribution curve
RSV	respiratory syncytial virus
RSV A	respiratory syncytial virus subgroup A
RSV B	respiratory syncytial virus subgroup B
RSVpreF	respiratory syncytial virus stabilized prefusion F subunit vaccine
SAE	serious adverse event
SAP	statistical analysis plan
SOC	system organ class
WHO	World Health Organization

Appendix 2. Specific Birth Outcomes

- Specific birth outcomes of interest for this study include:
  - AEs categorized as AESIs in the database
  - Neonatal death
  - Congenital malformations/anomalies
  - Other neonatal problems
  - Final Apgar score (at either 1, 5, or 10 minutes) less than 7
  - GA at birth
  - Length of hospitalization at birth

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Signed By:	Date(GMT)	Signing Capacity
PPD	21-Nov-2024 13:03:12	Final Approval