GlaxoSmithKline	**Statistical Analysis Plan**
Detailed Title:	A Phase 1/2 randomised observer-blind placebo-controlled study to evaluate the safety, reactogenicity and immunogenicity of different dose levels of GSK Biologicals' investigational unadjuvanted RSV maternal vaccine (GSK3888550A) compared to placebo when administered to healthy non-pregnant women aged 18-45 years
eTrack study number and Abbreviated Title	208068 (RSV-MAT-001)
Scope:	All data pertaining to the above study
Date of Statistical Analysis Plan	Final: 25-Oct-2018
Co-ordinating author:	PPD (Expert Biostatistician)
Reviewed by:	PPD (Clinical and Epidemiology Project Lead) PPD (Clinical Research and Development Lead) PPD (Lead statistician) PPD (Lead statistical analyst) PPD (Scientific writer) PPD (Regulatory Affair) PPD (SERM physician) PPD (Public disclosure representative)
Approved by:	PPD (Clinical and Epidemiology Project Lead); PPD (Clinical Research and Development Lead); PPD (Lead statistician); PPD (Lead stat Analyst); PPD (Study Statistician)

APP 9000058193 Statistical Analysis Plan Template (Effective date: 14 April 2017)

TABLE OF CONTENTS

PAGE

LIST OF TABLES

PAGE

LIST OF FIGURES

PAGE

LIST OF TEMPLATES

PAGE

LIST OF ABBREVIATIONS

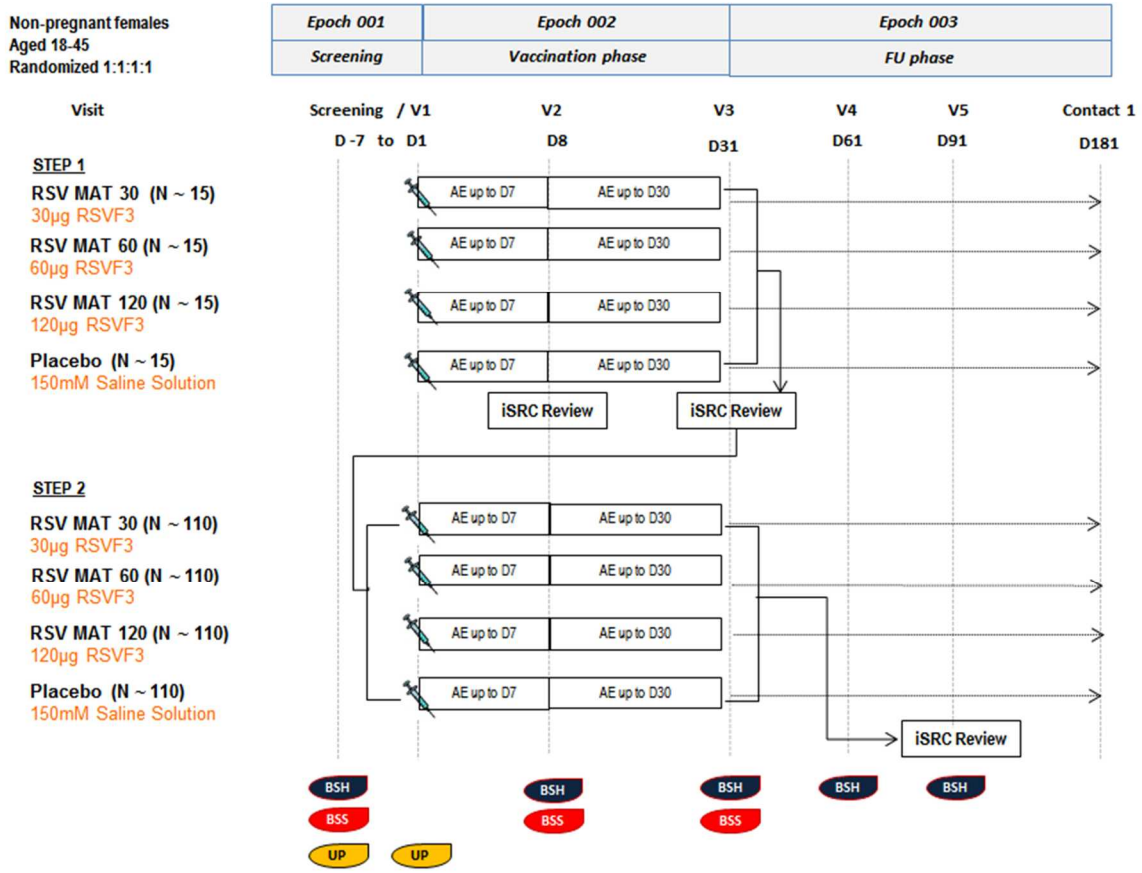
AE	Adverse event
ANCOVA	Analysis of Covariance
ANOVA	Analysis of Variance
CI	Confidence Interval
ELISA	Enzyme-linked immunosorbent assay
ES	Exposed Set
GMC	Geometric mean antibody concentration
GMT	Geometric mean antibody titre
LL	Lower Limit of the confidence interval
MedDRA	Medical Dictionary for Regulatory Activities
N.A.	Not Applicable
PD	Protocol Deviation
PPS	Per Protocol Set
SAE	Serious adverse event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SR	Study Report
TFL	Tables Figures and Listings
TOC	Table of Content
UL	Upper Limit of the confidence interval

1. DOCUMENT HISTORY

Date	Description	Protocol Version
25-OCT-2018	first version	Final Version 2- 13-AUG-2018

2. STUDY DESIGN

Figure 1 Study Design



AE – Adverse Events: solicited (Day 1 to Day 7); unsolicited (Day 1 to Day 30) and serious (Enrolment to Study conclusion)

BSS – Blood samples for haematology/biochemistry will be collected (~5.5 mL) from all subjects at Screening, Visit 2 (Day 8), and Visit 3 (Day 31)

BSH – Blood samples for humoral immunogenicity will be collected (~30 mL) from all subjects at Screening, Visit 2 (Day 8) Visit 3 (Day 31), Visit 4 (Day 61), and Visit 5 (Day 91)

iSRC – Internal Safety Review Committee

Contact 1- will be completed for all subjects at Day 181 (preferred contact is Phone Call)

RSV MAT 30/60/120 – RSV maternal 30/60/120µg, respectively, of the RSV maternal vaccine

Screening can occur ≤ 7 days prior to Visit 1 or on the same day, when possible

UP – Urine Pregnancy test (serum pregnancy test in country/local specific regulation) from all subjects (if Screening and Visit 1 are on the same day UP will not be repeated)

- **Experimental design**: Phase I/II, randomised, observer-blind, placebo control, multicentre study with four parallel groups
- **Duration of the study:** for each subject enrolled will be approximately 6 months from Visit 1.
  - Epoch 001: Screening Visit
  - Epoch 002: Active Vaccination phase starting at (Day 1) and concluding at, and including, Visit 3 (Day 31)
  - Epoch 003: Long Term Follow-up starting after Visit 3 (Day 31) and concluding at Contact 1 (Day181)

Any safety data collected beyond Day 31 will be collected in Epoch 003.

- **Primary Completion Date**: Visit 3 (Day 31) or last visit of Epoch 002
- **Control:** placebo control
- **Vaccination schedule**: Single intramuscular injection at Visit 1 (Day 1)
- **Treatment allocation:** Subjects will be randomised using a centralized randomisation system on internet (SBIR) at Visit 1 (Day 1). The randomisation algorithm will use a minimization procedure accounting for age (18 - 32 years or 33 - 45 years) and centre.
- **Blinding:**

Table 1 Blinding of study epochs

Study Epochs	Blinding
001	N/A
002	observer-blind
003	single-blind *

* The study will be conducted in an observer-blind fashion through Day 91. After this day, the study will continue in a single-blind fashion.

- **Sampling schedule**
  - **Blood samples for haematology/biochemistry**: will be collected (~5.5 mL) from all subjects at Screening, Visit 2 (Day 8), Visit 3 (Day 31) and any Unscheduled Visit(s).
  - **Blood samples for humoral immunogenicity:** will be collected (~30 mL) from all subjects at Screening, Visit 2 (Day 8), Visit 3 (Day 31), Visit 4 (Day 61) and Visit 5 (Day 91).
- **Safety monitoring**: This study will be monitored by a blinded SRT and by an unblinded iSRC. The analyses for iSRC evaluation will be described in SAP for iSRC.

3. OBJECTIVES

3.1. Primary objective

- To evaluate the safety and reactogenicity of three dose levels (30, 60, 120 µg) of the RSV maternal investigational vaccine administered as a single intramuscular injection, as compared to placebo up to 1-month post vaccination (Day 31).

3.2. Secondary objective

- To evaluate the safety of three dose levels (30, 60, 120µg) of the RSV maternal investigational vaccine compared to placebo up to 6 months post vaccination (Day 181).
- To evaluate the humoral immune response to three dose levels (30, 60, 120µg) of the RSV maternal investigational vaccine compared to placebo up to 3 months post vaccination (Day 91).

3.3. Tertiary objective

- To further evaluate the humoral immune response to the RSV maternal vaccine.

4. ENDPOINTS

4.1. Primary endpoints

- Occurrence of any adverse events (AEs) from vaccination during a 30-day follow up period, for all subjects in all groups:
  - Occurrence of each solicited local and general symptom during a 7-day follow-up period;
  - Occurrence of any unsolicited AE during a 30-day follow up period;
  - Occurrence of Serious AEs during a 30-day follow up period;
  - Occurrence of any haematological (Leukocytes, Neutrophils, Lymphocytes, Eosinophils, Haemoglobin, Platelets) and biochemical (alanine aminotransferase [ALT], aspartate aminotransferase [AST], creatinine, blood urea nitrogen [BUN]) laboratory abnormalities at Day 8 and Day 31.

4.2. Secondary endpoints

- Occurrence of SAEs from vaccination up to Day 91 and up to Day 181 for all subjects, in all groups.
- Humoral immune response to the investigational vaccine at Day 8, Day 31, Day 61 and Day 91 for all subjects in each investigational RSV vaccine groups:
  - RSV-A neutralising antibody (Nab) titres;
  - RSVPreF3 IgG antibody concentration.

4.3. Tertiary endpoint

- Additional humoral response which may include but not limited to, RSVPreF3 specific IgG1 subclass antibody concentrations, RSV-B neutralising antibody titres, antibody competing for binding to specific epitopes on RSVPreF3 and antibody concentrations to residual host cell proteins in the RSVPreF3 vaccines.

5. ANALYSIS SETS

5.1. Definition

Two cohorts will be defined for the purpose of the analysis: the Exposed Set (ES) and the Per-protocol set (PPS) for analysis of immunogenicity. All analyses will be performed per treatment actually administered.

5.1.1. Exposed Set (ES)

The ES will include all subjects with study vaccine administration documented.

- A **safety** analysis based on the ES will include all vaccinated subjects.
- An **immunogenicity** analysis based on the ES will include all vaccinated subjects for whom immunogenicity data are available.

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

The PPS for immunogenicity will be defined by time-point (Day 8, Day 31, Day 61 and Day 91) and will include all vaccinated subjects:

- Meeting all eligibility criteria (i.e. no protocol violation linked to the inclusion/ exclusion criteria, including age);
- Who received the study vaccine according to protocol procedures;
- Who did not receive a concomitant vaccination/medication/product leading to elimination from the PPS analysis up to the corresponding time-point as described in Section 6.6 of the protocol;
- Who did not present with an intercurrent medical condition leading to elimination from the PPS analysis up to the corresponding time-point, as described in Section 6.7 of the protocol;
- Who complied with the post-vaccination immunogenicity blood sampling schedule at the corresponding time-point, as specified in Table 2 of the SAP;
- For whom post-vaccination immunogenicity results are available for at least 1 assay at the corresponding time-point.
- The intervals allowed for the inclusion in the PPS for analysis of immunogenicity as specified in Table 2 of the SAP as bellow:

Table 2 Intervals between study visits

	Interval	Optimal length of interval	Allowed interval for PPS immunogenicity
Interval to be considered for enrollment	DOB → Visit 1 (Day 1)	18-45 years	18-45 years
	SCR – Visit 1 (Day 1)	0-7 days	0-7 days
Interval to be considered for blood sampling	Visit 1 (Day 1) → Visit 2 (Day 8)	7 days	7 - 10 days
	Visit 1 (Day 1) → Visit 3 (Day 31)	30 days	30 - 45 days
	Visit 1 (Day 1) → Visit 4 (Day 61)	60 days	56 – 70 days
	Visit 1 (Day 1) → Visit 5 (Day 91)	90 days	86 - 100 days

When presenting different time-points, the PPS for immunogenicity will be adapted for each time-point (Day 8, Day 31, Day 61 and Day 91).

5.2. Criteria for eliminating data from Analysis Sets

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

5.2.1. Elimination from Exposed Set (ES)

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

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

5.2.2.1. Excluded subjects

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

Code	Condition under which the code is used
900	Invalid informed consent or fraud data (*Subjects receiving a code 900 should not receive any other elimination codes)*
1030	Study vaccine not administered at all (*Subjects receiving a code 1030 should not receive any other elimination codes)*
1050	Randomization failure (subject not randomized in the correct group) *Comment: To check for manual randomisation, treatment not compatible with one assigned by SBIR*
1060	Randomization code was broken
1070**	Study vaccine dose not administered according to protocol Incorrect volume of the vaccine given Administration not according to protocol for reason specified by the investigator, other than side, site and route Site of the injection of vaccine is wrong or unknown Route of the study vaccine is wrong or unknown Wrong reconstitution of administered vaccine
1080	Vaccine temperature deviation
1090	Expired vaccine administered
2010	Protocol violation (inclusion/exclusion criteria including age) SCR – VIST 1 – 0-7 days# DOB – VISIT 1 – 18-45 years

*Attribution of these elimcodes to subject need CRDL review of individual listing
** Attribution of code 1070 to a subject requires CRDL confirmation
# need to be confirmed in the Pre-analysis meeting

5.2.2.2. Right censored Data

- Data from a subject will be censored from visit x for the PPS analysis under the following conditions. The code ****.Vx will be used to identify subjects whose immunogenicity data should be eliminated from a specific visit onwards. For Day 8, Day 31, Day 61 and Day 91 PP, the information will be checked from vaccination up to Day 7, Day 30, Day 60 and Day 90, respectively.

- The code ****.Vx+ will also be used to identify study withdrawal.

1040.Vx+*	Administration of concomitant vaccine(s) forbidden in the protocol • Use of any investigational or non-registered product (drug or vaccine) other than the study vaccine up to study completion (Contact 1 [Day 181]) • A vaccine not foreseen by the study protocol administered during 30 days following vaccination, with the exception of seasonal influenza vaccine which may be administered ≥ 15 days after the dose of study vaccine. (*To note – this code will only be checked at Day 8 and Day 31 PP and will be carried forward for D61 and D91 PPS*)
2040.Vx+*	Administration of any medication forbidden by the protocol • Any investigational or non-registered product (drug) other than the study vaccines used during the study period. • Immunoglobulins and/or any blood products administered up to 90 days post study vaccination. • Immunosuppressants or other immune-modifying drugs administered chronically (i.e. more than 14 days in total) or any long-acting immune-modifying drugs (e.g. infliximab) administered any time up to 90 days post-vaccination. For corticosteroids, this will mean ≥5mg/day prednisone or equivalent.
2050.Vx+*	Intercurrent medical condition • Intercurrent medical condition (up to Day 91/Visit 5) that has the capability of altering immune response which may influence immune response
2070.Vx+*	Concomitant infection which may influence immune response
2071.Vx+	Withdrawal from the study impacting PPS

*Attribution of these elimcodes to subject need CRDL review of individual listing

5.2.2.3. Visit-specific censored Data

Data from visit x will be censored for the PPS analysis under the following conditions.

Code	Condition under which the code is used
2090.Vx	Subjects did not comply with blood sample schedule **Applicable visits** • For Day 8 PP, to check for DOSE to DAY 8 BS = 7-10 days • For Day 31 PP, to check for DOSE to DAY 31 BS = 30-45 days • For Day 61 PP, to check for DOSE to DAY 61 BS = 56-70 days • For Day 91 PP, to check for DOSE to DAY 91 BS = 86-100 days
2100.Vx	Serological results not available post-vaccination → No immunological result at all for the specific blood sample collection timepoint Comment: - To check for availability of RSV-A neutralising antibody and/or RSVPreF3 IgG antibody result at each applicable PPS timepoint
2120.Vx	Obvious incoherence or abnormality or error in immunogenicity (antibody) data*** To check on RSV-A neutralising antibody and RSVPreF3 IgG antibody result at each applicable PPS timepoint

*** *Elimination criteria for implausible RSV serum immune responses (neut and/or ELISA): More than 4-fold decrease from pre-vaccination to Day 30; After Day 30, more than 4-fold increase or more than 8 fold decrease within a 30 day period*

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

The following important protocol deviations will be reported by groups:

- Forced randomization: In case of supplies shortage for the next assigned vaccine according to the randomization schedule at the clinical site, the randomization system will use the forced randomization procedure in order to continue to enrol and vaccinate subjects. The system moves seamlessly to the next treatment/randomization number for which vaccine supplies are available. The site will not be aware of the forced randomization event.
- Manual randomization: In case the randomization system is unavailable, the investigator has the option to request randomization to the SBIR helpdesk.
- Short follow-up: subjects who completed the last study contact before the minimum length of follow-up requirement.

6. STATISTICAL ANALYSES

6.1. Demography

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

The analysis of demographics will be performed on the ES and on the PPS for immunogenicity.

Demographic characteristics such as age at vaccination in years, race, ethnicity, vital signs and cohort description will be summarised by group using descriptive statistics:

- Frequency tables will be generated for categorical variable such as race.
- Mean, median, standard error and range will be provided for continuous data such as age.

The distribution of subjects will be tabulated as a whole and per group and for each age category (18 - 32 years and 33 - 45 years).

Withdrawal status will be summarised by group using descriptive statistics:

- The number of subjects enrolled into the study as well as the number of subjects excluded from PPS analyses will be tabulated.
- The number of withdrawn subjects will be tabulated according to the reason for withdrawal.

6.1.2. Additional considerations

- Vital signs will be presented at all time point(s) the information is collected on Exposed Set and Per Protocol Set.
- Summary of important protocol deviation leading to elimination will be presented. An individual listing will also be presented for this.
- The following table will be performed for web public disclosure
  - Percentage of Enrolled subjects by country will be tabulated by group,
  - Percentage of Enrolled subjects by age categories (18 - 64 years) will be tabulated by group.

6.2. Exposure

6.2.1. Analysis of exposure planned in the protocol

None

6.3. Immunogenicity

6.3.1. Analysis of immunogenicity planned in the protocol

The analysis will be performed on the applicable PPS cohort for immunogenicity and, if in any group the percentage of vaccinated subjects with serological results excluded from the PPS for analysis of immunogenicity is ≥ 5%, a second analysis will be performed on the ES.

6.3.1.1. Within group assessment

Humoral Immune response to RSV vaccine

For each group, at each time point that blood samples are collected and for each assay (RSV-A NAb and RSVPreF3 IgG) (unless specified otherwise):

- GMTs/GMCs will be tabulated with 95% CI based on log-transformed values and represented graphically.
- Percentage of subjects above the sero-positivity threshold will be tabulated with exact 95% CI.
- Pre- and Post- titres/concentrations will be displayed using reverse cumulative curves.
- The distributions of RSV-A NAb titres (Percentage of subjects greater than or equal to specified thresholds (< 128, 128-256, > 256-512, > 512-1024, > 1024-2048, > 2048-4096, >4096-8192 and >8192) will be tabulated.

- Individual post-vaccination versus pre-vaccination results will be plotted using scatter plots. Results of the control group will be used as a reference.
- Geometric mean of ratios of antibody titres/concentrations post-vaccination over pre-vaccination will be tabulated with 95% CI.
- Distribution of the fold increase of the antibody titres (post- over pre-vaccination titers) will be tabulated.
    - Percentage of subjects with a fold increase equal to or above 2, 4, 6, 8, 10 and12 by pre-vaccination titre category: (< 128, 128-256, > 256-512, > 512-1024, > 1024-2048, > 2048-4096, > 4096, and by cumulative category: <128, ≥128, ≥256, ≥512, ≥1024, ≥2048, ≥4096.).
- The kinetics of individual antibody titres/concentrations will be plotted as a function of time for subjects with results available at all time points.
- An analysis of variance model for repeated measures will be fitted to assess the mean profile in each group.

If deemed necessary (minimum of 10% subjects is required in both the age-category), the same analyses may be performed by age category (18 - 32 years and 33 - 45 years).

Fold increase of RSVPreF3 immunoglobulin G (IgG) antibody concentrations over fold increase of RSV-A Nab titres (Ratio of fold increase Post- over Pre-vaccination) will be tabulated using descriptive statistics. This analysis will include calculation on:

- Geometric mean ratios with corresponding 95% CIs of RSVPreF3 immunoglobulin G (IgG) antibody concentration over anti-RSV-A plaque reduction Nab titres at pre-vaccination for each group and
- Geometric mean ratios with corresponding 95% CIs of fold increase post/pre (Day 8, Day 31, Day 61 and Day 91/Day 1) between RSVPreF3 immunoglobulin G (IgG) antibody concentration and anti-RSV-A plaque reduction Nab titres for each group

6.3.1.2. Between group assessment

Exploratory comparisons will be performed for RSV-A Nab titres and RSVPreF3 IgG antibody concentrations between the different RSV vaccine groups at Day 31. If deemed necessary, this exploratory comparison may also be done at other time-points.

- The three RSV formulations will be first compared to the Placebo in order to identify groups whose means are significantly different from the mean of the Placebo group, (alpha=2.5%, Dunnett's adjustment test for multiplicity). The model will include vaccine group as fixed effect, pre-vaccination titre/concentration. Age categories (18 - 32 years and 33 - 45 years) and/or centre will be added as the categorical covariate, if deemed necessary and is significant. For this analysis, the model will be explored and fitted via the proc mixed procedure according to the following code:

```
PROC MIXED data=sero;
CLASS subjid group age_cat center;
MODEL log_val = baseline group age_cat center
/ddfm=kenwardroger outp = pred;
Random Subjid;
lsmeans group/pdiff=control('1') adjust=dunnett cl alpha=0.05;
RUN;
```

- Estimation of GMT/GMC ratios between groups with corresponding 95% CI using an ANCOVA model on the logarithm10 transformation of the titres/concentrations. This model includes:
  - The vaccine group as the fixed effect
  - The pre-vaccination titre/concentration as the covariate
  - Age groups (18 - 32 years and 33 - 45 years) and/or centre as the categorical covariate if deemed necessary
- Linear and quadratic trend of dose response will be tested using appropriate contrasts.

For the between group analysis among groups and trend tests, the model will be explored and fitted via the proc mixed procedure according to the following code:

```
PROC MIXED data=sero;
CLASS subjid group age_cat center;
MODEL log_val = baseline group age_cat center
/ddfm=kenwardroger outp = pred;
Random Subjid;
lsmeans group/pdiff, cl alpha=0.05;
ods output diffs = diff lsmeans = lsm covparms=cov;
Contrast 'Linear' group 0 -4 -1 5;
Contrast 'Quadratic' group 0 -3 1 2;
RUN:
```

6.3.2. Additional considerations

Few points have been added as additional consideration: -

- The immune analysis at Day 31 for Step 1 subject will only be performed on Exposed Set.
- Summary statistics of RSV-A Nab titres and RSVPreF3 IgG concentration (Minimum, Mean, median, SD, 1st quartile, 3rd quartile, Maximum) will be presented.
- The thresholds for presentation of titres in distribution table and for fold increase will be further adjusted at Day 91 analysis as needed.
- Area under curve (AUC) for each individual will be calculated using linear trapezoid method on titres/concentrations up to 91 days as data permit and summary statistics will be presented. Following loge-transformation, AUC will be analyzed by analysis of covariance (ANCOVA) fitting baseline as covariate and vaccine group as a fixed effect. Point estimates and associated 95% confidence intervals for the group difference will be constructed using the residual error term. These point estimates and associated 95% confidence intervals will then be exponentially back-transformed to provide point estimates and 95% confidence intervals for ratio on fold change. Trend of dose response will also be explored using AUC. The program for the analysis will be similar to between group analysis among vaccine groups and trend tests at day 31. The AUC will be calculated as

$$AUC = \sum_{i=2}^{n} \frac{1}{2}(m_{i-1} - m_i) * (t_{i-1} - t_i)$$

  where m_i corresponds to the i^{th} measurement and t_i corresponds to the i^{th} time point. Each subject's rectangular areas must be added together to estimate the AUC.
- Only subjects having at least 3 post vaccination immune results will be considered for AUC calculation.
- An analysis of variance model for repeated measures will be fitted to assess the mean profile in each group over time.

```
PROC MIXED data=sero;
CLASS subjid group visit age_cat center;
  MODEL log_val = baseline group | visit age_cat
center/ddfm=kenwardroger outp = pred;
  Random Subjid;
lsmeans group*visit/pdiff, cl alpha=0.05;
ods output diffs = diff lsmeans = lsm covparms=cov;
RUN;
```

6.4. Analysis of safety

6.4.1. Analysis of safety planned in the protocol

The analysis of safety will be performed on the ES.

6.4.1.1. Within group analysis

The percentage of subjects with at least one **local AE** (solicited and unsolicited), with at least one **general AE** (solicited and unsolicited) and with any AE during the 7-day or 30-day follow-up period after vaccination will be tabulated with exact 95% CI. The same computations will be done for any ≥ Grade 2 AEs, for any AEs considered related to vaccination, for any Grade 3 AEs considered related to vaccination and for AEs resulting in medically attended visit.

The percentage of subjects reporting each individual **solicited local AE** (any, each grade, resulting in medically attended visit) during the 7-day follow-up period after vaccination will also be tabulated based on maximum intensity per subject for each study vaccine group. The percentage of subjects reporting each individual **solicited general AE** (any, each grade, any related, any Grade 2 related, any Grade 3 related, resulting in medically attended visit) during the 7-day follow-up period after vaccination will also be based on maximum intensity per subject for each study vaccine group.

For fever during the 7-day follow-up period after vaccination, the number and percentage of subjects reporting any fever and fever by half degree (°C) cumulative increments will be reported. Similar tabulations will be performed for causally related fever, Grade 3 causally related fever and fever resulting in a medically attended visit. In addition, the prevalence of any and Grade 3 fever will be presented graphically over time after vaccination.

The percentage of subjects with any **unsolicited** symptoms within 30 days after vaccination with its exact 95% CI will be tabulated by group and by MedDRA System Organ Class and preferred term. Similar tabulation will be done for Grade 3 unsolicited symptoms, for any causally related unsolicited symptoms, for Grade 3 causally related unsolicited symptoms and for unsolicited symptoms resulting in a medically attended visit (the verbatim reports of unsolicited symptoms will be reviewed by a physician and the signs and symptoms will be coded according to the MedDRA Dictionary for Adverse Reaction Terminology. Every verbatim term will be matched with the appropriate Preferred Term).

SAEs reported throughout the study will be described in detail.

Pregnancy exposures throughout the study and pregnancy outcomes will be described in detail (if applicable).

The percentage of subjects using **concomitant medication** (any medication, any antipyretic and any antipyretic taken prophylactically, respectively) during the 7-day follow-up period (Day 1 - 7), 30 days follow-up (Day 1 – 30), between Day 1 – Day 91 and between Day 1- Day 181 after vaccination, will be summarized by group.

For all subjects in each group and each **haematology and biochemistry** parameter:

- The percentage of subjects having haematology and biochemistry results below or above the local laboratory normal ranges will be tabulated for each time point.
- The maximum grading post-vaccination (up to Day 8 and up to Day 31) versus baseline (Screening) and the percentage of subjects with laboratory parameters above or equal to Grade 1, Grade 2, Grade 3 and Grade 4 will be tabulated (Grades will be based on the FDA Guidance for Industry "Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials", see Table 4 and Table 5: FDA toxicity grading scale. Those laboratory parameters not included on FDA Toxicity Grading Scale will not be graded).

6.4.2. Additional considerations

The percentage of subjects with at least one grade 3 **local AE** (solicited and unsolicited), with at least one grade 3 **general AE** (solicited and unsolicited) and with any grade 3 AE during the 7-day or 30-day follow-up period after vaccination will be tabulated with exact 95% CI.

Descriptive summary of the number of days with solicited local/general adverse event during the 7 day (Days 1-7) post-vaccination period will be presented.

The percentage of subjects with SAE within 30 days (Day 1-30) after vaccination with its exact 95% CI will be tabulated by group and by MedDRA preferred term. Similar table will be generated for SAE from study start up to Day 90 and from study start up to study end.

SAEs, death, and withdrawal due to AE(s) reported during the entire study will be tabulated.

6.4.2.1. Exclusion of implausible solicited Adverse Event

Some local and systemic adverse events will be directly measured by the subject and will be subject to a reconciliation process, even if they are biologically implausible. Therefore, these implausible measurements will be removed from the analysis but included in listings. Implausible measurements are summarized in the table below:

Table 3 Implausible Solicited Adverse Events

Parameter	Implausible measurements
Body temperature	≤ 33°C or ≥ 42°C
Erythema	Measurements < 0 mm For subjects ≥ 6 years: ≥ 900 mm
Swelling	Measurements < 0 mm For subjects ≥ 6 years: ≥ 500 mm

6.4.2.2. Combined Solicited and Unsolicited Adverse Events

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

Solicited symptom	Lower level term code	Corresponding Lower level term decode
Pain	Injection site pain	10022086
Redness	Redness at injection site	10022098
Swelling	Swelling at injection site	10053425
Fatigue	Fatigue	10016256
Fever	Fever	10016558
Headache	Headache	10019211
Gastrointestinal symptoms	Gastrointestinal disorder	10017944

Please note – to check for AE term in cDISC during dry run

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

7. ANALYSIS INTERPRETATION

All comparative analyses will be descriptive with the aim to characterise the difference in immunogenicity between groups. These descriptive analyses should be interpreted with caution considering that there is no adjustment for multiplicity for most of these comparisons.

8. CONDUCT OF ANALYSES

8.1. Sequence of analyses

In order to obtain early immunogenicity data of the different formulations of the investigational RSV Maternal vaccine, an interim analysis will be performed on Exposed Set when immunogenicity data up to Day 31 for the Step 1 subjects becomes available. This analysis will be performed on Exposed Set on data as available (i.e partially clean or non-clean data). The templates and listings to be reported for this analysis will be detailed in TFL TOC of this SAP.

To ensure the study team remains blinded, the analysis will be performed by an unblinded statistician outside GSK and the iSRC will act as a firewall team, to review the aggregated summaries for risk of unblinding of individual subjects, before these are released to the team. For this analysis only a statistical report will be prepared

The final statistical analyses will be performed in 2 steps:

- A first analysis will be performed when all safety and immunogenicity data up to at least Day 91 is available in all subjects. At this point, the study statistician will be unblinded (i.e. will have access to the individual subject treatment assignments), but no individual listings will be provided to investigators until the final study report. However, summary results may lead to the unblinding of some specific subjects in case an event occurred only in one group; steps will be taken to minimize this risk.
- The final analysis covering all primary and secondary endpoints as well as any evaluated tertiary endpoint(s) will be performed when all data up to study conclusion are available. A clinical study report will only be written at this stage and individual listings will be provided as part of it.

If the data for tertiary endpoints becomes available at a later stage, (an) additional analysis/analyses will be performed. These data will be documented in annex(es) to the study report and will be made available to the investigators at that time

Description	Analysis ID	Disclosure Purpose (CTRS=public posting, SR=study report, internal)	Dry run review needed (Y/N)	*Study Headline Summary (SHS)*requiring expedited communication to upper management (Yes/No)	Reference for TFL
Final - Up to Day 181	E1_01	CTRS, Study report	Y	Y	See sheet TOC-DAY181 in TFL TOC
D31-Step 1	E1_02	Internal	Y	Y	See sheet TOC-S1-D31 in TFL TOC
Up to Day 91	E1_03	CTRS	Y	Y	See sheet TOC-DAY91 in TFL TOC

8.2. Statistical considerations for interim analyses

All analyses are descriptive. Therefore, the conduct of interim analyses has no impact on interpretation of study results.

9. CHANGES FROM PLANNED ANALYSES

None

10. LIST OF FINAL REPORT TABLES, LISTINGS AND FIGURES

The TFL TOC provides the list of tables/listings and figures needed for the study report. It also identifies the tables eligible for each analyses and their role (synopsis, in-text, post-text, SHS, CTRS,…). Note that all TFL aimed to be included as post-text are noted as post-text even if these are tabulation of individual data such as listing of SAE. The post-text material contains all source material for the study report and accordingly a post-text table may be redundant with an in-text table.

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

Group order in tables	Group label in tables	Group definition for footnote
1	RSV MAT 30	Subject receiving RSVPreF3 low dose
2	RSV MAT 60	Subject receiving RSVPreF3 mid dose
3	RSV MAT 120	Subject receiving RSVPreF3 high dose
4	Placebo	Subject receiving placebo

The following sub-group names will be used in the TFLs

Sub-group order in tables	Sub-group label in tables	Sub-group definition for footnote
1	18-32Y	Subjects 18-32 years of age
2	33-45Y	Subjects 33-45 years of age

11. ANNEX 1 STANDARD DATA DERIVATION RULE AND STATISTICAL METHODS

11.1. Statistical Method References

The exact two-sided 95% CIs for a proportion within a group will be the Clopper-Pearson exact CI [Clopper CJ, Pearson ES. The use of confidence or fiducial limits illustrated in the case of binomial. *Biometrika*. 1934;26:404-413].

11.2. Standard data derivation

11.2.1. Date derivation

- SAS date derived from a character date: In case day is missing, 15 is used. In case day & month are missing, 30June of the year will be used.
- Onset day for an event (AE, medication, etc.): The onset day is the number of days between the study vaccination and the onset/start date of the event. This is 1 for an event starting on the same day as a vaccination. See SAS date derived in case the start date of the event is incomplete.
- Duration: Duration of an event is expressed in days. It is the number of days between the start & the stop dates + 1. Therefore, duration is 1 day for an event starting & ending on the same day.

11.2.2. Demography

- For computation of age, following rules need to be considered:
  - Age will be calculated as the number of years between the date of birth and the date of first vaccination.
  - To ensure that the collection of date of birth will not jeopardise the privacy of Personally Identifiable Information (PII), only a partial date of birth (MMYYYY or YYYY as per local regulation) will be collected.
  - Note that due to incomplete date, the derived age may be incorrect by 1 year when month is missing from the birthdate. This may lead to apparent inconsistency between the derived age and the eligibility criteria/the age category used for randomization.

- For the summary of vital sign, the descriptive statistics will be presented in:
  - Height in cm
  - Weight in kg
  - BMI in kg/m2
  - Temperature in celsius
  - Heart rate in beats per minute
  - Respiratory rate in breaths per minute
  - Systolic and Diastolic Blood pressure in mmHg
- Conversion of weight to kg - The following conversion rule is used:
  - Weight in Kilogram= weight in Pounds / 2.2

The result is rounded to 2 decimals.

- Conversion of height to cm - The following conversion rule is used:
  - Height in Centimetres = Height in Inch * 2.54

The result is rounded to the unit (ie no decimal).

- Conversion of temperature to °C - The following conversion rule is used:
  - Temperature in °Celsius = ((Temperature in °Fahrenheit -32) *5)/9

The result is rounded to 1 decimal.

11.2.3. Immunogenicity

- For a given subject and given immunogenicity measurement, missing or non-evaluable measurements will not be replaced. Therefore, an analysis will exclude subjects with missing or non-evaluable measurements.
  - For the within-group assessment, the descriptive analysis performed for each assay at each timepoint will exclude subjects with a missing or non-evaluable measurement.
  - For the between group assessments, the Analysis of covariance (ANCOVA) model will be fitted at each timepoint based on the subjects having a result at both the baseline and the considered timepoint.
- The Geometric Mean Concentrations/Titres (GMC/Ts) calculations are performed by taking the anti-log of the mean of the log titre transformations. Antibody titres below the cut-off of the assay will be given an arbitrary value of half the cut-off of the assay for the purpose of GMC/T calculation. The cut-off value will be defined by the laboratory before the analysis.

- The 95% CI for GMT will be obtained within each group separately. The 95% CI for the mean of log-transformed titre will be first obtained assuming that log-transformed titres were normally distributed with unknown variance. The 95% CI for the GMT will then be obtained by exponential transformation of the 95% CI for the mean of the log-transformed titres.
- A seronegative subject is a subject whose antibody titre is below the cut-off value of the assay. A seropositive subject is a subject whose antibody titre is greater than or equal to the cut-off value of the assay.
- GMT/GMC ratios will be obtained using an ANCOVA model on the logarithm-transformed titres. The ANCOVA model will include the vaccine group as fixed effect, pre-vaccination titre as covariate and age groups (18 - 32 years and 33 - 45 years) and/or centre as the categorical covariate if deemed necessary. GMT/GMC ratios and their CI (based on Tukey multiple adjustment) will be derived as exponential-transformation of the corresponding group contrast in the model.
- The CI for GMT ratio will be obtained by exponential-transformation of the CI for the group least square mean of the log-transformed titres/concentration of the above ANCOVA model. Confidence intervals adjusted for multiple testing or other kind of significance adjustment will be produced.
- All CI computed will be two-sided 95% CI.

11.2.4. Safety

- For a given subject and the analysis of solicited symptoms within 7 days post-vaccination, missing or non-evaluable measurements will not be replaced. Therefore, the analysis of the solicited symptoms based on the Exposed Set will include only vaccinated subjects with documented safety data (i.e., symptom screen completed). More specifically the following rules will be used:
  - Subjects who documented the absence of a solicited symptom after vaccination will be considered not having that symptom after vaccination.
  - When a specific symptom is marked as having occurred following a specific vaccination (i.e. SDTM CE.CEOCCUR=Y for the specified post-vaccination period for the symptom in question), any missing daily recordings will be given imputed values to allow them to contribute to the ‘Any’ rows but not to specific grade rows of the symptom summary tables.
  - Dose without symptom sheets documented will be excluded.
- For analysis of unsolicited adverse events, such as serious adverse events or adverse events by primary MedDRA term, and for the analysis of concomitant medications, all vaccinated subjects will be considered. Subjects who did not report the event or the concomitant medication will be considered as subjects without the event or the concomitant medication respectively.

Note that for all tables described in this section, the way the percentage of subjects will be derived will depend on the event analysed (see table below for details). As a result, the N value will differ from one table to another.

Event	N used for deriving % per subject for Vaccination phase
Concomitant vaccination	All subjects with study vaccine administered
Solicited general symptom	All subjects with at least one solicited general symptom documented as either present or absent (i.e., symptom screen completed)
Solicited local symptom	All subjects with at least one solicited local symptom documented as either present or absent (i.e., symptom screen completed)
Unsolicited symptom	All subjects with study vaccine administered
Concomitant medication	All subjects with study vaccine administered

11.2.5. Number of decimals displayed:

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

Display Table	Parameters	Number of decimal digits
Demographic characteristics	Mean, median age	1
Demographic characteristics	SD (age)	1
Immunogenicity	Ratio of GMT/C	2
All summaries	% of difference, including LL & UL of CI	2
All summaries	p-value	3

12. ANNEX 2: TOXICITYGRADING SCALE FOR LABORATORY ASSESSMENTS

Table 4 FDA toxicity grading scales for biochemistry parameters

Serum*	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)	Potentially Life Threatening (Grade 4)**
Creatinine – mg/dL	1.5 – 1.7	1.8 – 2.0	2.1 – 2.5	> 2.5 or requires dialysis
Blood Urea Nitrogen BUN mg/dL	23 – 26	27 – 31	> 31	Requires dialysis
Liver Function Tests -ALT, AST increase by factor	1.1 – 2.5 x ULN	2.6 – 5.0 x ULN	5.1 – 10 x ULN	> 10 x ULN

ULN = upper limit of the normal range.
* The laboratory values provided in the tables serve as guidelines and are dependent upon institutional normal parameters. Institutional normal reference ranges should be provided to demonstrate that they are appropriate.
** The clinical signs or symptoms associated with laboratory abnormalities might result in characterization of the laboratory abnormalities as Potentially Life Threatening (Grade 4). For example, a low sodium value that falls within a Grade 3 parameter (125-129 mE/L) should be recorded as a Grade 4 hyponatremia event if the subject had a new seizure associated with the low sodium value.

Table 5 FDA toxicity grading scales for hematology parameters

Hematology*	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)	Potentially Life Threatening (Grade 4)
Hemoglobin (Female) - gm/dL	11.0 – 12.0	9.5 – 10.9	8.0 – 9.4	< 8.0
Hemoglobin (Female) change from baseline value - gm/dL	Any decrease - 1.5	1.6 – 2.0	2.1 – 5.0	> 5.0
WBC Increase - cell/mm3	10 800 – 15 000	15 001 – 20 000	20 001 – 25 000	> 25 000
WBC Decrease - cell/mm3	2 500 – 3 500	1 500 – 2 499	1 000 – 1 499	< 1 000
Lymphocytes Decrease - cell/mm3	750 – 1 000	500 – 749	250 – 499	< 250
Neutrophils Decrease - cell/mm3	1 500 – 2 000	1 000 – 1 499	500 – 999	< 500
Eosinophils - cell/mm3	650 – 1 500	1 501 - 5 000	> 5 000	Hypereosinophilic
Platelets Decreased - cell/mm3	125 000 – 140 000	100 000 – 124 000	25 000 – 99 000	< 25 000

* The laboratory values provided in the tables serve as guidelines and are dependent upon institutional normal parameters. Institutional normal reference ranges should be provided to demonstrate that they are appropriate.

13. ANNEX 3: STUDY SPECIFIC MOCK TFL

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

13.1. List of individual data listing

Appendix Table I.A - Elimination codes

Appendix Table I.Ai – Important Protocol deviations

Appendix Table I.B – Demography

Appendix Table IBii - Physical examination/vital signs

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

Appendix Table I.Cii - Reason for visit not done

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

Appendix Table I.Ei – Study Conclusion

Appendix Table I.Eii – Screening conclusion

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

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

Appendix Table I.J - Reason for non-eligibility

Appendix Table II.Ai - Solicited local adverse events

Appendix Table II.B - Solicited general adverse events

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

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

Appendix Table II.Di - Concomitant medications

Appendix Table II.Dii - Concomitant vaccinations

Appendix Table III.A – Immunogenicity

Appendix Table IV.A – Haematology and Biochemistry

Appendix Table V.A – Pregnancy report

13.2. Template of Tables and Figures

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

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

<each group>:
RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
n = number of subjects in a given center or country
N = total number of subjects
% = n/N x 100
Center = GSK Biologicals assigned center number

Template 2 Number of subjects vaccinated, completed and withdrawn with reason for withdrawal – up to <Day 31, Day 91, study end> <Exposed set>

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

<each group>:
RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
Vaccinated = number/percentage of subjects who were vaccinated in the study
Completed = number/percentage of subjects who completed last study visit
Withdrawn = number/percentage of subjects who did not perform the last study visit
Unknown = number/percentage of subjects who have not come for the last visit yet

Template 3 Visit attendance – up to <Day 31, Day 91, study end> <Exposed set>

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

RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
N = Number of subjects in each group or in total
n/% = number / percentage of subjects in a given category
Conclusion = date of last study visit or withdrawal

Template 4 Summary of important protocol deviation leading to elimination from Per protocol set <Enrolled Set>

	Each group N=		Total N=	
Title	**n**	**%**	**n**	**%**
At least one Important Protocol Deviation				
Assessment or time point completion				
Missed assessment				
Out of window assessment for immunogenicity				
Eligibility Criteria Not Met				
Inclusion Exclusion Criteria Not Met				
Excluded medication, vaccine or device				
Medication, excluded by the protocol, was administered				
Vaccine, excluded by the protocol, was administered				
Intercurrent medical conditions				
Developed intercurrent medical condition leading to PPS exclusion				
Fraudulent Data				
Fraudulent Data				
Informed Consent				
Informed consent not signed and/or dated by subject				
Study procedures				
Randomization procedures				
Wrong study treatment/administration/dose				
Not administering any study treatment				
Study treatment not administered per protocol				
Essential serological data missing				
Obvious incoherence or abnormality or error in data				

RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
N = Number of subjects in each group or in total
Occ = number of occurrences = number of important protocol deviations
n/% = number / percentage of subjects with important protocol deviations

Template 5 Consort flow - Part 1 from enrolment to randomization <All Enrolled Set>

	Total N=	
	n	**%**
NUMBER OF SUBJECTS ELIMINATED PRIOR TO RANDOMIZATION Consent Withdrawal, Not Due To A Serious Adverse Event		
Consent Withdrawal, Not Due To An Adverse Event Eligibility Criteria Not Fulfilled	2	0.3
Lost To Follow-Up Migrated / Moved From The Study Area		
Missing Other		
NUMBER OF SUBJECTS INCLUDED IN RANDOMIZED SET		

N = Number of subjects
n = Number of subjects enrolled by site
% = n / Number of subjects with available results x100
All Enrolled Set includes Screen Failures and non-Randomized subjects
Withdrawal reason "Other" corresponds to Subject Enrollment target reached before Randomization

Template 6 Consort – Part II from randomization to exposure for each study group <All Randomised Set>

	Each group N=		Total N=	
			n	%
NUMBER OF SUBJECTS ELIMINATED PRIOR TO EXPOSURE Consent Withdrawal, Not Due To A Serious Adverse Event Consent Withdrawal, Not Due To An Adverse Event Eligibility Criteria Not Fulfilled			2	0.3
Lost To Follow-Up Migrated / Moved From The Study Area				
NUMBER OF SUBJECTS INCLUDED IN EXPOSED SET				

RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
N = Number of subjects
n = Number of subjects randomised by site
% = n / Number of subjects with available results x 100

Template 7 Consort flow - Part 3 from exposure to per protocol set, per study group <Exposed Set>

	Each group N=		Total N=	
	n	%	n	%
NUMBER OF SUBJECTS ELIMINATED FROM PER PROTOCOL SET AT DAY <8, 31, 61, 91>				
ELIMINATIONS Eligibility Criteria Not Met (2010)				
Missed Assessment (2100) Out Of Window Treatment Administration (2080)				
Study Treatment Not Administered Per Protocol (1070)				
WITHDRAWALS				
Consent Withdrawal, Not Due To An Adverse Event				
Lost To Follow-Up Serious Adverse Event				
NUMBER OF SUBJECTS INCLUDED IN PER PROTOCOL SET AT DAY <8, 31, 61, 91>				

N = Number of subjects
n = Number of subjects enrolled by site
% = n / Number of subjects with available results x 100

Template 8 Summary of demographic characteristics <Exposed set, PPS for immunogenicity at Day <8, 31, 61, 91>>

	<Each group> N=XXXX		<Each group> N=XXXX		Total N=XXXX	
	Value or n	**%**	**Value or n**	**%**	**Value or n**	**%**
Age in years at <timepoint>						
N with data	xxx		xxx		xxx	
Mean	xxx.x		xxx.x		xxx.x	
SD	xxx.x		xxx.x		xxx.x	
Median	xxx.x		xxx.x		xxx.x	
Minimum	xxx		xxx		xxx	
Maximum	xxx		xxx		xxx	
Age category at (vaccination)						
18-32 years	xxx	xx.x	xxx	xx.x	xxx	xx.x
33-64 years	xxx	xx.x	xxx	xx.x	xxx	xx.x
Ethnicity						
<EACH ETHNICITY>	xxx	xx.x	xxx	xx.x	xxx	xx.x
…	xxx	xx.x	xxx	xx.x	xxx	xx.x
Geographic Ancestry						
<EACH GEOGRAPHIC ANCESTRY>	xxx	xx.x	xxx	xx.x	xxx	xx.x
…	xxx	xx.x	xxx	xx.x	xxx	xx.x

<each group>:
RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
N = total number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
N with data = number of subjects with documentation of the corresponding data
SD = standard deviation

Template 9 Summary of vital signs characteristics <Exposed set, PPS for immunogenicity at Day <8, 31, 61, 91>>

			<each group> N =	Total N =
Visit	**Characteristics**	**Parameters**	**Value**	**Value**
<Each visit>	Height (Cm)	N with data		
		Mean		
		SD		
		Median		
		Minimum		
		Maximum		
	Weight (Kg)	N with data		
		Mean		
		SD		
		Median		
		Minimum		
		Maximum		
	BMI	N with data		
		Mean		
		SD		
		Median		
		Minimum		
		Maximum		
	Heart rate (Beats per minute)	N with data		
		Mean		
		SD		
		Median		
		Minimum		
		Maximum		
	Respiratory rate (Breaths per minute)	N with data		
		Mean		
		SD		
		Median		
		Minimum		
		Maximum		
	Temperature/(Oral) (°C)	N with data		
		Mean		
		SD		
		Median		
		Minimum		
		Maximum		
	Systolic Blood pressure (mmHg)	N with data		
		Mean		
		SD		
		Median		
		Minimum		
		Maximum		
	Diastolic Blood pressure (mmHg)	N with data		
		Mean		
		SD		
		Median		
		Minimum		
		Maximum		

<each group>:
RSV MAT 30 = Subject receiving RSVPreF3 low dose

RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
N = total number of subjects
N with data = number of subjects with documentation of the corresponding data
Value = value of the considered parameter
SD = standard deviation

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

			<each group>		<each group>	
Type of interval	**Interval range**		**Value or n**	**%**	**Value or n**	**%**
Age	18 - 45 years	N	xxx		xxx	
		n	xxx	xx.x	xxx	xx.x
		Minimum	xxx		xxx	
		Maximum	xxx		xxx	
SCR – VISIT 1	0 – 7 Days	N	xxx		xxx	
		n	xxx	xx.x	xxx	xx.x
		Minimum	xxx		xxx	
		Maximum	xxx		xxx	
VISIT 1 – VISIT 2	7 – 10 Days	N	xxx		xxx	
		n	xxx	xx.x	xxx	xx.x
		Minimum	xxx		xxx	
		Maximum	xxx		xxx	
VISIT 1 – VISIT 3	30 – 45 Days	N	xxx		xxx	
		n	xxx	xx.x	xxx	xx.x
		Minimum	xxx		xxx	
		Maximum	xxx		xxx	
VISIT 1 – VISIT 4	56 – 70 Days	N	xxx		xxx	
		n	xxx	xx.x	xxx	xx.x
		Minimum	xxx		xxx	
		Maximum	xxx		xxx	
VISIT 1 – VISIT 5	86 – 100 Days	N	xxx		xxx	
		n	xxx	xx.x	xxx	xx.x
		Minimum	xxx		xxx	
		Maximum	xxx		xxx	
VISIT 1 – PHC 1	165 – 195 Days	N	xxx		xxx	
		n	xxx	xx.x	xxx	xx.x
		Minimum	xxx		xxx	
		Maximum	xxx		xxx	

<each group (pooled groups)>:
RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
N = total number of subjects with available results
n/% = number / percentage of subjects with results outside of the interval
range = minimum-maximum for age and intervals

Template 11 Study Population – Up to <Day 91, study end> <Exposed Set>

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

<each group>:
RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
N = Total number of subjects
SD = Standard deviation

Template 12 Number of enrolled subjects by country

	<each group> N =	Total N =
Characteristics	**n**	**n**
Country		

<each group>:
RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
N = Number of enrolled subjects
n= number of enrolled subjects included in each group or in total for a given country or for all countries

Template 13 Number of enrolled subjects by age category

		<each group> N =	Total N =
Characteristics	**Categories**	**n**	**n**
Age category	Adults [18-45 years]		
	Missing		

<each group>:
RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
N = Number of enrolled subjects
n= number of enrolled subjects included in each group or in total for a given age category or for all age categories
Missing = age at study vaccination unknown

Template 14 Minimum and maximum activity dates <Exposed set>

		<each group>	<each group>	Overall
Visit Description	**Parameter**	**Date**	**Date**	**Date**
<inform consent>	Minimum			
	Maximum			
[Randomisation]	Minimum			
	Maximum			
<each visit>	Minimum			
	Maximum			

<each group>:
RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo

Template 15 Compliance in completing solicited symptoms information <Exposed Set>

	<each group>			<each group>		
Symptom information	**N**	**n**	**Compliance (%)**	**N**	**n**	**Compliance (%)**
General SS						
Local SS						

RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
N=Number of administered doses
n = number of doses with SS returned
General SS = Symptom screens used for the collection of general solicited AEs
Local SS = Symptom screens used for the collection of local solicited AEs
Compliance (%) = (n / N) X 100

Template 16 Incidence and nature of <any, grade 2 and 3, grade 3, related, grade 3 related, > adverse events (unsolicited and solicited) <requiring medical attention> reported during the <7,30>-days (Day 1-<7,30>) post-vaccination period <Exposed Set>

	<Each group>					<Each group>				
				95% CI					95% CI	
Symptoms	**N**	**n**	**%**	**LL**	**UL**	**N**	**n**	**%**	**LL**	**UL**
Any symptom										
General symptoms										
Local symptoms										

RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
N = number of subjects with the administered dose
n/% = number/percentage of subjects presenting at least one type of symptom
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit

Template 17 Incidence of solicited local adverse events reported during the 7-day (Days 1-7) post-vaccination period by maximum grading <Exposed Set>

		<each group>				
					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**
Pain	All					
	Grade 1					
	Grade 2					
	Grade 3					
	Medical advice					
	Onset ≤48h					
Redness (mm)	All					
	>20 - ≤50					
	>50 - ≤100					
	>100					
	Medical advice					
	Onset ≤48h					
Swelling (mm)	All					
	>20 - ≤50					
	>50 - ≤100					
	>100					
	Medical advice					
	Onset ≤48h					

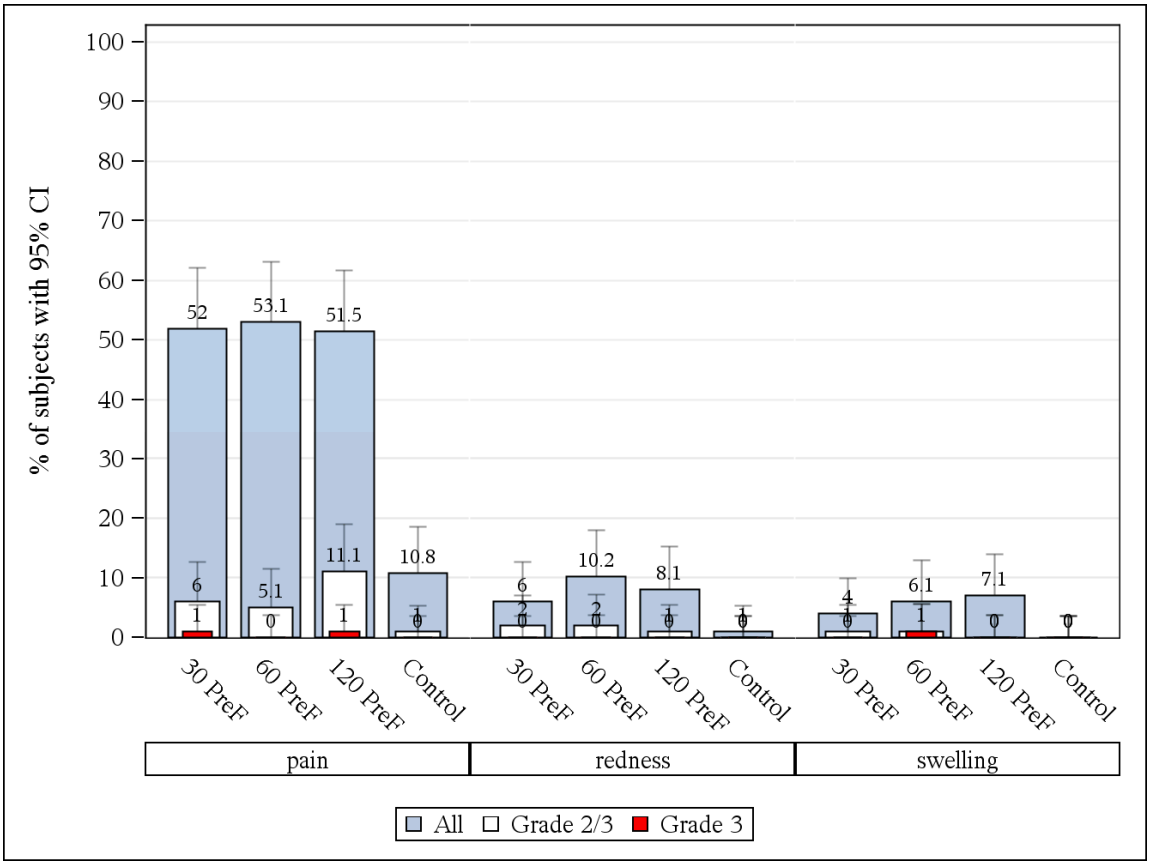
RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
N = number of subjects with the documented dose
n/% = number/percentage of subjects reporting the type of symptoms as maximum intensity during the follow-up
CI = Exact 95% confidence interval; LL = lower limit, UL = upper limit
The maximum intensity of local injection site redness/swelling was coded as follows:
1: >20 mm to ≤ 50 mm
2: > 50 mm to ≤ 100 mm
3: > 100 mm
Please note – to check for AE term in cDISC during dry run

Template 18 Number of days with solicited local adverse event during the 7-day (Days 1-7) post-vaccination period <Exposed Set>

		<Each group>	<Each group>
Symptom	**Statistic**	**value**	**value**
Pain	n	xxxx	xxxx
	Mean	xx.x	xx.x
	Minimum	xx.x	xx.x
	Q1	xx.x	xx.x
	Median	xx.x	xx.x
	Q3	xx.x	xx.x
	Maximum	xx.x	xx.x
Redness (mm)	n	xxxx	xxxx
	Mean	xx.x	xx.x
	Minimum	xx.x	xx.x
	Q1	xx.x	xx.x
	Median	xx.x	xx.x
	Q3	xx.x	xx.x
	Maximum	xx.x	xx.x
Swelling (mm)	n	xxxx	xxxx
	Mean	xx.x	xx.x
	Minimum	xx.x	xx.x
	Q1	xx.x	xx.x
	Median	xx.x	xx.x
	Q3	xx.x	xx.x
	Maximum	xx.x	xx.x

<each group>:
RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
n = number of doses with the symptom
Q1 = 25th percentile
Q3 = 75th percentile
Please note – to check for AE term in cDISC during dry run

Template 19 Percentage of subjects reporting solicited local adverse events (any grade /grade 2,3/ grade 3) during the 7-day (Days 1-7) post-vaccination period by maximum intensity <Exposed set>



RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
Please note – to check for AE term in cDISC during dry run

Template 20 Incidence of solicited general adverse event reported during the 7-day (Days 1-7) post-vaccination period by maximum grading <Exposed Set>

		Each group				
					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**
Fatigue	All					
	Grade 1					
	Grade 2					
	Grade 3					
	Related					
	Grade 2 Related					
	Grade 3 Related					
	Medical advice					
	Onset ≤48h					
Gastrointestinal symptoms	All					
	Grade 1					
	Grade 2					
	Grade 3					
	Related					
	Grade 2 Related					
	Grade 3 Related					
	Medical advice					
	Onset ≤48h					
Headache	All					
	Grade 1					
	Grade 2					
	Grade 3					
	Related					
	Grade 2 Related					
	Grade 3 Related					
	Medical advice					
	Onset ≤48h					
Temperature/(Oral) (°C)	All					
	≥38.0					
	>38.5					
	>39.0					
	>39.5					
	>40.0					
	Related					
	>38.5 Related					
	>39.0 Related					
	>39.5 Related					
	>40.0 Related					
	Medical advice					
	Onset ≤48h					

RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
N = number of subjects with the documented dose
n/% = number/percentage of subjects reporting the type of symptom as maximum intensity during the follow-up period
95%CI = Exact 95% confidence interval; LL = lower limit, UL = upper limit
All=any grade>0 for Fatigue, Gastrointestinal symptoms, Headache and any ≥38.0°C for Temperature

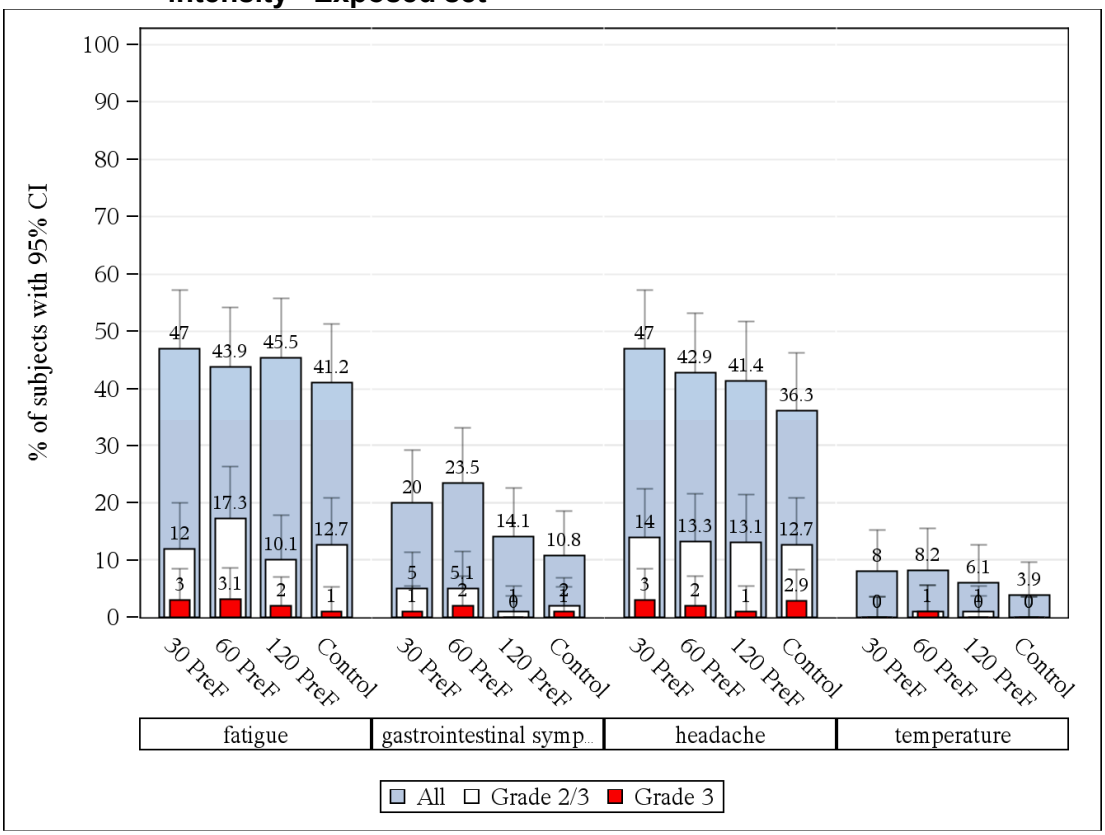
Related*= any grade>0 for Fatigue, Gastrointestinal symptoms, Headache and any ≥38.0°C for Temperature considered related to vaccination by the investigator
Please note – to check for AE term in cDISC during dry run

Template 21 Number of days with solicited general adverse event during the 7-day (Days 1-7) post-vaccination period <Exposed Set>

		<Each group>	<Each group>
Symptom	**Statistic**	**value**	**value**
Fatigue	n	xxxx	xxxx
	Mean	xx.x	xx.x
	Minimum	xx.x	xx.x
	Q1	xx.x	xx.x
	Median	xx.x	xx.x
	Q3	xx.x	xx.x
	Maximum	xx.x	xx.x
Gastrointestinal symptoms	n	xxxx	xxxx
	Mean	xx.x	xx.x
	Minimum	xx.x	xx.x
	Q1	xx.x	xx.x
	Median	xx.x	xx.x
	Q3	xx.x	xx.x
	Maximum	xx.x	xx.x
Headache	n	xxxx	xxxx
	Mean	xx.x	xx.x
	Minimum	xx.x	xx.x
	Q1	xx.x	xx.x
	Median	xx.x	xx.x
	Q3	xx.x	xx.x
	Maximum	xx.x	xx.x
Temperature (Oral) (°C)	n	xxxx	xxxx
	Mean	xx.x	xx.x
	Minimum	xx.x	xx.x
	Q1	xx.x	xx.x
	Median	xx.x	xx.x
	Q3	xx.x	xx.x
	Maximum	xx.x	xx.x

<each group>:
RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
n = number of doses with the symptom
Q1 = 25th percentile
Q3 = 75th percentile
Please note – to check for AE term in cDISC during dry run

Template 22 Percentage of subjects reporting fever (any and grade 3) and other solicited general adverse events (any grade /grade 2,3/ grade 3) during the 7-day (Days 1-7) post-vaccination period by maximum intensity <Exposed set>



RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
Grade 3 fever = Temperature >39.0 °C
Please note – to check for AE term in cDISC during dry run

Template 23 Percentage of subjects reporting the occurrence of <any, grade 3> <unsolicited symptoms, serious adverse events> classified by MedDRA Primary System Organ Class and Preferred Term <with causal relationship to vaccination, with medically attended visit>, within the 30-day (Days 1-30) post-vaccination period <Exposed Set>

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

RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = = number of subjects included in the considered analysis set in each group
n* = number of events reported
n/% = number/percentage of subjects reporting the symptom at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit
n* will only be generated for the CTRS posting

Template 24 Percentage of subjects reporting the occurrence of <serious adverse events> classified by MedDRA Primary System Organ Class and Preferred Term from <vaccination up to Day 91 visit, from vaccination up to study end> <Exposed Set>

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

RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects included in the considered cohort in each group
n/% = number/percentage of subjects reporting the symptom at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Template 25 Number and percentage of subjects taking a concomitant medication <during the <7,30>- day (Days 1-<7,30>) post-vaccination period, from vaccination to Day 91 visit/study end> <Exposed Set>

	<each group>				
				95% CI	
Type	**N**	**n**	**%**	**LL**	**UL**
Any					
Any antipyretics					
Prophylactic antipyretics					

<each group>:
RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
N = total number of subjects with the administered dose
n/% = number/percentage of subjects took the specified type of concomitant medication at least once during the considered period
95%CI = Exact 95% confidence interval; LL = lower limit, UL = upper limit

Template 26 Distribution of change from baseline in hematology and biochemistry with respect to normal laboratory ranges <Exposed Set>

				<each group>		
Laboratory parameter	**Timing**	**Range indicator at Baseline (SCR)**	**Range indicator at timing**	**N**	**n**	**%**
Alanine Aminotransferase	PI(D8)	Unknown	Unknown			
			Below			
			Within			
			Above			
		Below	Unknown			
			Below			
			Within			
			Above			
		Within	Unknown			
			Below			
			Within			
			Above			
		Above	Unknown			
			Below			
			Within			
			Above			
	PI (D31)	…				
Aspartate Aminotransferase	…	…				
Creatinine	…	…				
Blood Urea Nitrogen						
Hemoglobin						
Leukocytes (White Blood Cells)	…	…				
Neutrophil						
Eosinophil						
Platelets	…	…				

<each group>:
RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
N = number of subjects with available results for the specified laboratory parameter and timing in a given baseline category
n/% = number/percentage of subjects in the specified category
Below = below the normal laboratory range defined for the specified laboratory parameter
Within = within the normal laboratory range defined for the specified laboratory parameter
Above = above the normal laboratory range defined for the specified laboratory parameter
SCR= Screening
PI (D8): Post-vaccination at Day 8
PI (D31): Post-vaccination at Day 31

Template 27 Summary of hematology and biochemistry results by maximum grade up to <VISIT 2 (D8), VISIT 3 (D31)> post vaccination versus baseline <Exposed Set>

			<each group >		
Laboratory parameter	**Baseline (SCR)**	**Visit 2 to Visit X**	**N**	**n**	**%**
Alanine Aminotransferase(ALT)	Unknown	Unknown			
		Grade 0			
		Grade 1			
		Grade 2			
		Grade 3			
		Grade 4			
	Grade 0				
	Grade 1				
	Grade 2				
	Total				
Aspartate Aminotransferase(AST)					
Creatinine					
Eosinophils increase					
Hemoglobin decrease					
Lymphocytes decrease					
Neutrophil (decrease)	…				
Platelet count decrease					
White Blood Cells (WBC) decrease					
White Blood Cells (WBC) increase					

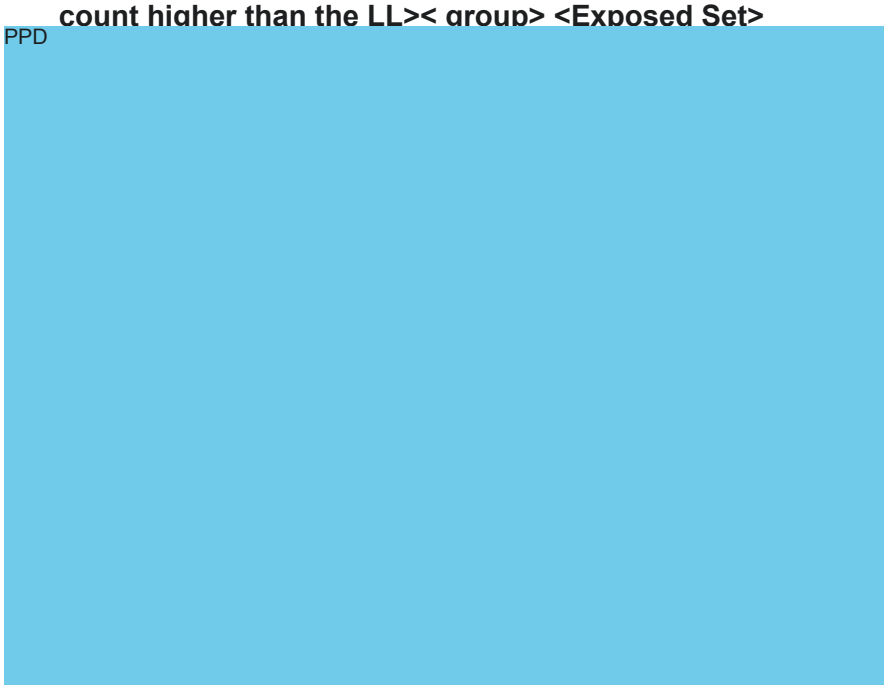
<each group>:
RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
N = number of subjects with at least one available result for the specified laboratory parameter and follow-up period
n/% = number/percentage of subjects reporting at least once the laboratory event when the maximum grading over the follow-up period is considered
SCR=Screening

Template 28 Summary of haematology change from baseline by maximum grade in the specified category <up to VISIT2 (D8), up to VISIT 3 (D31) ><Exposed set>

		RSV MAT 30 N =		**RSV MAT 60 N =**		**RSV MAT 120 N =**		**Placebo N =**		**Total N =**	
Laboratory parameter	**Maximum grade**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Hemoglobin (Change from baseline)	Other										
	Grade 2										
	Grade 3										
	Grade 4										

RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
N = number of subjects with at least one available result for the specified laboratory parameter and follow-up period
% = percentage of subjects reporting at least once the laboratory event when the maximum grading over the follow-up period is considered
% = n / Number of subjects with available results x 100
Other=all Unknown, Grade 0 and Grade 1

Template 29 Individuals results of <hemoglobin levels, platelet count, White Blood cells, ALT, AST, Creatinine, Blood urea nitrogen <equal and above grade 2, outside the normal range, count lower than the LL, count higher than the LL>< group> <Exposed Set>



Note: This figure is just a template.

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

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

<each group>:
RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with the administered dose
n* = number of events reported
n/% = number/percentage of subjects reporting the symptom at least once

Template 31 Number (%) of subjects with serious adverse events including number of events reported <within 30 days (Days 1-30) post vaccination period><from vaccination up to Day 91 visit, Study end> <Exposed Set>

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

<each group>:
RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
N = number of subjects with the administered dose
n* = number of events reported
n/% = number/percentage of subjects reporting the symptom at least once

Template 32 Listing of all SAEs <within 30 day (Days 1-30) post-vaccination period, from vaccination up to <Day 91, study end> ><Exposed Set>

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

RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
Please note that this table will be presented on group blinded during Day 91 analysis.

Template 33 Listing of adverse events, SAEs and solicited symptoms leading to withdrawal from the study <within 30 days (Days 1-30) post-vaccination period><during vaccination up to <Day 91, study end> <Exposed Set>

Group	Subject No.	Country	Race	AE Description	SAE	Causality	Outcome	Type of discontinuation

RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
Please note that this table will be presented on group blinded during Day 91 analysis.

Template 34 Listing of all pregnancies from vaccination up to study end <Exposed Set>

Group	Sub. No.	Country	Race	Age at vaccination	LMP date	Age at pregnancy (Year)	Date of delivery	Pregnancy Outcome	Date of outcome	Gestational weeks at birth/miscarriage /termination

RSV MAT 30 = Subject receiving RSV PreF3 low dose
RSV MAT 60 = Subject receiving RSV PreF3 mid dose
RSV MAT 120 = Subject receiving RSV PreF3 high dose
Placebo = Subject receiving placebo

Template 35 Number and percentage of subjects with <RSV-A neutralising antibody titre, RSV IgG antibody concentration> equal to or above <cut-off> and <GMTs/GMCs> <PPS for immunogenicity, Exposed Set>

				≥cut-off unit				GMT/GMC				
						95% CI			95% CI			
Antibody	**Group**	**Timing**	**N**	**n**	**%**	**LL**	**UL**	**value**	**LL**	**UL**	**Min**	**Max**
<RSV-A NAb, RSV IgG antibody>	<each group>	PRE										
		PI(D8)										
		PI(D31)										
		PI(D61)										
		PI(D91)										

<each group>:
RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
GMT/GMC = geometric mean antibody titre/concentration calculated on all subjects
N = Number of subjects with available results
n/% = number/percentage of subjects with titre equal to or above specified value
95% CI = 95% confidence interval; LL = lower limit, UL = upper limit
MIN/MAX = Minimum/Maximum
PRE= Pre-vaccination at screening
PI(D8) = Post-vaccination at Day 8
PI(D31) = Post-vaccination at Day 31
PI(D61) = Post-vaccination at Day 61
PI(D91) = Post-vaccination at Day 91
To check for the disclosure name for the antibody for 1st column of the table

Template 36 Distribution of RSV-A neutralising antibody titre <PPS for immunogenicity <at Day X>>

			Each group		
Antibody	**Timing**	**Titre**	**N**	**n**	**%**
RSV-A NAb	<PRE, PI(D8), PI(D31), PI(D61), PI(D91)>	<128			
		≥128			
		≥256			
		≥512			
		≥1024			
		≥2048			
		≥4098			

<each group>:
RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
N = number of subjects with available results
n/% = number/percentage of subjects with titre within the specified criterion
PRE= Pre-vaccination at screening
PI(D8) = Post-vaccination at Day 8
PI(D31) = Post-vaccination at Day 31
PI(D61) = Post-vaccination at Day 61
PI(D91) = Post-vaccination at Day 91
Please note that the categories of the titre presentation are not fixed and will be adjusted at time of D91 analysis

Template 37 Distribution of fold of anti-RSV-A neutralising antibody titre by pre-vaccination titre category <PPS for immunogenicity>

				Each group		
Antibody	**Fold change**	**Pre-vaccination status**	**Timing**	**N**	**n**	**%**
RSV-A NAb	<1	<128	PI(D8)			
			PI(D31)			
			PI(D61)			
		≥128-≤256				
		>256-≤512				
		>1024-≤2048				
		>2048-≤4096				
		>4096				
		Total				
	≥1 - <2					
	≥2					
	≥4					
	≥6					
	≥8					
	≥10					
	≥12					

<each group>:
RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo

N = number of subjects with pre- and corresponding post-vaccination results available
n/% = number/percentage of subjects with titre fold change meeting the specified criterion
PI(D8) = Post-vaccination at Day 8
PI(D31) = Post-vaccination at Day 31
PI(D61) = Post-vaccination at Day 61
PI(D91) = Post-vaccination at Day 91
Please note that the categories of the titre presentation are not fixed and will be adjusted at time of D91 analysis

Template 38 Geometric mean of the individual ratio of <RSV-A neutralizing antibody titres, RSV IgG antibody concentrations> at <Day 8, Day 31, Day 61, Day 91> compared to pre-vaccination with 95% CI <PPS for immunogenicity<at Day 31>>

						<GMT,C> ratio			
								95% CI	
Group	N	Time point description	<GMC,T>	Time point description	<GMT,C>	Ratio order	Value	LL	UL
RSV MAT 30		PI(D31)		PRE		PI(D31) / PRE			
RSV MAT 60		PI(D31)		PRE		PI(D31) / PRE			
RSV MAT 120		PI(D31)		PRE		PI(D31) / PRE			
Placebo		PI(D31)		PRE		PI(D31) / PRE			

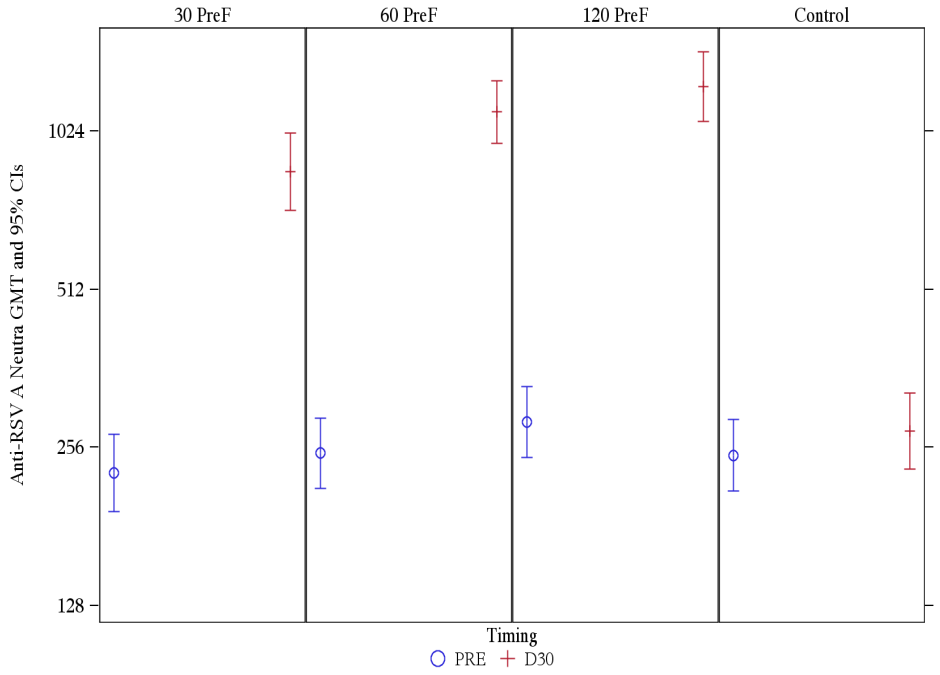
RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
<GMT,C> = geometric mean antibody <titres, concentration> calculated on all subjects
N = Number of subjects with available results at the two considered time points
95% CI = 95% confidence interval; LL = lower limit, UL = upper limit
PRE= Pre-vaccination at screening
PI(D8) = Post-vaccination at Day 8
PI(D31) = Post-vaccination at Day 31
PI(D61) = Post-vaccination at Day 61
PI(D91) = Post-vaccination at Day 91

Template 39 Estimated <GMTs,GMCs> and 95% CIs for <RSV-A neutralising antibody titre, RSV IgG antibody concentration> (PPS for immunogenicity)

				Estimated GMT		
					95% CI	
Antibody	**Group**	**Timing**	**N**	**Value**	**LL**	**UL**
<RSV-A NAb, RSV IgG antibody concentration>	RSV MAT 30	PRE				
		PI(D8)				
		PI(D31)				
		PI(D61)				
		PI(D91)				
	RSV MAT 60	PRE				
		PI(D8)				
		PI(D31)				
		PI(D61)				
		PI(D91)				
	RSV MAT 120	PRE				
		PI(D8)				
	Placebo	PRE				
		PI(D8)				

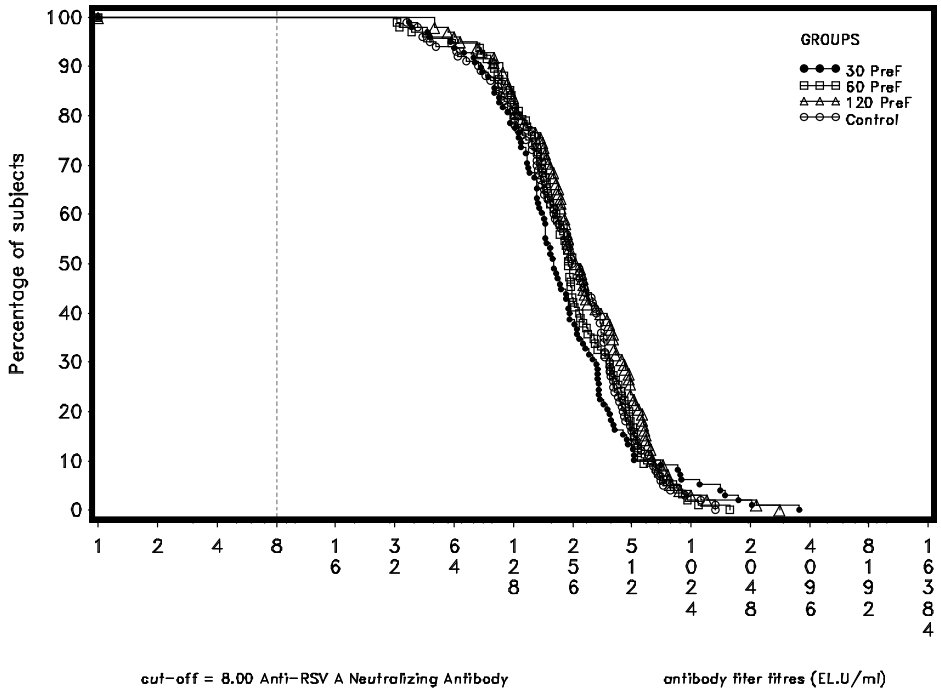
RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
GMT/C = geometric mean for <anti-RSV A Neutralizing antibody titre, RSV IgG antibody concentration> estimated by the ANOVA model for repeated measures
N = Number of subjects with available results
95% CI = 95% confidence interval (ANOVA model); LL = lower limit, UL = upper limit
PRE= Pre-vaccination at screening
PI(D8) = Post-vaccination at Day 8
PI(D31) = Post-vaccination at Day 31
PI(D61) = Post-vaccination at Day 61
PI(D91) = Post-vaccination at Day 91

Template 40 <GMTs, GMCs> and their 95% CIs for <RSV-A neutralising antibody titres, RSV IgG antibody concentration> at each timepoint up to Day <31,91> <PPS for immunogenicity>



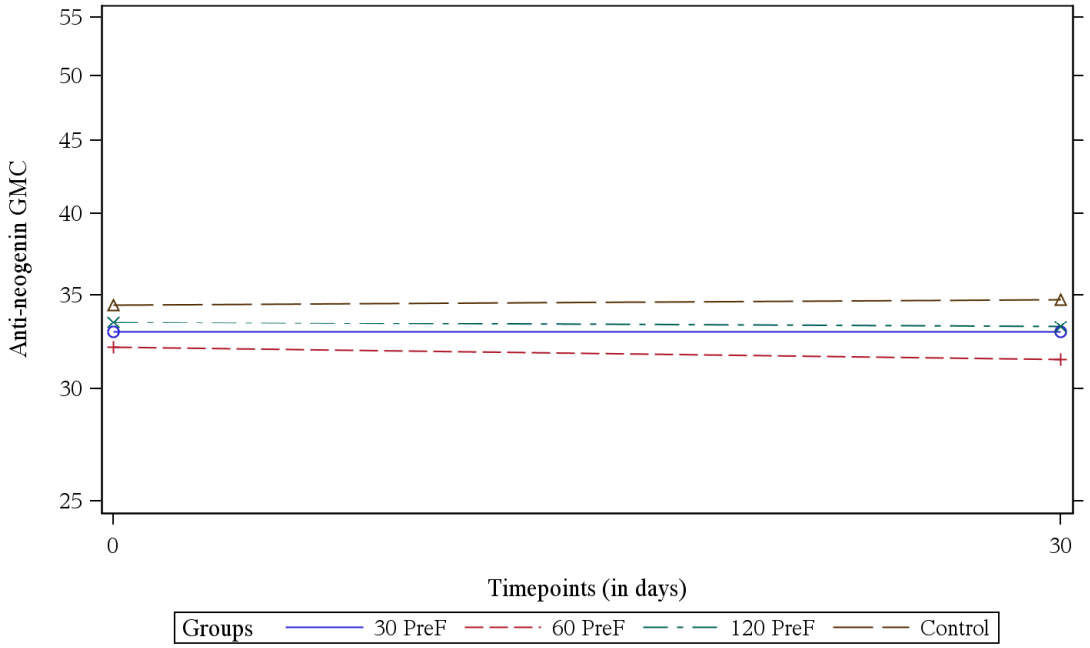
RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
<GMT,C> = geometric mean antibody <titre, concentration> calculated on all subjects
95% CI = 95% confidence interval
PRE = Pre-vaccination at screening
PI(D8) = Post-vaccination at Day 8
PI(D31) = Post-vaccination at Day 31
PI(D61) = Post-vaccination at Day 61
PI(D91) = Post-vaccination at Day 91
Note: This graph is provided as an example. For each assay separately, this graph will display the 4 groups and the 5 immuno timepoints: PRE, PI(D8), PI(D31), PI(D61) and PI(D91)

Template 41 Reverse cumulative distribution curves for <anti-RSV-A neutralising antibody titres, RSV IgG antibody concentrations> in each group at pre-vaccination and <Day 8, Day 31, Day 61, Day 91> <PPS for immunogenicity>



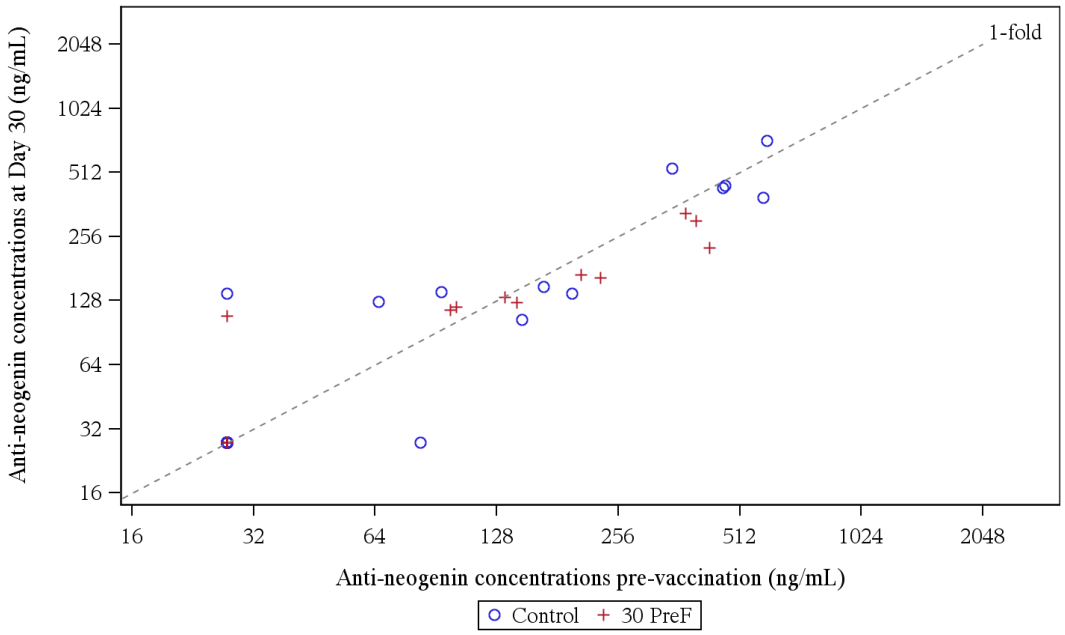
RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo

Template 42 Kinetics of <GMTs, GMCs> for <anti-RSV A neutralizing antibody titres, RSV IgG antibody concentration> on subjects with results available at all timepoints up to Day 91 <PPS for immunogenicity>



RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
Please note that graph is provided as example (our groups and timepoints are different)

Template 43 Individual results of <anti-RSV neutralizing antibody titres, RSV IgG antibody concentration> at <Day 31,61,91> versus pre-vaccination in <RSV MAT 30, RSV MAT 60, RSV MAT 120> and Placebo <PPS for immunogenicity>



RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
Figure is only a template. Actual will be done for the assays mentioned in the titles and for each group.

Template 44 Geometric Mean ratios with corresponding 95% confidence interval between anti-RSV F IgG antibody concentrations and anti-RSV-A neutralising antibody titres at pre-vaccination (PPS for immunogenicity)

									GM ratio		
				95% CI			95% CI			95% CI	
Timing	Group description	N	IgG Total GMC	LL	UL	RSV-A neut GMT	LL	UL	Value	LL	UL
PRE	<each group>										
PRE											
PRE											
PRE											

<each group>:
RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
N = Number of subjects with available results at pre-vaccination for IgG antibody concentration and RSV-A neutralizing antibody
GMC = Geometric mean antibody concentration calculated on all subjects for anti-RSV F IgG antibody concentration
GMT = Geometric mean antibody titre calculated on all subjects for RSV-A neutralizing antibody titres
GM Ratio=Geometric mean of individual ratio of IgG antibody concentration to RSV-A neutralizing antibody titre for each group
95% CI = 95% confidence interval; LL = lower limit, UL = upper limit
PRE = Pre-vaccination at screening

Template 45 Geometric Mean ratios of fold increase post/pre) with corresponding 95% confidence interval between anti-RSV F IgG antibody concentrations and anti-RSV-A neutralising antibody titres at <Day 8, Day 31, Day 61, Day 91> adjusted by pre-vaccination ratio <PPS for immunogenicity at Day <8, 31, 61, 91>>

									GMF Ratio		
										95% CI	
Timepoint	Group	N	IgG Total GMF	95% CI		RSV-A neut GMF	95%		Value	LL	UL
				LL	UL		LL	UL			
PI(D31)	<each group>										
PI(D61											
PI(D91)											

<each group>:
RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
N = Number of subjects with available results at the two considered time points for IgG antibody concentration and anti-RSV-A neutralizing antibody titres
GMF = Geometric mean of fold increase post over pre-vaccination
GMF Ratio= Geometric mean of individual ratio of fold increase for each group
95% CI = 95% confidence interval; LL = lower limit, UL = upper limit
PRE = Pre-vaccination at screening
PI(D8) = Post-vaccination at Day 8
PI(D31) = Post-vaccination at Day 31
PI(D61) = Post-vaccination at Day 61
PI(D91) = Post-vaccination at Day 91

Template 46 Exploratory comparisons (<GMT, GMC> ratios) between RSV groups with corresponding 95% confidence interval for <anti-RSV A neutralizing antibody titre, anti-RSV F IgG antibody concentration> at Day 31 – Tukey's adjustment <PPS for immunogenicity at Day 31>

							GMT ratio			
									Tukey's 95% CI	
Antibody	Group description	N	Adjusted <GMT, GMC>	Group description	N	Adjusted <GMT, GMC>	Ratio order	Value	LL	UL
<Anti-RSV A Neutralizing Antibody, RSV IgG antibody> PI(D8)	RSV MAT 120			RSV MAT 30			RSV MAT 120/RSV MAT 30			
	RSV MAT 120			RSV MAT 60			RSV MAT 120/ RSV MAT 60			
	RSV MAT 60			RSV MAT 30			RSV MAT 60/RSV MAT 30			

RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Adjusted GMT = geometric mean antibody titre adjusted for age_cat, center and baseline titre
N = Number of subjects with both pre- and post-vaccination results available
Tukey's 95% CI = 95% confidence interval for the GMT/GMC ratio (ANCOVA model: adjustment for age_cat, center and baseline titre - pooled variance;Tukey's adjustment), LL = lower limit, UL = upper limit
Age_cat is 1 for subject within age interval of 18-32 years and 2 for 33-45 years
PI(D31) = Post-vaccination at Day 31

Template 47 Exploratory comparisons (<GMT, GMC> ratios) between RSV groups with corresponding 95% confidence interval for <anti-RSV A neutralizing antibody titre, anti-RSV F IgG antibody concentration> at Day 31 <PPS for immunogenicity at Day 31>

							GMT ratio			
									95% CI	
Antibody	**Group description**	**N**	**Adjusted <GMT, GMC>**	**Group description**	**N**	**Adjusted <GMT, GMC>**	**Ratio order**	**Value**	**LL**	**UL**
<Anti-RSV A Neutralizing Antibody, RSV IgG antibody> PI(D8)	RSV MAT 120			RSV MAT 30			RSV MAT 120/RSV MAT 30			
	RSV MAT 120			RSV MAT 60			RSV MAT 120/ RSV MAT 60			
	RSV MAT 60			RSV MAT 30			RSV MAT 60/RSV MAT 30			

RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Adjusted GMT = geometric mean antibody titre adjusted for age_cat, center and baseline titre
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the GMT/GMC ratio (ANCOVA model: adjustment for age_cat, center and baseline titre - pooled variance), LL = lower limit, UL = upper limit
Age_cat is 1 for subject within age interval of 18-32 years and 2 for 33-45 years
PI(D31) = Post-vaccination at Day 31

Template 48 Exploratory comparisons (Geometric mean ratios) between RSV groups with corresponding 95% confidence interval for area under curve (AUC) up to Day 91 for <anti-RSV A neutralizing antibody titre, anti-RSV F IgG antibody concentration> <PPS for immunogenicity>

							GM ratio			
									95% CI	
Antibody	**Group description**	**N**	**Adjusted <GM>**	**Group description**	**N**	**Adjusted <GM>**	**Ratio order**	**Value**	**LL**	**UL**
<Anti-RSV A Neutralizing Antibody, RSV IgG antibody> PI(D8)	RSV MAT 120			RSV MAT 30			RSV MAT 120/RSV MAT 30			
	RSV MAT 120			RSV MAT 60			RSV MAT 120/ RSV MAT 60			
	RSV MAT 60			RSV MAT 30			RSV MAT 60/RSV MAT 30			

RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Adjusted GM = geometric mean of area under curve (AUC) adjusted for age_cat, center and baseline titre
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the GMT/GMC ratio (ANCOVA model: adjustment for age_cat, center and baseline titre - pooled variance), LL = lower limit, UL = upper limit
Age_cat is 1 for subject within age interval of 18-32 years and 2 for 33-45 years

Template 49 Exploratory comparisons (<GMT, GMC> ratios) between RSV groups and placebo with corresponding 95% confidence interval for <RSV A neutralizing antibody titre, RSV F IgG antibody concentration> at Day 31 <PPS for immunogenicity at Day 31>

								GMT ratio				
										Adjusted 95% CI		Adjusted p-value
Antibody	**Timepoint**	**Group description**	**N**	**<GMT, GMC>**	**Group description**	**N**	**<GMT, GMC>**	**Ratio order**	**Value**	**LL**	**UL**	
<RSV-A NAb, RSV IgG antibody>	PI(D8)	RSV MAT 120			Placebo			RSV MAT 120/Placebo				
		RSV MAT 60			Placebo			RSV MAT 60/ Placebo				
		RSV MAT 30			Placebo			RSV MAT 30/Placebo				

RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
Adjusted GMT = geometric mean antibody titre adjusted for age_cat, center and baseline titre
N = Number of subjects with both pre- and post-vaccination results available
95% CI = 95% confidence interval for the GMT/GMC ratio (ANCOVA model: adjustment for age_cat, center and baseline titre - pooled variance), LL = lower limit, UL = upper limit
P-values were adjusted according to Dunnett for multiple comparisons to placebo
Age_cat is 1 for subject within age interval of 18-32 years and 2 for 33-45 years
PI(D31) = Post-vaccination at Day 31

Template 50 Descriptive statistics of <anti-RSV A neutralizing antibody titre, anti-RSV F IgG antibody concentration>at pre-vaccination, Day <8, 31, 61, 91><PPS for immunogenicity>

		Each Group N=		
			95% CI	
Visit	**Parameters**	**Value**	**LL**	**UL**
PRE	N with data			
	Mean			
	SD			
	Q1			
	Median			
	Q3			
PI(D8)	…			
PI(D31)	…			
PI(D61)	…			
PI(D91)	…			

<each group>:
RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
N = total number of subjects
N with data = number of subjects with available results
Value = value of the considered parameter
SD = standard deviation
Q1 and Q3 = 1st and 3rd quantiles
LL, UL = Exact 95% Lower and Upper confidence limits
PRE = Pre-vaccination at screening
PI(D8) = Post-vaccination at Day 8
PI(D31) = Post-vaccination at Day 31
PI(D61) = Post-vaccination at Day 61
PI(D91) = Post-vaccination at Day 91

Template 51 Descriptive statistics of area under the curve up to Day 91 for <anti-RSV A neutralizing antibody titre, anti-RSV F IgG antibody concentration> 91><PPS for immunogenicity>

		Each Group N=		
			95% CI	
Timepoint	**Parameters**	**Value**	**LL**	**UL**
Up to Day 91	N with data			
	Mean			
	SD			
	Q1			
	Median			
	Q3			

<each group>:
RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Placebo = Subject receiving placebo
N = total number of subjects
N with data = number of subjects with documentation of the corresponding data
Value = value of the considered parameter
SD = standard deviation
Q1 and Q3 = 1st and 3rd quantiles
LL, UL = Exact 95% Lower and Upper confidence limits

Template 52 Assessment of trend (linear or quadratic) of dose response for <<anti-RSV A neutralizing antibody titre, anti-RSV F IgG antibody concentration> between three RSV vaccine groups at Day 31 <PPS for immunogenicity at Day 31>

Antibody	**Trend Test**	**N**	**P value**
<Anti-RSV A Neutralizing Antibody, RSV IgG antibody>	Linear		
	Quadratic		

<each group>:
RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Analysed using ANCOVA fitting treatment as fixed effect and age_cat, center and baseline titre as covariate
Contrast used for evaluating <linear,quadratic> trend is
Age_cat is 1 for subject within age interval of 18-32 years and 2 for 33-45 years

Template 53 Assessment of trend (linear or quadratic) of dose response using area under curve up to Day 91 for <<anti-RSV A neutralizing antibody titre, anti-RSV F IgG antibody concentration> between three RSV vaccine groups <PPS for immunogenicity>

Antibody	Trend Test	N	P value
<Anti-RSV A Neutralizing Antibody, RSV IgG antibody>	Linear		
	Quadratic		

<each group>:

RSV MAT 30 = Subject receiving RSVPreF3 low dose
RSV MAT 60 = Subject receiving RSVPreF3 mid dose
RSV MAT 120 = Subject receiving RSVPreF3 high dose
Analysed using ANCOVA fitting treatment as fixed effect and age_cat, center and baseline titre as covariate
Age_cat is 1 for subject within age interval of 18-32 years and 2 for 33-45 years