GlaxoSmithKline	**Statistical Analysis Plan**
Detailed Title:	A Phase 1/2, randomized, observer-blind, controlled, multi-center study to evaluate safety, reactogenicity and immunogenicity of GSK Biologicals' (RSV) investigational vaccine based on the RSV viral proteins F, N and M2-1 encoded by chimpanzee-derived adenovector (ChAd155-RSV) (GSK3389245A), when administered intramuscularly ***as*** a single dose or as two doses according to a 0, 1-month schedule**,** to infants aged 6 and 7 month
eTrack study number and Abbreviated Title	204894 (RSV PED-011)
Scope:	All data pertaining to the above study
Date of Statistical Analysis Plan	Final: 27 March 2019
Co-ordinating author:	PPD (Statistician)
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 Affairs); PPD (SERM physician); PPD – safety scientist; PPD (Public disclosure representative)
Approved by:	PPD (Clinical and Epidemiology Project Lead); PPD (Lead statistician); PPD (Study Statistician); PPD (Lead Scientific writer); PPD (Lead statistical Analyst)

APP 9000058193 Statistical Analysis Plan Template (Effective date: 5th March 2019)

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LIST OF ABBREVIATIONS

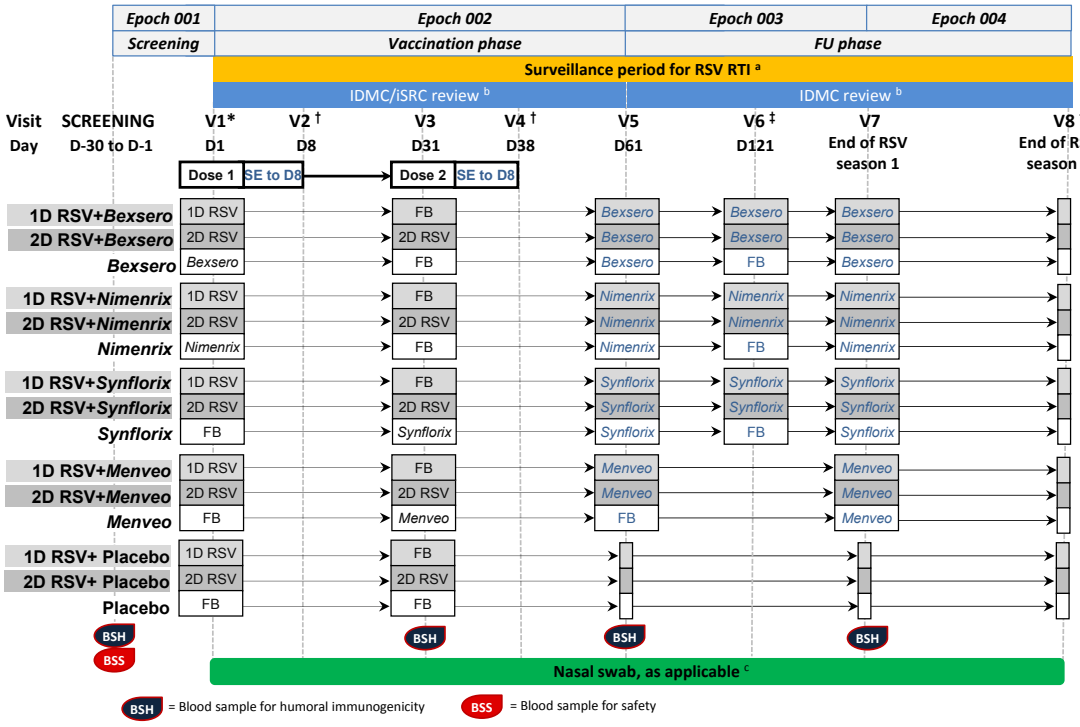
AE	Adverse event
AESI	Adverse Events of Special Interest
ChAd155-RSV	Investigational recombinant chimpanzee adenovirus Type 155-vectored RSV vaccine
CI	Confidence Interval
ERD	Enhanced Respiratory Disease
ES	Exposed Set
GMC	Geometric mean antibody concentration
GMT	Geometric mean antibody titre
GSK	GlaxoSmithKline
LL	Lower Limit of the confidence interval
LLOQ	Lower Limit of Quantification
LRTI	Lower respiratory tract infection
MedDRA	Medical Dictionary for Regulatory Activities
NA	Not Applicable
PD	Protocol Deviation
PPS	Per-Protocol Set
RR	Relative Risk
RSV	Respiratory Syncytial Virus
RTI	Respiratory Tract Infection
SAE	Serious adverse event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SDTM	Study Data Tabulation Model
SPM	Study Procedure Manual
SR	Study Report
TFL	Tables Figures and Listings
ToC	Table of Content
UL	Upper Limit of the confidence interval
ULOQ	Upper Limit of Quantification

1. DOCUMENT HISTORY

Date	Description	Protocol Version
27 MAR 2019	Final	Amendment 3: 21 MAR 2019

2. STUDY DESIGN

Figure 1 Study design



D: Day; **FU**: follow-up; **IDMC**: Independent Data Monitoring Committee; **iSRC**: internal Safety Review Committee; **RSV**: respiratory syncytial virus; **RTI**: respiratory tract infection; **SE**: solicited events; **V**: Visit **1D**: 1 Dose ($1.5x10^{10}$ vp/dose); **2D**: 2 Dose ($5x10^{10}$ vp/dose); FB: Formulation buffer S9b.

* Vaccine Dose 1 at Day 1 will be administered before the first RSV season (refer to Section 5.1 of the protocol for definition of RSV season).

† Visit 2 (Day 8), Visit 4 (Day 38), and Visit 8 (no blood sampling for immune response and no vaccine administration) may take place in the subject's home or at the investigators clinical facility as appropriate to the circumstances in the judgment of the investigator. For authorized sites only, Visit 5 (Day 61) and Visit 7 (both with blood sampling) may also take place in the subject's home or at the investigators clinical facility as appropriate to the circumstances in the judgment of the investigator

‡ In countries where *Menveo* or Placebo is used as a comparator, no administration will be performed at Day 121 and therefore in those countries there will be no Visit 6 and it will be administered at the end of the first RSV season at Visit 7 (refer to Table 2 and Table 7 of the protocol).

[a] Surveillance for RSV-RTI comprises monthly nasal swab collected to detect asymptomatic RSV infections during RSV season and active and passive surveillance contacts for RSV symptomatic RTI. Of note the swab may be omitted if a nasal swab has been taken at a symptomatic visit in the same month (see Section 9.2 of the protocol). Data about RSV–RTI incidence will be reviewed monthly by an IDMC.

[b] An iSRC will review all accumulating safety data monthly until the IDMC reviews has reviewed all safety data up to 30 days after administration of Dose 2 (i.e., Day 61). The IDMC will review all accumulating safety data monthly throughout the period of vaccination and accumulating SAEs until the end of the second RSV transmission season. Refer to Sections 9.10.2 and 9.10.3 of the protocol.

c Refer to Section 6.6.12.3 of the protocol

Table 1 Vaccines administered and vaccination schedules

Groups	Age* (Months) / (Visit, Day)				
	6-7 / (V1, D1)	**7-8 / (V3, D31)**	**8-9 / (V5, D61)**	**10-11 / (V6, D121)****	**14-18 / (V7)**
1D RSV + *Bexsero*	1D RSV ChAd	FB	*Bexsero*	*Bexsero*	*Bexsero*
2D RSV + *Bexsero*	2D RSV ChAd	2D RSV ChAd	*Bexsero*	*Bexsero*	*Bexsero*
Bexsero	*Bexsero*	FB	*Bexsero*	FB	*Bexsero*
1D RSV + *Nimenrix*	1D RSV ChAd	FB	*Nimenrix*	*Nimenrix*	*Nimenrix*
2D RSV + *Nimenrix*	2D RSV ChAd	2D RSV ChAd	*Nimenrix*	*Nimenrix*	*Nimenrix*
Nimenrix	*Nimenrix*	FB	*Nimenrix*	FB	*Nimenrix*
1D RSV + *Synflorix*	1D RSV ChAd	FB	*Synflorix*	*Synflorix*	*Synflorix*
2D RSV + *Synflorix*	2D RSV ChAd	2D RSV ChAd	*Synflorix*	*Synflorix*	*Synflorix*
Synflorix	FB	*Synflorix*	*Synflorix*	FB	*Synflorix*
1D RSV + *Menveo*	1D RSV ChAd	FB	*Menveo*		*Menveo*
2D RSV + *Menveo*	2D RSV ChAd	2D RSV ChAd	*Menveo*		*Menveo*
Menveo	FB	*Menveo*	FB		*Menveo*
1D RSV + Placebo	1D RSV ChAd	FB			
2D RSV + Placebo	2D RSV ChAd	2D RSV ChAd			
Placebo	FB	FB			

V: Visit; **D**: Day; **1D**: 1 Dose ($1.5x10^{10}$ vp/dose); **2D**: 2 Dose ($5x10^{10}$ vp/dose); **RSV ChAd**: ChAd155-RSV vaccine; **FB**: Formulation buffer S9b.

* Assumes enrolled at 6 and 7 months of age for the vaccine Dose 1 to be administered before the first RSV season; the second dose will be given one month after the first dose. (RSV seasons will be determined for each country based on local epidemiological data [The RSV season is defined as the period of the year when 70% of the RSV cases have occurred in previous years. For the calculation, where available, data from up to the ten previous years should be applied. If the data permit calculation of the actual date of the beginning of the season, rather than approximation to the nearest month, this is desirable. Refer to the SPM for RSV seasons per country.])

** In countries where *Menveo* or Placebo is used as a comparator, no administration will be performed at Day 121 and therefore in those countries there will be no Visit 6 and it will be administered at the end of the first RSV season at Visit 7.

- Experimental design: Phase I/II, observer-blind, randomized, controlled, multi-centric study with three parallel groups
- Duration of the study: approximately 24 months.
  - Epoch 001: Screening Visit starting up to 30 days before first vaccination and ending on Day -1.
  - Epoch 002: primary starting at Visit 1 (Day 1) and ending at Visit 5 (Day 61).
  - Epoch 003: follow-up starting after Visit 5 (Day 61)* and ending at Visit 7 (end of the first RSV transmission season).
  - Epoch 004: follow-up starting after Visit 7 (end of the first RSV transmission season)* and ending at Visit 8 (end of the second RSV transmission season).

  *Any safety, immunogenicity and disease surveillance data collected beyond Visit 5 (Day 61) will be collected in Epoch 003. Any safety, immunogenicity and disease surveillance data collected beyond Visit 7 (end of the first RSV transmission season) will be collected in Epoch 004. Refer to the SPM for RSV transmission seasons per country.
- Primary Completion Date (PCD): Visit 5 (Day 61).

- End of Study (EoS): Last testing results released of samples collected at Visit 8 (end of the second RSV transmission season) related to primary and secondary endpoints.*

  * Up to Visit 8 (end of the second RSV season), there will be monthly nasal swab to detect asymptomatic RSV infections during the RSV season ***or*** if following active or a passive surveillance contacts, a subject presents symptoms of respiratory tract infection (RTI), a nasal swab will be collected.

- Study groups:

Table 2 Study groups and epochs foreseen in the study

Study groups	Target Number of subjects	Age (Min/Max)	Epochs			
			Epoch 001	Epoch 002	Epoch 003	Epoch 004
1D RSV + *Bexsero*	50	6 – 7 months	N/A	x	x	x
1D RSV + *Nimenrix*		6 – 7 months	N/A	x	x	x
1D RSV + *Synflorix*		6 – 7 months	N/A	x	x	x
1D RSV + *Menveo*		6 – 7 months	N/A	x	x	x
1D RSV + *Placebo*		6 – 7 months	N/A	x	x	x
2D RSV + *Bexsero*	50	6 – 7 months	N/A	x	x	x
2D RSV + *Nimenrix*		6 – 7 months	N/A	x	x	x
2D RSV + *Synflorix*		6 – 7 months	N/A	x	x	x
2D RSV + *Menveo*		6 – 7 months	N/A	x	x	x
2D RSV + *Placebo*		6– 7 months	N/A	x	x	x
Bexsero	50	6 – 7 months	N/A	x	x	x
Nimenrix		6 – 7 months	N/A	x	x	x
Synflorix		6 – 7 months	N/A	x	x	x
Menveo		6 – 7 months	N/A	x	x	x
Placebo		6 – 7 months	N/A	x	x	x

1D: 1 Dose ($1.5x10^{10}$ vp/dose); **RSV**: ChAd155-RSV vaccine; **2D**: 2 Dose ($5x10^{10}$ vp/dose); N/A: Not Applicable.

Table 3 Study groups and treatment foreseen in the study

Treatment name	*1D RSV ChAd*	*2D RSV ChAd*	*Bexsero*	*Nimenrix*	*Synflorix*	*Menveo*	*FB*
Vaccine/ Product name	*1D ChAd155-RSV 1.5X10[10] vp/dose*	*2D ChAd155-RSV 5X10[10] vp/dose*	*Bexsero*	*Nimenrix*	*Synflorix*	*Menveo*	*FB*
Study Groups							
1D RSV + Bexsero	*x*		*x*				*x*
1D RSV + Nimenrix	*x*			*x*			*x*
1D RSV + Synflorix	*x*				*x*		*x*
1D RSV + Menveo	*x*					*x*	*x*
1D RSV + Placebo	*x*						*x*
2D RSV + Bexsero		*x*	*x*				
2D RSV + Nimenrix		*x*		*x*			
2D RSV + Synflorix		*x*			*x*		
2D RSV + Menveo		*x*				*x*	
2D RSV + Placebo		*x*					
Bexsero			*x*				*x*
Nimenrix				*x*			*x*
Synflorix					*x*		*x*
Menveo						*x*	*x*
Placebo							*x*

ChAd155-RSV: Chimpanzee Adenovirus Type 155 RSV vaccine; **FB**: Formulation buffer S9b; **RSV ChAd**: ChAd155-RSV vaccine; **1D**: 1 Dose ($1.5x10^{10}$ vp/dose); **2D**: 2 Dose ($5x10^{10}$ vp/dose).

- Controls: active comparator vaccines (*Bexsero*, or *Nimenrix*, or *Synflorix*, or *Menveo*, or Placebo (FB)*.

  * The choice of active comparator vaccine (*Bexsero*, *Nimenrix*, *Synflorix*, or *Menveo*) or Placebo is done at the country level. Refer to the ICF for the local choice of comparator/Placebo.

- Vaccination schedules:

  – **RSV investigational vaccine:** In the 1 Dose (1D) groups, a single lower dose of $1.5x10^{10}$ vp will be administered IM at Day 1 (Visit 1). Formulation buffer will be administered in the 1D groups at Day 31 (Visit 3). In the 2 Dose (2D) groups, two doses of $5x10^{10}$ vp will be administered IM according to a 0, 1-month schedule, (i.e., at Day 1 [Visit 1] and Day 31 [Visit 3]) (see Figure 1 and Table 1). Dose 1 will be administered before the first RSV season and the second dose will be given one month after the first dose (RSV seasons will be determined for each country based on local epidemiological data and documented in the Study Procedures Manual [SPM]. The RSV season is defined as the period of the year when 70% of the RSV cases have occurred in previous years. For the calculation, where available, data from up to the ten previous years should be applied. If the data permit calculation of the actual date of the beginning of the season, rather than approximation to the nearest month, this is desirable.)

  – **Comparator or Placebo:** In countries where *Bexsero* or *Nimenrix* is used as a control, two doses will be administered IM with at least a 2-month interval between these primary doses. A booster dose will be administered IM in the second year of life at Visit 7, with an interval of at least 2 months between the

primary series and booster dose. The first *Bexsero* or *Nimenrix* dose will be administered at Day 1 (Visit 1) (in the groups receiving only *Bexsero* or *Nimenrix*, respectively). In the groups receiving only *Bexsero* or *Nimenrix*, the second dose will be at Day 61 (Visit 5). The first *Bexsero* or *Nimenrix* dose to be administered to the 1D and 2D RSV groups will be at Day 61 (Visit 5), following the 1 or 2 RSV vaccine doses, respectively. The second dose of *Bexsero* or *Nimenrix* in the 1D and 2D groups will be at Day 121 (Visit 6). Formulation buffer will be administered, when neither RSV vaccine nor comparator is scheduled, at the 5 vaccination visits (see Figure 1 and Table 1).

- In countries where *Synflorix* is used as a control, two doses will be administered IM with at least a 1 month interval between these primary doses. A booster dose will be administered IM in the second year of life at Visit 7. The first *Synflorix* dose will be administered at Day 31 (Visit 3) (in the group receiving only *Synflorix*). In the group receiving only *Synflorix*, the second dose will be at Day 61 (Visit 5). The first *Synflorix* dose to be administered to the 1D and 2D RSV groups will be at Day 61 (Visit 5), following the 1 or 2 RSV vaccine doses, respectively. The second dose of *Synflorix* in the 1D and 2D groups will be at Day 121 (Visit 6). Formulation buffer will be administered, when neither RSV vaccine nor comparator is scheduled, at the 5 vaccination visits (see Figure 1 and Table 1).
- In countries where *Menveo* is used as a control, two doses will be administered IM at least 3 months apart with the second dose in the second year of life at Visit 7. The first *Menveo* dose will be administered at Day 31 (Visit 3) (in the group receiving only *Menveo*). The first *Menveo* dose to be administered to the 1D and 2D RSV groups will be at Day 61 (Visit 5), following the 1 or 2 RSV vaccine doses, respectively. Since the second *Menveo* dose has to be administered in the second year of life at Visit 7, no administration will be performed at Day 121 (Visit 6). Formulation buffer will be administered, when neither RSV vaccine or comparator is scheduled, at the 4 vaccination visits (see Figure 1 and Table 1).
- In countries where Placebo is used as a control, one dose will be administered IM at Day 31 (Visit 3) in the 1D RSV + Placebo group and two IM doses will be administered IM according to a 0, 1-month schedule at Day 1 (Visit 1) and Day 31 (Visit 3) in the Placebo group (see Figure 1 and Table 1)**.**

- Treatment allocation: infants will be randomized using a centralized randomization system on internet (SBIR) before first vaccination and after assessment of eligibility (i.e., after screening conclusion) (refer to Section 6.2.2 of the protocol for details about randomization of treatment). The randomization algorithm will use a minimization procedure accounting for country as a minimization factor and the grouping comparator/placebo as a stratification factor.
- Blinding: not applicable for Epoch 001 (Screening Visit), observer-blind in Epoch 002 and single-blind in Epoch 003 and Epoch 004. Refer to Section 6.3 of the protocol for details of blinding procedure.

- Blinding of study epochs

Study Epochs	Blinding
Epoch 001	N/A
Epoch 002	observer-blind
Epoch 003	single-blind
Epoch 004	single-blind

- Sampling schedule:
  - Blood samples for **hematology/biochemistry** will be taken from all infants at Screening (up to 30 days before first vaccination to Day -1). Blood samples for **hematology/biochemistry** may be taken from infants at any timepoints, if deemed necessary by the investigator. Refer to Table 12 of the protocol for the list of parameters to be tested.
  - Refer to Section 6.6.1.2.2 and Figure 2 of the protocol for information about the re-testing of samples in case of any Grade 1 abnormality with potential clinical relevance (according to investigators judgment) or any ≥ Grade 2 abnormality.
  - Blood samples for **humoral immunogenicity** will be taken from all subjects at Screening and on Day 31, Day 61, and at the visit occurring at the end of the first RSV transmission season.
  - Blood sample for **assessment of mechanism of illness (potential ERD)** will be taken from subjects hospitalized for LRTI (only for RSV-positive subjects using a locally available RSV test).
  - Nasal swab: there will be monthly nasal swab to detect asymptomatic RSV infections during the RSV season and if following active or a passive surveillance contacts, a subject present symptoms of RTI, a nasal swab will be collected (as well as a sample for local testing i.e., the type of sample to be determined locally [e.g., swab, etc.]) (Refer to the SPM).
- Study visits: Other than the screening visit and assessment visits for active/passive surveillance, there will be 8 study visits except in countries where *Menveo* or Placebo is used as a control where there will be 7 study visits.
  - In countries where *Menveo* is used as a comparator, no administration will be performed at Day 121 and therefore in those countries there will be no Visit 6 and it will be administered at the end of the first RSV season at Visit 7 (refer to Table 2 and 7 of the protocol).
  - In countries where Placebo is used as a control, no vaccine administration will be performed after Visit 3 and therefore in those countries there will be no Visit 6. There will be a Visit 5 and Visit 7 for countries using Placebo and all other study procedures will occur at these visits except vaccination.
  - Visit 2 (Day 8), Visit 4 (Day 38), and Visit 8 (no blood sampling for immune response and no vaccine administration) may take place in the subject's home or at the investigators clinical facility as appropriate to the circumstances in the judgment of the investigator.

- For authorized sites only, Visit 5 (Day 61) and Visit 7 (both with blood sampling) may also take place in the subject's home or at the investigators clinical facility as appropriate to the circumstances in the judgment of the investigator.
- Data collection: electronic Case Report Form (eCRF).
- Safety monitoring: internal safety review committee (iSRC) and IDMC (refer to Section 9.10 of the protocol).

- **Surveillance for RSV-RTI, difficulty in breathing, and wheezing episodes** Surveillance period will be carried out from Visit 1 (after Dose 1) until the last study visit (end of the second RSV transmission season). In order to detect asymptomatic RSV-RTI, monthly nasal swabs for analysis at sponsor laboratory will be performed for all subjects during the RSV season. In order to timely detect RSV-RTI and to ensure cases are timely captured by the study sites, both active and passive surveillance will be conducted:
  - **Passive surveillance**: parent(s)/LAR(s) are instructed to contact the investigator/study staff as soon as the subject experiences new RTI symptoms (cough, runny nose or blocked nose) or worsening of RTI symptoms, or in case of difficulty in breathing or wheezing.
  - **Active surveillance**: parent(s)/LAR(s) of all the subjects will be contacted by the investigator/study staff on a regular basis (weekly during the RSV season and every month outside the RSV season) to identify any potential RSV-RTI and to remind the parent(s)/LAR(s) of the subjects to report any new occurrence of RTI symptoms (cough, runny nose or blocked nose), or in case of difficulty in breathing or wheezing as soon as possible.

Refer to Section 9.2 of the protocol for more information about active and passive surveillance.

- Surveillance for spontaneous or excessive bleeding - Subjects' parent(s)/LAR(s) will be instructed to contact the investigator/study staff if their child presents symptoms of spontaneous bleeding or easy bruising or if their child develops a rash, within 30 days after either vaccination (Visit 1 and Visit 3), in order to detect any thrombocytopenic petechiae or purpura. The investigator will, based on his/her medical judgment, measure the total blood count and appropriately investigate infants with clinical suspicion of low platelets**.**
- **Group description**: - For the blinded report on safety/reactogenicity, the analyses will be presented as one group (RSV groups and Placebo group being pooled).

The following group names for the unblinded analysis 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	Pooled Groups label in tables – UNBLINDED ANALYSIS	Pooled definition for footnote - UNBLINDED ANALYSIS
1	RSVBEX1D	RSV 1D + BEXERO 3D	RSV 1D	Pooled 1D RSV
2	RSVNIM1D	RSV 1D +NIMENRIX 3D		
3	RSVSYN1D	RSV 1D +SYNFLORIX 3D		
4	RSVMEN1D	RSV 1D +MENVEO 2D		
5	RSVPBO1D	RSV 1D + PLACEBO		
6	RSVBEX2D	RSV 2D + BEXERO 3D	RSV 2D	Pooled 2D RSV
7	RSVNIM2D	RSV 2D +NIMENRIX 3D		
8	RSVSYN2D	RSV 2D +SYNFLORIX 3D		
9	RSVMEN2D	RSV 2D +MENVEO 2D		
10	RSVPBO2D	RSV 2D + PLACEBO		
11	BEXERO	BEXERO 3D	COMP_PLB	Pooled comparator
12	NIMENRIX	NIMENRIX 3D		
13	SYNFLORIX	SYNFLORIX 3D		
14	MENVEO	MENVEO 2D		
15	PLACEBO	PLACEBO		

3. OBJECTIVES/ENDPOINTS

3.1. Objectives

3.1.1. Primary Objective

- To evaluate the safety and reactogenicity of the RSV investigational vaccine when administered IM as one ($1.5x10^{10}$ vp) dose or as two ($5x10^{10}$ vp) doses according to a 0, 1-month schedule**,** up to 60 days after Dose 1 (i.e., Day 61) in infants aged 6 and 7 months.

3.1.2. Secondary Objective

- To evaluate the occurrence of RSV respiratory tract infections of any severity from Visit 1 (Day 1, after Dose 1) up to the end of the first RSV transmission season, in infants aged 6 and 7 months
- To evaluate the safety of the RSV investigational vaccine when administered IM as one ($1.5x10^{10}$ vp) dose or as two ($5x10^{10}$ vp) doses according to a 0, 1-month schedule, from study start (Day 1) up to the end of the second RSV transmission season in infants aged 6 and 7 months
- To evaluate the occurrence of RSV respiratory tract infections from Visit 1 (Day 1, after Dose 1) up to the end of the second RSV transmission season, in infants aged 6 and 7 months.

- To evaluate the occurrence of very severe RSV-LRTI from Visit 1 (Day 1, after Dose 1) up to the end of the first RSV transmission season in RSV infected infants aged 6 and 7 months with a negative RSV exposure status (at screening based on in-stream baseline serological testing.
- To evaluate the humoral immunogenicity induced by the RSV investigational vaccine when administered IM as one ($1.5x10^{10}$ vp) dose or as two ($5x10^{10}$ vp) doses according to a 0, 1-month schedule, from study start (Day 1) up to the end of the first RSV transmission season, in infants aged 6 and 7 months.

3.1.3. Tertiary objective

- If deemed necessary, to further characterize the immune response of the RSV investigational vaccine when one ($1.5x10^{10}$ vp) dose or two ($5x10^{10}$ vp) doses are administered IM according to a 0, 1-month schedule to infants aged 6 and 7 months

3.2. Endpoints

3.2.1. Primary endpoints

- Occurrence of adverse events (AEs) from first vaccination (Day 1) up to Day 61
  - Occurrence of each solicited local and general AE, during a 7-day follow-up period after each vaccination (i.e., the day of vaccination and 6 subsequent days)
  - Occurrence of any unsolicited AE, during a 30-day follow-up period after each vaccination (i.e., the day of vaccination and 29 subsequent days)
  - Occurrence of any serious adverse event (SAE) from Day 1 up to Day 61
  - Occurrence of episode of spontaneous or excessive bleeding (AE of special interest), during a 30-day follow-up period after each vaccination

3.2.2. Secondary endpoints

- Occurrence of RSV-RTI, RSV-LRTI, severe RSV-LRTI and very severe RSV-LRTI (according to standardized case definitions) as from first vaccination (Day 1) up to the end of the first RSV transmission seasons.
- Occurrence of RSV-RTI, RSV-LRTI, severe RSV-LRTI and very severe RSV-LRTI (according to standardized case definitions) as from first vaccination (Day 1) up to the end of the second RSV transmission seasons.
- Occurrence of SAEs from first vaccination (Day 1) up to the end of the second RSV transmission seasons.
- Occurrence of RSV-LRTI (AE of special interest) as from first vaccination (Day 1) up to the end of the first RSV transmission season, and up to the end of the second RSV transmission seasons.

- Occurrence of very severe RSV-LRTI (according to standardized case definitions) among RSV infected infants with a negative RSV exposure status (at screening based on in-stream baseline serological testing) from first vaccination (Day 1) up to the end of the first RSV transmission seasons.
- Humoral response to the investigational RSV vaccine, pre-vaccination (Screening), post-Dose 1 (Day 31) and post-Dose 2 (Day 61 and at the end of the first RSV transmission season):
  - Neutralizing antibody titers against RSV-A
  - RSV F antibody concentrations

3.2.3. Tertiary endpoints

- Humoral response to the investigational RSV vaccine, pre-vaccination (Screening), post-Dose 1 (Day 31) and post-Dose 2 (Day 61)
  - Palivizumab-competing antibody concentrations
- Any further exploratory immunology to detect disease-related or vaccine-related immune responses, such as but not limited to
  - Anti-vector immunity: neutralization

4. ANALYSIS SETS

4.1. Definition

4.1.1. Exposed Set

The Exposed Set (ES) will include all subjects with at least one study vaccine administration documented.

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

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

4.1.2. Exposed Set of subjects with a negative RSV exposure status

The Exposed Set of subjects with a negative RSV exposure status will include all vaccinated subjects assessed as RSV unexposed at screening based on in-stream baseline serological testing

The safety analysis of incidence of RSV-LRTI will be conducted on the cohort of subjects with a negative RSV exposure status (at screening based on in-stream baseline serological testing) as well as on the entire ES.

4.1.3. Per-protocol Set for analysis of immunogenicity

The per-protocol set (PPS) cohort for analysis of immunogenicity will be defined by timepoint (Day 31, Day 61 and End of the first RSV transmission season) and will consist of all subjects from the ES who complied with eligibility criteria, study procedures up to the end of the study and had immunogenicity results in the epoch as described below,

More specifically, the PPS cohort for analysis of immunogenicity for specific timepoint (Day 31 [Visit 3], Day 61 [Visit 5] and at end of the first RSV transmission season [Visit 7]) will include all evaluable subjects:

- Who met all eligibility criteria (i.e., no protocol violation linked to the inclusion/exclusion criteria, including age).
- Who received study vaccine as scheduled per protocol.
- For whom the administration route and site of the vaccine was as according to protocol.
- Who received the vaccine according to protocol procedures.
- Who complied with the vaccination schedule, as specified Table 4 in of the SAP.
- Who did not receive a concomitant medication/product/vaccine leading to exclusion from a PPS analysis, as described in Section 7.6.2 of the protocol, up to Day 31 (Visit 3)/up to Day 61 (Visit 5) /at Visit 7 (end of the first RSV transmission season).
- Who complied with the timings of the post vaccination blood sampling for immune response evaluation, up to Day 31 (Visit 3)/up to Day 61 (Visit 5) /at Visit 7 (end of the first RSV transmission season), as specified in Table 4 of the SAP.

When presenting different time-points, the PPS for immunogenicity will be adapted for each time-point (Day 31, Day 61 and End of first RSV transmission season).

Table 4 presents the intervals between study visits that determine subjects' eligibility for inclusion in the PPS analysis.

Table 4 Maximum allowed interval between study visits for PPS

Interval	Allowed length of interval[1]
Visit 1 (Day 1) → Visit 3 (Day 31)	23 - 44 days
Visit 1 (Day 1) → Visit 5 (Day 61)	60 - 81 days
Visit 3 (Day 31) → Visit 5 (Day 61)	28 - 37 days [2]
Visit 5 (Day 61) → Visit 7 (end of the first RSV transmission season)	90 days to the defined end of transmission season or up to 4 weeks after

[1] Subjects will not be eligible for inclusion in the PP cohort for analysis of immunogenicity if they make the study visit outside this interval.

[2] The interval between Visit 1 and Visit 5 must be a minimum of 60 days to be in line with the active comparator vaccination schedules as per the respective approved labels.

4.2. Criteria for eliminating data from Analysis Sets

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

4.2.1. Elimination from Exposed Set (ES)

Code 1030 (Study vaccine not administered at all), code 900 (invalid informed consent) and code 800 (fraudulent data) will be used for identifying subjects eliminated from ES.

4.2.2. Elimination from Exposed Set (ES) subjects with a negative RSV exposure status

Code 1030 (Study vaccine not administered at all), code 900 (invalid informed consent) and code 800 (fraudulent data) will be used for identifying subjects eliminated from ES. Additionally, code 2020 (RSV- seropositive antibody status at baseline) will be used to identify all the subject with negative RSV exposure status.

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

4.2.3.1. Excluded subjects

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

For codes 1040, 1070, 1080, 1090, 2040, 2060, 2070, 2080: subjects will be eliminated from a specific visit (at which the condition is met) onwards.

For codes 2090, 2100, 2120: subjects will be eliminated at the specific visit at which the condition is met

Code	Condition under which the code is used	Visit (timepoints) where the code is applicable	Applicable for analysis set
800	Fraudulent data	All	All
900	Invalid informed consent	All	all
1030	Study vaccine not administered at all	All	Safety, immunology
1040	Administration of concomitant vaccine(s) forbidden in the protocol:- • Any investigational or non-registered product (drug or vaccine) other than the study vaccines used during the study period • A vaccine not foreseen by the study protocol administered during the period starting 30 days before the first dose and ending 30 days after the last dose of vaccine*, with the exception of: – Scheduled routine pediatric vaccines which may be administered ≥ 7 days before a dose and ≥ 7 days after a dose of study vaccines, with the exception of live viral vaccines which may be administered	Visit 3,5, 7	Immunogenicity

Code	Condition under which the code is used	Visit (timepoints) where the code is applicable	Applicable for analysis set
	≥ 14 days before a dose or ≥ 7 days after a dose. – Vaccines needed for urgent individual medical need (e.g., rabies prophylaxis		
1050	Randomisation failure	All	Immunogenicity
1060	Randomisation code was broken	All	Immunogenicity
1070	Subjects got vaccinated with the correct vaccine but containing a lower volume	All	Immunogenicity
1070	Vaccination not according to protocol: • Wrong replacement or study vaccine administered (not compatible with the vaccine regimen associated to the treatment number) • Site or route of study vaccine administration wrong or unknown • Administration not according to protocol for reason specified by the investigator, other than side, site and route	All	Immunogenicity
1080	Vaccine temperature deviation (vaccine administered despite a Good Manufacturing Practices (GMP) no-go temperature deviation for RSV vaccines only)	All	Immunogenicity
1090	Expired vaccine administered (only applicable for RSV vaccine)	All	Immunogenicity
2010	Protocol violation (inclusion/exclusion criteria including age)	All	Immunogenicity
2040	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 • Long-acting immune-modifying drugs administered at any time during the study period • Immunosuppressants or other immune-modifying drugs administered chronically (i.e., more than 14 days in total) during the study period • Immunoglobulins and/or any blood products administered during the study period	Visit 3, 5, 7	Immunogenicity
2050	Underlying medical condition forbidden by the protocol	Visit 3, 5, 7	Immunogenicity
2060	Intercurrent medical condition → Intercurrent medical condition that has the capability of altering immune response, or alteration of initial immune status (suspected or confirmed immunosuppressive or immunodeficient condition) which may influence immune response	Visit 3, 5, 7	Immunogenicity
2070	Concomitant infection not related to the vaccine which may influence immune response	Visit 3, 5, 7	Immunogenicity
2080	Subjects did not comply with vaccination schedule:- Number of days between dose 1 and dose 2 is outside [23-44 days]	Visit 3	Immunogenicity

Code	Condition under which the code is used	Visit (timepoints) where the code is applicable	Applicable for analysis set
2090	Subjects did not comply with blood sample schedule • Number of days between dose 1 and visit 3 blood sample is outside [23-44 days] • Number of days between dose 1 and visit 5 blood sample is outside [60-81 days] • Number of days between dose 2 and visit 5 blood sample is outside [28-37 days] for RSV 2D group • Number of days between visit 5 blood sample and visit 7 blood sample is outside [92-148 days]	Visit 3, 5, 7	Immunogenicity
2100	Serological results not available post-vaccination:- No immunological result at visit x for all 2 tests - RSV A Neutralising antibody titer and RSVPreF3-specific IgG antibody concentration	Visit 3, 5 and 7	Immunogenicity
2120	Obvious incoherence or abnormality or error in data :- Incoherence between CRF and results, wrong sample labelling, Central/internal/external lab deviations; incorrect spinning/processing of sample including processing within the time required by protocol; temperature deviations from range defined in protocol and/or SPM - room temperature/refrigerator/freezer; an assessment was completed but was not completed according to protocol or SPM.	Visit 3, 5, 7	Immunogenicity

5. STATISTICAL ANALYSES

Note that standard data derivation rules and stat methods are described in "business rules document" and will not be repeated below. The study specific data derivation rules and stat methods will be described in section 9.

5.1. Demography

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

The analysis of demographics will be performed on the ES and on the PPS cohort for immunogenicity for each RSV + comparator vaccine group and each active control comparator group and also for the pooled RSV vaccine and pooled comparator group.

Demographic characteristics (age at vaccination in months, sex, country and race and vital signs), cohort description will be summarized by group using descriptive statistics:

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

The distribution of subjects will be tabulated as a whole and per group.

Withdrawal status will be summarized by group using descriptive statistics:

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

5.1.2. Additional considerations

- Summary of important protocol deviation leading to elimination will be presented. An individual listing will also be presented for this.
- Consort tables for flow of subject from enrolment to randomization and randomization to exposed will also be presented.
- 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 will be tabulated by group.

5.2. Immunogenicity

5.2.1. Analysis of immunogenicity planned in the protocol

The primary analysis will be performed on the PPS for immunogenicity and, if in any group the percentage of vaccinated subjects with serological results excluded from the PPS for immunogenicity is more than 10%, a second analysis will be performed on the ES. The results from immunogenicity analysis will be reported by the pooled RSV vaccine group and the pooled comparator group

For the final analysis, the Adapted PPS for immunogenicity analysis will be used which allows the summary of immunogenicity results by time point. In summary table on the Adapted PPS for immunogenicity, immunogenicity summary result at Day 31, Day 61 and end of first RSV transmission season will be presented on PPS for immunogenicity at Day 31, Day 61 and end of first RSV transmission season, respectively.

The infants are monitored for RSV infection starting from dose 1 and, therefore, immunogenicity analyses can be adjusted to exclude those infants with an infection prior to sampling.

5.2.1.1. Within groups assessment

5.2.1.1.1. Analysis of secondary objectives

For three pooled groups, at each timepoint that blood samples are collected for humoral immune response against the investigational RSV vaccine (neutralizing antibody titers against RSV-A, RSV F antibody concentrations).

- Geometric mean titers/concentrations (GMTs/GMCs) will be tabulated with 95% CI and represented graphically.
- Percentage of subjects above the sero-positivity threshold will be tabulated with exact 95% CI.
- Antibody titers/concentrations will be displayed using reverse cumulative curves.
- The distributions (< 128, 128-256, > 256-512, > 512-1024, > 1024-2048, > 2048-4096, > 4096) of neutralizing antibody titers/concentrations will be tabulated.
- Individual post-vaccination versus pre-vaccination results will be plotted using scatter plots. Results of the comparator group will be used as a reference.
- Geometric mean of ratios of antibody titers/concentrations at each post-vaccination timepoint over pre-vaccination will be tabulated with 95% CI.
- Distribution of the fold increase of the neutralizing antibody titers will be tabulated by pre-vaccination titer category.
- The kinetics of individual antibody titers/antibody concentrations results will be plotted as a function of time for subjects with results available at all timepoints.

An immunogenicity analysis will also be performed on the ES with a negative RSV exposure status (at screening based on in-stream baseline serological testing) for whom immunogenicity data are available**.**

At study end, an additional analysis of immunogenicity will be performed on infants by baseline values (as per the cut-off used to define RSV naïve serostatus).

5.2.1.1.2. Analysis of tertiary objective

If available, any further exploratory immunology results (including, but not limited to anti-vector immunity and palivizumab-competing antibody concentrations) will be reported by timepoint for the two pooled RSV vaccine group***s*** and the pooled comparator group using descriptive summary statistics.

5.2.2. Additional considerations

- Summary statistics for neutralizing antibody titers against RSV-A, RSV F antibody concentrations (Minimum, Mean, median, SD, 1st quartile, 3rd quartile, Maximum) will be presented.
- Distribution of the fold increase of the neutralizing antibody titers will be tabulated by pre-vaccination titer category (percentage of subjects with a fold increase equal to

or above 1, 2, 2.5, 3, 4, 6, 8 10, 11 and 12 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 thresholds for presentation of titres in distribution table and for fold increase will be further adjusted at Day 61 analysis as needed.

- For three pooled groups, at each timepoint that blood samples are collected for humoral immune response against the investigational RSV vaccine (neutralizing antibody titrs against RSV-A, RSV F antibody concentrations, following additional analysis will be performed on PPS by baseline values (sero-negative vs sero-positive for RSV as per cut-off defined for RSV naïve serostatus) at the end of study:-
  - Geometric mean titers/concentrations (GMTs/GMCs) will be tabulated with 95% CI and represented graphically.
  - The distributions of neutralizing antibody titers/concentrations will be tabulated.
  - Geometric mean of ratios of antibody titers/concentrations at each post-vaccination timepoint over pre-vaccination will be tabulated with 95% CI
  - Summary statistics for neutralizing antibody titers against RSV-A, RSV F antibody concentrations (Minimum, Mean, median, SD, 1st quartile, 3rd quartile, Maximum) will be presented.

5.3. Analysis of safety and reactogenicity

5.3.1. Analysis of safety and reactogenicity planned in the protocol

5.3.1.1. Within groups assessment

The safety will be descriptively summarized based on the ES. The analysis of local AEs, general AEs and fever will be reported for each RSV + comparator vaccine group and each active control comparator group and also for the pooled RSV vaccine and pooled comparator groups. For the analysis of SAEs and AE of specific interest, the analysis will be performed only on the pooled RSV and pooled comparator groups.

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 will be tabulated with exact 95% confidence interval (CI) after each vaccine dose and overall. The percentage of doses followed by at least one local AE (solicited and unsolicited), by at least one general AE (solicited and unsolicited) and by any AE during the 7-day or 30-day follow-up period will be tabulated, overall vaccination course, with exact 95% CI. The same computations will be done for Grade 3 AEs, for any AEs considered related to vaccination for any Grade 3 AEs considered related to vaccination and AEs resulting in a medically attended visit.

The percentage of subjects reporting each individual solicited local AE (any grade, Grade 2, Grade 3, resulting in a medically attended visit) and solicited general AE (any grade, Grade 2, Grade 3, any related, Grade 2 related, Grade 3 related, resulting in medically attended visit) during the 7-day follow-up period (Day 1-7) will be tabulated for each

RSV + comparator vaccine group and each active control comparator group and also for the pooled RSV vaccine and pooled comparator groups after each vaccine dose and overall. Similarly, the percentage of doses followed by each individual solicited local and general AE and their sub-categories, will be tabulated, overall vaccination course, with exact 95% CI.

For fever, the number and percentage of subjects reporting fever by half degree (°C) cumulative increments during the 7-day follow-up period (Day 1-7) will be tabulated for each RSV + comparator vaccine group and each active control comparator group and also for the pooled RSV vaccine and pooled comparator groups after each vaccine dose and overall. Similar tabulations will be performed for any fever with a causal relationship to vaccination, Grade 3 (> 40.0°C) causally related fever and for any 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.

For clinical safety laboratory parameters, a listing of laboratory value outside the normal range for the unscheduled visits will be provided as per the toxicity scale referred in the protocol. Laboratory values will be classified according to toxicity criteria (Table 7) of the SAP.

Laboratory values that are outside the normal range will also be flagged in the data listings, along with corresponding normal ranges and assessment of clinical significance

The percentage of subjects with unsolicited AEs within 30 days (Day 1-30) after each vaccine dose (overall doses) with its exact 95% CI will be tabulated RSV + comparator vaccine group and each active control comparator group and also for the pooled RSV vaccine and pooled comparator groups and by MedDRA preferred term. Similar tabulation will be done for Grade 3 unsolicited AEs, for any causally related unsolicited AEs, for Grade 3 causally related unsolicited AEs and for unsolicited AEs resulting in a medically attended visit. The verbatim reports of unsolicited AEs will be reviewed by a physician and the signs and AEs will be coded according to the MedDRA Dictionary for Adverse Reaction Terminology. Every verbatim term will be matched with the appropriate Preferred Term.

The percentage of subject with episode of spontaneous or excessive bleeding (AE of specific interest), during a 30-day follow-up period after each vaccination will be tabulated according to associated Preferred Term code mentioned in Section 9.4 of the SAP.

The percentage of subjects with RSV-LRTI (AE of specific interest) from Dose 1 up to end of the first RSV transmission season and from Dose 1 up to end of second RSV season will be tabulated according to associated Preferred Term code presented in the Section 9.4 of the SAP.

The percentage of subjects with SAE within 30 days (Day 1-30) after each vaccine dose with its exact 95% CI will be tabulated and by MedDRA preferred term. Similar tables will be generated for SAEs from Dose 1 to end of first RSV season and from Dose 1 to end of the second RSV season.

SAEs reported throughout the study and AE of special interest will be described in detail.

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) and during the 30-day follow-up period (Day 1-30) will be summarized by the pooled RSV vaccine and pooled comparator groups after each vaccine dose and overall.

5.3.1.2. Between groups assessment

Exploratory comparisons between the pooled RSV vaccine group and the pooled comparator group will be done in terms of the percentage of subjects, overall doses, reporting any Grade 2/3 AE during the 7-day follow-up period (Day 1-7) after vaccination, and/ or any fever >39.0°C during the 7-day follow-up period (Day 1-7) after vaccination, and/ or any vaccine-related SAE during the 7-day follow-up period (Day 1-7) after vaccination.

The standardized asymptotic 95% CI for the difference between the pooled RSV group and (minus) the pooled comparator group will be computed.

The standardized asymptotic 95% CI for the following differences will be computed:

- RSV1D minus COMP_PLB
- RSV2D minus COMP_PLB

5.3.2. Additional considerations

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.

Percentage of subjects reporting fever (any and grade 3) and other solicited general adverse events (any grade, grade 2,3 and grade 3) during the 7-day (Days 1-7) post-vaccination period by maximum intensity will be presented in figure.

Percentage of subjects reporting solicited local adverse events (any grade, grade 2,3 and grade 3) during the 7-day (Days 1-7) post-vaccination period by maximum intensity will be presented in figure.

5.3.2.1. Combined Solicited and Unsolicited Adverse Events

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

Solicited symptom	Lower level term name	Lower level term code	Corresponding Primary Term code
Pain	Pain	10033371	10033371
Redness	Erythema	10015150	10015150
Swelling	Swelling	10042674	10042674
Drowsiness	Drowsiness	10013649	10013649
Fever	Fever	10016558	10016558
Irritability/Fussiness	Irritability	10022998	10022998
Loss of appetite	Appetite lost	10003028	10003028

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.

5.3.2.2. Exclusion of implausible solicited Adverse Event

Some local and systemic adverse events will be directly measured by the subject and will not 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 5 Implausible Solicited Adverse Events

Parameter	Implausible measurements
Body temperature	≤ 33°C or ≥ 42°C
Swelling	For subjects < 6 years: ≥ 250 mm Measurements < 0 mm

5.3.2.3. Solicited Adverse Events

All analyses will be based on the 'as treated' analysis set. Solicited adverse events will be reported daily during the 7-day (from Day 1 to Day 7) follow up period after each vaccination, using structured diaries.

In order to summarize the data, the maximum intensity of local injection site redness/swelling (in mm) and fever (in °C) will be categorized as follows:

Grading	Redness/swelling	Fever
0:	None	< 38.0°C (100.4°F)
1:	<5 mm	≥ 38.0°C (100.4°F) - ≤ 39.0°C (102.2°F)
2:	> 5 - ≤ 20 mm	> 39.0°C (102.2°F) - ≤ 40.0°C (104.0°F)
3:	> 20 mm	> 40.0°C (104.0°F)

Fever is defined as temperature ≥ 38.0°C / 100.4°F (regardless of the location of measurement). The preferred location for measuring temperature in this study will be the oral cavity. Body temperature will also be summarized by 0.5°C increments as follows: ≥38.0, >38.5, >39.0, >39.5, >40.0 °C.

For each of the time points or time intervals presented in the summaries, only subjects with at least one plausible observation (i.e., any non-missing values but excluding "Not done/unknown" and implausible values) for the solicited adverse events in the interval of interest will be considered. Subjects without plausible data (i.e. missing values or reported as "Not done/unknown" and implausible values) will be removed from the denominator to prevent a downward bias (towards zero).

5.3.2.4. Unsolicited Adverse Events

All the unsolicited adverse events occurring during the study, judged either as related, or not related to vaccination by the investigator, will be recorded. All the unsolicited adverse events/AE of specific interest (Spontaneous or excessive bleeding) occurring during the 30-day (Day 1 to Day 30) follow up period after each vaccination, and all serious adverse events/AE of specific interest (RSV LRTI) occurring from Dose 1 up to study end will be recorded according to the protocol-specified reporting rules. The original verbatim terms used by investigators to identify adverse events in the CRFs will be mapped to preferred terms using the MedDRA dictionary. The unsolicited adverse events will then be grouped by MedDRA preferred terms into frequency tables according to system organ class. Adverse events judged by the investigator as at least possibly related to study vaccine will be summarized by vaccine group, according to system organ class and preferred term within system organ class. When an unsolicited adverse event occurs more than once for a subject, the maximal severity and strongest relationship to the vaccine group will be counted.

Only vaccine-emergent adverse events will be analyzed, i.e., excluding those after a subject has given informed consent but before vaccination. The selection of unsolicited adverse events and the assignment to time intervals will be done by day of onset and not by days ongoing/persisting.

The analysis of unsolicited adverse events during the 30-day post vaccination period includes the following categories:

- Any unsolicited adverse event.
- Possibly related unsolicited adverse events.
- Grade 3 unsolicited adverse events
- Grade 3 related unsolicited adverse events.
- Serious adverse events (SAEs)
- Possibly related SAEs.
- Medically attended adverse events
- AE of specific interest (spontaneous or excessive bleeding)

SAE and AE of specific interest (RSV-LRTI) has to be reported from Day 1 up to Day 61, from Day 1 to end of 1st RSV season and from Day 1 to end of 2nd RSV season.

5.4. Analysis of RTI and LRTI

5.4.1. Analysis of RTI and LRTI planned in protocol

The primary analysis will be performed on the ES of subjects with a negative RSV exposure status (at screening based on in-stream baseline serological testing) in the pooled single dose RSV vaccine group, the pooled two dose RSV vaccine group, and the pooled comparator group separately for first and second RSV seasons and overall. A similar analysis will be performed on the entire ES. As primary analysis, the assessment of RSV infection will be performed using the quantitative RT-PCR according to standardized case definitions (see Table 6 of the SAP) based on the available WHO case definitions.

The number of RSV infections within each group and the maximum disease severity of the event will be tabulated. The rate (with 95% CI) of RSV-RTI and RSV-LRTI and infections progressing to hospitalization will be evaluated for each of the three pooled groups.

The rate of very severe RSV-LRTI among RSV infected infants with a negative RSV exposure status (at screening based on in-stream baseline serological testing) from first vaccination (Day 1) up to the end of the first RSV transmission season will be estimated as well as 95% one-sided lower CI.

The proportion and the relative risk of subjects with at least one RSV-associated RTI (with 95% CI) between each of two pooled RSV vaccine groups and the pooled control group will be calculated for both the cohort of subjects with a negative RSV exposure status (at screening based on in-stream baseline serological testing) on the ES and on the entire ES. The same descriptive analysis will be performed for subjects with at least one RSV-associated LRTI and those with at least one RSV-associated severe LRTI.

Descriptive analyses (mean, median, min, max) of viral load assessed by the quantitative RT-PCR (RSV-A/B) of all cases as listed in Table 6 of the SAP will be tabulated by case category. This analysis will also be done on the three pooled groups.

The incidence rate of all cases as listed in Table 6 of the SAP (with 95% CI) will be calculated by the three pooled groups. The same descriptive analysis will be performed for all cause LRTI and all cause severe LRTI. These will also be presented for each viral etiology identified by the multiplex PCR.

The incidence rate of asymptomatic RSV infections (with 95% CI) detected by the quantitative PCR (RSV-A/B), will be tabulated by the three pooled groups. Descriptive analyses (mean, median, min, max) of viral load assessed by the quantitative RT-PCR (RSV-A/B) of those asymptomatic RSV infections will also be done on the three pooled groups.

The RVP (Multiplex PCR) on specimens from all RSV-A/B positive and confirmed LRTI cases, according to case definition presented in Table 6 (Figure 3 of the protocol for the decision tree), will be tabulated as a qualitative assessment profiling the potential co-infections occurring in these subjects.

5.4.2. Additional consideration

In addition to above planned analysis for RTI and LRTI, following additional analysis is planned: -

- Descriptive analysis on maximum viral load per subject based on qRT-PCR confirmed RSV infection of maximum severity will be performed.
- Listing will be presented for all cases of RSV infection at Day 731 with the details of gender, age at episode, country, site, day of event (i.e days since first visit), classification according to maximum severity of episode as RSV RTI/RSV LRTI/ RSV severe LRTI and RSV very severe LRTI, RSV hospitalization 'Yes/No', SpO2 value, respiratory rate, result of RSV qRT-PCR and RVP result will be presented.
- Listings will be generated at Day 731 for all hospitalized cases with gender, age at episode, classification according to maximum severity of episode as (RSV RTI/RSV LRTI/ RSV severe LRTI and RSV very severe LRTI), RVP result, total number of calendar days on which the child was hospitalized, days requiring monitoring/nursing observation, days requiring nasogastric or intravenous fluids, days requiring supplemental oxygen, days requiring respiratory support excluding mechanical ventilation, days requiring mechanical ventilation and days requiring pediatric intensive care unit management.

6. ANALYSIS INTERPRETATION

For the occurrence of very severe RSV-LRTI among RSV infected infants with a negative RSV exposure status (at screening based on in-stream baseline serological testing) from first vaccination (Day 1) up to the end of the first RSV transmission season, if the upper boundary of the 95% one-sided lower CI of the rate is under 80%, it indicates that the very severe RSV-LRTI rate is less than that of the historic RSV-FI trials [Kim, 1969].

Comparative analyses will be exploratory and should be interpreted with caution considering that there is no adjustment for multiplicity and that group sizes are small for these comparisons.

7. CONDUCT OF ANALYSES

7.1. Sequence of analyses

The statistical analyses will be performed in 3 steps:

- An analysis will be performed when all data up to Day 61 are available. Additional safety data available at the time of this analysis will be described. At this point, the statistician will be unblinded (i.e., individual subject treatment assignments will be available) and the study will be conducted in a single blind manner, with patients remaining blinded up to the last study visit (end of the second RSV transmission season). Summary results may unblind some specific subjects, but no individual listings will be provided and the investigator will not have access to the treatment

allocation up to the last study visit (end of the second RSV transmission season), except in case of emergency unblinding (see Section 9.8 of the protocol)

- An analysis will be performed when all data up to Visit 7 (end of the first RSV transmission season, i.e., data that are as clean as possible) are available. No individual listings will be provided.
- The final analysis will be performed when all data up to study conclusion (end of the second RSV transmission season) are available. An integrated clinical study report containing all data will be written and made available to the investigators at that time.

If the data for tertiary endpoints become 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	Disclosure Purpose (CTRS=public posting, SR=study report, internal)
Day 61 analysis	Internal, web disclosure
End of RSV season 1	Internal
End of RSV season 2	Web disclosure, Study report

7.2. Statistical considerations for interim analyses

No interim analyses are planned

8. CHANGES FROM PLANNED ANALYSES

Following are few changes from planned analysis:-

- In the protocol, we have PPS up to Day 61 which included Day 31 as well. To have better clarity with respect to PPS for Day 31, the text has been re-worded for the definition of PPS population. PPS has also been defined for Day 31 timepoint along with PPS at Day 61 and end of 1st RSV transmission season. Also, as the timepoint 'End of 1st RSV transmission season is not exactly Day 365, so the Day 365 has been removed and only kept as PPS at end of 1st RSV transmission season. The criteria of eliminating subject from the PPS of respective timepoint is accordingly reworded.
- In the protocol amendment 3, it is mentioned under Analysis of Immunogenicity section that 'In summary table on the Adapted PPS for immunogenicity, PPS for immunogenicity at Day 61 will be used for Pre, Day 31 and Day 61 immunogenicity summary and PPS for immunogenicity at Day 365 for Day 365 immunogenicity summary.' As we have added the PPS for Day 31 in the SAP, accordingly the summary table presentation has been modified as 'In summary table on the Adapted PPS for immunogenicity, immunogenicity summary result at Day 31, Day 61 and end of first RSV transmission season) will be based on PPS of Day 31, Day 61 and end of first RSV transmission season, respectively'.
- Table to present percentage of responders in terms of neutralizing antibody titers with 95% CI has been removed as there is no definition of response available.

9. NON-STANDARD DATA DERIVATION RULES AND STATISTICAL METHODS

The following sections describe additional derivation rules and statistical methods which are not presented in section 10.1 (Business rules for standard data derivations and statistical methods).

9.1. Immunogenicity

- Assay cut-off for the humoral immunity will be per the following table

Component	Method	Unit	Cut-off
Respiratory Syncytial Virus A Ab	NEUTRALIZATION	ED60	18
Respiratory Syncytial Virus F protein Ab.IgG (Anti-RSV PreF antibody)	ELISA	EU/ml	10
Respiratory Syncytial Virus F protein Ab.IgG (Palivizumab competing Ab)	ELISA	µg/ml	9.6

- For RSV neutralizing assay, the LLOQ and ULOQ is set at 18ED60 and 21654 ED60. For analysis, the cut-off is set at the lower limit of quantification. For results below the cut-off, an arbitrary value of half of the cut-off will be considered for calculation of GMC and fold increase. The result above the ULOQ is set at ULOQ for analysis.
- For anti-RSV PreF antibody and RSV PCA, the cut-off is set at the level of detection. For results below the cut-off (LOD), an arbitrary value of half of the cut-off will be considered for calculation of GMC and fold increase.

9.2. RTI and LRTI

During the analysis of the study, all cases identified during the surveillance of RSV-RTI will be definitively classified as either RTI, LRTI, severe LRTI or very severe LRTI according to the standardized case definitions (Table 6 in the SAP) based on the available World Health Organization (WHO) case definitions (Table 6 in the protocol)

Table 6 Case definitions for data analysis

Case	***At sea level up to 2500 meters elevation***	***Above 2500 meters elevation***
RSV-RTI	Runny nose OR blocked nose OR cough AND Confirmed RSV infection [4]	***Same***
RSV-LRTI	History of cough OR difficulty breathing [1] AND SpO_2 < 95% [2], OR RR increase [3] AND Confirmed RSV infection [4]	***Same but with SpO2 <92%***
severe *RSV*-LRTI	Meeting the case definition of RSV-LRTI AND SpO_2 < 93% [2], OR lower chest wall in-drawing	***Same but with SpO2 <90%***
very severe *RSV*-LRTI	Meeting the case definition of RSV-LRTI AND SpO_2 < 90% [2], OR inability to feed, OR failure to respond / unconscious	***Same but with SpO2 <88%***

Case	*At sea level up to 2500 meters elevation*	*Above 2500 meters elevation*
RSV hospitalization	Confirmed RSV infection [5] AND Hospitalized for acute medical condition [6]	***Same***
All-cause LRTI	History of cough OR difficulty breathing [1] AND SpO_2 < 95% [2], OR RR increase [3]	***Same but with SpO2 <92%***

LRTI = lower respiratory tract infections; **RR** = respiratory rate; **RTI** = respiratory tract infections; **SpO2** = blood oxygen saturation.

[1] Based on history reported by parents.

[2] The lowest value during the course of illness will be used.

[3] RR increase defined as:≥ 50/minute (2 to 11 months of age) ; ≥ 40/minute (12 months of age or above) ; The highest value during the course of the illness will be used.

[4] RSV infection confirmed on nasal swab positive for RSV A or B by quantitative Reverse Transcription Polymerase Chain Reaction (qRT-PCR).

[5] RSV sampling and testing is based on medical judgment of medical practitioner or driven by algorithm.

[6] Hospitalization is defined as a medical decision that the infant requires admission for observation or treatment.

- For the analysis of RTI episode, a new RTI episode will be defined as any occurrence of cough, runny nose, blocked nose, wheezing or difficulty breathing with an interval of at least 7 symptom free days since the last episode of RTI that was diagnosed.
- For molecular biology (qRT-PCR test), the following cut-off will be applied: -

System	Component	Method	Unit	Cut-off
Nasal swab	RSV-A RNA	Quantitative real-time PCR (qRT-PCR)	Copies/ml	1.12 X 10^3
Nasal swab	RSV-B RNA	Quantitative real-time PCR (qRT-PCR)	Copies/ml	1.47 x 10^3

9.3. Hematology and Biochemistry parameters

The grading of the hematology and biochemistry lab result will be done as per the toxicity grading scales provided in the Table 7 below (Table 28 of the protocol).

Table 7 Toxicity grading scales for hematology and biochemistry parameters applicable for this study

Component	Grade 1	Grade 2	Grade 3	Grade 4
Hemoglobin (g/dL)	9.0 to < 10.5	8.0 to < 9.0	7.0 to < 8.0	< 7.0
Leukocytes (cell/mm^3)	2500 to < 3500	1500 to < 2500	1000 to < 1500	< 1000
Absolute neutrophil count (cell/mm^3)	1000 to < 1300	750 to < 1000	500 to < 750	< 500
Absolute lymphocyte count (cell/mm^3)	600 to < 650	500 to < 600	350 to < 500	< 350
Platelets (cell//mm^3)	75000 to < 150000	50000 to < 75000	25000 to < 50000	< 25000
Alanine Aminotransferase (increase by factor)	1.1 to < 2.0 xULN	2.0 to < 3.0 xULN	3.00 to ≤ 8.0 xULN	> 8.0 xULN
Aspartate Aminotransferase (increase by factor)	1.1 to < 2.0 xULN	2.0 to < 3.0 xULN	3.00 to ≤ 8.0 xULN	> 8.0 xULN
Creatinine (mg/dL)	0.6 to < 0.9	0.9 to < 1.2	1.2 to ≤ 1.5	> 1.5

ULN: upper limit of normal.

9.4. Coding for the AE of specific interest

Any of the below listed preferred term reported as an Expedited Adverse Event must be immediately escalated to the CRDL or Central Safety Physician to assess or confirm the need for an urgent IDMC review.

The list of preferred terms and associated PT codes is given below:

HAEMATOMA

Preferred term	PT code
abdominal wall haematoma	10067383
administration site haematoma	10075100
adrenal haematoma	10059194
aortic intramural haematoma	10067975
application site haematoma	10068317
arterial intramural haematoma	10074971
auricular haematoma	10003797
basal ganglia haematoma	10077031
brain stem haematoma	10073230
breast haematoma	10064753
broad ligament haematoma	10006375
bursal haematoma	10077818
catheter site haematoma	10055662
cephalhaematoma	10008014
cerebellar haematoma	10061038
cerebral haematoma	10053942
cervix haematoma uterine	10050020
chest wall haematoma	10076597
colonic haematoma	10009996
deep dissecting haematoma	10074718
extradural haematoma	10015769
eyelid haematoma	10064976
haematoma	10018852
haematoma evacuation	10060733
haematoma infection	10051564
hepatic haematoma	10019676
incision site haematoma	10059241
infusion site haematoma	10065463
injection site haematoma	10022066
instillation site haematoma	10073609
intestinal haematoma	10069829
intra-abdominal haematoma	10056457
intracerebral haematoma evacuation	10062025

Preferred term	PT code
intracranial haematoma	10059491
intraocular haematoma	10071934
laryngeal haematoma	10070885
lip haematoma	10066304
mediastinal haematoma	10049941
medical device site haematoma	10075577
mesenteric haematoma	10071557
nasal septum haematoma	10075027
oesophageal intramural haematoma	10077486
oral mucosa haematoma	10074779
ovarian haematoma	10033263
paranasal sinus haematoma	10069702
pelvic haematoma	10054974
penile haematoma	10070656
perineal haematoma	10034520
periorbital haematoma	10034544
periosteal haematoma	10077341
perirenal haematoma	10049450
peritoneal haematoma	10058095
pharyngeal haematoma	10068121
post procedural haematoma	10063188
pulmonary haematoma	10054991
renal haematoma	10038459
retroperitoneal haematoma	10058360
scrotal haematoma	10039749
spinal cord haematoma	10076051
spinal epidural haematoma	10050162
spinal subdural haematoma	10050164
splenic haematoma	10041646
spontaneous haematoma	10065304
subarachnoid haematoma	10076701
subcutaneous haematoma	10042345
subdural haematoma	10042361
subgaleal haematoma	10069510
subretinal haematoma	10071935
tongue haematoma	10043959
uterine haematoma	10063875
vaccination site haematoma	10069472
vaginal haematoma	10046909
vitreous haematoma	10071936
vulval haematoma	10047756

HAEMORRHAGE

Preferred term	PT code
abdominal wall haemorrhage	10067788
acute haemorrhagic conjunctivitis	10067817
administration site haemorrhage	10075101
adrenal haemorrhage	10001361
anal haemorrhage	10049555
anastomotic haemorrhage	10056346
angina bullosa haemorrhagica	10064223
application site haemorrhage	10072694
arterial haemorrhage	10060964
basal ganglia haemorrhage	10067057
bone marrow haemorrhage	10073581
brain stem haemorrhage	10006145
brain stem microhaemorrhage	10071205
breast haemorrhage	10006254
bronchial haemorrhage	10065739
catheter site haemorrhage	10051099
central nervous system haemorrhage	10072043
cerebellar haemorrhage	10008030
cerebellar microhaemorrhage	10071206
cerebral haemorrhage	10008111
cerebral microhaemorrhage	10067277
cervix haemorrhage uterine	10050022
ciliary body haemorrhage	10057417
conjunctival haemorrhage	10010719
diverticulitis intestinal haemorrhagic	10013541
diverticulum intestinal haemorrhagic	10013560
duodenitis haemorrhagic	10013865
ear haemorrhage	10014009
encephalitis haemorrhagic	10014589
gastric haemorrhage	10017788
gastroduodenal haemorrhage	10053768
gastrointestinal haemorrhage	10017955
genital haemorrhage	10061178
haemarthrosis	10018829
haematemesis	10018830
haematochezia	10018836
haematotympanum	10063013
Haematuria	10018867
haemorrhage	10055798
haemorrhage coronary artery	10055803

Preferred term	PT code
haemorrhage intracranial	10018985
haemorrhage subcutaneous	10018999
haemorrhage subepidermal	10019001
haemorrhage urinary tract	10055847
haemorrhagic anaemia	10052293
haemorrhagic diathesis	10062713
haemorrhagic disorder	10019009
haemorrhagic infarction	10019013
haemorrhagic ovarian cyst	10060781
haemorrhagic pneumonia	10077933
haemorrhagic thyroid cyst	10072256
haemorrhagic urticaria	10059499
injection site haemorrhage	10022067
internal haemorrhage	10075192
intestinal haemorrhage	10059175
intra-abdominal haemorrhage	10061249
intraventricular haemorrhage	10022840
iris haemorrhage	10057418
joint microhaemorrhage	10077666
lacrimal haemorrhage	10069930
large intestinal haemorrhage	10052534
laryngeal haemorrhage	10065740
lip haemorrhage	10049297
lower gastrointestinal haemorrhage	10050953
lymph node haemorrhage	10074270
mediastinal haemorrhage	10056343
mesenteric haemorrhage	10060717
mouth haemorrhage	10028024
mucocutaneous haemorrhage	10076048
mucosal haemorrhage	10061298
muscle haemorrhage	10028309
myocardial haemorrhage	10048849
naevus haemorrhage	10062955
ocular retrobulbar haemorrhage	10057571
oesophageal haemorrhage	10030172
optic disc haemorrhage	10030919
optic nerve sheath haemorrhage	10030941
ovarian haemorrhage	10065741
pancreatic haemorrhage	10033625
papillary muscle haemorrhage	10059164
parathyroid haemorrhage	10059051

Preferred term	PT code
parotid gland haemorrhage	10051166
pelvic haemorrhage	10063678
penile haemorrhage	10034305
pericardial haemorrhage	10034476
periorbital haemorrhage	10071697
peritoneal haemorrhage	10034666
Petechiae	10034754
pharyngeal haemorrhage	10034827
pituitary haemorrhage	10049760
post procedural haemorrhage	10051077
procedural haemorrhage	10071229
prostatic haemorrhage	10036960
pulmonary alveolar haemorrhage	10037313
pulmonary haemorrhage	10037394
putamen haemorrhage	10058940
rectal haemorrhage	10038063
renal haemorrhage	10038460
respiratory tract haemorrhage	10038727
retinal haemorrhage	10038867
retroperitoneal haemorrhage	10038980
scleral haemorrhage	10050508
skin haemorrhage	10064265
small intestinal haemorrhage	10052535
soft tissue haemorrhage	10051297
spermatic cord haemorrhage	10065742
spinal cord haemorrhage	10048992
spinal epidural haemorrhage	10049236
spinal subarachnoid haemorrhage	10073564
spinal subdural haemorrhage	10073563
splenic haemorrhage	10041647
spontaneous haemorrhage	10074557
subarachnoid haemorrhage	10042316
subdural haemorrhage	10042364
testicular haemorrhage	10051877
thalamus haemorrhage	10058939
thoracic haemorrhage	10062744
thyroid haemorrhage	10064224
tongue haemorrhage	10049870
tracheal haemorrhage	10062543
upper gastrointestinal haemorrhage	10046274
ureteric haemorrhage	10065743

Preferred term	PT code
urethral haemorrhage	10049710
urinary bladder haemorrhage	10046528
urogenital haemorrhage	10050058
uterine haemorrhage	10046788
vaccination site haemorrhage	10069475
vaginal haemorrhage	10046910
venous haemorrhage	10065441
vitreous haemorrhage	10047655
vulval haemorrhage	10063816

THROMBOCYTOPENIA

Preferred term	PT code
bleeding time abnormal	10049227
bleeding time prolonged	10005140
coagulation test abnormal	10063557
platelet count abnormal	10035526
platelet count decreased	10035528
platelet disorder	10035532
platelet dysfunction	10073391
Thrombocytopenia	10043554
thrombocytopenic purpura	10043561

LOWER RESPIRATORY TRACT INFECTION

Preferred term	PT code
atypical pneumonia	10003757
Bronchitis	10006451
bronchitis viral	10053160
haemorrhagic pneumonia	10077933
lower respiratory tract infection	10024968
lower respiratory tract infection viral	10065188
lung infection	10061229
Pneumonia	10035664
pneumonia respiratory syncytial viral	10035732
pulmonary sepsis	10051739
respiratory syncytial virus bronchiolitis	10038718
respiratory syncytial virus bronchitis	10069811
respiratory tract infection	10062352
respiratory tract infection viral	10062106

10. ANNEXES

As the SAP and TFL TOC has been developed using the old template and process, we will not have TFL as annex to this SAP. All the template applicable to the study has been added in the SAP in Section 13.

10.1. Business rules for standard data derivations and statistical methods

10.1.1. Attributing events to vaccine doses

The dose relative to an event is the most recent study dose given to a subject prior to the start of a given event. For example, if the start date of an adverse event is between Dose 1 and Dose 2, the relative dose will be Dose 1.

If an event starts on the same day as a study dose, the relative dose will be derived from the additional information provided in the CRF using the contents of the flag indicating if the event occurred before or after vaccination. If 'after vaccination' is selected, the relative dose for the event will be the one administered on the start day of the event. If 'before vaccination' is selected, the relative dose for the event will be the dose prior to this one.

10.1.2. Handling of missing data

10.1.2.1. Dates

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

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

The following exceptions apply:

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

year. If 'before vaccination' is selected, the imputed date will be one day before the first (or only) study dose given during that year.

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

10.1.2.2. Laboratory data

Missing laboratory results (including immunological data) will not be replaced.

10.1.2.3. Daily recording of solicited symptoms

10.1.2.3.1. Studies with paper diaries

For studies using paper diaries which have questions in the CRF indicating the presence or absence of solicited symptoms, the following rules are applicable.

Denominators for the summary of local (or general) solicited symptoms will be calculated using the number of subjects who respond "Yes" or "No" to the question concerning the occurrence of local (or general) symptoms.

When a specific symptom is marked as having not occurred following a specific vaccination (i.e. SDTM CE.CEOCCUR=N for the specified post-vaccination period for the symptom in question), all daily measurements will be imputed as Grade 0.

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.

When the occurrence of a specific symptom is not present (i.e. SDTM CE.CEOCCUR is neither Y nor N for the specified post-vaccination period for the symptom in question) but the group of symptoms (local or general) is marked as having occurred (i.e. SDTM CE.CEOCCUR=Y), all 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.

The following table shows how subjects contribute to each category for a specific solicited symptom over the Day X to Day Y post-vaccination period:

Solicited symptom category	Subjects included in the calculation of the numerator
Any	All subjects with at least one occurrence of the symptom at grade 1, grade 2, or grade 3 between Day X and Day Y or with the symptom marked as present and at least one missing daily recording between Day X and Day Y
At least grade 1	All subjects with at least one occurrence of the symptom at grade 1, grade 2, or grade 3 between Day X and Day Y
At least grade 2	All subjects with at least one occurrence of the symptom at grade 2 or grade 3 between Day X and Day Y
At least grade 3	All subjects with at least one occurrence of the symptom at grade 3 between Day X and Day Y

10.1.2.4. Unsolicited adverse events

Missing severity, relationship with study vaccine, and outcome of unsolicited adverse events will not be replaced and will appear as 'UNKNOWN' in all statistical output.

10.1.3. Data derivation

10.1.3.1. Age at vaccination in days

When age at vaccination is to be displayed in days, it will be calculated as:

Age = date of vaccination minus date of birth

10.1.3.2. Age at vaccination in months

When age at vaccination is to be displayed in months, it will be calculated as the number of complete calendar months between the date of birth (DOB) and the date of vaccination. For example:

DOB = 10JUN2017, Date of vaccination = 09JUL2018 -> Age = 12 months

DOB = 10JUN2017, Date of vaccination = 10JUL2018 -> Age = 13 months

10.1.3.3. Age at vaccination in years

When age at vaccination is to be displayed in years, it will be calculated as the number of complete calendar years between the date of birth and the date of vaccination. For example:

DOB = 10SEP1983, Date of vaccination = 09SEP2018 -> Age = 34 years

DOB = 10SEP1983, Date of vaccination = 10SEP2018 -> Age = 35 years

10.1.3.4. Weight

Weight will be presented in kilograms. Weights reported in pounds will be converted as follows:

Weight in kilograms = Weight in pounds / 2.2

10.1.3.5. Height

Height will be presented in centimeters. Heights reported in feet and inches will be converted as follows:

Height in centimeters = Height in inches x 2.54

10.1.3.6. Body mass index (BMI)

BMI will be calculated as follows:

BMI = (Weight in kilograms) / (Height in meters)^2

10.1.3.7. Temperature

Temperatures will be presented in degrees Celsius (°C). Temperatures reported in degrees Fahrenheit (°F) will be converted as follows:

Temperature (Celsius) = ((Temperature (Fahrenheit) - 32) x 5)/9

10.1.3.8. Numerical serology results

Numerical serology results will be derived from the content of IS.ISORRES in the SDTM dataset. For assays with a specific cut-off, the following derivation rules apply:

IS.ISORRES	Derived value
“value” and value is >= cut-off	value
“value” and value is < cut-off	cut-off/2
“value” and value is >ULOQ (applicable for RSV neutralizing assay)	ULOQ
“value” and value is <LLOQ (applicable for RSV neutralizing assay)	LLOQ/2
value” and value is >=LLOQ and <ULOQ (applicable for RSV neutralizing assay)	value
All other cases	missing

10.1.3.9. Geometric mean titers (GMTs) and concentrations (GMCs)

Geometric Mean Titer (GMT) or Concentration (GMC) calculations are performed by taking the inverse logarithm of the mean of the log titer or concentration transformations. Antibody titers or concentrations 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 GMT/GMC calculation. The cut-off value is defined by the laboratory before the analysis and is described in the protocol.

10.1.3.10. Onset day

The onset day for an event (e.g. AE, medication, vaccination) is the number of days between the last study vaccination and the start date of the event. This is 1 for an event occurring on the same day as a vaccination (and reported as starting after vaccination).

10.1.3.11. Duration of events

The duration of an event with a start and end date will be the number of days between the start and end dates plus one day, i.e. an event that starts on 03MAR2018 and ends on 12MAR2018 has a duration of 10 days.

The duration of solicited events will be calculated as the sum of the individual days with the symptom reported at grade 1 or higher.

10.1.3.12. Counting rules for combining solicited and unsolicited adverse events

For output combining solicited and unsolicited adverse events, all serious adverse events will be considered general events since the administration site flag is not included in the expedited adverse event CRF pages.

Multiple events with the same preferred term which start on the same day are counted as only one occurrence.

10.1.3.13. Counting rules for occurrences of solicited adverse events

When the occurrences of solicited adverse events are summarized, each event recorded as having occurred during a specific period will be counted as only one occurrence regardless of the number of days on which it occurs. Also, in the case of co-administered study vaccines, an injection site reaction recorded for a subject following multiple vaccines will be counted as only one occurrence.

10.1.3.14. Display of decimals

10.1.3.15. Percentages

Percentages and their corresponding confidence limits will be displayed with:

- no decimals when there are fewer than 50 subjects in each tabulated group
- one decimal when there are at least 50 subjects in at least one tabulated group
  - Exceptions will be made for percentages that are not 0% or 100% but appear as 0% or 100% due to rounding. For these specific cases the number of decimals will be increased until the displayed value is no longer 0% or 100%. Examples are given in the following table.

n/N	Displayed percentage
10/45	22%
1/45	2%
10/55	18.2%
1/55	1.8%
1/300	0.3%
1/3000	0.03%
1/30000	0.003%
299/300	99.7%
2999/3000	99.97%
29999/30000	99.997%

  - The display of additional decimals for values close to 0% or 100% will be applied only to point estimates and not confidence limits, which can be rounded and displayed as 0% or 100%.
  - Values of exactly 0% or 100% will be presented with no decimals regardless of the number of subjects per tabulated group.

10.1.3.16. Differences in percentages

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

10.1.3.17. Demographic/baseline characteristics statistics

The mean, median, and standard deviation for continuous baseline characteristics (height, weight, body mass index (BMI), pre-vaccination body temperature) will be presented with one decimal.

The minimum and maximum values and quartile values (if required) will be presented with the same number of decimals as the observed values.

The maxima and minima of transformed height variables will be displayed with no decimals.

The maxima and minima of transformed weight variables will be displayed with no decimals with the exception of values are below 10kg where one decimal will be displayed.

The maximum and minima of transformed body temperatures will be displayed with one decimal.

10.1.3.18. Serological summary statistics

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

GMT or GMC value	Number of decimals to display
<0.1	3
>=0.1 and <10	2
>=10 and <1000	1
>=1000	0

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

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

10.1.3.19. Statistical methodology

10.1.3.20. Exact confidence intervals around proportions

The exact confidence intervals around within-group proportions are derived using the method of Clopper and Pearson [Clopper, 1934].

10.1.3.21. Standardized asymptotic confidence intervals around differences in proportions

The standardized asymptotic confidence intervals around differences in proportions are derived using the method of Mietinnen and Nurminen [Miettinen, 1985].

10.2. TFL and/or TFL ToC

The TFL ToC can be found in eTMF folder section 11.1.1. As the process of TFL came when the SAP was already developed using previous process, no separate TFL has been prepared. The mock template are present in the SAP in Section 13 and tables to be generated for synopsis, in-text, post-text and posting has been flagged in the TFL ToC for different timepoints when the analysis is planned.

11. REFERENCES

Clopper CJ, Pearson E. The Use of Confidence or Fiducial Limits Illustrated in the case of the Binomial. *Biometrika.* 1934;26:404-13.

Miettinen, O. S. and Nurminen, M. Comparative analysis of two rates. Statistics in Medicine, 1985;4,213-226.

Kim HW, Canchola JG, Brandt CD, et al. Respiratory syncytial virus disease in infants despite prior administration of antigenic inactivated vaccine. *Am J Epidemiol*. 1969; 89(4): 422-34

12. LIST OF LISTINGS FOR THE FINAL ANALYSIS

The following listings will be generated using the macros developed by DSCS

Appendix Table I.B – Demography

Appendix Table IBii - Vital signs

Appendix Table I.Cii - Reason for visit not done

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

Appendix Table I.Eii – Screening conclusion

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

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 IV.A – Haematology and Biochemistry

Appendix Table V.A - RTI Assessment, Surveillance / Asymptomatic visit and Worsening data

Randomisation list

13. MOCK TABLES

Template 1 Number of subjects by country and center - <RSV 1D, RSV 2D, Comparator/Placebo> groups (Exposed Set)

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

Short group label = long group label
N = total number of subjects
n = number of subjects in a given center or country
% = n/N x 100
Center = GSK Biologicals assigned center number

Template 2 Summary of study completion with reasons for withdrawal <RSV 1D, RSV 2D, Comparator/Placebo> <groups> < pooled RSV 1D, RSV 2D, Comparator/Placebo groups> (Exposed Set)

	<Each Group> N=XXXX		<Total> N=XXXX	
	n	**%**	**n**	**%**
Completed the study	xxx	xx.x	xxx	xx.x
Withdrawn from the study	xxx	xx.x	xxx	xx.x
Primary reason for withdrawal				
Adverse Event Requiring Expedited Reporting	xxx	xx.x	xxx	xx.x
Unsolicited Non-Serious Adverse Event	xxx	xx.x	xxx	xx.x
Solicited Adverse Event	xxx	xx.x	xxx	xx.x
Protocol Deviation	xxx	xx.x	xxx	xx.x
Withdrawal By Subject	xxx	xx.x	xxx	xx.x
Sponsor Study Termination	xxx	xx.x	xxx	xx.x
Lost To Follow-up	xxx	xx.x	xxx	xx.x
Migrated / Moved From The Study Area	xxx	xx.x	xxx	xx.x
Other	xxx	xx.x	xxx	xx.x

Short group label = long group label
Completed = number of subjects who completed last study visit
Withdrawn = number of subjects who did not come for the last study visit

Template 3 Summary of visit attendance/phone contact completion <RSV 1D, RSV 2D, Comparator/Placebo> groups (Exposed Set)

	<Group 1> N=XXXX		<Group 2> N=XXXX		Total N=XXXX	
	n	%	n	%	n	%
Visit 1 (Day 1)						
Attended	xxx	xx.x	xxx	xx.x	xxx	xx.x
Did not attend yet	xxx	xx.x	xxx	xx.x	xxx	xx.x
Withdrawal at visit or earlier	xxx	xx.x	xxx	xx.x	xxx	xx.x
Did not attend	xxx	xx.x	xxx	xx.x	xxx	xx.x
Visit X (Day Y)						
Phone contact X (Day Y)						
Completed	xxx	xx.x	xxx	xx.x	xxx	xx.x
Did not complete yet	xxx	xx.x	xxx	xx.x	xxx	xx.x
Withdrawal at visit or earlier	xxx	xx.x	xxx	xx.x	xxx	xx.x
Did not complete	xxx	xx.x	xxx	xx.x	xxx	xx.x
Phone contact X (Day Y)						
Visit X (Day Y)						
Last study contact (Day Y)						
Completed	xxx	xx.x	xxx	xx.x	xxx	xx.x
Did not complete yet	xxx	xx.x	xxx	xx.x	xxx	xx.x
Withdrawal at visit or earlier	xxx	xx.x	xxx	xx.x	xxx	xx.x
Did not complete	xxx	xx.x	xxx	xx.x	xxx	xx.x

Short group label = long group label
N = Number of subjects in each group or in total
n/% = number / percentage of subjects in a given category

Template 4 Summary of important protocol deviations leading to elimination from any analyses <RSV 1D, RSV 2D, Comparator/Placebo> <groups>< -pooled RSV 1D, RSV 2D, Comparator/Placebo groups>

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

Short group label = long group label
N = Total number of subjects
Occ = number of occurrences = number of important protocol deviations
n/% = number / percentage of subjects with important protocol deviations

Template 5 Summary of subject disposition from enrolled set to randomized set (Exposed Set)

	Total N=XXX	
	n	**%**
Withdrawals prior to randomization	xxx	xx.x
<Withdrawal reason 1>	xxx	xx.x
<Withdrawal reason 2>	xxx	xx.x
	xxx	xx.x
Number of subjects included in randomized set	xxx	xx.x

Short group label = long group label
N = Number of subjects
n = number of subjects enrolled by center
% = n / Number of subjects with available results x 100

Template 6 Summary of subject disposition from randomized set to exposed set

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

Short group label = long group label
N = Number of subjects
n = number of subjects enrolled by center
% = n / Number of subjects with available results x 100

Template 7 Summary of subject disposition from Exposed Set to Per Protocol Set at <Day 31/Day 61/end of first RSV season> <RSV 1D, RSV 2D, Comparator/Placebo> groups (Exposed set)

	<Group 1> N=XXX		<Group 2> N=XXX		Total N=XXX	
	n	%	n	%	n	%
Withdrawals	xxx	xx.x	xxx	xx.x	xxx	xx.x
<Withdrawal reason 1>	xxx	xx.x	xxx	xx.x	xxx	xx.x
<Withdrawal reason 2>	xxx	xx.x	xxx	xx.x	xxx	xx.x
Eliminations	xxx	xx.x	xxx	xx.x	xxx	xx.x
<Elimination reason 1	xxx	xx.x	xxx	xx.x	xxx	xx.x
(code)>	xxx	xx.x	xxx	xx.x	xxx	xx.x
<Elimination reason 2 (code)>						
	xxx	xx.x	xxx	xx.x	xxx	xx.x
Number of subjects included in Per Protocol Set at <Day 31/Day 61/End of first RSV season>						

Short group label = long group label
N = Number of subjects
n = number of subjects enrolled by center
% = n / Number of subjects with available results x 100

Template 8 Summary of subject disposition from Exposed Set to End of study <RSV 1D, RSV 2D, Comparator/Placebo> groups (Exposed set)

	<Group 1> N=XXX		<Group 2> N=XXX		Total N=XXX	
	n	%	n	%	N	%
Eliminations	xxx	xx.x	xxx	xx.x	xxx	xx.x
<Elimination reason 1	xxx	xx.x	xxx	xx.x	xxx	xx.x
(code)>	xxx	xx.x	xxx	xx.x	xxx	xx.x
<Elimination reason 2						
(code)>						
	xxx	xx.x	xxx	xx.x	xxx	xx.x
Withdrawals	xxx	xx.x	xxx	xx.x	xxx	xx.x
<Withdrawal reason 1>	xxx	xx.x	xxx	xx.x	xxx	xx.x
< Withdrawal reason 2>						
Number of subjects who	xxx	xx.x	xxx	xx.x	xxx	xx.x
completed the study	xxx	xx.x	xxx	xx.x	xxx	xx.x
Completed with 1 dose	xxx	xx.x	xxx	xx.x	xxx	xx.x
Completed with X doses						

Short group label = long group label
N = Number of subjects
n = number of subjects enrolled by center
% = n / Number of subjects with available results x 100

Template 9 Deviations from protocol for age and intervals between study visits <RSV 1D, RSV 2D, Comparator/Placebo> groups (Exposed Set)

Type of interval	Interval range			<Group 1>		<Group 2	
				Value	%	Value	%
Age (years) at first vaccine administration	From <x> to <y> years	N		xxx		xxx	
		n		xxx		xxx	xx.x
		Below <x>	xx.x			xxx	xx.x
				xxx		xxx	xx.x
		Above <y>	xx.x				
				xxx			
Number of days between vaccination <x> and vaccination <y>	From <x> to <y> days		xx.x				
Number of days between vaccination <x> and visit <y>	From <x> to <y> days						
Number of days between vaccination <x> and blood sampling <y>							

Short group label = long group label
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 10 Minimum and maximum visit dates <RSV 1D, RSV 2D, Comparator/Placebo> groups (Exposed Set)

Visit Description	Parameter	<each group> Date	<each group> Date	Overall Date
< each informed consent>	Minimum	DDMMYYYY	DDMMYYYY	DDMMYYYY
	Maximum	DDMMYYYY	DDMMYYYY	DDMMYYYY
[Randomization]	Minimum	DDMMYYYY	DDMMYYYY	DDMMYYYY
	Maximum	DDMMYYYY	DDMMYYYY	DDMMYYYY
<each visit>	Minimum	DDMMYYYY	DDMMYYYY	DDMMYYYY
	Maximum	DDMMYYYY	DDMMYYYY	DDMMYYYY

Short group label = long group label

Template 11 Summary of demographic characteristics - <RSV 1D, RSV 2D, Comparator/Placebo> <groups>< -pooled RSV 1D, RSV 2D, Comparator/Placebo groups> (Exposed Set, PPS for immunogenicity at <Day 31/Day 61/end of first RSV season>)

	<Group 1> N =		<Group 2> N =		<Group 3> N =		Total N =	
	Value or n	%	Value or n	%	Value or n	%	Value or n	%
Age (months) at first vaccination								
n								
Mean								
Standard Deviation								
Median								
Minimum								
Maximum								
Sex								
Female								
Male								
Geographic Ancestry								
African Heritage / African American								
American Indian or Alaskan Native								
Asian - Central/South Asian Heritage								
Asian - East Asian Heritage								
Asian - Japanese Heritage								
Asian - South East Asian Heritage								
Native Hawaiian or Other Pacific Islander								
White - Arabic / North African Heritage								
White - Caucasian / European Heritage								
Other								

<each group>:
N = total number of subjects
n/% = number / percentage of subjects in a given category
Value = value of the considered parameter
SD = standard deviation

Template 12 Summary of vital signs characteristics - <RSV 1D, RSV 2D, Comparator/Placebo> <groups>< pooled RSV 1D, RSV 2D, Comparator/Placebo groups> (Exposed set, PPS for immunogenicity at <Day 31/Day 61/end of first RSV season>)

Visit	Characteristics	Parameters	<each group> N = Value	Total N = Value
<Each visit>	Height (Cm)	N with data		
		Mean		
		SD		
		Median		
		Minimum		
		Maximum		
	Weight (Kg)	N with data		
		Mean		
		SD		
		Median		
		Minimum		
		Maximum		
	Heart rate (Beats per minute)	N with data		
		Mean		
		SD		
		Median		
		Minimum		
		Maximum		
	Respiratory rate (Breadth per minute)	N with data		
		Mean		
		SD		
		Median		
		Minimum		
		Maximum		
	Temperature/(Axillary) (°C)	N with data		
		Mean		
		SD		
		Median		
		Minimum		
		Maximum		

<each group>:
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 13 Number of enrolled subjects by age category <RSV 1D, RSV 2D, Comparator/Placebo> groups

Characteristics	Categories	<*each group*> N = n	Total N = n
Age category	1=Infants and toddlers (28 days-23 month)		
	Missing		

<each group>:
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 dose 1 unknown

Template 14 Compliance in completing solicited adverse events information <RSV 1D, RSV 2D, Comparator/Placebo> groups (Exposed Set)

		<Group 1>			<Group 2>		
		N	n	Compliance (%)	N	n	Compliance (%)
<Vaccination at visit 1>	General solicited adverse events	xxx	xxx	xx.x	xxx	xxx	xx.x
	Local solicited adverse events	xxx	xxx	xx.x	xxx	xxx	xx.x
<Vaccination at visit X>		xxx	xxx	xx.x	xxx	xxx	xx.x
	General solicited adverse events	xxx	xxx	xx.x	xxx	xxx	xx.x
Per vaccination	Local solicited adverse events	xxx		xx.x	xxx	xxx	xx.x
		xxx		xx.x	xxx	xxx	xx.x
	General solicited adverse events	xxx	xxx				
	Local solicited adverse events						

Short group label = long group label
N=Number of administered vaccination
n = number of vaccination with Adverse Event Screen returned
Compliance (%) = (n / N) X 100

Template 15 Summary of <grade 3> adverse events (solicited and unsolicited) <with causal relationship to vaccination, with medically attend visit> within <7, 30> days following first and second vaccination and overall <RSV 1D, RSV 2D, Comparator/Placebo> <groups>< pooled RSV 1D, RSV 2D, Comparator/Placebo groups> (Exposed Set)

		<Each Group >			
				95% CI	
		n	%	LL	UL
<Vaccination at visit 1>	N	xxx			
	Any adverse event	xxx	xx.x	xx.x	xx.x
	Local adverse event	xxx	xx.x	xx.x	xx.x
	General adverse event	xxx	xx.x	xx.x	xx.x

<Vaccination at visit X>

Per subject
Per vaccination

Short group label = long group label
For each vaccination:
N = number of subjects with the corresponding administered vaccination
n/% = number/percentage of subjects presenting at least one type of adverse event following the corresponding dose
For per vaccination:
N = number of administered vaccination
n/% = number/percentage of vaccination followed by at least one type of adverse event
For per subject:
N = number of subjects with at least one administered vaccination
n/% = number/percentage of subjects presenting at least one type of adverse event
95% CI = Exact 95% confidence interval; LL = lower limit, UL = upper limit

Template 16 Percentage of subjects with solicited local adverse events by maximum intensity within the 7-day (Days 1-7) following first and second vaccination and overall - <RSV 1D, RSV 2D, Comparator/Placebo> <groups> < pooled RSV 1D, RSV 2D, Comparator/Placebo groups>(Exposed Set)

Adverse event: Pain

		<Group 1>				<Group 2>			
				95% CI				95% CI	
		n	%	LL	UL	n	%	LL	UL
<Vaccination at visit 1>	N	xxx				xxx			
	Any	xxx	xx.x	xx.x	xx.x	xxx	xx.x	xx.x	xx.x
	Grade 2	xxx	xx.x	xx.x	xx.x	xxx	xx.x	xx.x	xx.x
	Grade 3	xxx	xx.x	xx.x	xx.x	xxx	xx.x	xx.x	xx.x
	Medically attended visits								
<Vaccination at visit 3>									
Per subject									
Per vaccination									

Adverse event: Swelling/Redness

		<Group 1>				<Group 2>			
				95% CI				95% CI	
		n	%	LL	UL	n	%	LL	UL
<Vaccination at visit 1>	N	xxx				xxx			
	Any	xxx	xx.x	xx.x	xx.x	xxx	xx.x	xx.x	xx.x
	≥5 - ≤ 20	xxx	xx.x	xx.x	xx.x	xxx	xx.x	xx.x	xx.x
	>20	xxx	xx.x	xx.x	xx.x	xxx	xx.x	xx.x	xx.x
	Medically attended visits								
<Vaccination at visit 3>									
Per subject									
Per vaccination									

<each group>:
For each vaccination:
N = number of subjects with the corresponding documented vaccination
n/% = number/percentage of subjects reporting the type of adverse event at least once following the corresponding vaccination
For Per vaccination:
N = number of documented vaccination
n/% = number/percentage of vaccination followed by at least one type of adverse event
For Per subject:
N = number of subjects with at least one documented vaccination

n/% = number/percentage of subjects reporting the type of adverse event at least once
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit
The maximum intensity of local injection site redness/swelling was coded as follows:
1: > 0.1 mm to < 5 mm
2: ≥ 5 mm to ≤ 20 mm
3: > 20 mm
Please note – The N may vary for each symptom depending on how many subjects has filled in diary card for particular symptom.

Template 17 Duration in days of solicited <general, local> adverse events within 7 days following first and second vaccination and overall <RSV 1D, RSV 2D, Comparator/Placebo> groups (Exposed Set)

	Symptom	<Group 1> Value	<Group 2> Value
<Vaccination at visit 1>	<Symptom 1>		
	n	xxx	xxx
	Mean	xxx.x	xxx.x
	Minimum	xxx	xxx
	Q1	xxx.x	xxx.x
	Median	xxx.x	xxx.x
	Q3	xxx.x	xxx.x
	Maximum	xxx	xxx
	<Symptom 2>		
<Vaccination at visit X>			

Per vaccination

Short group label = long group label
n = number of doses with the adverse event
Q1 = 25th percentile
Q3 = 75th percentile

Template 18 Percentage of subjects with solicited general adverse events by maximum intensity within the 7-day (Days 1-7) following first and second vaccination and overall - <RSV 1D, RSV 2D, Comparator/Placebo> <groups> < pooled RSV 1D, RSV 2D, Comparator/Placebo groups >(Exposed Set)

Adverse event: Irritability/Fussiness or Drowsiness or Loss of appetite

		<Group 1>				<Group 2>			
				95% CI				95% CI	
		n	%	LL	UL	n	%	LL	UL
<Vaccination at visit 1>	N	xxx				xxx			
	Any	xxx	xx.x	xx.x	xx.x	xxx	xx.x	xx.x	xx.x
	Grade 2	xxx	xx.x	xx.x	xx.x	xxx	xx.x	xx.x	xx.x
	Grade 3	xxx	xx.x	xx.x	xx.x	xxx	xx.x	xx.x	xx.x
	Any related								
	Grade 2 related								
	Grade 3 related								
	Medically attended visits								
<Vaccination at visit 3>									
Per subject									
Per vaccination									

Adverse event: Temperature (C)

		<Group 1>				<Group 2>			
				95% CI				95% CI	
		n	%	LL	UL	n	%	LL	UL
<Vaccination at visit 1>	N	xxx				xxx			
	Any	xxx	xx.x	xx.x	xx.x	xxx	xx.x	xx.x	xx.x
	≥38.0	xxx	xx.x	xx.x	xx.x	xxx	xx.x	xx.x	xx.x
	≥38.5	xxx	xx.x	xx.x	xx.x	xxx	xx.x	xx.x	xx.x
	≥39.0								
	≥39.5								
	>40.0								
	Related								
	>39.0 - ≤40.0 Related								
	>40.0 Related								
	Medically attended visits								
<Vaccination at visit 3>									
Per subject									
Per vaccination									

<each group>:

For each vaccination:

N = number of subjects with the corresponding documented vaccination

n/% = number/percentage of subjects reporting the type of adverse event at least once following the corresponding vaccination

For Per vaccination:

N = number of documented vaccination

n/% = number/percentage of vaccination followed by at least one type of adverse event

For Per subject:

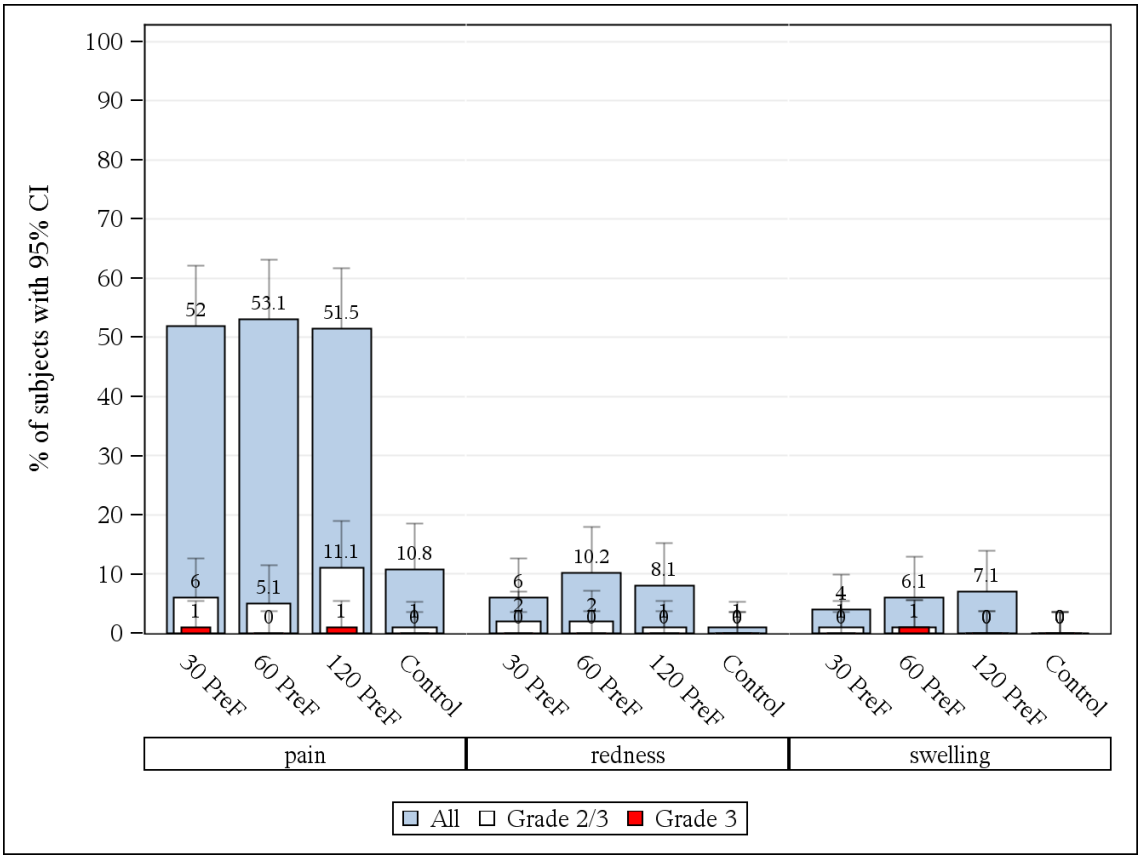
N = number of subjects with at least one documented vaccination

n/% = number/percentage of subjects reporting the type of adverse event at least once

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

Please note – The N may vary for each adverse event depending on how many subjects has filled in diary card for particular symptom.

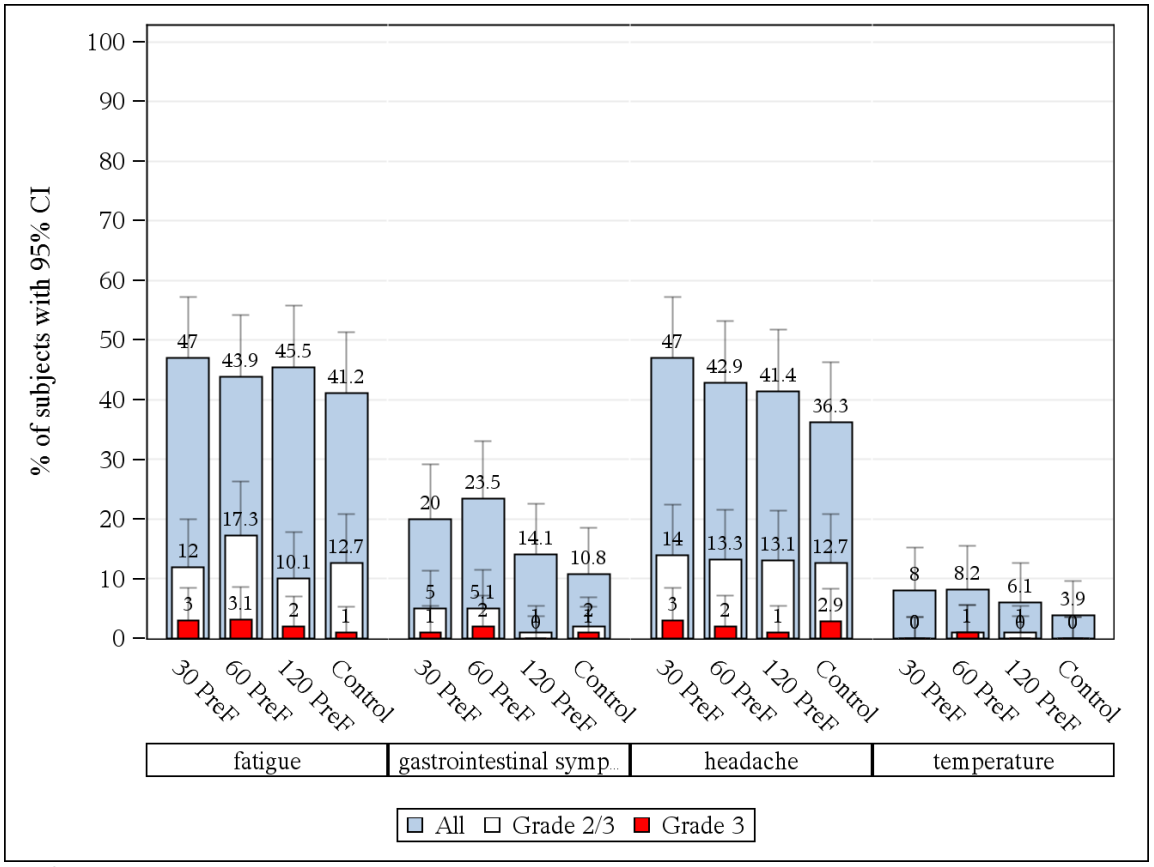
Template 19 Percentage of subjects reporting solicited local adverse events (any grade /grade 2,3/ grade 3) within 7-days following first and second vaccination by maximum intensity for pooled RSV 1D, RSV 2D, Comparator/Placebo groups (Exposed Set)



<each group>

Please note – this graph will be presented on pooled group only

Template 20 Percentage of subjects reporting fever (any and grade 3) and other solicited general adverse events (any grade /grade 2,3/ grade 3) within 7-days following first and second vaccination by maximum intensity for pooled RSV 1D, RSV 2D and Comparator/Placebo groups (Exposed Set)



<each group>
Please note the figure is only template
Please note – this graph will be presented on pooled group only

Template 21 Summary of subjects with at least one <Ø/grade 3/ related/ grade 3 related/serious/ medically attended> unsolicited adverse event <episode of spontaneous or excessive bleeding> classified by MedDRA Primary System Organ Class and Preferred Term <with onset within 30 days of first and second vaccination><from vaccination dose 1 up to Day 61> <pooled> <RSV 1D, RSV 2D, Comparator/Placebo> groups (Exposed Set)

	<Group 1> N=XXXX				<Group 2> N=XXXX			
Primary System Organ Class (CODE)			**95% CI**				**95% CI**	
Preferred Term (CODE)	**n**	**%**	**LL**	**UL**	**N**	**%**	**LL**	**UL**
Any <Ø, grade 3, related, grade3 related> unsolicited adverse event	xxx	xx.x	xx.x	xx.x	Xxx	xx.x	xx.x	xx.x
<SOC 1 (code)>	xxx	xx.x	xx.x	xx.x	Xxx	xx.x	xx.x	xx.x
<Preferred Term 1 (code)>	xxx	xx.x	xx.x	xx.x	Xxx	xx.x	xx.x	xx.x
<Preferred Term 2 (code)>	xxx	xx.x	xx.x	xx.x	Xxx	xx.x	xx.x	xx.x
<SOC 2 (code)>	xxx	xx.x	xx.x	xx.x	xxx	xx.x	xx.x	xx.x
<Preferred Term 1 (code)>	xxx	xx.x	xx.x	xx.x	xxx	xx.x	xx.x	xx.x
<Preferred Term 2 (code)>	xxx	xx.x	xx.x	xx.x	xxx	xx.x	xx.x	xx.x

Short group label = long group label
Any adverse event = at least one adverse event experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered vaccination
n* = number of events reported
n/% = number/percentage of subjects reporting the adverse event at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Template 22 Summary of subjects with at least one <episode of RSV-LRTI (AE of specific interest)/serious adverse event> classified by MedDRA Primary System Organ Class and Preferred Term <from vaccination dose 1 up to end of <first/second> RSV season for pooled RSV 1D, RSV 2D and Comparator/Placebo groups (Exposed Set)

	<Group 1> N=XXXX				<Group 2> N=XXXX			
Primary System Organ Class (CODE)			**95% CI**				**95% CI**	
Preferred Term (CODE)	**n**	**%**	**LL**	**UL**	**N**	**%**	**LL**	**UL**
Any <Ø, grade 3, related, grade3 related> unsolicited adverse event	xxx	xx.x	xx.x	xx.x	Xxx	xx.x	xx.x	xx.x
<SOC 1 (code)>	xxx	xx.x	xx.x	xx.x	Xxx	xx.x	xx.x	xx.x
<Preferred Term 1 (code)>	xxx	xx.x	xx.x	xx.x	Xxx	xx.x	xx.x	xx.x
<Preferred Term 2 (code)>	xxx	xx.x	xx.x	xx.x	Xxx	xx.x	xx.x	xx.x
<SOC 2 (code)>	xxx	xx.x	xx.x	xx.x	xxx	xx.x	xx.x	xx.x
<Preferred Term 1 (code)>	xxx	xx.x	xx.x	xx.x	xxx	xx.x	xx.x	xx.x
<Preferred Term 2 (code)>	xxx	xx.x	xx.x	xx.x	xxx	xx.x	xx.x	xx.x

Short group label = long group label
Any adverse event = at least one adverse event experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered vaccination
n* = number of events reported
n/% = number/percentage of subjects reporting the adverse event at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Template 23 Listing of SAE from vaccination dose 1 up to <Day 61/end of first RSV season/study end> (Exposed Set)

Group	Subject number	Gender	Country	Race	Age at onset (Year)	Verbatim	Preferred Term
xxxxx	xxxxx	xxxxx	xxxxxxx	xxxxxx	xx	xxxxx	xxxxx

Group	Subject number	Primary System Organ Class	Medical visit type	Vaccination	Day of onset	Duration	Intensity	Causality	Outcome
xxxxx	xxxxx	xxxxx	xxxxxxx	xxxxxx	xx	xx	xxxx	: : :	xxxxx

Group	Subject number	Seriousness criteria	Potential AESI (prefered term)
xxxxx	xxxxx	xxxxx	xxxxxxx

Group	Subject number	Seriousness criteria	Potential AESI (prefered term)	Vaccination	Day of onset	Duration	Intensity	Causality	Outcome
xxxxx	xxxxx	xxxxx	xxxxxxx	xxxxxx	xx	xx	xxxx	: : :	xxxxx

Template 24 Listing of AEs related to LRTI and association to RSV infection from vaccination dose 1 up to <Day 61/end of first RSV season/study end> (Exposed Set)

Group	**Sub. No.**	**Age at onset (month)**	**Verbatim**	**Preferred term**	**MED type**	**Previous Dose**	**Day of onset**	**Start date**	**End date**	**Duration**	**Intensity**	**Causality**	**Outcome**	**Local RSV test result**	**Date of sample for local testing**	**Central test RSV A**	**Central test RSV B**	**Date of sample for central testing**	**AESI**

<each group>:
AESI: AEs of Special Interest - LRTI identified by the Investigator
*AEs related to LRTI will be identified based on the list of preferred terms described in in section 9.4–Annex 2

Template 25 Listing of AEs related to spontaneous or excessive bleeding together with hemoglobin and platelet count results with 30 days of first and second vaccination (Exposed Set)

Group	Sub. No.	Age at onset (month)	Verbatim	Preferred term*	Previous Dose	Day of onset	Duration	Intensity	Start date	End date	AESI	Date of sample	Laboratory parameter	Raw result	Unit
xx	xx		xx	xx	xx	xx			xx	xx		xx	Hemoglobin		
													Platelet count		
												xx	Hemoglobin		
													Platelet count		
												…			

<each group>:

*AEs related to spontaneous or excessive bleeding will be identified based on the list of preferred terms described in section 9.4 –Annex

AESI: AEs of Special Interest – Spontaneous or excessive bleeding identified by the Investigator

Template 26 Listing of adverse events, SAEs and solicited symptoms leading to study or treatment discontinuation from vaccination dose 1 up to <Day 61/end of first RSV season/end of second RSV season>(Exposed Set)

Type of discontinuation: <study/treatment>

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

Template 27 Listing of unscheduled safety visit from vaccination dose 1 up to <Day 61/end of first RSV season/study end> (Exposed Set)

Group	Sub.No.	Gender	Country	Race	Age at unscheduled visit (Month)	Date of previous safety BS	Date of unscheduled safety BS	Result of previous safety BS out of lab range	Grade of abnormality per protocol – previous safety BS	Result of biochemistry/ hematology at unscheduled visit	Outcome of unscheduled safety visit

<each group>:

Please note that only unscheduled safety visits with abnormal safety parameters will be presented.

Template 28 Summary of subjects taking a concomitant medication within <7/30> days following each vaccination and overall <RSV 1D, RSV 2D, Comparator/Placebo> <groups>< for pooled RSV 1D, RSV 2D and Comparator/Placebo groups> (Exposed Set)

		<Group 1>				<Group 2>			
				95% CI				95% CI	
		n	%	LL	UL	n	%	LL	UL
<Vaccination at visit 1>	N	xxx				xxx			
	Any	xxx	xx.x	xx.x	xx.x	xxx	xx.x	xx.x	xx.x
	Any antipyretic	xxx	xx.x	xx.x	xx.x	xxx	xx.x	xx.x	xx.x
	Any prophylactic antipyretic	xxx	xx.x	xx.x	xx.x	xxx	xx.x	xx.x	xx.x

<Vaccination at visit X>

Per subject

Per vaccination

Short group label = long group label
For each vaccination:
N = number of subjects with the corresponding administered vaccination
n/% = number/percentage of subjects who took the specified type of concomitant medication at least once during the considered period
For per vaccination:
N = number of administered vaccination
n/% = number/percentage of vaccines after which the specified type of concomitant medication was taken at least once during the considered period
For per subject:
N = number of subjects with at least one administered vaccination
n/% = number/percentage of subjects who 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 29 Summary of occurrences and subjects with at least one solicited and unsolicited adverse event classified by MedDRA Primary System Organ Class and Preferred Term with onset within 30 days of first and second vaccination – SAE excluded <RSV 1D, RSV 2D, Comparator/Placebo> groups (Exposed Set)

Primary System Organ Class (CODE) Preferred Term (CODE)	<Group 1> N=XXXX occ	 n	 %	<Group 2> N=XXXX occ	 n	 %
Any solicited and unsolicited adverse event	xxx	xxx	xx.x	xxx	xxx	xx.x
<SOC 1 (code)>	xxx	xxx	xx.x	xxx	xxx	xx.x
<Preferred Term 1 (code)>	xxx	xxx	xx.x	xxx	xxx	xx.x
<Preferred Term 2 (code)>	xxx	xxx	xx.x	xxx	xxx	xx.x
<SOC 2 (code)>	xxx	xxx	xx.x	xxx	xxx	xx.x
<Preferred Term 1 (code)>	xxx	xxx	xx.x	xxx	xxx	xx.x
<Preferred Term 2 (code)>	xxx	xxx	xx.x	xxx	xxx	xx.x

Short group label = long group label
Any adverse event = at least one adverse event experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered vaccination
n* = number of events reported
n/% = number/percentage of subjects reporting the adverse event at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Template 30 Number (%) of subjects with serious adverse events <from Day 1 up to <Day 61/end of second RSV season>, including number of events reported for pooled RSV 1D, RSV 2D and Comparator/Placebo> groups (Exposed Set)

			<Each group> N=XXXX			<Each group> N=XXXX		
Type of Event	**Primary System Organ Class (CODE)**	**Preferred Term (CODE)**	**n***	**n**	**%**	**n***	**n**	**%**
SAE		At least one symptom	xxx	xxx	xx.x	xxx	xxx	xx.x
	<each SOC (SOC code)>	<each PT (PT code)>	xxx	xxx	xx.x	xxx	xxx	xx.x
			xxx	xxx	xx.x	xxx	xxx	xx.x
Related SAE		At least one symptom	xxx	xxx	xx.x	xxx	xxx	xx.x
	<each SOC (SOC code)>	<each PT (PT code)>	xxx	xxx	xx.x	xxx	xxx	xx.x
			xxx	xxx	xx.x	xxx	xxx	xx.x
Fatal SAE		At least one symptom	xxx	xxx	xx.x	xxx	xxx	xx.x
	<each SOC (SOC code)>	<each PT (PT code)>	xxx	xxx	xx.x	xxx	xxx	xx.x
			xxx	xxx	xx.x	xxx	xxx	xx.x
Related Fatal SAE		At least one symptom	xxx	xxx	xx.x	xxx	xxx	xx.x
	<each SOC (SOC code)>	<each PT (PT code)>	xxx	xxx	xx.x	xxx	xxx	xx.x
			xxx	xxx	xx.x	xxx	xxx	xx.x

Short group label = long group label
N = number of subjects with administered vaccination
n/% = number/percentage of subjects reporting the adverse event at least once
n* = Number of adverse events reported
Related = assessed by the investigator as related

Template 31 Number and percentage of subjects with <anti-RSV A antibody titre, anti-RSV F concentration> equal to or above <cut-off ><unit> and gm<t,c> for pooled RSV 1D, RSV 2D and Comparator/Placebo> groups (<Adapted>PPS of immunogenicity at <Day X, end of 1st RSV season>)

Antibody	Time point	Cut-off		<Group 1>					<Group 2>				
						95% CI						95% CI	
			N	**n**	**value**	**LL**	**UL**	**N**	**n**	**value**	**LL**	**UL**
<Antibody 1>	<Time point 1>	<Cut-off 1>	%=<cut-off 1> <unit>	xxx	xxx	xx.x	xx.x	xx.x	xxx	xxx	xx.x	xx.x	xx.x
			GM<T,C>	xxx		xx.x	xx.x	xx.x	xxx		xx.x	xx.x	xx.x

Short group label = long group label
GMT/C = geometric mean antibody titer/concentration
N = Number of subjects with available results
n/% = number/percentage of subjects with titer/concentration equal to or above specified value
95% CI = 95% confidence interval; LL = lower limit, UL = upper limit
PRE= Pre-vaccination
D31 = Post-vaccination at Day 31
D61 = Post-vaccination at Day 61
RSV1S = End of 1st RSV transmission season

Template 32 Distribution of <RSV-A neutralising antibody titre, RSV-F antibody concentration> for pooled RSV 1D, RSV 2D and Comparator/Placebo> groups (<Adapted>PPS for immunogenicity <at Day X, end of 1st RSV season>)

Antibody	Time point	Cut-off	<Group 1>					<Group 2>				
						95% CI					95% CI	
			N	n	value	LL	UL	N	n	value	LL	UL
<Antibody 1>	<Time point 1>	<cut-off 1	xxx	xxx	xx.x	xx.x	xx.x	xxx	xxx	xx.x	xx.x	xx.x
		>=cut-off 2	xxx	xxx	xx.x	xx.x	xx.x	xxx	xxx	xx.x	xx.x	xx.x
		>=cut-off 3	xxx	xxx	xx.x	xx.x	xx.x	xxx	xxx	xx.x	xx.x	xx.x
	<Time point 2>	<cut-off 1	xxx	xxx	xx.x	xx.x	xx.x	xxx	xxx	xx.x	xx.x	xx.x
		>=cut-off 2	xxx	xxx	xx.x	xx.x	xx.x	xxx	xxx	xx.x	xx.x	xx.x
		>=cut-off 3	xxx	xxx	xx.x	xx.x	xx.x	xxx	xxx	xx.x	xx.x	xx.x

Short group label = long group label
N = number of subjects with available results
n/% = number/percentage of subjects with <titer, concentration> within the specified criterion
<95>% CI = <95>% confidence interval; LL = Lower Limit, UL = Upper Limit
PRE= Pre-vaccination
D31 = Post-vaccination at Day 31
D61 = Post-vaccination at Day 61
RSV1S = End of 1st RSV transmission season

Template 33 Vaccine response for anti-RSV-A neutralising antibody titre at each post-vaccination timepoint for pooled RSV 1D, RSV 2D and Comparator/Placebo> groups (PPS for analysis of immunogenicity at <Day X, End of 1st RSV season>)

Antibody	Time point	Pre-vaccination Category	<Group 1>					<Group 2>				
						95% CI					95% CI	
			N	n	value	LL	UL	N	n	value	LL	UL
<Antibody 1>	<Time point 1>	<128	xxx	xxx	xx.x	xx.x	xx.x	xxx	xxx	xx.x	xx.x	xx.x
		≥128 - ≤256	xxx	xxx	xx.x	xx.x	xx.x	xxx	xxx	xx.x	xx.x	xx.x
		>256-≤1024	xxx	xxx	xx.x	xx.x	xx.x	xxx	xxx	xx.x	xx.x	xx.x
		≥1024										
		Total response	xxx	xxx	xx.x	xx.x	xx.x	xxx	xxx	xx.x	xx.x	xx.x

Short group label = long group label
Total = all subjects with pre-and post- vaccination result available
Vaccine response defined as :
For subjects with pre-vaccination titer <128: antibody titer at post-vaccination>= 4 fold the pre-vaccination antibody titer
For subjects with pre-vaccination titer in ≥128 - ≤256: antibody titer at post-vaccination >= 3 fold the pre-vaccination antibody titer
For subjects with pre-vaccination titer in >256-≤1024: antibody titer at post-vaccination>= 2.5 fold the pre-vaccination antibody titer
For subjects with pre-vaccination titer >1024: antibody titer at post-vaccination >= 1 fold the pre-vaccination antibody titer
N = number of subjects with both pre- and post-vaccination results available
n/% = number/percentage of responders
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit
PRE= Pre-vaccination
<D31 = Post-vaccination at Day 31>
<D61 = Post-vaccination at Day 61>
<RSV1S = End of 1st RSV transmission season>

Template 34 Number and percentage of subjects with <anti-RSV A antibody titre, anti-RSV F concentration> equal to or above <cut-off ><unit> and GMR for pooled RSV 1D, RSV 2D and Comparator/Placebo> groups (PPS of immunogenicity at <Day X, End of 1st RSV season>)

Antibody Cut-off	Time point		<Group 1>					<Group 2>				
						95% CI					95% CI	
			N	n	value	LL	UL	N	n	value	LL	UL
<Antibody 1> <Cut-off 1>	<Time point 1>	%>=<cut-off 1> <unit>	xxx	xxx	xx.x	xx.x	xx.x	xxx	xxx	xx.x	xx.x	xx.x
		GMC/T	xxx		xx.x	xx.x	xx.x	xxx		xx.x	xx.x	xx.x
		Visit comparison / baseline										
		GMR	xxx		xx.x	xx.x	xx.x	xxx		xx.x	xx.x	xx.x

Short group label = long group label
GMT = geometric mean antibody titer
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
D31 = Post-vaccination at Day 31
D61 = Post-vaccination at Day 61
RSV1S = End of 1st RSV transmission season

Template 35 Distribution of fold of anti-RSV-A neutralising antibody titer by <cumulative> pre-vaccination titer category for pooled RSV 1D, RSV 2D and Comparator/Placebo> groups (PPS for analysis of immunogenicity at <Day X, end of first RSV season>)

Antibody Fold	Time point	Pre-vaccination status	<Group 1>					<Group 2>				
					95% CI					95% CI		
			N	n	Value	LL	UL	N	n	Value	LL	UL
<Antibody 1>	<Time point 1>	<1 <128	xxx	xxx	xx.x	xx.x	xx.x	xxx	xxx	xx.x	xx.x	xx.x
		≥128-≤256	xxx	xxx	xx.x	xx.x	xx.x	xxx	xxx	xx.x	xx.x	xx.x
		>256-≤512	xxx	xxx	xx.x	xx.x	xx.x	xxx	xxx	xx.x	xx.x	xx.x
		>1024-≤2048	xxx	xxx	xx.x	xx.x	xx.x	xxx	xxx	xx.x	xx.x	xx.x
		>2048-≤4096	xxx	Xxx	xx.x	xx.x	xx.x	xxx	xxx	xx.x	xx.x	xx.x
		>4096	xxx	Xxx	xx.x	xx.x	xx.x	xxx	xxx	xx.x	xx.x	xx.x
		Total	xxx	xxx	xx.x	xx.x	xx.x	xxx	xxx	xx.x	xx.x	xx.x
		≥1 <128 <unit>	xxx	xxx	xx.x	xx.x	xx.x	xxx	xxx	xx.x	xx.x	xx.x
		≥2 <128 <unit>	xxx	xxx	xx.x	xx.x	xx.x	xxx	xxx	xx.x	xx.x	xx.x

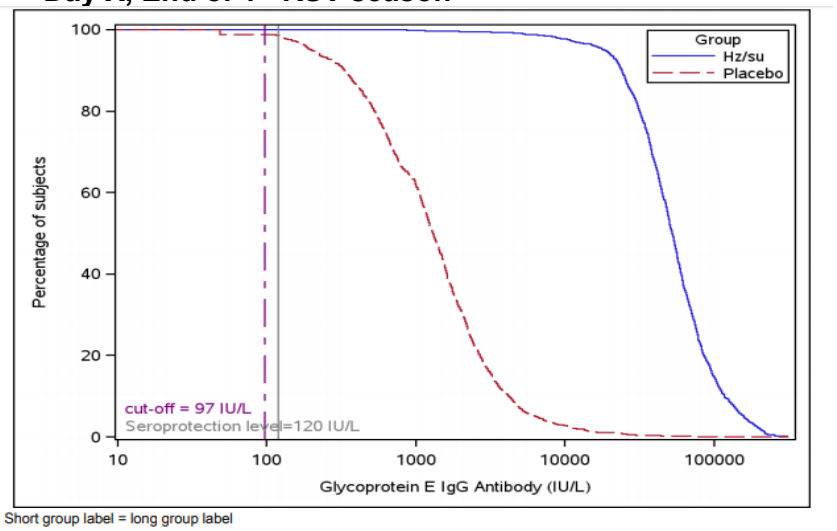
Short group label = long group label
N = number of subjects with pre and corresponding post-vaccination results available
n/% = number/percentage of subjects with titre fold change meeting the specified criterion
PRE= Pre-vaccination
D31 = Post-vaccination at Day 31
D61 = Post-vaccination at Day 61
RSV1S = End of 1st RSV transmission season

Template 36 Descriptive statistics of <anti-RSV A neutralizing antibody titre, anti-RSV F antibody concentration>at pre-vaccination, Day <31, 61,> <and end of 1st RSV transmission season> for pooled RSV 1D, RSV 2D and Comparator/Placebo> groups (<Adapted> PPS for immunogenicity)

		Each Group N=XXXX
Visit	**Characteristics**	**Value**
PRE	N with data	
	Mean	
	SD	
	Q1	
	Median	
	Q3	
	95% CI	(xx.x ; xx.x)
PI(D8)	…	
PI(D31)	…	
PI(D61)	…	
PI(D91)	…	

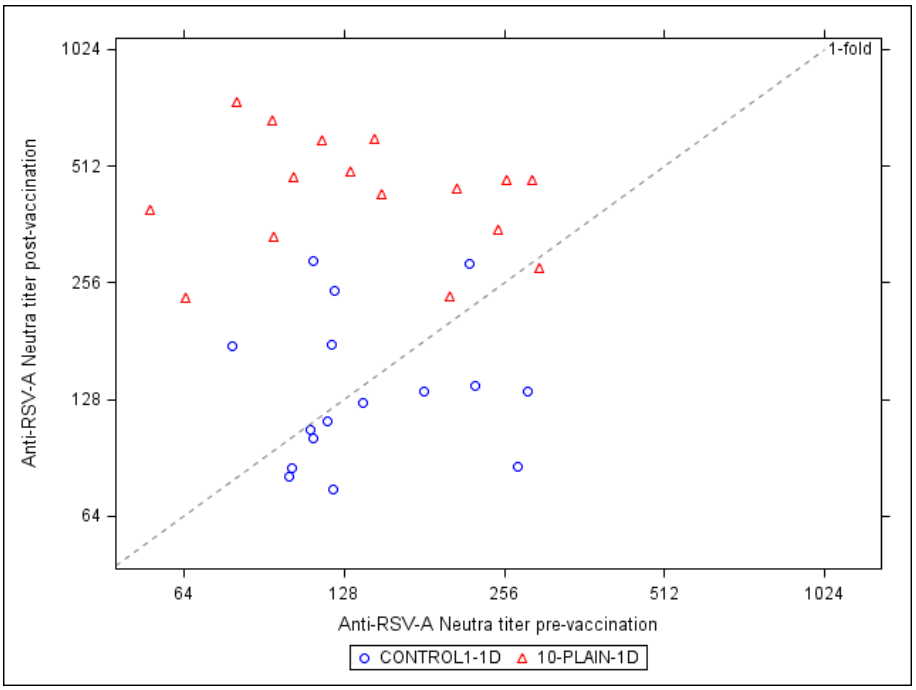
Short group label = long group label
N = total number of subjects
N with data = number of subjects with available results
Value = value of the considered parameter
SD = standard deviation
Q1 and Q3 = 1st and 3rd quantiles
LL, UL = Exact 95% Lower and Upper confidence limits
PRE= Pre-vaccination
D31 = Post-vaccination at Day 31
D61 = Post-vaccination at Day 61
RSV1S = End of 1st RSV transmission season

Template 37 Reverse cumulative distribution curves for anti-RSV-A neutralising antibody titres in each group at baseline and <Day 31, Day 61, End of first RSV season> for pooled RSV 1D, RSV 2D and Comparator/Placebo> group <PPS for analysis of immunogenicity at <Day X, End of 1st RSV season>



Short group label = long group label

Template 38 Individual results of anti-RSV-A neutralising antibody titre at Day <61/end of first RSV season> versus pre-vaccination in <each pooled <RSV 1D, RSV 2D> group> and Comparator/placebo group> (PPS for analysis of immunogenicity at <Day X>)



Short group label = long group label

Note: This graph is provided as an example. The same graph will be generated for each assay and each timepoint separately (Days 61, end of first RSV season)

Template 39 Number and percentage of subjects with at least one RSV infection, RSV-RTI, RSV-LRTI, RSV-severe LRTI, RSV-very severe LRTI, All-cause LRTI and RSV hospitalization (based on WHO case definition) from vaccination dose 1 up to end of <first, second> RSV season for pooled RSV 1D, RSV 2D and Comparator/Placebo group (<Exposed Set, Exposed Set with a negative RSV exposure status>)

	<each group> N =				Total N =			
			95% CI				95% CI	
Categories	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
No infection								
RSV-infection symptomatic or asymptomatic*								
RSV-RTI								
RSV-LRTI								
RSV-severe LRTI								
RSV-very severe LRTI								
All-cause LRTI								
RSV hospitalization**								

Short group label = long group label

* Association to RSV based on central testing only for asymptomatic visit (no local test available)

** Confirmed RSV infection and hospitalized for acute medical condition

N = number of subjects with at least one administered dose

n/%= number/percentage of subjects reporting at least once the symptom

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

Template 40 Proportion of subjects with at least one RSV hospitalization over the number of subjects with at least one RSV infection (symptomatic or asymptomatic*) from vaccination dose 1 up to end of <first, second> RSV season for pooled RSV 1D, RSV 2D and Comparator/Placebo group <Exposed Set, Exposed Set with negative RSV baseline status>

	<each group> N=			
			95 % CI	
Symptom	**n**	**%**	**LL**	**UL**
RSV hospitalization**				

Short group label = long group label

* Association to RSV based on central testing only for asymptomatic visit (no local test available)

** Confirmed RSV infection and hospitalized for acute medical condition

N= number of subjects with at least one RSV infection (symptomatic or asymptomatic)

n/%= number/percentage of subjects reporting at least one RSV hospitalization

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

Template 41 Number and percentage of subjects reporting the RSV infection of different severity (based on WHO case definition) by number of events experienced between vaccination dose 1 up to end of <first, second> RSV season for pooled RSV 1D, RSV 2D and Comparator/Placebo group <Exposed Set, Exposed Set with negative RSV baseline status>

		<Each group> N=xx			
				95% CI	
Characteristics	**Categories**	**n**	**%**	**LL**	**UL**
RSV infection-symptomatic or asymptomatic*	0				
	1				
	2				
RSV-RTI	0				
	1				
RSV-LRTI	0				
	1				
	2				
RSV-Severe LRTI	0				
	1				
RSV-very severe LRTI	0				
	1				
All cause LRTI	0				
	1				
	2				
	3				
RSV hospitalization$	0				
	1				
	2				
	3				

Short group label = long group label
N = number of subjects in each group
n = number of subjects in a given category
% =100*n/N
LL, UL for percentage = Exact 95% Lower and Upper confidence limits
Please note – Single episode can be considered in multiple category depending on the symptom experienced
* Association to RSV based on central testing only for asymptomatic visit (no local test available)
$Confirmed RSV infection and hospitalized for acute medical condition

Template 42 Number and percentage of RSV infections and associated disease severity (based on WHO case definition) and relative risk from vaccination dose 1 up to end of <first, second> RSV season for pooled RSV 1D, RSV 2D and Comparator/Placebo group <Exposed Set, Exposed Set with negative RSV baseline status>

	<Each Group> N =				Relative risk (RSV1D vs Comparator/Placebo)			Relative risk (RSV2D vs Comparator/Placebo)		
			95% CI			95% CI			95% CI	
Categories	**n**	**%**	**LL**	**UL**	**Values**	**LL**	**UL**	**Values**	**LL**	**UL**
RSV asymptomatic (Excluding RSV-RTI, LRTI, RSV-severe LRTI or RSV-very severe LRTI)										
RSV RTI (Excluding LRTI, RSV-severe or very severe LRTI)										
RSV LRTI (Excluding RSV-severe or very severe LRTI)										
RSV-severe LRTI (Excluding RSV-very severe LRTI)										
RSV-very severe LRTI										

Short group label = long group label

* Association to RSV based on central testing only for asymptomatic visit (no local test available)

N = number of RSV positive samples in each group

n** = number of cases in each category

n/%= number/percentage of cases in each category

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

Please note – Single episode is considered in single category of highest severity based on the symptom experienced

Template 43 Number and percentage of RSV infections (based on WHO case definition) requiring hospitalization between vaccination dose 1 up to end of <first, second> RSV season for pooled RSV 1D, RSV 2D and Comparator/Placebo group <Exposed Set, Exposed Set with negative RSV baseline status>

	Group N =					Total N =				
				95% CI					95% CI	
Categories	**n****	**n**	**%**	**LL**	**UL**	**n****	**N**	**%**	**LL**	**UL**
RSV RTI*(Excluding LRTI, severe or very severe LRTI)										
RSV LRTI (Excluding severe or very severe LRTI)										
RSV-severe LRTI (Excluding very severe LRTI)										
RSV-very severe LRTI										

Short group label = long group label

N = number of RSV infections in each group

n** = number of cases in each category

n/%= number/percentage of subjects reporting at least once the case

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

Template 44 Descriptive statistics of viral load calculated on all qRT-PCR confirmed RSV infection episodes with varying disease severity (based on WHO case definition) from vaccination dose 1 up to end of <first, second> RSV season for pooled RSV 1D, RSV 2D and Comparator/Placebo group <Exposed Set, Exposed Set with negative RSV baseline status>

		Group N=		
Symptoms	**Parameters**	**Value**	**LL**	**UL**
RSV asymptomatic* (Excluding RSV-RTI, RSV-LRTI, RSV-severe LRTI or RSV-very severe LRTI)	n			
	GM			
	95% CI			
	SD			
	Q1			
	Median			
	Q3			
	Min/Max			
RSV RTI (Excluding RSV-LRTI, RSV-severe LRTI or RSV-very severe LRTI)				
RSV LRTI (Excluding RSV-severe or RSV-very severe LRTI)				
RSV-severe LRTI (Excluding RSV-very severe LRTI)				
RSV-very severe LRTI				
RSV hospitalization$				

Short group label = long group label
N = number of RSV infections episodes in each group
n= Number of events in each category
SD=Standard Deviation
Q1 and Q3 = 1st and 3rd quantiles
Min/Max = Minimum/Maximum
GM = Geometric mean
LL, UL for GM = Exact 95% Lower and Upper confidence limits
Total RSV viral load computed as RSV A Viral load + RSV B Viral load
* Association to RSV based on central testing only for asymptomatic visit (no local test available)
$Confirmed RSV infection and hospitalized for acute medical condition
Please note: each episode for a subject is considered to be independent. We may have multiple swab for one episode. We have considered the swab with maximum viral load from one episode for the table
Please note – Except for RSV hospitalization, single episode is considered in single category of highest severity based on the symptom experienced

Please check:- To check for cases where asymptomatic swab has been taken but the subject hasve symptoms of RTI or LRTI. In this case, asymptomatic is also considered as RSV RTI/LRTI and maximum viral load of all the episode should be considered.

Template 45 Descriptive statistics of maximum viral load per subjects based on qRT-PCR confirmed episode with varying disease severity (based on WHO case definition) form vaccination dose 1 up to end of <first, second> RSV season for pooled RSV 1D, RSV 2D and Comparator/Placebo group <Exposed Set, Exposed Set with negative RSV baseline status>

		Each Group N=		
			95% CI	
Symptoms	**Parameters**	**Value**	**LL**	**UL**
RSV asymptomatic* (Excluding RSV-RTI, RSV-LRTI, RSV-severe LRTI or RSV-very severe LRTI)	n			
	GM			
	95% CI			
	SD			
	Q1			
	Median			
	Q3			
	Min/Max			
RSV RTI (Excluding RSV-LRTI, RSV-severe or RSV-very severe LRTI)	…			
RSV LRTI (Excluding RSV-severe or RSV-very severe LRTI)	…			
RSV-severe LRTI (Excluding RSV-very severe LRTI)	…			
RSV-very severe LRTI	…			
RSV hospitalization$	…			

Short group label = long group label
N = number of RSV positive subjects in each group
n= Number of subjects in each category
SD=Standard Deviation
Q1 and Q3 = 1st and 3rd quantiles
Min/Max = Minimum/Maximum
GM = Geometric mean
LL, UL for GM = Exact 95% Lower and Upper confidence limits
Total RSV viral load computed as RSV A Viral load + RSV B Viral load
Please note: Except of RSV hospitalization, the subject has been considered only once in one of the category based on the maximum severity of event experienced
* Association to RSV based on central testing only for asymptomatic visit (no local test available)
$Confirmed RSV infection and hospitalized for acute medical condition

Template 46 Frequency of multiple respiratory pathogen for qRT-PCR confirmed RSV-RTI episodes from vaccination dose 1 up to end of <first, second> RSV season for pooled RSV 1D, RSV 2D and Comparator/Placebo groups <Exposed Set, Exposed Set with negative RSV baseline status>

	Group N =				Total N =			
			95% CI				95% CI	
Categories	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Influenza Virus A/California/7/2009(H1N1)								
Adenovirus								
Human Coronavirus OC43								
Human Coronavirus 229E								
Human Coronavirus NL63								
Human Coronavirus HKU1								
Enterovirus + Rhinovirus								
Influenza Virus A								
Influenza Virus B								
Influenza Virus A (H1N1)								
Influenza Virus A (H3N2)								
Human bocavirus								
Human metapneumovirus								
Parainfluenza virus 1								
Parainfluenza virus 2								
Parainfluenza virus 3								
Parainfluenza virus 4								

Short group label = long group label
N = number of qRT-PCR confirmed RSV-RTI infection episodes in each group
n = number of episodes in a given category
% =100*n/N
LL, UL for percentage = Exact 95% Lower and Upper confidence limits

Template 47 Frequency of multiple respiratory pathogen for confirmed LRTI episodes from vaccination dose 1 up to end of <first, second> RSV season for pooled RSV 1D, RSV 2D and Comparator/Placebo groups <Exposed Set, Exposed Set with negative RSV baseline status>

	Group N =				Total N =			
			95% CI				95% CI	
Categories	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
Respiratory syncytial virus								
Influenza Virus A/California/7/2009(H1N1)								
Adenovirus								
Human Coronavirus OC43								
Human Coronavirus 229E								
Human Coronavirus NL63								
Human Coronavirus HKU1								
Enterovirus + Rhinovirus								
Influenza Virus A								
Influenza Virus B								
Influenza Virus A (H1N1)								
Influenza Virus A (H3N2)								
Human bocavirus								
Human metapneumovirus								
Parainfluenza virus 1								
Parainfluenza virus 2								
Parainfluenza virus 3								
Parainfluenza virus 4								

Short group label = long group label
N = number of confirmed LRTI infection episodes in each group
n = number of episodes in a given category
% =100*n/N
LL, UL for percentage = Exact 95% Lower and Upper confidence limits

Template 48 Listing of RSV-RTI cases identified according to WHO case definitions from vaccination dose 1 up to end of second RSV season <Exposed Set, Exposed Set with negative RSV baseline status>

Group	**Sub. No.**	**Sex**	**Age at episode(month)**	**Country**	**Site**	**Surveillance type**	**Episode nb**	**Dose nb.**	**Dose seq**	**Onset day**	**SpO2**	**Respiratory rate**	**Central test RSV A**	**Central test RSV B**	**RSV-RTI**	**RSV-LRTI**	**Severe RSV-LRTI**	**RSV-very severe LRTI**	**Hospitalization**	**RVP result**
															Yes/No	Yes/No	Yes/No	Yes/No	Yes/No	

Short group label = long group label

Template 49 Listing of RSV-RTI requiring hospitalization and type of inpatient facility required from vaccination dose 1 up to end of second RSV season <Exposed Set, Exposed Set with negative RSV baseline status>

Group	Sub No.	Sex	Age at episode (month)	Country	Classification of episode per WHO*	Total days hospitalized	No. of days of monitoring or nursing	No. of days of nasogastric or intravenous fluids given	No. of days oxygen administered	No. of days respiratory support given	No. of days mechanical ventilation given	No. of days child kept in paediatrics intensive care unit	RVP result	Pathogen identified in RVP
													Yes/ No	

Short group label = long group label

*subject will be classified per maximum severity experienced

Template 50 Number and percentage of subjects with highest associated severity of RSV infection (based on WHO case definition) from vaccination dose 1 up to <first, second> RSV season for pooled RSV 1D, RSV 2D and Comparator/Placebo groups <Exposed Set, Exposed Set with negative RSV baseline status>

	Group N =					Total N =				
				95% CI					95% CI	
Categories	n**	n	%	LL	UL	n**	n	%	LL	UL
No Infection										
RSV asymptomatic (Excluding RSV-RTI, RSV-LRTI, RSV-severe LRTI or RSV-very severe LRTI)										
RSV RTI (Excluding RSV-LRTI, RSV-severe or very severe LRTI)										
RSV LRTI (Excluding RSV-severe or very severe LRTI)										
RSV-severe LRTI (Excluding RSV-very severe LRTI)										
RSV-very severe LRTI										

Short group label = long group label

N = number of subjects in each group

n** = number of cases in each category

n/%= number/percentage of subjects reporting at least once the case

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

Please note – Single episode can be considered in single category depending on the highest severity symptom experienced

Template 51 Number and percentage of subjects reporting the RSV infection of maximum severity (based on WHO case definition) by number of events experienced between vaccination dose 1 up to end of <first, second> RSV season for pooled RSV 1D, RSV 2D and Comparator/Placebo groups <Exposed Set, Exposed Set with negative RSV baseline status >

		Total				
					95% CI	
Characteristics	**Categories**	**N**	**n**	**%**	**LL**	**UL**
RSV asymptomatic (Excluding RSV-RTI, RSV-LRTI, RSV-severe LRTI or RSV-very severe LRTI)	0					
	1					
	2					
RSV-RTI (Excluding RSV-LRTI, RSV severe or very severe LRTI)	0					
	1					
RSV-LRTI (Excluding RSV severe or very severe LRTI)	0					
	1					
RSV-Severe LRTI Excluding RSV very severe LRTI)	0					
	1					
RSV-very severe LRTI	0					
	1					

Short group label = long group label
N = number of subjects in each group
n = number of subjects in a given category
% =100*n/N
LL, UL for percentage = Exact 95% Lower and Upper confidence limits
Please note – Single episode will be considered in single category depending on the maximum severity experienced

Template 52 Number and percentage of subjects with <anti-RSV A antibody titre, anti-RSV F concentration> equal to or above <cut-off ><unit> and gm<t,c> for pooled RSV 1D, RSV 2D and Comparator/Placebo> groups – by RSV baseline status (<Adapted>PPS of immunogenicity at <Day X, end of 1st RSV season>)

			<Each group>									
Antibody off	Time point	Cut-off	<RSV+ve>					<RSV-ve>				
						95% CI					95% CI	
			N	n	value	LL	UL	N	n	value	LL	UL
<Antibody 1> off 1>	<Time point 1>	<Cut-off 1>	%>=<cut-off 1> <unit>	xxx	xxx	xx.x	xx.x	xx.x	xxx	xxx	xx.x	xx.x	xx.x
			GM<T,C>	xxx		xx.x	xx.x	xx.x	xxx		xx.x	xx.x	xx.x

Short group label = long group label
GMT/C = geometric mean antibody titer/concentration
N = Number of subjects with available results
n/% = number/percentage of subjects with titer/concentration equal to or above specified value
95% CI = 95% confidence interval; LL = lower limit, UL = upper limit
PRE= Pre-vaccination
D31 = Post-vaccination at Day 31
D61 = Post-vaccination at Day 61
RSV1S = End of 1st RSV transmission season
RSV+ve = Subjects are RSV positive at baseline
RSV-ve = Subject are RSV negative at baseline

Template 53 Distribution of <RSV-A neutralising antibody titre, RSV-F antibody concentration> for pooled RSV 1D, RSV 2D and Comparator/Placebo> groups – by RSV baseline status(<Adapted>PPS for immunogenicity <at Day X, end of 1st RSV season>)

			<Each group>									
Antibody	Time point	Cut-off	<RSV+ve>					<RSV-ve>				
						95% CI					95% CI	
			N	n	value	LL	UL	N	n	value	LL	UL
<Antibody 1>	<Time point 1>	<cut-off 1	xxx	xxx	xx.x	xx.x	xx.x	xxx	xxx	xx.x	xx.x	xx.x
		>=cut-off 2	xxx	xxx	xx.x	xx.x	xx.x	xxx	xxx	xx.x	xx.x	xx.x
		>=cut-off 3	xxx	xxx	xx.x	xx.x	xx.x	xxx	xxx	xx.x	xx.x	xx.x
	<Time point 2>	<cut-off 1	xxx	xxx	xx.x	xx.x	xx.x	xxx	xxx	xx.x	xx.x	xx.x
		>=cut-off 2	xxx	xxx	xx.x	xx.x	xx.x	xxx	xxx	xx.x	xx.x	xx.x
		>=cut-off 3	xxx	xxx	xx.x	xx.x	xx.x	xxx	xxx	xx.x	xx.x	xx.x

Short group label = long group label
N = number of subjects with available results
n/% = number/percentage of subjects with <titer, concentration> within the specified criterion
<95>% CI = <95>% confidence interval; LL = Lower Limit, UL = Upper Limit
PRE= Pre-vaccination
D31 = Post-vaccination at Day 31
D61 = Post-vaccination at Day 61
RSV1S = End of 1st RSV transmission season
RSV+ve = Subjects are RSV positive at baseline
RSV-ve = Subject are RSV negative at baseline

Template 54 Number and percentage of subjects with <anti-RSV A antibody titre, anti-RSV F concentration> equal to or above <cut-off ><unit> and GMR for pooled RSV 1D, RSV 2D and Comparator/Placebo> groups – by RSV baseline status (PPS of immunogenicity at <Day X, End of 1st RSV season>)

			<Each group>									
Antibody Cut-off	Time point		<RSV+ve>					<RSV-ve>				
						95% CI					95% CI	
			N	n	value	LL	UL	N	n	value	LL	UL
<Antibody 1> <Cut-off 1>	<Time point 1>	%>=<cut-off 1> <unit>	xxx	xxx	xx.x	xx.x	xx.x	xxx	xxx	xx.x	xx.x	xx.x
		GMC/T	xxx		xx.x	xx.x	xx.x	xxx		xx.x	xx.x	xx.x
		Visit comparison / baseline										
		GMR	xxx		xx.x	xx.x	xx.x	xxx		xx.x	xx.x	xx.x

Short group label = long group label
GMT = geometric mean antibody titer
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
D31 = Post-vaccination at Day 31
D61 = Post-vaccination at Day 61
RSV1S = End of 1st RSV transmission season
RSV+ve = Subjects are RSV positive at baseline
RSV-ve = Subject are RSV negative at baseline

Template 55 Descriptive statistics of <anti-RSV A neutralizing antibody titre, anti-RSV F antibody concentration>at pre-vaccination, Day <31, 61,> <and end of 1st RSV transmission season> for pooled RSV 1D, RSV 2D and Comparator/Placebo> groups – by RSV baseline status (<Adapted> PPS for immunogenicity)

		Each Group N=XXXX	
		RSV+ve N=XXXX	RSV-ve N=XXXX
Visit	**Characteristics**	**Value**	**Value**
PRE	N with data		
	Mean		
	SD		
	Q1		
	Median		
	Q3		
	95% CI	(xx.x ; xx.x)	(xx.x ; xx.x)
D31	…		
D61	…		
RSV1S	…		

Short group label = long group label
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
D31 = Post-vaccination at Day 31
D61 = Post-vaccination at Day 61
RSV1S = End of 1st RSV transmission season
RSV+ve = Subjects are RSV positive at baseline
RSV-ve = Subject are RSV negative at baseline

Template 56 Summary of subjects by unsolicited adverse event category with onset within 30 days of first and second vaccination (Exposed Set)

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

Any adverse event = at least one adverse event experienced (regardless of the MedDRA Preferred Term)
N = number of subjects with at least one administered vaccination
n/% = number/percentage of subjects reporting the adverse event at least once
95% CI = exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit

Template 57 Number and percentage of subjects with at least one RSV-RTI progressing to RSV-LRTI, RSV-severe LRTI, RSV-very severe LRTI and RSV hospitalization from vaccination dose 1 up to end of <first, second> RSV season for pooled RSV 1D, RSV 2D and Comparator/Placebo groups <ES, Exposed Set with negative RSV exposure status>

	<each group> N =				Total N =			
			90% CI				90% CI	
Categories	**n**	**%**	**LL**	**UL**	**n**	**%**	**LL**	**UL**
RSV-LRTI								
RSV-severe LRTI								
RSV-very severe LRTI								
RSV hospitalization*								

<Blinded = Blinded group>
<RSV 1D = Pooled 1D RSV>
<RSV 2D = Pooled 2D RSV>
<COMP_PLB = Pooled comparator or placebo>
* Confirmed RSV infection and hospitalized for acute medical condition
N = number of subjects with at least one RSV-RTI infection
n/%= number/percentage of subjects reporting at least once the symptom
90%CI= Exact 90% confidence interval; LL = lower limit, UL = upper limit
Please note – Single episode is considered in single category of highest severity based on the symptom experienced