ModernaTX, Inc.

mRNA-1345-P202

A Phase 2, randomized, observer-blind study to evaluate the safety, reactogenicity, and immunogenicity of mRNA-1345, an mRNA vaccine targeting respiratory syncytial virus, in children 2 to <18 years of age at high risk of respiratory syncytial virus disease

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Statistical Analysis Plan

Version 3.0

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DOCUMENT HISTORY

Version	Date	Description of main modifications
1.0	01Apr2024	Original SAP version per Original Protocol.
1.1	12Jul2024	Update SAP per Protocol Amendment 1.
1.2	29Jul2024	Update per Moderna's comments.
2.0	2Aug2024	Final version 2.0.
2.1	7Feb2025	Update per Protocol Amendment 2 (remove Cohort 3 references and include Part B Cohort 1 Extension).
2.2	28Feb2025	Update per Moderna's comments.
2.3	7Mar2025	Remove "eligible" wording from section 6.3.4.
2.4	30May2025	Add Appendix M.
3.0	2Jun2025	Final version 3.0.

List of Abbreviations

Abbreviation	Definition
Ab	Antibody
AE	Adverse Event
AESI	Adverse Event Of Special Interest
AR	Adverse Reaction
ATC	Anatomical Therapeutic Chemical
bAb	Binding Antibodies
BMI	Body Mass Index
CAT	Clinical Assessment Team
CDC	Centers For Disease Control And Prevention
CEAC	Cardiac Event Adjudication Committee
CHD	Congenital Heart Disease
CI	Confidence Interval
CMI	Cell-Mediated Immunity
COVID-19	Coronavirus Disease 2019
CRF	Case Report Form
CRO	Contract Research Organization
CSP	Clinical Study Protocol
CSR	Clinical Study Report
DBL	Database Lock
DM	Diabetes Mellitus
DSMB	Data Safety Monitoring Board
eCRF	Electronic Case Report Form
eDiary	Electronic Diary
EoS	End of Study
FAS	Full Analysis Set
GMC	Geometric Mean Concentration
GMFR	Geometric Mean Fold-Rise
GMR	Geometric Mean Titer Ratio
GMT	Geometric Mean Titer
HCP	Health Care Provider
HLGT	High Level Group Term
IcEv	Intercurrent Event
ICF	Informed Consent Form
IP	Investigational Product
IRT	Interactive Response Technology
IST	Internal Safety Team
LAR	Legally Authorized Representative
LB	Lower Bound
LLOQ	Lower Limit Of Quantification
LRTD	Lower Respiratory Tract Disease
MA	Medically Attended

MAAE	Medically Attended Adverse Event
MedDRA	Medical Dictionary for Regulatory Activities
mRNA	Messenger Ribonucleic Acid
nAb	Neutralizing Antibody
NEC	Necrotizing Enterocolitis
PBMC	Peripheral Blood Mononuclear Cell
PCR	Polymerase chain reaction
POCBP	Person of Childbearing Potential
PP	Per-Protocol
PT	Preferred Term
RSV	Respiratory Syncytial Virus
RSV-A	Respiratory Syncytial Virus Subtype A
RSV-B	Respiratory Syncytial Virus Subtype B
RSV-F	Respiratory Syncytial Virus Fusion Protein
RTD	Respiratory Tract Disease
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SAS	Statistical Analysis System
SD	Standard Deviation
SoA	Schedule Of Activities
SOC	System Organ Class
SMQ	Standardized MedDRA Queries
TFLs	Tables, Figures, and Listings
ULOQ	upper limit of quantification
US DHHS	United States Department of Health and Human Services
WHO-DD	World Health Organization Drug Dictionary

1. Introduction

This statistical analysis plan (SAP), version 3.0, is based on clinical study protocol (CSP) amendment 2, dated 02-Oct-2024 and the approved electronic case report form (eCRF) Version 6.004 BCR (1749), dated 31-Oct-2024.

In addition to the information presented in the statistical considerations section of the protocol (Section 9) which provides the principal features of analyses for this study, this SAP provides statistical analysis details/data derivations. It also documents modifications or additions to the analysis plan which are not "principal" in nature and result from information that was not available at the time of protocol finalization. If the methods in this SAP differ from the methods described in the protocol, the SAP will prevail.

Study mRNA-1345-P202 is a Phase 2, randomized, observer-blind study to evaluate the safety reactogenicity, and immunogenicity of mRNA-1345, an mRNA vaccine targeting RSV, in children 2 to <5 years of age (Cohort 1) and children at high risk of RSV disease 5 to <18 years of age (Cohort 2).

PPD Biostatistics and programming team, designee of Moderna Biostatistics and Programming department, will perform the statistical analysis; Statistical Analysis System (SAS) Version 9.4 or higher will be used.

In this document, injection, and dose are used interchangeably.

2. Study Objectives

2.1. Primary Objectives

The primary objective for Part A Cohort 1 is to evaluate the safety and reactogenicity of a single injection of mRNA-1345 vaccine in participants of 2 to <5 years of age.

The primary objective for Part A Cohort 2 is to evaluate the safety and reactogenicity of a single injection of mRNA-1345 vaccine in participants of 5 to <18 years of age.

The primary objective for Part B Cohort 1 is to evaluate the incidence of RSV-RTD during 6 months after re-enrollment.

2.2. Secondary Objectives

The secondary objective for Part A Cohort 1 is to evaluate the immunogenicity of a single injection of mRNA-1345 vaccine in participants of 2 to <5 years of age.

The secondary objective for Part A Cohort 2 is to evaluate the immunogenicity of a single injection of mRNA-1345 vaccine in participants of 5 to <18 years of age.

The secondary objective for Part B Cohort 1 is to evaluate the safety of a single study injection administered in Part A during 6 months after re-enrollment in Part B.

2.3. Exploratory Objectives

The exploratory objective for Part A Cohort 1 may be performed to further characterize the immune response to a single mRNA-1345 injection.

The exploratory objective for Part A Cohort 2 may be performed to evaluate immune response biomarkers as potential correlates of protection or risk of RSV disease.

The exploratory objective for Part B Cohort 1 may be performed to evaluate the persistence of the immunogenicity of a single study injection administered in Part A, and to explore immune response biomarkers.

3. Study Endpoints

3.1. Primary Endpoints

The primary objective for Part A Cohort 1 will be evaluated by the following safety endpoints:

- Solicited local and systemic adverse reactions (ARs) through 7 days postinjection.
- Unsolicited adverse events (AEs) through 28 days postinjection.
- Medically attended AEs (MAAEs) from Day 1 to Month 6/ end of study (EoS) Visit.
- Adverse events of special interest (AESIs) from Day 1 to Month 6/ EoS Visit.
- Serious AEs (SAEs) from Day 1 to Month 6/ EoS Visit.
- AEs leading to discontinuation from Day 1 to Month 6/ EoS Visit.

The primary objective for Part A Cohort 2 will be evaluated by the following safety endpoints:

- Solicited local and systemic ARs through 7 days postinjection.
- Unsolicited AEs through 28 days postinjection.
- MAAEs from Day 1 to Month 6/ end of study (EoS) Visit.
- AESIs from Day 1 to Month 6/ EoS Visit.
- SAEs from Day 1 to Month 6/ EoS Visit.
- AEs leading to discontinuation from Day 1 to Month 6/ EoS Visit.

The primary objective for Part B Cohort 1 will be evaluated by the following endpoints:

- RSV-RTD from Part B Day 1 to Part B EoS Visit.

- RSV-LRTD from Part B Day 1 to Part B EoS Visit.
- Severe RSV-LRTD from Part B Day 1 to Part B EoS Visit.
- Very severe RSV-LRTD from Part B Day 1 to Part B EoS Visit.
- RSV hospitalization from Part B Day 1 to Part B EoS Visit.

3.2. Secondary Endpoints

The secondary objectives for Part A Cohort 1 will be evaluated by the following endpoints:

- GMT of serum RSV neutralizing antibody at Day 1, Day 29, and Month 6/EoS Visit.
- GMC of serum RSV prefusion F binding antibody at Day 1, Day 29, and Month 6/ EoS Visit.
- GMFR of Postbaseline/Baseline neutralizing antibody titers and binding antibody concentrations at Day 29 and Month 6/ EoS Visit.
- Percentage of participants with a seroresponse (defined as a postinjection titer >4-fold-rise if Baseline is >LLOQ or >4 × LLOQ if Baseline titer is <LLOQ) in the above immunogenicity measures.

The secondary objectives for Part A Cohort 2 will be evaluated by the following endpoints:

- GMT of serum RSV neutralizing antibody at Day 1 and Day 29.
- GMC of serum RSV prefusion F binding antibody at Day 1 and Day 29.
- GMFR of Postbaseline/Baseline neutralizing antibody titers and binding antibody concentrations at Day 29.
- Percentage of participants with a seroresponse (defined as a postinjection titer >4-fold-rise if Baseline is >LLOQ or >4 × LLOQ if Baseline titer is <LLOQ) in the above immunogenicity measures.

The secondary objectives for Part B Cohort 1 will be evaluated by the following endpoints:

- AESIs from Part B Day 1 to Part B EoS Visit.

SAEs from Part B Day 1 to Part B EoS Visit.

3.3. Exploratory Endpoints

The exploratory objective of Part A Cohort 1 may be evaluated by the following endpoints:

- Transcriptome analysis may be conducted to further evaluate immune responses.

- Frequency, magnitude, and/or phenotype of vaccine-specific T-cell and B-cell responses by flow cytometry or other methods.
- Frequency, specificities, or other endpoints to be determined for the further characterization of immune responses.

The exploratory objective of Part A Cohort 2 may be evaluated by the following endpoints:

- Frequency, specificities, or other endpoints to be determined for the further characterization of immune responses.

The exploratory objective of Part B Cohort 1 may be evaluated by the following endpoints:

- GMT of serum RSV neutralizing antibody at Part B Day 1.
- GMC of serum RSV prefusion F and postfusion F binding antibody at Part B Day 1.
- Frequency, specificities, or other endpoints to be determined, for the further characterization of immune responses, including cell-mediated immunogenicity.

Note: The exploratory analysis for the above endpoints may be performed by another analysis group and not included in the scope of this SAP.

4. Study Design

4.1. Overall Study Design

This is a Phase 2, randomized, observer-blind, study to evaluate the safety, reactogenicity, and immunogenicity of a single injection of mRNA-1345 vaccine in approximately 160 participants 2 to <5 years of age (Cohort 1) and 180 participants 5 to <18 years of age (Cohort 2). The study will be conducted in 2 Parts:

Part A:

In Cohort 1, approximately 60 of the estimated 160 participants will be 2 to <3 years of age. In Cohort 2, approximately 90 of the estimated 180 participants will be 5 to <12 years of age, and approximately 90 participants will be 12 to <18 years of age. The study will enroll a total of approximately 340 participants.

For Part A, study details include:

- Potential participants will have a Screening Visit for the purpose of determining eligibility for the study.
- Cohort 1: The Immunization Visit (Day 1) will occur within 28 days of Screening. The Screening Visit and the Day 1 Visit may also occur on the same day. Enrolled

participants will be randomized (1:1:1:1) on Day 1 to receive a single injection of mRNA-1345 CCI µg, CCI µg, or CCI µg) or placebo (normal saline), with approximately 40 participants in each study group. Randomization and enrollment will be stratified by age categories at Day 1 (40%/60%; 2 to <3 years old and 3 to <5 years old). Blood samples to assess immunogenicity will be taken at timepoints specified in the SoA (Appendix F).

- Cohort 2: The Immunization Visit (Day 1) will occur within 28 days of Screening. The Screening Visit and the Day 1 Visit may also occur on the same day. Enrolled participants will be randomized on Day 1 to receive a single injection of mRNA-1345 (1:1:1 randomization; CCI µg, CCI µg, or CCI µg), with approximately 60 participants in each study group. Randomization and enrollment will be stratified by age categories (50%/50%; 5 to <12 years old and 12 to <18 years old). Blood samples to assess immunogenicity will be taken at timepoints specified in the SoA (Appendix G).
- Subsequent sample collection and assessments will occur as per the SoA (Appendix F and Appendix G).

Part B:

For Part B, all Cohort 1 participants (approximately 160) who were enrolled and dosed in Part A, will be offered to re-enroll into this safety follow-up study, in which surveillance for RSV disease will be conducted over a 6-month period. This will include the next RSV season in the United States (approximately 01 Oct 2025 to 30 Apr 2025). RSV surveillance will be performed weekly during RSV season and monthly during RSV off season,

Part B of the study aims to provide surveillance for RSV disease for the next RSV season (6 months after re-enrollment) and safety follow-up for Cohort 1 participants that were enrolled and dosed in Part A.

For Part B, study details include:

- There will be no Screening Visit. The first visit will be the Part B Day 1, which is the day of re-enrollment of Cohort 1 participants into the study.
- No treatment will be administered to the participants in Part B of the study.
- There will be at least 1 in-person visit (Part B Day 1), weekly text messages during RSV season (from 01 Oct 2024 to 30 Apr 2025), and 3 safety phone calls (Month 2, Month 4, and Month 6 [EoS]) as specified in the SoA (Appendix H).Additional unscheduled visits will occur if a participant experiences relevant RSV symptoms. Convalescent visits may occur after confirmed RSV-LRTD.

- Interim medical history: SAEs and AESIs that may have occurred subsequent to Part A EoS Visit/discontinuation until the time of signing the ICF for Part B will be collected.
- SAEs and AESIs will be collected from signing of the ICF for Part B through Part B Month 6/EoS Visit.
- Subsequent sample collection and assessments will occur as per the SoA (Appendix H).

Overall, the study will require up to 6 months of participants for each participant in Part A and up to an additional 6 months of participation for each participant in Part B.

The study will be conducted with the oversight of an unblinded IST and DSMB and pause rules will be implemented. An independent CEAC will review all reported suspected cases of myocarditis, pericarditis, and myopericarditis.

Study visits and assessments are defined in the SoA (Part A: Appendix F for Cohort 1 and Appendix G for Cohort 2; Part B: Appendix H for Cohort 1). The maximum planned volumes of blood sampled at each visit (as indicated in the SoA) are summarized in Section 8 of the protocol.

4.2. Statistical Hypothesis

There is no formal statistical hypothesis testing planned for the study. All statistical analyses will be descriptive in nature.

4.3. Sample Size Determination

As shown in Table 1, a sample size of 60 or 40 participants in each study group has approximately 95% or 87% probability, respectively, to observe at least 1 participant with an AE given the true underlying incidence rate of 5%, which should allow for a preliminary assessment of the reactogenicity profile for each dose level.

Table 1: Probability of AEs Based on Sample Size

Sample Size Per Group (n)	True AE Rate	Probability of at Least 1 AE Observed
60	2%	70%
60	3%	84%
60	4%	91%
60	5%	95%
60	10%	>99%
40	2%	55%
40	3%	70%

40	4%	80%
40	5%	87%
40	10%	99%

Abbreviations: AE = adverse event; n = number of participants

4.4. Randomization (Part A)

In Cohort 1, approximately 160 participants 2 to <5 years of age at the time of randomization will be randomized (1:1:1:1 ratio) to receive either a single injection of mRNA-1345 (CCI µg, CCI µg, or CCI µg) or placebo (normal saline), with approximately 40 participants in each study group. Randomization and enrollment will be stratified by age categories (40%/60%; 2 to <3 years old and 3 to <5 years old). Approximately 60 of the estimated 160 participants will be 2 to <3 years of age.

In Cohort 2, approximately 180 participants 5 to <18 years of age at the time of randomization will be randomized (1:1:1 ratio) to receive a single injection of mRNA-1345 (CCI µg, CCI µg, or CCI µg), with approximately 60 participants in each study group. Randomization and enrollment will be stratified by age categories (50%/50%; 5 to <12 years old and 12 to <18 years old).

The randomization will be in a blinded manner using a centralized Interactive Response Technology (IRT) system, in accordance with pre-generated randomization schedules.

4.5. Blinding and Unblinding

This is an observer-blind study. The investigator, study site staff, study participants, participant's parent(s)/LAR(s), site monitors, and Sponsor personnel (or its designees) will be blinded to the trial intervention administered until the study database is locked and unblinded, with certain exceptions or in the event of an emergency, please refer to Section 6.4 and Section 9.1 of the protocol and the Data Blinding Plan for details.

5. Analysis Sets

Analysis sets for Part A statistical analyses are Randomization Set, Full Analysis Set (FAS), Per-protocol (PP) Set, Safety Set, and Solicited Safety Set.

Analysis set for Part B statistical analyses is Safety Set. (Note: FAS might be needed for immunogenicity listing in Part B if results are available).

5.1. Randomization Set (Part A)

The Randomization Set consists of all participants who are randomized in the study, regardless of the participant's treatment status in the study. Participants will be included in the treatment group to which they are randomized.

5.2. Full Analysis Set

Part A:

The Part A FAS consists of all participants who are randomly assigned and receive the study injection and have a Baseline and at least 1 postinjection antibody assessment. Participants will be included in the treatment group to which they are randomized.

Part B:

The Part B Cohort 1 FAS consists of all participants in the Part A Cohort 1 FAS who re-enroll in Part B of the study and have Part B Day 1 antibody assessment. Participants will be included in the treatment group to which they are randomized in Part A. The Part B Cohort 1 FAS will be used for the potential immunogenicity listing if immunogenicity results are available.

5.3. Per-Protocol Set (Part A)

The PP Set consists of all participants in the FAS who receive the planned dose of the study intervention, comply with the immunogenicity testing schedule, have a Baseline and Day 29 assessment, and have no important protocol deviations that affect the immune response. Important protocol deviations leading to exclusion of participants from the PP Set are defined in Section 6.2.8 (Important Protocol Deviations).

The PP Set will be used as the primary analysis set for analyses of immunogenicity unless otherwise specified. Participants will be included in the treatment group to which they are randomized.

Participants with dosing error will be considered as having a protocol deviation. However, the determination of whether to exclude such participants from the PP Set will be based on the difference between the actual dose received and the randomized dose. The dosing error criteria for PP Set exclusion are described in Table 2.

Table 2: Dosing Error Criteria for PP Set Exclusion

Randomized Treatment Group	Actual Dose of mRNA-1345 Received
mRNA-1345 CCI µg	< CCI µg or > CCI µg
mRNA-1345 µg	< CCI µg or > CCI µg
mRNA-1345 µg	< CCI µg or > CCI µg
mRNA-1345 µg	< CCI µg or > CCI µg
Placebo	> 0 µg

In the immunogenicity analysis based on the PP Set, for participants receiving immune modifying medication(s) after Day 29 visit, immunogenicity assessments at Part A Month 6/EoS

(Cohort 1) visit will be excluded from the analysis. Also, immunogenicity assessments falling out of analysis visit window (Appendix B) will be excluded from the analysis.

5.4. Safety Set

Part A:

The Part A Safety Set consists of all participants who are randomly assigned and receive the study intervention.

The Part A Safety Set will be used for all analyses of safety except for the solicited ARs. Participants will be included in the treatment group corresponding to the study intervention they actually received according to Table 3 below.

Table 3: Actual Treatment Group Mapping Scheme

Actual Treatment Group	Actual Dose of mRNA-1345 Received
mRNA-1345 [redacted] µg	≤ [redacted] µg
mRNA-1345 [redacted] µg	> [redacted] µg and ≤ [redacted] µg
mRNA-1345 [redacted] µg	> [redacted] µg and ≤ [redacted] µg
mRNA-1345 [redacted] µg	> [redacted] µg
Placebo	0 µg

Part B:

The Part B Cohort 1 Safety Set consists of all participants in the Part A Cohort 1 Safety Set who re-enroll in Part B of the study. The Part B Cohort 1 Safety Set will be used for all Part B analyses except for the potential immunogenicity listing if immunogenicity results are available.

5.5. Solicited Safety Set (Part A)

The Solicited Safety Set consists of all participants in the Safety Set who contribute any solicited AR data.

The Solicited Safety Set will be used for the analyses of solicited ARs, and participants will be included in the treatment group corresponding to the study intervention that they actually received.

6. Statistical Analysis

6.1. General Considerations

For Part A the SoA is provided in Appendix F for Cohort 1 and Appendix G for Cohort 2; for Part B the SoA is provided in Appendix H for Cohort 1.

Continuous variables will be summarized using the following descriptive summary statistics: the number of participants (n), mean, standard deviation (SD), median, minimum (min), and Confidential

maximum (max). For the summary statistics of all numerical variables, unless otherwise specified, the display precision will follow programming standards. Please see Appendix A for variable display standards.

Categorical variables will be summarized using counts and percentages. When count data are presented, the percentage will be suppressed when the count is zero in order to draw attention to the non-zero counts. A row denoted "Missing" will be included in count tabulations where specified on the shells to account for dropouts and missing values. The denominator for all percentages will be the number of participants in that treatment group within the analysis set of interest, unless otherwise specified.

Baseline value is defined as the most recent non-missing measurement (scheduled or unscheduled) collected before the first injection, unless otherwise specified. For immunogenicity tests, the baseline is defined as the most recent non-missing result/measurement (scheduled or unscheduled) collected before or on the date of the injection (Day 1).

Study day relative to Part A Day 1 injection will be calculated as below:

a) Study day prior to the date of Part A Day 1 injection will be calculated as: date of assessment/event – date of Part A Day 1 injection (resulting in negative study day);

b) Study day on or after the date of Part A Day 1 injection will be calculated as: date of assessment/event – date of Part A Day 1 injection + 1.

Study day relative to Part B Day 1 will be calculated as below:

a) Study day prior to the date of Part B Day 1 will be calculated as: date of assessment/event – date of Part B Day 1 Visit (resulting in negative study day);

b) Study day on or after the date of Part B Day 1 will be calculated as: date of assessment/event – date of Part B Day 1 Visit + 1.

For GMT, GMC and GMFR calculation, antibody values reported as below the LLOQ will be replaced by 0.5 × LLOQ and antibody values that are greater than the upper limit of quantification (ULOQ) will be converted to the ULOQ. Missing Values will not be imputed.

Unscheduled visits: Unscheduled visit measurements will be included in analysis as follows:

- In the derivation of baseline measurements.
- In scheduled visit windows per specified visit windowing rules.
- In individual participant data listings as appropriate.

Visit windowing rules: The analysis visit windows for protocol-defined visits are provided in Appendix B.

Incomplete/missing data:

- Imputation rules for missing dates of prior/concomitant medications and non-study vaccinations are provided in Appendix C.
- Imputation rules for missing dates of prior/concomitant procedures are provided in Appendix D.
- Imputation rules for missing AE dates are provided in Appendix E.
- Other incomplete/missing data will not be imputed, unless specified otherwise.

Treatment groups:

The following treatment groups will be used for summary purposes:

- Cohort 1: mRNA-1345 CCI µg
- Cohort 1: mRNA-1345 µg
- Cohort 1: mRNA-1345 µg
- Cohort 1: Placebo
- Cohort 2: mRNA-1345 CCI µg
- Cohort 2: mRNA-1345 µg
- Cohort 2: mRNA-1345 µg

Placebo is used in Cohort 1, but not for Cohort 2 due to the likely higher background rate of solicited adverse reactions expected to be reported for the youngest age group, which could confound tolerability assessment, as well as naturally occurring increases in neutralizing antibody titers against RSV over time up to age 5+. The same concerns are not present for the older age groups (5 to < 18 years); therefore, no placebo is used in cohort 2.

All analyses and data summaries/displays will be provided by the above treatment groups using appropriate analysis population, unless otherwise specified. Cohort 1, and Cohort 2 will be summarized separately. For Cohort 1 and Cohort 2, additional data summaries for the total mRNA-1345 group, by pooling all participants from the 3 dose groups of mRNA-1345 in the cohort, may be provided if deemed necessary.

6.2. Background Characteristics

6.2.1. Participant Disposition

Part A:

The number and percentage of participants in the following categories (analysis sets defined in Section 5) will be summarized by treatment group as defined in Section 6.1 based on Randomization Set:

- Randomization Set
- Full Analysis Set
- Per-protocol Set
- Safety Set
- Solicited Safety Set

The percentages will be based on the number of participants in the Randomization Set, except that for the Solicited Safety Set the percentages will be based on the number of participants in the Safety Set (as treated).

The number and percentage of participants in each of the following disposition categories will be summarized by treatment group based on the Randomization Set:

- Received any study injection
- Completed Part A of the study
- Prematurely discontinued from Part A of the study and the reason for discontinuation

A participant disposition listing will be provided, including informed consent for Part A, completion of study injection (Yes/No), study injection date or reason not administered, Part A study completion (Yes/No), date of Part A study completion or discontinuation, and reasons for Part A study discontinuation.

A participant, who has completed the last scheduled procedure at the Part A final visit (EoS visit) (i.e., 6 months after study injection on Day 1), is considered to have completed Part A of the study.

The number of participants in the following categories will be summarized based on participants screened:

- Number of participants screened
- Number and percentage of screen failure participants and the reason for screen failure

The percentage of participants who screen failed will be based on the number of participants screened. The percentage of participants reporting each reason for screen failure will be based on the number of participants who screen failed.

A separate listing will be provided for screen failure participants with age at screening (years), sex, race, ethnicity, and reasons for screen failure.

In addition, participants with any inclusion and exclusion criteria violation will also be provided in a listing.

Part B:

The number and percentage of participants in each of the following disposition categories will be summarized by treatment group based on the Part B Cohort 1 Safety Set:

- Completed Part B of the study
- Prematurely discontinued from Part B of the study and the reason for discontinuation

A participant disposition listing will be provided, including study injection date in Part A, Part B informed consent date, age at Part B enrollment (years), Part B study completion (Yes/No), date of Part B study completion or discontinuation, and reasons for Part B study discontinuation.

A participant, who has completed the last scheduled procedure at the Part B final visit (EoS visit) (i.e., 6 months after Part B Day 1), is considered to have completed Part B of the study.

6.2.2. Demographics and Baseline Characteristics

Part A:

Descriptive statistics will be calculated for the following continuous demographic and baseline characteristics: age at screening (years), age at randomization from CRF (years), weight (kg), height (cm), and body mass index (BMI) (kg/m^2). The number and percentage of participants will be provided for categorical variables such as age group at randomization from IRT and from CRF (≥ 2 to < 3 years, ≥ 3 to < 5 years for Cohort 1, and ≥ 5 to < 12 years, ≥ 12 to <18 years for Cohort 2), sex, race, and ethnicity. The summaries will be presented by treatment group as defined in Section 6.1. The summaries will be provided separately based on the Randomization Set, FAS, Safety Set, Solicited Safety Set and PP Set.

Part B:

The above summary of demographic and baseline characteristics for Part A will be provided by treatment group for Part B Cohort 1 Safety Set. In addition, age at Part B enrollment from CRF (years) will be also summarized.

6.2.3. Medical History

Part A:

Medical history data will be coded by system organ class (SOC) and preferred term (PT) using the Medical Dictionary for Regulatory Activities (MedDRA Version 25.0, 2022).

The number and percentage of participants with any medical history will be summarized by SOC and PT for each treatment group defined in Section 6.1 based on the Safety Set. A participant will be counted only once for multiple events within each SOC and PT. SOC will be displayed in internationally agreed order. PT will be displayed in descending order of frequency of the total mRNA-1345 group, and then alphabetically within SOC.

Number of events and number of participants with selected medical conditions, as indicated in Appendix L, will also be summarized by SOC, high level group term (HLGT), and PT for each treatment group.

Part B:

The above summary of medical history for Part A will be provided by treatment group for Part B Cohort 1 Safety Set.

6.2.4. Interim Medical History (Part B)

Interim medical history will include SAEs and AESIs that may have occurred subsequent to Part A EoS Visit/discontinuation until the time of signing the ICF for Part B.

Interim medical history data will be coded by system organ class (SOC) and preferred term (PT) using the Medical Dictionary for Regulatory Activities (MedDRA Version 25.0, 2022).

Interim medical history will be summarized by SOC and PT in the same way for medical history as described in Section 6.2.3 for Part B Cohort 1 Safety Set. Interim medical history will be also presented in a listing for Part B Cohort 1 Safety Set.

6.2.5. Prior and Concomitant Medications

Part A:

Medications administered within the period starting 28 days before the study intervention will be recorded in the eCRF. Any medications (including any prescription or over-the-counter medications, vaccines, or blood products) that the participant is receiving at the time of enrollment or receives during Part A of the study will be recorded in the eCRF, with the exception of dietary supplements (eg, vitamins) and nonsteroidal topical therapy. Information regarding any prior history of mRNA vaccination will be documented.

Prior and concomitant medications will be coded using the World Health Organization drug dictionary (WHO-DD). The summary of concomitant medications will be presented by treatment group defined in Section 6.1 based on the Safety Set. Imputation rules for missing/partial dates for medications is detailed in Appendix C.

For analysis purpose, a medication taken prior to the injection date, regardless of whether the end date is before or after the injection date, is defined "prior"; if the medication is taken between the injection date and up to Part A Month 6/EoS Visit, then it is considered "concomitant", regardless of whether the start date is before or after the injection date.

An overall summary table of concomitant medications and non-study vaccinations will be provided to present the number and percentage of participants who take the following:

- Any concomitant medications and non-study vaccinations within 7 days after injection
- Any concomitant medications and non-study vaccinations within 28 days after injection
- Any concomitant medications and non-study vaccinations up to Part A Month 6/EoS Visit

Summary tables of concomitant medications and non-study vaccinations within 28 days after injection and up to Part A Month 6/EoS Visit will be provided by Anatomical Therapeutic Chemical (ATC) level 2 and preferred term (PT) based on the Safety Set. PTs will be displayed in descending order of frequency of the total mRNA-1345 group.

An overall summary of medications taken to prevent or treat fever or pain within 7 days post injection will also be provided based on Solicited Safety Set. The summary will be based on participants' response to eDiary questions regarding whether they have taken any medications to prevent or treat fever/pain within 7 days post injection.

Prior and concomitant medications and non-study vaccinations will be presented in a listing.

Part B:

Concomitant medications and non-study vaccinations associated with SAEs and AESIs occurring from Part B Day 1 to Part B Month 6/EoS Visit will be recorded in the eCRF and coded using the World Health Organization drug dictionary (WHO-DD).

For analysis purpose, a medication taken from Part B Day 1 to Part B Month 6/EoS Visit is considered "concomitant", regardless of whether the start date is before or after the date of Part B Day 1 Visit.

Summary tables of concomitant medications and non-study vaccinations from Part B Day 1 to Part B Month 6/EoS Visit will be provided by ATC level 2 and PT based on the Part B Cohort 1

Safety Set. PTs will be displayed in descending order of frequency of the total mRNA-1345 group.

Concomitant medications and non-study vaccinations from Part B Day 1 to Part B Month 6/EoS Visit will be presented in a listing.

6.2.6. Concomitant Procedures/Surgeries (Part A)

Procedures and/or surgeries data will be coded by SOC and PT using the MedDRA Version 25.0, 2022. Imputation rules for missing/partial dates of procedures/surgeries are detailed in Appendix D.

For analysis purpose, a procedure/surgery that occurred prior to the injection date (including cases where the procedure/surgery date is completely missing) is defined "prior"; if the procedure/surgery is performed on or after the injection date and up to Part A Month 6/EoS Visit, then it is considered "concomitant".

The number of procedures/surgeries and number and percentage of participants with any concomitant procedure/surgery up to 28 days after injection and up to Part A Month 6/EoS will be summarized by SOC and PT for each treatment group defined in Section 6.1 based on the Safety Set. A participant will be counted only once for multiple procedures/surgeries within each SOC and PT. SOC will be displayed in internationally agreed order. PT will be displayed in descending order of frequency of the total mRNA-1345 group, and then alphabetically within SOC.

Prior and concomitant procedures/surgeries will be presented in a listing.

6.2.7. Study Exposure

Part A:

Study IP administration data will be summarized in disposition table and presented in a listing.

Study duration for each participant in Part A will be defined relative to randomization and injection as the following:

- Time on study from randomization: calculated as date of Part A study discontinuation/completion – date of randomization +1
- Time on study from injection: calculated as date of Part A study discontinuation/completion – date of Part A Day 1 injection +1

Descriptive statistics will be provided for the above definitions of time on study in Part A by treatment group defined in Section 6.1 based on Safety Set and PP set. Additionally, the number

and percentage of participants in each of the following categories will be displayed by treatment group in Safety Set and PP Set:

- Time on study ≥7 days from injection
- Time on study ≥28 days from injection
- Time on study ≥3 months from injection
- Time on study ≥6 months from injection

Part B:

Study duration for each participant in Part B will be defined relative to Part A injection and Part B Day 1 as the following:

- Time from Part A injection: calculated as date of Part B study discontinuation/completion – date of Part A Day 1 injection +1
- Time on study from Part B Day 1: calculated as date of Part B study discontinuation/completion – date of Part B Day 1 Visit +1

Descriptive statistics will be provided for the above definitions of time on study in Part B by treatment group defined in Section 6.1 based on Part B Cohort 1 Safety Set.

6.2.8. Important Protocol Deviations

Important protocol deviations are a subset of protocol deviations that may significantly impact the completeness, accuracy, and/or reliability of the study data or that may significantly affect a participant's rights, safety, or well-being. Important protocol deviations will be identified based on the protocol at the start of the study and during the conduct of the study and finalized before database lock (DBL) by the study team.

Part A:

The number and percentage of the participants with any important protocol deviation in each category will be provided by treatment group as defined in Section 6.1 based on the Randomization Set.

A subset of important protocol deviations in Part A, which impact critical or key study data and thus lead to exclusion of participants from the PP set, may include (but are not limited to) the following:

- Received a wrong study intervention dose defined in Table 2 in Section 5.3
- Did not have a baseline immunogenicity assessment

- Did not have any Day 29 immunogenicity assessment
- Received immune modifying medication(s) before Day 29 visit

The important protocol deviations in Part A leading to exclusion from the PP Set will be determined and documented by the study team prior to DBL and unblinding. Reasons of exclusion from PP Set will be summarized by treatment group.

Part B:

The number and percentage of the participants with any important protocol deviation in Part B in each category will be provided by treatment group as defined in Section 6.1 based on the Part B Cohort 1 Safety Set.

6.2.9. COVID-19 Impact (Part A)

An individual data listing on Coronavirus Disease 2019 (COVID-19) impact will be provided for the Randomization Set and it will include which visit(s)/assessment(s) has (have) been missed or out of the window due to COVID-19, along with the specific relationship to COVID-19.

6.3. Safety Analysis

Part A:

Safety and reactogenicity will be assessed by clinical review of all relevant parameters including solicited ARs (local and systemic), unsolicited AEs, SAEs, MAAEs, AESI, AEs leading to study discontinuation, vital signs, and physical examination findings. Solicited ARs will be coded according to the MedDRA Version 25.0, 2022 for AR terminology and unsolicited AEs will be coded by SOC and PT according to the MedDRA Version 25.0, 2022. The Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials (DHHS 2007) will be used in this study.

All safety analyses will be based on the Safety Set, except summaries of solicited ARs, which will be based on the Solicited Safety Set. All safety analyses will be provided by treatment group as defined in Section 6.1, unless otherwise specified.

Part B:

For Part B, SAEs and AESIs will be collected from signing of the ICF for Part B through Part B Month 6/EoS Visit and coded by SOC and PT according to the MedDRA Version 25.0, 2022. Vital signs and physical examination will be performed at Part B Day 1 Visit and whenever participants experience symptoms of RSV disease (RSV surveillance). All safety analyses will be based on Part B Cohort 1 Safety Set.

6.3.1. Solicited Adverse Reactions (Part A)

An AR is any AE for which there is a reasonable possibility that the test product caused the AE. The term "Solicited Adverse Reactions" refers to selected signs and symptoms occurring after injection administration during a specified postinjection follow-up period (day of injection and 6 subsequent days). The eDiary will solicit daily participant reporting of ARs using a structured checklist (Section 8.3.2 of the study protocol). Participants will record such occurrences in an eDiary from Day 1 through Day 7 (i.e., the day of injection and 6 subsequent days). Severity grading of reactogenicity will occur automatically based on participant entry into the eDiary according to the grading scales presented in Table 12 of the study protocol, which are modified from the toxicity grading scale for healthy adult and adolescent volunteers enrolled in preventive vaccine clinical trials (US DHHS 2007). All solicited ARs (local and systemic) reported in the eDiary will be considered causally related to study injection.

If a participant reports a solicited AR with onset during the solicited period and did not record the event in the eDiary, the event should be recorded on the Reactogenicity eCRF. If the event starts during the solicited period, but continues beyond 7 days after injection, the participants should notify the site to provide an end date and close out the event on the Reactogenicity eCRF. If the participant reports an event that started after the solicited period (i.e., beyond 7 days after injection), it should be recorded as an AE on the AE eCRF. Causality for these events will be determined per assessment by the Investigator.

The following local ARs for each injection site (left and right arm or leg) will be solicited by the eDiary: injection site pain, injection site erythema (redness), injection site swelling/induration (hardness), and axillary (underarm or groin) swelling or tenderness ipsilateral to the side of injection. The following systemic ARs will be solicited by the eDiary: headache, fatigue, myalgia (muscle aches all over the body), arthralgia (joint aches in several joints), nausea/vomiting, chills, and fever.

All analyses of solicited ARs will be provided by treatment group based on the Solicited Safety Set.

The number and percentage of participants with any solicited ARs, any solicited local ARs and any solicited systemic ARs during the 7-day follow-up period after injection will be summarized by treatment group with a 2-sided 95% exact CI using the Clopper-Pearson method. Refer to Safety Estimand 1a in Appendix I, Table 7.

The following summaries for solicited ARs will be presented by treatment group:

- The number and percentage of participants who reported any solicited ARs, any solicited local ARs (has a severity grade of Grade 1 or greater) and any solicited systemic ARs

(has a severity grade of Grade 1 or greater) within 30 minutes after injection will be summarized.

- The number and percentage of participants who reported each individual solicited AR (has a severity grade of Grade 1 or greater) during the 7-day follow-up period after injection will be summarized by severity grade.
- The number and percentage of participants who reported each individual solicited AR will be summarized by the onset day relative to the injection (Day 1 through Day 7). The onset day of an individual solicited AR is defined as the timepoint after injection at which the respective solicited AR first occurred.
- The duration (days) of each solicited AR will be summarized. The duration will be calculated as: end date of solicited AR event – reaction start date of solicited AR event +1, no matter if it is intermittent or continued or if the solicited AR continues beyond 7 days.

Bar plots may be created to display the percentage of participants who reported solicited AR.

The above summaries of solicited ARs may be provided for the following subgroups if deemed necessary:

- Cohort 1: Age group (≥ 2 to < 3 years, ≥ 3 to < 5 years)
- Cohort 2: Age group (≥ 5 to < 12 years, ≥ 12 to <18 years)
- Sex (Male, Female)

These summaries may be provided for additional subgroups of selected baseline characteristics. All solicited ARs will be listed.

6.3.2. Adverse Events

Part A:

An AE is any untoward medical occurrence in a clinical study, temporally associated with the use of study intervention, whether or not considered related to the study intervention.

AEs will also be evaluated by the investigator for the occurrence of any MAAEs, which is defined as an AE that leads to an unscheduled visit to a healthcare practitioner.

For analysis purpose, an AE is defined as any event occurring during the study not present before exposure to study intervention. Worsening of a pre-existing condition after study intervention will be reported as a new AE.

An unsolicited AE is any AE reported by the participant that is not specified as a solicited AR in the protocol or is specified as a solicited AR but starts outside the protocol-defined period for reporting solicited ARs (i.e., 7 days after injection). For analysis and reporting purpose, unsolicited AEs will include the following:

- AEs that are reported by participants and recorded on the AE eCRF
- Solicited ARs that meet SAE criteria and are recorded on the Reactogenicity eCRF

Unsolicited AEs will be collected for up to 28 days after injection; SAEs, MAAEs, AESIs, and AEs leading to study discontinuation will be collected throughout the study (up to Part A Month 6/EoS). Analyses of unsolicited AEs will be summarized up to 28 days after injection unless otherwise specified. Additionally, SAEs, MAAEs, AESIs, and AEs leading to study discontinuation will be summarized throughout the study (up to Part A Month 6/EoS). Refer to Safety Estimands 1b and 1c in Appendix I, Table 7.

All summary tables (except for the overall summary of AEs) for unsolicited AEs will be presented by SOC and PT (or by PT). SOC will be displayed in internationally agreed order. PTs will be displayed in descending order of frequency in the total mRNA-1345 group, and then alphabetically within SOC. When summarizing the number and percentage of participants with an event, participants with multiple occurrences of the same AE or a continuing AE will be counted once. In addition, the number of events will also be included in those summaries.

For the by-severity summaries, the toxicity grade of a solicited AR meeting SAE criteria will be mapped to a severity level of Mild/Grade 1, Moderate/Grade 2 or Severe/≥ Grade 3 and the maximum severity level in the case of multiple events will be presented.

Part B:

SAEs and AESIs will be collected from Part B Day 1 to Part B Month 6/EoS Visit.

Summary tables for SAEs and AESIs from Part B Day 1 to Part B EoS Visit will be presented by SOC and PT (or by PT). SOC will be displayed in the internationally agreed order. PTs will be displayed in descending order of frequency in the total mRNA-1345 group, and then alphabetically within SOC. When summarizing the number and percentage of participants with an event, participants with multiple occurrences of the same AE or a continuing AE will be counted once. In addition, the number of events will also be included in those summaries.

6.3.2.1. Overview of AEs (Part A)

An overall summary of unsolicited AEs up to 7 days after injection, between 8 to 28 days after injection, and up to 28 days after injection will be provided for the number and percentage of

participants, along with the number of events, by treatment group who experience at least one of the categories:

- Any unsolicited AEs
- Any serious AEs
- Any fatal AEs
- Any unsolicited medically-attended AEs
- Any unsolicited AEs leading to study discontinuation
- Any unsolicited severe AEs
- Any unsolicited non-serious AEs (no SAE)
- Any unsolicited non-serious severe AEs (no SAE)
- Any unsolicited non-serious AEs (regardless of SAE)
- Any unsolicited non-serious severe AEs (regardless of SAE)
- Any unsolicited AESI

Note: Severe AEs include both unsolicited severe AEs and ≥ Grade 3 solicited ARs that meet SAE criteria.

The above overall summaries will also include number and percentage of participants with unsolicited AEs that are treatment-related in each of the above categories.

Additionally, the overall summary for the categories of SAEs, MAAEs, AESIs, and AEs leading to study discontinuation will be provided for these AEs throughout the study (up to Part A Month 6/EoS).

Separate listings containing individual participant AE data throughout the study (up to Part A Month 6/EoS) for AEs, treatment-related AEs, serious AEs, serious treatment-related AEs, medically-attended AEs, treatment-related medically-attended AEs, AEs leading to study discontinuation, severe AEs, treatment-related severe AEs, AESIs, and fatal AEs will be provided. Listing of deaths, including cause of death, will be provided.

6.3.2.2. AEs by System Organ Class and Preferred Term

Part A:

The following summary tables of unsolicited AEs up to 28 days after injection will be provided by SOC and PT using frequency counts and percentages (i.e., number and percentage of participants with an event):

- All unsolicited AEs
- All unsolicited AEs that are treatment-related
- All serious AEs
- All serious AEs that are treatment-related
- All unsolicited non-serious AEs
- All unsolicited non-serious severe AEs
- All unsolicited medically-attended AEs
- All unsolicited medically-attended AEs that are treatment-related
- All unsolicited AEs leading to study discontinuation
- All unsolicited severe AEs
- All unsolicited severe AEs that are treatment-related
- All unsolicited AESI

Note: Severe AEs include both unsolicited severe AEs and ≥ Grade 3 solicited ARs that meet SAE criteria.

Summary tables by SOC and PT will also be provided for unsolicited AEs up to 7 days after injection, and between 8 to 28 days after injection.

Additionally, summary tables of SAEs, treatment-related SAEs, MAAEs, treatment-related MAAEs, AEs leading to study discontinuation, and AESIs will be also provided by SOC and PT considering all events reported throughout the study (up to Part A Month 6/EoS).

Part B:

The following summary tables of SAEs, and AESIs will be provided by SOC and PT using frequency counts and percentages (i.e., number and percentage of participants with an event) considering all events reported from Part B Day 1 to Part B Month 6/EoS Visit:

- All SAEs
- All AESIs

6.3.2.3. AEs by Preferred Term (Part A)

A summary table for all unsolicited AEs up to 28 days after injection will be provided by PT in descending order of frequency in the total mRNA-1345 group.

6.3.2.4. AEs by Severity (Part A)

The following summary tables of AEs up to 28 days after injection will be provided by the severity, SOC and PT using frequency counts and percentages:

- All unsolicited AEs
- All unsolicited AEs that are treatment-related

6.3.2.5. AEs by SMQ (Part A)

The number of events and number of participants reported occurrence of selected AEs of clinical interests identified by SMQs up to 7 days after injection, up to 28 days after injection, and throughout the study (up to Part A Month 6/EoS) will be summarized by SMQ, subordinate SMQ, and PT. Two sets of summary tables will be provided, one will be based on combined broad and narrow scope of SMQ, the other will be based on narrow scope. SMQ and subordinate SMQ within each SMQ will be displayed in alphabetic order. PT will be displayed in descending order of frequency of the total mRNA-1345 group, and then alphabetically within subordinate SMQ or SMQ if no subordinate SMQ. Detail information for the selected SMQ is presented in Appendix J Table 10 and Table 11.

Selected AEs of clinical interests identified by SMQs up to Part A Month 6/EoS will be provided in listings.

6.3.2.6. AEs by System Organ Class, High Level Group Term and Preferred Term (Part A)

Certain AEs, as indicated in Appendix L, will also be summarized by SOC, HLGT, and PT for each treatment group and presented by three time periods: up to 7 days after injection, up to 28 days after injection, and throughout the study (up to Part A Month 6/EoS).

6.3.2.7. Independent Cardiac Event Adjudication Committee (CEAC) (Part A)

An independent CEAC of medically qualified personnel, including cardiologists, will review suspected cases of myocarditis, pericarditis, and myopericarditis to determine if they meet CDC criteria of "probable" or "confirmed" events, and to assess severity (see more details in Protocol Section 10.1.6.2) and provide the assessment to the Sponsor. The CEAC members will be blinded to study treatment. Details regarding the CEAC composition, responsibilities, procedures, and frequency of data review can be found in the CEAC charter.

A summary table will be provided based on the data adjudicated by the CEAC, as the primary analysis of cardiac events.

6.3.2.8. Subgroup Analysis of AEs (Part A)

The overview of AEs, AEs by SOC/PT, AEs by Severity, unsolicited treatment-related AEs by SOC/PT and serious AEs by SOC/PT may be provided for the following subgroups as deemed necessary:

- Cohort 1: Age group (≥ 2 to < 3 years, ≥ 3 to < 5 years)
- Cohort 2: Age group (≥ 5 to < 12 years, ≥ 12 to <18 years)

These summaries may be provided for additional subgroups of selected baseline characteristics.

6.3.3. Vital Sign Measurements

Part A:

Vital signs will be collected at Screening, on the day of injection (Part A Day 1) once before injection. Postinjection vital signs should only be obtained if the participant is showing concerning signs or symptoms (eg, signs of anaphylaxis). At subsequent scheduled visits, vital signs should only be obtained if necessary for the evaluation of an AE.

Vital sign measurements, including systolic and diastolic blood pressures, heart rate, respiratory rate, and axillary temperature will be presented in a data listing based on the Safety Set.

Part B:

Vital signs will be collected at Part B Day 1 Visit, and unscheduled visits for RSV surveillance. During unscheduled visits for RSV surveillance, the following vital signs will be recorded for every visit: temperature, respiratory rate, heart rate, oxygen saturation (SpO_2).

Vital sign measurements will be presented in a data listing for Part B Cohort 1 Safety Set.

6.3.4. RSV Cases (Part B)

To detect and capture RSV-RTD cases by study sites, in a timely manner, all children 2 to <5 years of age who were enrolled and dosed in Part A of Cohort 1 and opted for re-enrollment in Part B will be closely monitored for respiratory illnesses, by RSV surveillance, from Part B Day 1 until Part B EoS Visit.

All cases identified during the surveillance of RSV-RTD will be definitively classified as either RTD, LRTD, severe LRTD, very severe LRTD, or hospitalization according to the modified case definitions based on the available WHO case definitions for RSV. Case definitions are presented in Table 4.

Table 4: Case Definitions for RSV for Data Analysis

RSV-RTD	Runny nose **OR** blocked nose **OR** cough AND Confirmed RSV infection[a]
RSV-LRTD	Cough **OR** difficulty breathing[b] AND SpO_2 <95%[c], **OR** RR increase[d] AND Confirmed RSV infection[a]
RSV Severe-LRTD	Meeting the case definition of RSV-LRTD AND SpO_2 <93%[c], **OR** lower chest wall in-drawing
RSV Very Severe LRTD	Meeting the case definition of RSV-LRTD AND SpO_2 <90%[c], **OR** failure to respond/unconscious
RSV Hospitalization	Confirmed RSV[a,e] AND Hospitalized for acute medical condition[f]
For each of 'RSV-RTD,' 'RSV-LRTD,' 'RSV severe-LRTD,' and 'RSV very severe LRTD,' an additional category of 'Medically attended RSV-RTD (MA-RSV-RTD), MA-RSV-LRTD,' etc, will be created to include the subset of participants that meet these definitions that attended a health care consultation.	

Abbreviations: BPM = beats per minute; LRTD = lower respiratory tract disease; RT-PCR = reverse transcription polymerase chain reaction; RR = respiratory rate; RSV = respiratory syncytial virus; RTD = respiratory tract disease; SpO_2 = blood oxygen saturation.

a. RSV infection confirmed on nasal swab positive by positive RT-PCR or other local laboratory tests.
b. Based on observation by Investigator; difficulty breathing includes signs of wheezing, stridor, tachypnoea, chest in-drawing or subcostal or intercostal retractions.
c. For SpO2, the lowest stable value monitored will be used.
d. RR increased defined as >38 BPM for 2- to <3-year-olds, >33 BPM for -3 to <4-year-olds, and >29 BPM for ≥4-year-olds per 99th percentiles for age (Fleming et al 2011).
e. RSV sampling and testing is based on medical judgment of medical practitioner or driven by algorithm.
f. Hospitalization is defined as a medical decision in which the participant requires overnight admission for observation or treatment.

Respiratory Illness Episode:

When a participant is determined to have a new or worsening respiratory illness episode, the participant will be arranged to have an unscheduled visit for medical evaluation and testing. The unscheduled visit, called "Unscheduled Illness Visit", will be created in eCRF to collect the following assessments associated with the respiratory illness episode: visit date, respiratory illness symptoms, respiratory examination, physical examination, vital signs, nasal swab collection for central laboratory RT-PCR test, local diagnostic test, healthcare encounter.

RSV Cases Classified by Clinical Assessment Team:

Confidential

Classification of RSV cases will be made by the Clinical Assessment Team (CAT) of the Sponsor by evaluating all RSV surveillance data collected for each respiratory illness episode. The classification of RSV cases by CAT will be used as the primary analysis of RSV cases.

RSV Cases Classified Programmatically Based on Prespecified Criteria:

For a respiratory illness episode, a case of RSV-RTD, RSV-LRTD, RSV Severe LRTD or RSV Very Severe LRTD will be defined if prespecified symptoms and testing criteria (Table 4) are met based on the assessments collected under the same corresponding unscheduled illness visit folder in eCRF. Central laboratory RT-PCR or other local laboratory test results obtained from the same visit folder will be used. The date of each RSV-RTD/RSV-LRTD case will be the earliest date of the following dates:

- Earliest positive RSV test date
- Earliest date of prespecified symptoms (Table 4)

For a respiratory illness episode, a case of RSV hospitalization is defined if 1) an RSV-RTD or RSV-LRTD is defined and 2) there is a healthcare encounter of hospitalization stay due to respiratory tract infection collected under the same corresponding unscheduled illness visit folder in eCRF.

For a respiratory illness episode, a medically attended case of an RSV-RTD or RSV-LRTD is defined if 1) an RSV-RTD or RSV-LRTD is defined and 2) there is a healthcare encounter due to respiratory tract disease collected under the same corresponding unscheduled illness visit folder in eCRF.

Analyses of RSV Cases:

The number and percentage of participants with RSV-RTD, RSV-LRTD, RSV severe-LRTD, RSV very severe LRTD, RSV hospitalization, MA-RSV-RTD, MA-RSV-LRTD, MA-RSV severe-LRTD, and MA-RSV very severe LRTD from Part B Day 1 to Part B EoS will be summarized by treatment group. The above analyses will be performed based on RSV cases classified by CAT for Part B Cohort 1 Safety Set. Refer to Safety Estimand 1d in Appendix I, Table 7.

Additionally, the above analyses will be performed based on RSV cases classified programmatically for Part B Cohort 1 Safety Set. Refer to Appendix M for detailed RSV case classifications by programming.

The surveillance results will be presented in listings.

6.3.5. Pregnancy Test (Part A)

Pregnancy test results will be presented by participant in a listing.

6.4. Immunogenicity Analysis (Part A)

The primary analysis population of immunogenicity will be the PP Set. If the number of participants in the FAS and PP Set differ (defined as the difference divided by the total number of participants in the PP Set) by more than 10%, additional supportive analyses of immunogenicity may be conducted using the FAS based on Appendix I.

All the immunogenicity analyses will be provided by treatment group and by cohort, unless otherwise specified.

The GMT and GMC will be calculated using the following formula:

$$10^{\left\{\frac{1}{n}\sum_{i=1}^{n}\log_{10}(y_{it})\right\}}$$

where $y_{1t}, y_{2t}, \cdots, y_{nt}$ are *n* observed immunogenicity titers or levels for participants *i=1, 2, …, n* at time point *t*.

The GMFR measures the changes in immunogenicity titers from baseline within participants. The GMFR will be calculated using the following formula:

$$10^{\left\{\frac{1}{n}\sum_{i=1}^{n}\log_{10}\left(\frac{y_{it}}{y_{i0}}\right)\right\}} = 10^{\left\{\frac{1}{n}\sum_{i=1}^{n}[\log_{10}(y_{it})-\log_{10}(y_{i0})]\right\}}$$

where $y_{1t}, y_{2t}, \cdots, y_{nt}$ are observed immunogenicity titers or levels for participants i's at time point t. and $y_{10}, y_{20}, \cdots, y_{n0}$ are immunogenicity titers or levels for participants i's at time point 0 (baseline).

6.4.1. Immunogenicity Assessments

Immunogenicity assessments will include the following:

- RSV-A and RSV-B neutralizing antibody (nAb) as measured by microneutralization assay
- RSV prefusion F (preF) and postfusion F (postF) binding antibody (bAb) as measured by luminex

6.4.2. Analysis of Secondary Endpoints

The secondary endpoints will be analyzed on the PP Set in order to estimate Estimands 2a-1, 2b-1 and 2c-1 (refer to Appendix I, Table 8). In addition, this may be supported by estimation of a treatment policy estimand (Estimands 2a-2, 2b-2 and 2c-2) on the FAS Set.

The secondary endpoints for Part A Cohort 1 include the following:

- GMT of serum RSV-A and RSV-B nAbs at Baseline (Day 1), Day 29, and Part A Month 6
- GMC of serum RSV preF and postF bAbs at Baseline (Day 1), Day 29, and Part A Month 6
- GMFR of Postbaseline/Baseline nAb titers and bAb concentrations at Day 29 and Part A Month 6
- Proportion of participants with a seroresponse in nAb titers and bAb concentrations from Baseline at Day 29 and Part A Month 6

The secondary endpoints for Part A Cohort 2 include the following:

- GMT of serum RSV-A and RSV-B nAbs at Baseline (Day 1) and Day 29
- GMC of serum RSV preF and postF bAbs at Baseline (Day 1) and Day 29
- GMFR of postbaseline/Baseline nAb titers and bAb concentrations at Day 29
- Proportion of participants with a seroresponse in nAb titers and bAb concentrations from Baseline at Day 29

The statistical analyses include the following:

- GMT of RSV-A nAbs and RSV-B nAbs, and GMC of RSV preF bAbs, and postF bAbs with corresponding 95% CI will be provided at Baseline (Day 1), Day 29, and Month 6 (for Part A Cohort 1) by treatment group for each cohort. The 95% CIs will be calculated based on the t-distribution of the log-transformed values and then back transformed to the original scale for presentation. The following descriptive statistics will also be provided at Baseline (Day 1), Day 29, and Month 6 (for Part A Cohort 1), the number of participants (n), median, minimum and maximum. GMT and GMC with 95% CI may be plotted at each scheduled timepoint by treatment group for each cohort.
- GMFR of RSV-A nAbs, RSV-B nAbs, and RSV preF bAbs, and postF bAbs with corresponding 95% CI will be provided at each postbaseline timepoint over Baseline (Day 1) by treatment group for each cohort. The 95% CIs will be calculated based on the t-distribution of the log-transformed values, then back transformed to the original scale for presentation. GMFR and corresponding 95% CI will be plotted at each scheduled timepoint by treatment group for each cohort.

- Proportion of participants with a seroresponse from Baseline in RSV-A nAb titers, RSV-B nAb titers, and RSV preF bAb concentrations, and postF bAb concentrations at each post-baseline time point will be provided with 2-sided 95% CIs using the Clopper-Pearson method by treatment group for each cohort.

6.4.3. Subgroup Analysis

All the above specified immunogenicity analyses may be performed by the following subgroups if deemed necessary:

- Cohort 1: Age group (≥ 2 to < 3 years, ≥ 3 to < 5 years)
- Cohort 2: Age group (≥ 5 to < 12 years, ≥ 12 to <18 years)

6.5. Exploratory Analysis

The exploratory endpoints of Cohort 1 include the following:

- Transcriptome analysis may be conducted to further evaluate immune responses.
- Frequency, magnitude, and/or phenotype of vaccine-specific T-cell and B-cell responses by flow cytometry or other methods.
- Frequency, specificities, or other endpoints to be determined for the further characterization of immune responses.

The exploratory analysis may be performed by another analysis group and not included in the scope of this SAP.

The exploratory objectives of Part B Cohort 1 may be evaluated by the following endpoints:

- GMT of serum RSV neutralizing antibody at Part B Day 1.
- GMC of serum RSV preF and postF binding antibody at Part B Day 1.

Since the blood draw for immunogenicity assessments at Part B Day 1 is optional, a listing including available data may be presented for Part B Cohort 1 FAS.

- Frequency, specificities, or other endpoints to be determined, for the further characterization of immune responses, including cell-mediated immunogenicity.

The analysis on frequency, specificities, or other endpoints may be performed by another analysis group and not included in the scope of this SAP.

6.6. Multiplicity Adjustment

This study is descriptive, and no multiplicity adjustments will be applied.

6.7. Planned Analyses

Interim analyses and a final analysis will be conducted.

For Part A, an IA of reactogenicity, safety, and immunogenicity will be performed for each cohort after all participants in the cohort have completed the Day 29 Visit. The IAs will be performed by a separate team of unblinded programmers and statisticians. These analyses will be conducted on cleaned data and may be combined depending on study timelines.

Additional interim analysis may be performed as needed. Final analysis will be performed after all participants have completed the study and all data are available.

6.8. Data Safety Monitoring Board

An independent DSMB will review blinded and unblinded data at the scheduled data review meeting following the IA. The DSMB will review safety of the selected Phase 2 dose in each age group. For Part B Cohort 1, an additional safety data review for RTD cases will be completed by the Sponsor and DSMB at the end of Part B. Any emerging safety concerns from IST safety reviews or in case a pause rule trigger is confirmed by the IST, further evaluation will be referred to the DSMB.

The Sponsor may also request that the DSMB conduct ad hoc reviews of safety events from this study or other data, including new nonclinical or clinical information related to mRNA-1345 external to this study. The DSMB will review all available study data to adjudicate such events in accordance with the DSMB charter. Refer to the DSMB charter for additional details.

The DSMB composition, its remit and frequency of data review will be further defined in the DSMB charter.

7. Changes from Planned Analyses in Protocol

There is no change from planned analyses in protocol.

8. References

Miettinen O, Nurminen M. Comparative analysis of two rates. Stat Med. 1985;4:213-226.

United States Department of Health and Human Services (US DHHS), Food and Drug Administration, Center for Biologics Evaluation and Research. Guidance for industry: Toxicity grading scale for healthy adult and adolescent volunteers enrolled in preventive vaccine clinical trials. September 2007 [cited 2022 Jan 11]. Available from: https://www.fda.gov/media/73679/download.

Fleming S, Thompson M, Stevens R, Heneghan C, Plüddemann A, Maconochie I, et al. Normal ranges of heart rate and respiratory rate in children from birth to 18 years of age: a systematic review of observational studies. Lancet. 2011;377(9770):1011-8.

9. List of Appendices

9.1. Appendix A Standards for Variable Display in Tables, Figures and Listings (TFLs)

Continuous Variables: The precision for continuous variables will be based on the precision of the data itself. The mean and median will be presented to one more decimal number than the original results; the SD will be presented to two more decimal numbers than the original results; the minimum and maximum will be presented to the same precision as the original results. For immunogenicity values, the GMT, GMC, GMFR, and the corresponding confidence intervals will be presented to 2 decimal places.

Categorical Variables: Percentages will be presented to 1 decimal place. If the count is 0, the percentage will not be displayed. If the count equals the denominator, the percentage will be displayed as 100.

9.2. Appendix B Analysis Visit Windows (Part A)

Analysis visit windows will be utilized for immunogenicity assessments only.

Data will be mapped using the following approach:

Step 1: If the assessments are collected at a scheduled visit, the collected data will be mapped to the nominal scheduled visit.

Step 2: If the assessments are collected at an unscheduled visit or early termination visit, the collected data will be mapped using the analysis visit windows described in Table 5 a subject has multiple assessments within the same analysis visit, the following rule will be used:

- If multiple assessments occur within a given analysis visit, the assessment closest to the target study day will be used.
- If there are 2 or more assessments equal distance to the target study day, the last assessment will be used.

Table 5: Analysis Visit Windows for Immunogenicity Assessments

Visit	Target Study Day	Visit Window in Study Day
Day 1 (Cohort 1, and Cohort 2)	1	1

Day 29 (Cohort 1, and Cohort 2)	29	[22, 43]
Month 6/EoS (Cohort 1)	180	[152, 208]

For immunogenicity analysis based on PP Set, any immunogenicity assessment (regardless of scheduled or unscheduled visit) that is out of analysis window as described in Table 5 will be excluded from analysis.

9.3. Appendix C Imputation Rules for Missing Dates of Prior/Concomitant Medications

Imputation rules for missing or partial start/stop dates of medication are defined below:

1. Missing or partial medication start date:
   - If only Day is missing, use the first day of the month, unless:
     - The medication end date is on/after the date of the injection or is missing/partial AND the start month and year of the medication coincide with the start month and year of the injection. In this case, use the date of the injection.
   - If Day and Month are both missing, use the first day of the year, unless:
     - The medication end date is on/after the date of the injection or is missing/partial AND the start year of the medication coincide with the start year of the IP injection. In this case, use the date of the injection.
   - If Day, Month, and Year are all missing, the date will not be imputed, but the medication will be treated as though it began prior to the injection for purposes of determining if status as prior or concomitant.
2. Missing or partial medication stop date:
   a. If only Day is missing, use the earliest date of (last day of the month, study completion, discontinuation from the study, or death).
   b. If Day and Month are both missing, use the earliest date of (last day of the year, study completion, discontinuation from the study, or death).

c. If Day, Month, and Year are all missing, the date will not be imputed, but the medication will be flagged as a continuing medication.

9.4. Appendix D Imputation Rules for Missing Dates of Procedures/Surgeries

Imputation rules for missing or partial dates of procedures/surgeries are defined below:

- If only Day is missing, use the first day of the month, unless:
  - The start month and year of the procedure/surgery coincide with the start month and year of the injection. In this case, use the date of the injection.
- If Day and Month are both missing, use the first day of the year, unless:
  - The start year of the procedure/surgery coincide with the start year of the injection. In this case, use the date of the injection.
- If Day, Month, and Year are all missing, the date will not be imputed, but the procedure/surgery will be treated as concomitant.

9.5. Appendix E Imputation Rules for Missing Dates of AEs

Imputation rules for missing or partial start dates and stop dates of AEs are defined below:

1. Missing or partial start date:

- If only Day is missing, use the first day of the month, unless:
  - The AE end date is on/after the date of the injection or is missing/partial AND the start month and year of the AE coincide with the start month and year of the injection. In this case, use the date of the injection.
- If Day and Month are both missing, use the first day of the year, unless:
  - The AE end date is on/after the date of the injection or is missing/partial AND the start year of the AE coincides with the start year of the injection. In this case, use the date of the injection.
- If Day, Month, and Year are all missing, the date will not be imputed. However, if the AE end date is prior to the date of the injection, then the AE will be not included in the AE summaries.

2. Missing or partial end dates will not be imputed.

9.6. Appendix F Part A: Schedule of Activities for Cohort 1 (2 to Less than 5 Years)

Study Period	**SCR**	**Intervention**	**Follow-Up**					**Notes**
Visit Number		**1**	**2**	**3**	**4**	**5**	**USV[a]**	Reference to Protocol Section
Timepoint	**SCR**	**D1**	**D8**	**D29**	**M3**	**M6/ EoS Visit**		1 Month = 30 Days Screening Visit and D1 Visit may occur on the same day. Refer to Section 4.1
Window Allowance (Days)	**-28 before D1**		**+3**	**±4**	**±7**	**±7**		
Type of Visit	**V**	**V**	**SC**	**V**	**SC**	**V**	**V**	
Informed Consent	X							Refer to Section 10.1.3
Demographics and medical history	X							Refer to Section 8.1
Inclusion/exclusion criteria[b]	X	X						Refer to Section 5.1 and Section 5.2
Vital signs[b]	X	X					X	Refer to Section 8.3.4
Physical examination[b,c]	X	X		X		X	X	Refer to Section 8.3.3
Participants with CHD only: ECG (if not available within 6 months of Screening)	X							Refer to Section 8.3.5
Recording of concomitant medications and non-study vaccinations	X	X	X	X	X	X	X	Refer to Section 6.9
Randomization		X						Refer to Section 6.3
Study injection (including the 30-minute postdose observation period)[d]		X						Refer to Section 6.1
Blood for antibody-mediated immunogenicity		X[e]		X		X		Refer to Section 8 and Section 8.9
Blood for CMI (PBMC)[f]		X[e]		X		X		Refer to Section 8 and Section 8.9

Study Period	SCR	Intervention	Follow-Up					Notes
Visit Number		**1**	**2**	**3**	**4**	**5**	**USV[a]**	Reference to Protocol Section
Timepoint	**SCR**	**D1**	**D8**	**D29**	**M3**	**M6/ EoS Visit**		1 Month = 30 Days Screening Visit and D1 Visit may occur on the same day. Refer to Section 4.1
Window Allowance (Days)	**-28 before D1**		**+3**	**±4**	**±7**	**±7**		
Type of Visit	**V**	**V**	**SC**	**V**	**SC**	**V**	**V**	
eDiary activation for recording solicited Ars		X						Refer to Section 8.3.2
Review of solicited ARs eDiary[d]			X					Refer to Section 8.3.2
Follow-up safety phone call[g]			X		X			Refer to Section 8.3.1
Recording of unsolicited AEs		X	X	X				Refer to Section 10.3
MAAEs and concomitant medications associated with MAAEs[h]		X	X	X	X	X	X	Refer to Section 8.4.7
AESIs, AEs leading to discontinuation, and concomitant medications associated with these AEs[h]		X	X	X	X	X	X	Refer to Section 8.4.8 and Section 10.3
SAEs and concomitant medications associated with SAEs[h]	X[i]	X	X	X	X	X	X	Refer to Section 10.3
Study completion						X		

Note: If a participant cannot attend a scheduled in-person visit with the exception of the Screening Visit and Day 1, a home visit is acceptable if performed by appropriately delegated study site staff or a home healthcare service. If neither an in-person visit from the participant nor a home visit to the participant is possible (with the exception of the Screening Visit and Day 1), a safety phone call should be performed that includes the assessments scheduled for the safety phone calls.

Abbreviations: AE = adverse event; AESI = AE of special interest; AR = adverse reaction; CHD = congenital heart defect; CMI = cell-mediated immunity; D = day; eDiary = electronic diary; EoS = end-of-study; ICF = informed consent form; LAR = legally authorized representative; M = month (month = 30 days); MAAE = medically attended adverse event; PBMC = peripheral blood mononuclear cell; RSV = respiratory syncytial virus; SAE = serious adverse event; SC = safety phone call; SCR = Screening; USV = unscheduled visit; V = in-person visit.

a. Visit for participants who discontinue/withdraw from the study and unscheduled visits.

b. Vital sign measurements, check of inclusion/exclusion criteria, and physical examination do not need to be repeated if the Screening Visit and the Day 1 Visit occur on the same day. A complete physical examination will be performed at the Screening Visit.
c. A symptom-directed physical examination will be performed at in-person visits after the Screening Visit, at the discretion of the Investigator.
d. eDiary entries will be recorded by the participant's parent(s)/LAR(s) within approximately 30 minutes after study injection while at the clinic with instruction provided by the study site staff. Participant's parent(s)/LAR(s) will continue to record solicited ARs in the eDiary each day after they leave the clinic, on the day of study intervention and the subsequent 6 days following study intervention.
e. Prior to study intervention (ie, Baseline blood sample).
f. Blood for PBMC will be collected from a subset of participants at selected study sites for participants enrolled in Cohort 1 only.
g. Trained study site staff will remind the participant's parent(s)/LAR(s) to complete the eDiary and to collect information about any Grade 3 solicited ARs, any underarm/groin swelling or tenderness on same side as injection, any medications taken to prevent or treat pain or fever, and any medical visits, as applicable.
h. Trained study site staff will collect information relating to any MAAEs, AEs leading to study discontinuation, SAEs, AESI, and information on concomitant medications associated with those events, and any non-study vaccinations received.
i. After signing of the ICF.

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9.7. Appendix G Part A: Schedule of Activities for Cohort 2 (5 to Less than 18 Years)

Study Period	**SCR**	**Intervention**	**Follow-Up**					**Notes**
Visit Number		**1**	**2**	**3**	**4**	**5**	**USV[a]**	Reference to Protocol Section
Timepoint	**SCR**	**D1**	**D8**	**D29**	**M3**	**M6/ EoS Visit**		1 Month = 30 Days Screening Visit and D1 Visit may occur on the same day. Refer to Section 4.1
Window Allowance (Days)	**-28 before D1**		**+3**	**±4**	**±7**	**±7**		
Type of Visit	**V**	**V**	**SC**	**V**	**SC**	**SC**	**V**	
Informed Consent	X							Refer to Section 10.1.3
Demographics and medical history	X							Refer to Section 8.1
Inclusion/exclusion criteria[b]	X	X						Refer to Section 5.1 and Section 5.2
Vital signs[b]	X	X					X	Refer to Section 8.3.4
Physical examination[b,c]	X	X		X			X	Refer to Section 8.3.3
Pregnancy test (urine)[d] prior to injection and IRT registration (POCBP)	X	X						Refer to Section 8.3.6
Participants with CHD only: ECG (if not available within 6 months prior to Screening)	X							Refer to Section 8.3.5
Participants aged 12-<18 years only: 12-Lead ECG (predose) and collection of banked serum for potential cardiac biomarker testing		X						Refer to Section 8.3.5 and Section 8.8.
Recording of concomitant medications and non-study vaccinations	X	X	X	X	X	X	X	Refer to Section 6.9
Randomization		X						Refer to Section 6.3

Study Period	SCR	Intervention	Follow-Up					Notes
Visit Number		**1**	**2**	**3**	**4**	**5**	**USV[a]**	Reference to Protocol Section
Timepoint	**SCR**	**D1**	**D8**	**D29**	**M3**	**M6/ EoS Visit**		1 Month = 30 Days Screening Visit and D1 Visit may occur on the same day. Refer to Section 4.1
Window Allowance (Days)	**-28 before D1**		**+3**	**±4**	**±7**	**±7**		
Type of Visit	**V**	**V**	**SC**	**V**	**SC**	**SC**	**V**	
Study injection (including the 30-minute postdose observation period)[e]		X						Refer to Section 6.1
Blood for antibody-mediated immunogenicity		X[f]		X				Refer to Section 8 and Section 8.9
eDiary activation for recording solicited Ars		X						Refer to Section 8.3.2
Review of solicited ARs eDiary[e]			X					Refer to Section 8.3.2
Follow-up safety phone call[g]			X		X	X		Refer to Section 8.3.1
Recording of unsolicited AEs		X	X	X				Refer to Section 10.3
MAAEs and concomitant medications associated with MAAEs[h]		X	X	X	X	X	X	Refer to Section 8.4.7
AESIs, AEs leading to discontinuation, and concomitant medications associated with these AEs[h]		X	X	X	X	X	X	Refer to Section 8.4.8 and Section 10.3
SAEs and concomitant medications associated with SAEs[h]	X[i]	X	X	X	X	X	X	Refer to Section 10.3
Study completion						X		

Note: If a participant cannot attend a scheduled in-person visit with the exception of the Screening Visit and Day 1, a home visit is acceptable if performed by appropriately delegated study site staff or a home healthcare service. If neither an in-person visit from the participant nor a home visit to the participant is possible (with the exception of the Screening Visit and Day 1), a safety phone call should be performed that includes the assessments scheduled for the safety phone calls.

Abbreviations: AE = adverse event; AESI = AE of special interest; AR = adverse reaction; CHD = congenital heart disease;D = day; eDiary = electronic diary; ECG = electrocardiogram; EoS = end-of-study; ICF = informed consent form; IRT = Interactive Response Technology; LAR = legally authorized representative; M = month (month = 30 days); MAAE = medically attended adverse event; POCBP = person of childbearing potential; RSV = respiratory syncytial virus; SAE = serious adverse event; SC = safety phone call; SCR = Screening; USV = unscheduled visit; V = in-person visit.

a. Visit for participants who discontinue/withdraw from the study and unscheduled visits.
b. Vital sign measurements, check of inclusion/exclusion criteria, and physical examination do not need to be repeated if the Screening Visit and the Day 1 Visit occur on the same day. A complete physical examination will be performed at the Screening Visit.
c. A symptom-directed physical examination will be performed at in-person visits after the Screening Visit, at the discretion of the Investigator.
d. Applicable to female participants who have reached menarche only. Serum pregnancy test will be performed to confirm a positive result of a urine pregnancy test. Participants who become pregnant at any time should remain in the study and complete all study visits as scheduled.
e. eDiary entries will be recorded by the participant's parent(s)/LAR(s) or the participant within approximately 30 minutes after study injection while at the clinic with instruction provided by the study site staff. Participant's parent(s)/LAR(s) or the participant will continue to record solicited ARs in the eDiary each day after they leave the clinic, on the day of study intervention and the subsequent 6 days following study intervention.
f. Prior to study intervention (ie, Baseline blood sample).
g. Trained study site staff will remind the participant's parent(s)/LAR(s) and the participant to complete the eDiary and to collect information about any Grade 3 solicited ARs, any underarm/groin swelling or tenderness on same side as injection, any medications taken to prevent or treat pain or fever, and any medical visits, as applicable.
h. Trained study site staff will collect information relating to any MAAEs, AEs leading to study discontinuation, SAEs, AESI, and information on concomitant medications associated with those events, and any non-study vaccinations received.
i. After signing of the ICF.

9.8. Appendix H Part B: Schedule of Activities for Cohort 1 (2 to Less than 5 Years)

Study Period		RSV Surveillance					Notes
	Re-Enrollment	Follow-Up					
Visit Number	**1**	**2**	**3**	**4 (EoS Visit)**	**USV[a]** (RSV Surveillance)	**Convalescent Visit**	Reference to Protocol Section
Timepoint	**D1**	**M2**	**M4**	**M6**	Whenever experiencing respiratory symptoms	Following a confirmed RSV-LRTD	1 Month = 30 Days
Window Allowance (Days)	**-**	**±7**	**±7**	**±7**	**N/A**	**+3 to 24**	
Type of Visit	**V**	**SC**	**SC**	**SC**	**V**	**V**	
Informed Consent	X						Refer to Section 10.1.3
Demographics (age only)	X						Refer to Section 8.1
Interim SAE and AESI history from Part A EoS or discontinuation to signing of ICF for Part B	X						Refer to Section 8.3
Inclusion/exclusion criteria	X						Refer to Section 5.1 and Section 5.2
Vital signs[b]	X				X		Refer to Section 8.3.4
Physical examination[c]	X				X	X	Refer to Section 8.3.3
Follow-up safety phone calls[d]		X	X	X			Refer to Section 8.3.1
AESIs and concomitant medications associated with AESIs[e]	X	X	X	X	X		Refer to Section 8.4
SAEs and concomitant medications associated with SAEs[e]	X	X	X	X	X		Refer to Section 8.4
Blood for antibody-mediated immunogenicity (optional)[f]	X						

Study Period		RSV Surveillance					
	Re-Enrollment	Follow-Up					Notes
Visit Number	**1**	**2**	**3**	**4 (EoS Visit)**	**USV[a]** (RSV Surveillance)	**Convalescent Visit**	Reference to Protocol Section
Timepoint	**D1**	**M2**	**M4**	**M6**	Whenever experiencing respiratory symptoms	Following a confirmed RSV-LRTD	1 Month = 30 Days
Window Allowance (Days)	**-**	**±7**	**±7**	**±7**	**N/A**	**+3 to 24**	
Type of Visit	**V**	**SC**	**SC**	**SC**	**V**	**V**	
RSV surveillance[d, g]	Weekly during RSV season and monthly when not in RSV season						Refer to Section 8.3.7
Nasal or Nasopharyngeal Swab					X		
Blood for cell-mediated and antibody-mediated immunogenicity (optional)[h]						X	

Note: If a participant cannot attend a scheduled in-person visit with the exception of the Part B Day 1 visit, a home visit is acceptable if performed by appropriately delegated study site staff or a home healthcare service. If neither an in-person visit from the participant nor a home visit to the participant is possible (with the exception of the Part B Day 1 Visit), a safety phone call should be performed that includes the assessments scheduled for the safety phone calls.

Abbreviations: AE = adverse event; AESI = AE of special interest; AR = adverse reaction; CHD = congenital heart defect; CMI = cell-mediated immunity; D = day; EoS = end-of-study; ICF = informed consent form; LAR = legally authorized representative; M = month (month = 30 days); RSV = respiratory syncytial virus; SAE = serious adverse event; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; SC = safety phone call; USV = unscheduled visit; V = in-person visit.

a. Visit for participants who experience symptoms of RSV disease (USV for RSV surveillance) or discontinue/withdraw from the study.
b. Vital signs to be collected at USV include at minimum: temperature, respiratory rate, pulse oximetry (SpO_2), and heart rate.
c. A complete physical examination will be performed at the Re-enrollment Visit. A symptom-directed physical examination will be performed at unscheduled visits for RSV surveillance. Physical exam to be completed at RSV surveillance (unscheduled) visits include at minimum: Observation of breathing pattern and work of breathing, auscultation of the chest, hydration and perfusion status.
d. Trained study site staff will contact parent(s)/LAR(s) of all participants weekly via text message during the RSV season to remind the parent(s)/LAR(s) to call and report with any potential (any new or worsening) RSV-RTD symptoms.
e. Trained study site staff will collect information relating to any SAEs, AESI, and information on concomitant medications associated with those events, and any non-study vaccinations received.
f. Optional blood draw for antibody-mediated immunogenicity in participants with parent(s)/LAR(s) who have provided consent to the additional blood volume.
g. Participants will be followed from Part B Day 1 through EoS for RSV-suspected disease. Study staff will text parent(s)/LAR(s) weekly to remind them to call the site if child experiences any symptoms of an RSV-suspected disease (defined as congestion or runny nose for >24 hours, cough, difficulty breathing, or respiratory distress, including wheezing). Once the site is notified by parent(s)/LAR(s) of relevant symptoms, parent(s) or LAR(s) will be encouraged to bring the participant for an assessment visit,

preferably within 5 days of symptom(s) onset for evaluation and respiratory specimen collection. For assessment visits, evaluation and sample collections will be conducted for RSV and potentially for other respiratory viruses, including SARS-CoV-2.

h. An optional blood draw will occur 3 to 24 days after a confirmation of RSV-LRTD (following the USV or date of hospitalization, whichever is earlier) for cell-mediated and antibody-mediated immunogenicity in participants with parent(s)/LAR(s) who have provided consent to the additional blood volume.

9.9. Appendix I Estimands and Estimand Specifications

Table 6: Intercurrent Events

Label	Intercurrent Event Type
IcEv1 (Early discontinuation)	Discontinued early from study in Part A.
IcEv1b (Early discontinuation from Part B)	Discontinued early from study in Part B.
IcEv2 (Immune modifying medications in Part A)	Received of concomitant medications and/or vaccines deemed to affect the immune response in Part A. This includes RSV monoclonal antibody medications.
IcEv3 (Important protocol deviation impacting key study data in Part A)	Received wrong intervention dose, did not have a baseline immunogenicity assessment, did not have Day 29 postinjection immunogenicity assessment, or received immune modifying medication(s) before Day 29.
IcEv4 (Immunogenicity assessments falling out of visit window in Part A)	Had immunogenicity assessments falling out of analysis visit windows described in Appendix B.

Abbreviation: IcEv: intercurrent event.

Table 7: Summary of Primary Safety Estimands with Rationale for Strategies to Address Intercurrent Events

Objective: To evaluate the reactogenicity and safety of mRNA-1345 administered for Part A.			
Estimand Label	**Estimand 1a**	**Estimand 1b**	**Estimand 1c**
Estimand Description	• Proportion of participants reporting any solicited local ARs through 7 days after injection. • Proportion of participants reporting any solicited systemic ARs through 7 days after injection.	• Proportion of participants reporting any unsolicited AEs through 28 days after injection.	• Proportion of participants reporting any MAAEs up to Part A Month 6/EoS Visit. • Proportion of participants reporting any AESIs up to Part A Month 6/EoS Visit. • Proportion of participants reporting any SAEs up to Part A Month 6/EoS Visit • Proportion of participants reporting any AEs leading to discontinuation up to Part A Month 6/EoS Visit ..
Target Population	Participants 2 to <5 years of age (Part A Cohort 1) and participants 5 to <18 years of age at high risk of RSV disease (Part A Cohort 2) who receive the study intervention and contribute any solicited AR data.	Participants 2 to <5 years of age (Part A Cohort 1) and participants 5 to <18 years of age at high risk of RSV disease (Part A Cohort 2) who receive the study intervention.	Same as Estimand 1b.

Endpoint	• Incidence of solicited local ARs through 7 days after injection. • Incidence of solicited systemic ARs through 7 days after injection.	Incidence of unsolicited AEs through 28 days after injection.	• Incidence of MAAEs up to Part A Month 6/EoS Visit. • Incidence of AESIs up to Part A Month 6/EoS Visit. • Incidence of SAEs up to Part A Month 6/EoS Visit • Incidence of AEs leading to discontinuation up to Part A Month 6/EoS Visit
Treatment Conditions	Part A Cohort 1: mRNA-1345 CCI µg Part A Cohort 1: mRNA-1345 [redacted] µg Part A Cohort 1: mRNA-1345 [redacted] µg Part A Cohort 1: Placebo (Reference) Part A Cohort 2: mRNA-1345 CCI µg Part A Cohort 2: mRNA-1345 [redacted] µg Part A Cohort 2: mRNA-1345 [redacted] µg	Same as Estimand 1a.	Same as Estimand 1a.
Population-Level Summary	• Proportion of participants reporting any solicited local ARs through 7 days after injection by treatment group for each cohort. • Proportion of participants reporting any solicited systemic ARs through 7 days after injection by treatment group for each cohort.	• Proportion of participants reporting any unsolicited AEs through 28 days after injection by treatment group for each cohort.	• Proportion of participants reporting any MAAEs up to Part A Month 6/EoS Visit by treatment group for each cohort. • Proportion of participants reporting any AESIs up to Part A Month 6/EoS Visit by treatment group for each cohort. • Proportion of participants reporting any SAEs up to Part A Month 6/EoS Visit by treatment group for each cohort. • Proportion of participants reporting any AEs leading to discontinuation up to Part A Month 6/EoS Visit by treatment group for each cohort.
Intercurrent Event Strategy			
IcEv1 to IcEv4	Treatment Policy (Including all data collected)	Treatment Policy (Including all data collected)	Treatment Policy (Including all data collected)
Rationale for Strategies	Count all relevant safety events observed, irrespective of non-compliance of key protocol criteria.		

Objective: To evaluate the incidence of RSV-RTD during 6 months after re-enrollment for Part B	
Estimand Label	**Estimand 1d**
Estimand Description	• Proportion of participants reporting RSV-RTD. • Proportion of participants reporting RSV-LRTD. • Proportion of participants reporting severe RSV-LRTD. • Proportion of participants reporting RSV very severe LRTD. • Proportion of participants reporting RSV hospitalization.
Target Population	Participants 2 to <5 years of age (Part B Cohort 1) who receive the study intervention in Part A and re-enroll in Part B
Endpoint	• Incidence of RSV-RTD from Part B Day 1 to Part B EoS Visit. • Incidence of RSV-LRTD from Part B Day 1 to Part B EoS Visit. • Incidence of severe RSV-LRTD from Part B Day 1 to Part B EoS Visit. • Incidence of RSV very severe LRTD from Part B Day 1 to Part B EoS Visit. Incidence of RSV hospitalization from Part B Day 1 to Part B EoS Visit.
Treatment Conditions	Part B Cohort 1: mRNA-1345 CCI µg Part B Cohort 1: mRNA-1345 µg Part B Cohort 1: mRNA-1345 µg Part B Cohort 1: Placebo (Reference)
Population-Level Summary	• Proportion of participants reporting RSV-RTD by treatment group. • Proportion of participants reporting RSV-LRTD by treatment group. • Proportion of participants reporting severe RSV-LRTD by treatment group. • Proportion of participants reporting RSV very severe LRTD by treatment group. • Proportion of participants reporting RSV hospitalization by treatment group.
Intercurrent Event Strategy	
IcEv1b	Treatment Policy (Including all data collected)
Rationale for Strategies	Count all relevant safety events observed, irrespective of non-compliance of key protocol criteria.

Table 8: Summary of Secondary Immune Estimands with Rationale for Strategies to Address Intercurrent Events (Part A)

Objective: To evaluate the immunogenicity of a single injection of mRNA-1345

Estimand Label	Primary Immune Estimand 2a -1 (on the PP Set)	Supportive Immune Estimand 2a-2 (on the FAS Set)
Estimand Description	Immune response to mRNA-1345 RSV vaccine measured as GMT or GMC of serum RSV-A nAbs, RSV-B nAbs, RSV preF bAbs, and RSV postF bAbs at Day 1, Day 29, and Month 6/EoS (for Part A Cohort 1) in participants 2 to < 18 years of age who receive the planned dose of the study intervention, comply with the immunogenicity testing schedule, have a Baseline and Day 29 assessment, and have no important protocol deviations impacting the immune response.	Immune response to mRNA-1345 RSV vaccine measured as GMT of serum RSV-A and RSV-B nAbs at Day 1, Day 29, and Month 6/EoS (for Part A Cohort 1) in participants 2 to < 18 years of age who receive any study intervention dose, have a Baseline and at least 1 postinjection assessment irrespective of any important protocol deviations impacting the immune response.
Target Population	Participants 2 to <5 years of age (Part A Cohort 1) and participants 5 to <18 years of age at high risk of RSV disease (Part A Cohort 2) who receive the planned dose of the study intervention, comply with the immunogenicity testing schedule, have a Baseline and Day 29 assessment, and have no important protocol deviations impacting the immune response.	Participants 2 to <5 years of age (Part A Cohort 1) and participants 5 to <18 years of age at high risk of RSV disease (Part A Cohort 2) who receive any study intervention dose, have a Baseline and at least 1 postinjection assessment irrespective of any important protocol deviations impacting the immune response.
Endpoint	GMT or GMC of serum RSV-A nAbs, RSV-B nAbs, preF bAbs, and postF bAbs at Day 1, Day 29 and Month 6/EoS (for Part A Cohort 1).	Same as Estimand 2a-1.
Treatment Conditions	Cohort 1: mRNA-1345 CCI µg Cohort 1: mRNA-1345 [redacted] µg Cohort 1: mRNA-1345 [redacted] µg Cohort 1: Placebo (Reference) Cohort 2: mRNA-1345 CCI µg Cohort 2: mRNA-1345 [redacted] µg Cohort 2: mRNA-1345 [redacted] µg	Same as Estimand 2a-1.
Population-Level Summary	GMT or GMC of serum RSV-A nAbs, RSV-B nAbs, preF bAbs, and postF bAbs will be provided at Baseline (Day 1), Day 29, and Month 6/EoS (for Part A Cohort 1) by treatment group for each cohort.	Same as Estimand 2a-1.
Intercurrent Event Strategy		
IcEv1 (Early discontinuation)	Treatment policy (Including all data collected)	Treatment policy (Including all data collected)
IcEv2 (Immune modifying medications)	Hypothetical (Excluding related data)	Treatment policy (Including all data collected)

IcEv3 (Important protocol deviation impacting key study data)	Principal stratum (Excluding participants)	Treatment policy (Including all data collected)
IcEv4 (Immunogenicity assessments falling out of visit window)	Hypothetical (Excluding related data)	Treatment policy (Including all data collected)
Rationale for Strategies	This estimand seeks to understand immune response in participants who receive the planned dose of study intervention dose and comply with key protocol criteria. A principal stratum is used to exclude participants with important protocol deviations impacting key study data so that analysis is a sub-population composed of participants free from such intercurrent events. For early discontinuation, all collected data are included. For participants receiving immune modifying medications, all immunogenicity assessments after the start of the medications will be excluded. Immunogenicity assessments falling out of visit window will be excluded from that visit	A treatment policy strategy is used for following up immune response including all participants who receive any study intervention dose irrespective of whether they subsequently were found not to strictly meet the key protocol criteria. There is interest in understanding immune response in the light of poor compliance which may happen in clinical practice.
Estimand Label	**Primary Immune Estimand 2b-1 (on the PP Set)**	**Supportive Immune Estimand 2b-2 (on the FAS Set)**
Estimand Description	Immune response to mRNA-1345 RSV vaccine measured as GMFR of postbaseline/baseline nAb titers and bAb concentrations at Day 29, and Month 6/EoS (for Part A Cohort 1) in participants 2 to < 18 years of age who receive the planned dose of the study intervention, comply with the immunogenicity testing schedule, have a Baseline and Day 29 assessment, and have no important protocol deviations impacting the immune response.	Immune response to mRNA-1345 RSV vaccine measured as GMFR of postbaseline/baseline nAb titers and bAb concentrations at Day 29, and Month 6/EoS (for Part A Cohort 1) in participants 2 to < 18 years of age who receive any study intervention dose, have a Baseline and at least 1 postinjection assessment irrespective of any important protocol deviations impacting the immune response.
Target Population	Same as Estimand 2a-1	Same as Estimand 2a-2
Endpoint	GMFR of postbaseline/baseline nAb titers and bAb concentrations at Day 29 and Month 6/EoS (for Part A Cohort 1).	Same as Estimand 2b-1.
Treatment Conditions	Same as Estimand 2a-1	Same as Estimand 2a-1.

Population-Level Summary	GMFR of postbaseline/baseline nAb titers and bAb concentrations will be provided at Day 29, and Month 6/EoS (for Part A Cohort 1) by treatment group for each cohort.	Same as Estimand 2b-1.
Intercurrent Event Strategy		
IcEv1 (Early discontinuation)	Treatment policy (Including all data collected)	Treatment policy (Including all data collected)
IcEv2 (Immune modifying medications)	Hypothetical (Excluding related data)	Treatment policy (Including all data collected)
IcEv3 (Important protocol deviation impacting key study data)	Principal stratum (Excluding participants)	Treatment policy (Including all data collected)
IcEv4 (Immunogenicity assessments falling out of visit window)	Hypothetical (Excluding related data)	Treatment policy (Including all data collected)
Rationale for Strategies	Same as Estimand 2a-1.	Same as Estimand 2a-2.
Estimand Label	**Primary Immune Estimand 2c-1 (on the PP Set)**	**Supportive Immune Estimand 2c-2 (on the FAS Set)**
Estimand Description	Immune response to mRNA-1345 RSV vaccine measured as proportion with ≥4-fold increases in nAb titers and bAb concentrations from Baseline at Day 29, and Month 6/EoS (for Part A Cohort 1) in participants 2 to < 18 years of age who receive the planned dose of the study intervention, comply with the immunogenicity testing schedule, have a Baseline and Day 29 assessment, and have no important protocol deviations impacting the immune response.	Immune response to mRNA-1345 RSV vaccine measured as proportion with ≥4-fold increases in nAb titers and bAb concentrations from Baseline at Day 29, and Month 6/EoS (for Part A Cohort 1) in participants 2 to < 18 years of age who receive any study intervention dose, have a Baseline and at least 1 post-injection assessment irrespective of any important protocol deviations impacting the immune response.
Target Population	Same as Estimand 2a-1	Same as Estimand 2a-2
Endpoint	Proportion of participants with a seroresponse from Baseline in nAb titers and bAb concentrations at Day 29 and Month 6/EoS (for Part A Cohort 1).	Same as Estimand 2c1.

Treatment Conditions	Same as Estimand 2a-1	Same as Estimand 2a-1.
Population-Level Summary	Proportion of participants with a seroresponse from Baseline in nAb titers and bAb concentrations at Day 29, and Month 6/EoS (for Part A Cohort 1) by treatment group for each cohort.	Same as Estimand 2c-1.
Intercurrent Event Strategy		
IcEv1 (Early discontinuation)	Treatment policy (Including all data collected)	Treatment policy (Including all data collected)
IcEv2 (Immune modifying medications)	Hypothetical (Excluding related data)	Treatment policy (Including all data collected)
IcEv3 (Important protocol deviation impacting key study data)	Principal stratum (Excluding participants)	Treatment policy (Including all data collected)
IcEv4 (Immunogenicity assessments falling out of visit window)	Hypothetical (Excluding related data)	Treatment policy (Including all data collected)
Rationale for Strategies	Same as Estimand 2a-1.	Same as Estimand 2a-2.

Table 9: Summary of Secondary Safety Estimands with Rationale for Strategies to Address Intercurrent Events (Part B)

Objective: To evaluate the safety of a single study injection administered in Part A during 6 months after re-enrollment in Part B.	
Estimand Label	**Estimand 2d**
Estimand Description	• Proportion of participants reporting any AESIs from Part B Day 1 to Part B EoS Visit. • Proportion of participants reporting any SAEs from Part B Day 1 to Part B EoS Visit.
Target Population	Participants 2 to <5 years of age (Part B Cohort 1) who receive the study intervention in Part A and re-enroll in Part B

Endpoint	• AESIs from Part B Day 1 to Part B EoS Visit. • SAEs from Part B Day 1 to Part B EoS Visit.
Treatment Conditions	Part B Cohort 1: mRNA-1345 CCI µg Part B Cohort 1: mRNA-1345 µg Part B Cohort 1: mRNA-1345 µg Part B Cohort 1: Placebo (Reference)
Population-Level Summary	• Proportion of participants reporting any AESIs from Part B Day 1 to Part B EoS Visit by treatment group. • Proportion of participants reporting any SAEs from Part B Day 1 to Part B EoS Visit by treatment group.
Intercurrent Event Strategy	
IcEv1b	Treatment Policy (Including all data collected)
Rationale for Strategies	Count all relevant safety events observed, irrespective of non-compliance of key protocol criteria.

9.10. Appendix J Definition of AE of Clinical Interest by SMQ

Table 10: AE of Clinical Interest by SMQ to be applied

SMQ	Broad/Narrow Search	SMQ Search Criteria
Anaphylactic Reaction	Broad/Narrow	Specified PT terms and algorithmic approach specified in Table 11
Angioedema	Broad/Narrow	Specific PT terms
Arthritis	Broad/Narrow	Specific PT terms
Cardiac Arrhythmia	Broad/Narrow	Specific PT terms
Cardiac Failure	Broad/Narrow	Specific PT terms
Cardiomyopathy	Broad/Narrow	Specific PT terms
Central Nervous System Vascular Disorders	Broad/Narrow	Specific PT terms
Convulsions	Broad/Narrow	Specific PT terms
Demyelination	Broad/Narrow	Specific PT terms
Embolic and Thrombotic Events	Broad/Narrow	Specific PT terms
Guillain-Barre Syndrome	Broad/Narrow	Specific PT terms
Haematopoietic Cytopenias	Broad/Narrow	Specific PT terms
Hearing and Vestibular disorders	Broad/Narrow	Specific PT terms
Hypersensitivity	Broad/Narrow	Specific PT terms
Immune-mediated/Autoimmune disorders	Broad/Narrow	Specific PT terms
Ischemic Heart Disease	Broad/Narrow	Specific PT terms
Noninfectious Myocarditis/Pericarditis	Broad/Narrow	Specific PT terms
Peripheral Neuropathy	Broad/Narrow	Specific PT terms
Thrombophlebitis	Broad/Narrow	Specific PT terms
Vasculitis	Broad/Narrow	Specific PT terms

Table 11: Algorithmic Approach for Anaphylactic Reaction

The following criteria will be used to determine anaphylactic reaction:

- A term from Category A
- A term from Category B (Upper Airway/Respiratory) and a term from Category C (Angioedema/Urticaria/Pruritus/Flush) that occurred within 24 hours of each other.
- A term from Category D (Cardiovascular/Hypotension) and at least one of the following:
    - A term from Category B (Upper Airway/Respiratory) that occurred within 24 hours of each other.
    - A term from Category C (Angioedema/Urticaria/Pruritus/Flush) that occurred within 24 hours of each other.

Anaphylactic Reaction		
Category	**Scope**	**PT Search Term**
A	Narrow	Anaphylactic reaction
A	Narrow	Anaphylactic shock
A	Narrow	Anaphylactic transfusion reaction
A	Narrow	Anaphylactoid reaction
A	Narrow	Anaphylactoid shock
A	Narrow	Circulatory collapse
A	Narrow	Dialysis membrane reaction
A	Narrow	Kounis syndrome
A	Narrow	Procedural shock
A	Narrow	Shock
A	Narrow	Shock symptom
A	Narrow	Type I hypersensitivity
B	Broad	Asthma
B	Broad	Bronchial oedema
B	Broad	Bronchospasm
B	Broad	Cardio-respiratory distress
B	Broad	Chest discomfort
B	Broad	Choking
B	Broad	Choking sensation
B	Broad	Circumoral oedema
B	Broad	Cough
B	Broad	Cough variant asthma
B	Broad	Cyanosis
B	Broad	Dyspnoea
B	Broad	Hyperventilation

B	Broad	Irregular breathing
B	Broad	Laryngeal dyspnoea
B	Broad	Laryngeal oedema
B	Broad	Laryngospasm
B	Broad	Laryngotracheal oedema
B	Broad	Mouth swelling
B	Broad	Nasal obstruction
B	Broad	Oedema mouth
B	Broad	Oropharyngeal oedema
B	Broad	Oropharyngeal spasm
B	Broad	Oropharyngeal swelling
B	Broad	Pharyngeal oedema
B	Broad	Pharyngeal swelling
B	Broad	Respiratory arrest
B	Broad	Respiratory distress
B	Broad	Respiratory failure
B	Broad	Reversible airways obstruction
B	Broad	Sensation of foreign body
B	Broad	Sneezing
B	Broad	Stridor
B	Broad	Swollen tongue
B	Broad	Tachypnoea
B	Broad	Throat tightness
B	Broad	Tongue oedema
B	Broad	Tracheal obstruction
B	Broad	Tracheal oedema
B	Broad	Upper airway obstruction
B	Broad	Vaccine associated enhanced respiratory disease
B	Broad	Wheezing
C	Broad	Allergic oedema
C	Broad	Angioedema
C	Broad	Circumoral swelling
C	Broad	Erythema
C	Broad	Eye oedema
C	Broad	Eye pruritus
C	Broad	Eye swelling
C	Broad	Eyelid oedema
C	Broad	Face oedema

C	Broad	Flushing
C	Broad	Injection site urticaria
C	Broad	Lip oedema
C	Broad	Lip swelling
C	Broad	Nodular rash
C	Broad	Ocular hyperaemia
C	Broad	Oedema
C	Broad	Oedema blister
C	Broad	Periorbital oedema
C	Broad	Periorbital swelling
C	Broad	Pruritus
C	Broad	Pruritus allergic
C	Broad	Rash
C	Broad	Rash erythematous
C	Broad	Rash pruritic
C	Broad	Skin swelling
C	Broad	Swelling
C	Broad	Swelling face
C	Broad	Swelling of eyelid
C	Broad	Urticaria
C	Broad	Urticaria papular
D	Broad	Blood pressure decreased
D	Broad	Blood pressure diastolic decreased
D	Broad	Blood pressure systolic decreased
D	Broad	Cardiac arrest
D	Broad	Cardio-respiratory arrest
D	Broad	Cardiovascular insufficiency
D	Broad	Diastolic hypotension
D	Broad	Hypotension
D	Broad	Hypotensive crisis
D	Broad	Post procedural hypotension

9.11. Appendix L Medical Conditions or Adverse Events to be Presented by SOC/HLGT/PT

Table 12: Medical Conditions or Adverse Events to be Presented by SOC/HLGT/PT

SOC	HLGT
Cardiac Disorders	Cardiac arrhythmias
	Cardiac disorders, signs and symptoms, NEC
	Cardiac neoplasms
	Cardiac valve disorders
	Coronary artery disorders
	Endocardial disorders
	Heart failures
	Myocardial disorders
	Pericardial disorders
Nervous System Disorders	Peripheral neuropathies
	PT: Guillain-Barré Syndrome *
	Demyelinating disorders
	PT: Acute disseminated encephalomyelitis *
	Seizures (incl subtypes)
Nervous System Disorders	Central nervous system infections and inflammations
Immune System Disorders	Allergic conditions
	PT: Anaphylactic reaction *

*Only the PT under the HLGT will be presented.

9.12. Appendix M Detailed Case Definitions for RSV for Data Analysis

Table 13: Detailed Case Definitions for RSV for Data Analysis

Case	Definition	Full list to be considered
RSV-RTD	Runny nose **OR** blocked nose **OR** cough AND Confirmed RSV infection[a]	Symptom log (Runny Nose, Blocked Nose, Cough) AND Confirmed RSV infection[a]
RSV-LRTD	Cough **OR** difficulty breathing[b] AND SpO_2 <95%[c], **OR** RR increase[d] AND Confirmed RSV infection[a]	Symptom log (Cough, Difficulty Breathing, New or increased wheezing, Chest indrawing, Failure to respond/unconscious) **OR** Respiratory Exam (Wheezing, chest indrawing, failure to respond/unconscious) AND SpO_2 < 95%[c], **OR** RR increase[d] AND Confirmed RSV infection[a]
RSV Severe LRTD	Meeting the case definition of RSV-LRTD AND SpO_2 <93%[c], **OR** lower chest wall in-drawing	LRTD: Symptom log (Cough, Difficulty Breathing, New or increased wheezing, Chest indrawing, Failure to respond/unconscious) **OR** Respiratory Exam (Wheezing, chest indrawing, failure to respond/unconscious) AND SpO_2 < 95%[c], **OR** RR increase[d] AND Confirmed RSV infection[a] AND Severe LRTD SpO_2 < 93%[c], **OR** Respiratory exam (Chest indrawing)

RSV Very Severe LRTD	Meeting the case definition of RSV-LRTD AND SpO_2 <90%[c], **OR** failure to respond/unconscious	LRTD: Symptom log (Cough, Difficulty Breathing, New or increased wheezing, Chest indrawing, Failure to respond/unconscious) **OR** Respiratory Exam (Wheezing, chest indrawing, failure to respond/unconscious) AND SpO_2 < 95%[c], **OR** RR increase[d] AND Confirmed RSV infection[a] AND Very severe LRTD SpO_2 < 90%[c], **OR** Symptom log (Failure to respond/unconscious) **OR** Respiratory exam (Failure to respond/unconscious)
RSV Hospitalization	Confirmed RSV[a,e] AND Hospitalized for acute medical condition[f]	Confirmed RSV[a,e] AND Hospitalized for acute medical condition[f]

Abbreviations: BPM = beats per minute; LRTD = lower respiratory tract disease; RT-PCR = reverse transcription polymerase chain reaction; RR = respiratory rate; RSV = respiratory syncytial virus; RTD = respiratory tract disease; SpO_2 = blood oxygen saturation.

a. RSV infection confirmed on nasal swab positive by positive RT-PCR or other local laboratory tests.
b. Based on observation by Investigator; difficulty breathing includes signs of wheezing, stridor, tachypnoea, chest in-drawing or subcostal or intercostal retractions.
c. For SpO_2, the lowest stable value monitored will be used.
d. RR increased defined as >38 BPM for 2- to <3-year-olds, >33 BPM for -3 to <4-year-olds, and >29 BPM for ≥4-year-olds per 99th percentiles for age (Fleming et al 2011).
e. RSV sampling and testing is based on medical judgment of medical practitioner or driven by algorithm.
f. Hospitalization is defined as a medical decision in which the participant requires overnight admission for observation or treatment.

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PPD , ModernaTX, Inc	 Signature	05-Jun-2025 Date
PPD , ModernaTX, Inc	 Signature	09-Jun-2025 Date

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