Collaborative Influenza Vaccine Innovation Centers

STATISTICAL ANALYSIS PLAN
for
DMID Protocol: 20-0009
Study Title:

A Phase 1b, Double-Blind, Randomized, Dose-Escalating, Age De-Escalating, Placebo-Controlled Study to Assess the Safety and Immunogenicity of One or Two Doses of Sing2016 M2SR H3N2 Influenza Vaccine Delivered Intranasally in a Healthy Pediatric Population 6 Months through 17 Years of Age

NCT04960397

Version 1.0

DATE: 13-Aug-2024

STUDY TITLE

Protocol Number Code:	**DMID Protocol: 20-0009**
Development Phase:	Phase 1b
Products:	Sing2016 M2SR H3N2, SPG-NaCl buffer, seasonal inactivated influenza vaccine (IIV4), MAD300 sprayer device, and sodium chloride placebo
Form/Route:	Intranasally (except IIV4, administered intramuscularly)
Indication Studied:	Influenza
Sponsor:	Division of Microbiology and Infectious Diseases Division of Allergy, Immunology, and Transplantation National Institute of Allergy and Infectious Diseases National Institutes of Health
Clinical Trial Initiation Date:	September 10, 2021
Clinical Trial Completion Date:	April 13, 2024
Date of the Analysis Plan:	August 13, 2024
Version Number:	1.0

This study was performed in compliance with Good Clinical Practice.

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LIST OF ABBREVIATIONS

AE	Adverse Event
BAMA	Binding Antibody Multiplex Assay
C	Celsius
CDC	Center for Disease Control and Prevention
CI	Confidence Interval
COVID-19	Coronavirus Disease 2019
CSR	Clinical Study Report
DMID	Division of Microbiology and Infectious Diseases
ECL	Electrochemiluminescence
EDC	Electronic Data Capture
ELISA	Enzyme-linked Immunosorbent Assay
F	Fahrenheit
FDA	Food and Drug Administration
GMT	Geometric Mean Titer
GMFR	Geometric Mean Fold Rise
HAI	Hemagglutination Inhibition
ICH	International Conference on Harmonisation
IRB	Institutional Review Board
ITT	Intention to Treat
L	Liter
LOD	Lower Limit of Detection
LLOQ	Lower Limit of Quantification
MedDRA	Medical Dictionary for Regulatory Activities
mITT	Modified Intention to Treat
mL	Milliliter
MN	Microneutralization
N	Number (typically refers to Participants)

List of Abbreviations *(continued)*

NA	Neuraminidase
NAI	Neuraminidase Inhibition
PI	Principal Investigator
PP	Per Protocol
PT	Preferred Term
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SDMCC	Statistical and Data Management Coordinating Center
sIgA	Secretory IgA
SMC	Safety Monitoring Committee
SOC	System Organ Class
SRC	Safety Review Committee
ULOD	Upper Limit of Detection

1. PREFACE

The Statistical Analysis Plan (SAP) for "A Phase 1b, Double-Blind, Randomized, Dose-Escalating, Age De-Escalating, Placebo-Controlled Study to Assess the Safety and Immunogenicity of One or Two Doses of Sing2016 M2SR H3N2 Influenza Vaccine Delivered Intranasally in a Healthy Pediatric Population 6 Months through 17 Years of Age" (Division of Microbiology and Infectious Diseases [DMID] Protocol 20-0009) describes and expands upon the statistical information presented in the protocol.

This document describes all planned analyses and provides reasons and justifications for these analyses. It also includes sample tables, listings, and figures planned for the final analyses. Regarding the final analyses and Clinical Study Report (CSR), this SAP follows the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Guidelines, as indicated in Topic E3 (Structure and Content of Clinical Study Reports), and more generally is consistent with Topic E8 (General Considerations for Clinical Trials) and Topic E9 (Statistical Principles for Clinical Trials). The structure and content of the SAP provides sufficient detail to meet the requirements identified by the Food and Drug Administration (FDA) and ICH, while all work planned and reported for this SAP will follow internationally accepted guidelines published by the American Statistical Association and the Royal Statistical Society for statistical practice.

This document contains five broad sections: (1) a description of the purpose and timing(s) of analyses; (2) a description of the study design, its objectives; and the variables collected/assessed to be used in analyses; (3) general statistical principles; (4) comprehensive statistical analysis methods for study outcomes, and (5) a list of proposed tables and figures along with mock-ups (Appendices I, II, and III). Any deviation from this SAP will be described and justified in protocol amendments and/or in the CSR, as appropriate. The reader of this SAP is encouraged to also review the study protocol for details on conduct of the study and the operational aspects of clinical assessments.

2. INTRODUCTION

2.1. Purpose of the Analyses

Final analyses will assess the safety, tolerability/reactogenicity, and immunogenicity of the Sing2016 M2SR H3N2 vaccine at various doses for pediatrics aged 2 to 17 years as compared to saline placebo. The clinical study report will be generated after all primary and secondary endpoint data are available, the data have been cleaned, and the clinical database has been locked. Available exploratory endpoint data may be included as well, and remaining analyses will be presented in an addendum to the CSR after those data are available.

The protocol for DMID 20-0009 called for planned interim safety analyses and planned interim immunogenicity analyses. The planned interim safety analyses were performed to assess the safety prior to progressing to subsequent cohorts. The purpose of the planned interim immunogenicity analyses was to present the pharmaceutical partner with immunological response results for planning for future studies. Additional details about these interim analyses, including timing, can be found in Section 5.6.1. Analysis plans for interim immunogenicity analyses were defined in memorandums. The Interim Analysis Report and Addendums Part 1 and 2 were submitted to the IND in SN0046 on May 16, 2024.

3. STUDY OBJECTIVES AND ENDPOINTS

3.1. Study Objectives

Primary

- (Safety) To assess the safety and tolerability of one or two administrations of the Sing2016 M2SR H3N2 influenza vaccine at 10^8, or 10^9 $TCID_{50}$ delivered intranasally to healthy participants, 2 to 17 years of age

Secondary

- (Immunogenicity) To assess the humoral immunogenicity (serum antibody and mucosal antibody responses) directed against homologous viral strains after one or two administrations of Sing2016 M2SR H3N2 influenza vaccine at 10^8, or 10^9 $TCID_{50}$ delivered intranasally to healthy participants, 2 to 17 years of age

Exploratory

- (Immunogenicity) To assess the cellular immunogenicity (T-cell immune responses) against Sing2016 M2SR H3N2 influenza vaccine following one or two administrations of Sing2016 M2SR H3N2 influenza vaccine at 10^8, and 10^9 $TCID_{50}$ delivered intranasally to healthy participants, 2 to 17 years of age
- (Immunogenicity) To assess participant immunological response to neuraminidase (NA) following one and two administrations of Sing2016 M2SR H3N2 influenza vaccine at 10^8, or 10^9 $TCID_{50}$ delivered intranasally to healthy participants, 2 to 17 years of age
- (Immunogenicity) To assess the humoral immunogenicity (serum and/or plasma antibody) and mucosal antibody responses, and cellular immunogenicity (T-cell responses) after seasonal influenza vaccine (IIV4) following one or two administrations of Sing2016 M2SR H3N2 influenza vaccine at 10^8, and 10^9 $TCID_{50}$ delivered intranasally to healthy participants, 2 to 17 years of age
- (Immunogenicity) To assess mucosal antibody responses directed against homologous viral strains after one or two administrations of Sing2016 M2SR H3N2 influenza vaccine at 10^8, or 10^9 $TCID_{50}$ delivered intranasally to healthy participants, 2 to 17 years of age
- (Immunogenicity) To assess humoral immunogenicity (serum and/or plasma antibody), and mucosal antibody responses) directed against heterologous viral strains of one or two administrations of Sing2016 M2SR H3N2 influenza vaccine at 10^8 or 10^9 $TCID_{50}$ delivered intranasally to healthy participants, 2 to 17 years of age
- (Immunogenicity) To conduct additional characterization of humoral immunity against homologous and/or heterologous viral strains (e.g., extra-neutralizing antibody function) following one or two administrations of Sing2016 M2SR H3N2 influenza vaccine at 10^8, and 10^9 $TCID_{50}$ delivered intranasally to healthy participants, 2 to 17 years of age
- (Immunogenicity) To assess the effects of age, dose level, sex, prior receipt of seasonal influenza vaccine(s), and other variables on humoral immunogenicity (serum antibody and mucosal antibody responses) directed against homologous viral strains of one or two administrations of Sing2016 M2SR

H3N2 influenza vaccine at 10^8, and 10^9 $TCID_{50}$ delivered intranasally to healthy participants, 2 to 17 years of age

3.2. Endpoints

Primary

- (Safety) The number and percentage of study participants in Cohorts 1-4 each and across Cohorts 1-4 who experience solicited local reactogenicity events, of all severity grades and by grade, in the 7 days following administration of each dose of vaccine
- (Safety) The number and percentage of study participants in Cohorts 1-4 each and across Cohorts 1-4 who experience solicited systemic reactogenicity events, of all severity grades and by grade, in the 7 days following administration of each dose of vaccine
- (Safety) The number and percentage of study participants in Cohorts 1-4 each and across Cohorts 1-4 who experience unsolicited non-serious adverse events, of all severity grades and by grade, in the 28 days following administration of each dose of vaccine
- (Safety) The number and percentage of study participants in Cohorts 1-4 each and across Cohorts 1-4 who experience adverse events of special interest (AESIs) from the time of first vaccination through the end of the study period (final visit in the month of April of the calendar year following enrollment)
- (Safety) The number and percentage of study participants in Cohorts 1-4 each and across Cohorts 1-4 who experience Serious Adverse Events (SAEs) from the time of first vaccination through the end of the study period (final visit in the month of April of the calendar year following enrollment)
- (Safety) The number and percentage of study participants in Cohorts 1-4 each and across Cohorts 1-4 who experience new-onset chronic medical conditions (NOCMCs) from the time of the first study vaccination through the end of the study period (final visit in the month of April of the calendar year following enrollment)

Secondary

- (Immunogenicity) The number and percentage of participants in Cohorts 1, 2, and 3 with putative seroprotection at baseline (Day 1) and on approximately Day 29, defined as an HAI titer ≥1:40 in serum against an H3N2 M2SR-like virus
- (Immunogenicity) The number and percentage of participants in Cohort 4 with putative seroprotection at baseline (Day 1) and on approximately Day 57, defined as an HAI titer ≥1:40 in serum against an H3N2 M2SR-like virus
- (Immunogenicity) The number and percentage of participants in Cohorts 1, 2, 3 with neutralization titer ≥1:40 in serum against an H3N2 M2SR-like virus on approximately Day 29
- (Immunogenicity) The number and percentage of participants in Cohort 4 with neutralization titer ≥1:40 in serum against an H3N2 M2SR-like virus at baseline (Day 1) and on approximately Day 57
- (Immunogenicity) Geometric Mean Titers (GMTs) of serum HAI against an H3N2 M2SR-like virus at baseline (Day 1) and on approximately Day 29 for participants in Cohorts 1, 2, and 3
- (Immunogenicity) Geometric Mean Titers (GMTs) of serum HAI against an H3N2 M2SR-like virus at baseline (Day 1) and on approximately Day 57 for participants in Cohort 4

- (Immunogenicity) Geometric Mean Titers (GMTs) of serum neutralizing antibodies against an H3N2 M2SR-like virus for participants in Cohorts 1, 2, and 3 at baseline (Day 1) and on approximately Day 29
- (Immunogenicity) Geometric Mean Titers (GMTs) in serum neutralizing antibodies against an H3N2 M2SR-like virus for participants in Cohort 4 at baseline (Day 1) and on approximately Day 57
- (Immunogenicity) Geometric Mean Fold Rise (GMFR) and proportions in serum with greater than or equal to 2- and 4-fold rises from baseline (Day 1) in HAI titers against an H3N2 M2SR-like virus for participants in Cohorts 1, 2, and 3 on approximately Day 29
- (Immunogenicity) Geometric Mean Fold Rise (GMFR) and proportions in serum with greater than or equal to 2- and 4-fold rises from baseline (Day 1) in HAI titers against an H3N2 M2SR-like virus for participants in Cohort 4 on approximately Day 57
- (Immunogenicity) Geometric Mean Fold Rise (GMFR) and proportions with greater than or equal to 2- and 4-fold rises from baseline (Day 1) in serum neutralization titers against an H3N2 M2SR-like virus for participants in Cohorts 1, 2, and 3 on approximately Day 29
- (Immunogenicity) Geometric Mean Fold Rise (GMFR) and proportions with greater than or equal to 2- and 4-fold rises from baseline (Day 1) in serum neutralization titers against an H3N2 M2SR-like virus for participants in Cohort 4 on approximately Day 57
- (Immunogenicity) Mean secretory IgA (sIgA) responses, as measured by the binding antibody multiplex assay (BAMA) in nasal lavage specimens, against an H3N2 M2SR-like virus for participants in Cohorts 1, 2, and 3 before vaccination and on approximately Day 29
- (Immunogenicity) Mean secretory IgA (sIgA) responses, as measured by the binding antibody multiplex assay (BAMA) in nasal lavage specimens, against an H3N2 M2SR-like virus for participants in Cohort 4 before vaccination and on approximately Day 57
- (Immunogenicity) Mean change (difference) from baseline in secretory IgA (sIgA) responses, as measured by the binding antibody multiplex assay (BAMA) in nasal lavage specimens, against an H3N2 M2SR-like virus for participants in Cohorts 1, 2, and 3 on approximately Day 29
- (Immunogenicity) Mean change (difference) from baseline in secretory IgA (sIgA) responses, as measured by the binding antibody multiplex assay (BAMA) in nasal lavage specimens, against an H3N2 M2SR-like virus for participants in Cohort 4 on approximately Day 57

Exploratory

- (Immunogenicity) Antigen-specific T-cell responses to vaccine immunogens, at baseline (Day 1) and following one or two doses of vaccine
- (Immunogenicity) Humoral antibody, as detected by one or more assays that measure responses to NA, at baseline (Day 1) and following one or two doses of vaccine or IIV4
- (Immunogenicity) Serum antibody, as detected by HAI and neutralization, directed against homologous H3N2 strains at baseline (Day 1) and after IIV4 administration
- (Immunogenicity) Antigen-specific T-cell responses to vaccine immunogens, at baseline (Day 1) and measured after IIV4 administration

- (Immunogenicity) Serum antibody to additional influenza antigens, as detected by multiplex ELISA assays and/or protein microarrays with subsequent evaluation of HAI and neutralization when multiplex ELISA screen is positive, directed against heterologous strains at baseline (Day 1) and following one or two doses of Sing2016 M2SR H3N2 vaccine
- (Immunogenicity) Humoral and/or mucosal antibody neutralizing and extra-neutralizing function against homologous and heterologous strains based on positive responses detected by methods described above
- (Immunogenicity) Associations between serum antibody responses and age, dose level, sex, prior receipt of seasonal influenza vaccine(s) and other variables over time.
- (Immunogenicity) Associations between mucosal antibody responses and age, dose level, sex, prior receipt of seasonal influenza vaccine(s) and other variables over time.
- (Immunogenicity) Geometric Mean Titers (GMTs) of plasma HAI against an H3N2 M2SR-like virus at baseline (Day 1) and on approximately Day 29 for participants in Cohorts 1, 2, and 3
- (Immunogenicity) Geometric Mean Titers (GMTs) of plasma HAI against an H3N2 M2SR-like virus at baseline (Day 1) and on approximately Day 57 for participants in Cohort 4
- (Immunogenicity) Geometric Mean Titers (GMTs) of plasma neutralizing antibodies against an H3N2 M2SR-like virus for participants in Cohorts 1, 2, and 3 at baseline (Day 1) and on approximately Day 29
- (Immunogenicity) Geometric Mean Titers (GMTs) of plasma neutralizing antibodies against an H3N2 M2SR-like virus for participants in Cohort 4 at baseline (Day 1) and on approximately Day 57
- (Immunogenicity) Geometric Mean Fold Rise (GMFR) and proportions with greater than or equal to 2- and 4-fold rises from baseline (Day 1) in plasma HAI titers against an H3N2 M2SR-like virus for participants in Cohorts 1, 2, and 3 on approximately Day 29
- (Immunogenicity) Geometric Mean Fold Rise (GMFR) and proportions with greater than or equal to 2- and 4-fold rises from baseline (Day 1) in plasma HAI titers against an H3N2 M2SR-like virus for participants in Cohort 4 on approximately Day 57
- (Immunogenicity) Geometric Mean Fold Rise (GMFR) and proportions with greater than or equal to 2- and 4-fold rises from baseline (Day 1) in plasma neutralization titers against an H3N2 M2SR-like virus for participants in Cohorts 1, 2, and 3 on approximately Day 29
- (Immunogenicity) Geometric Mean Fold Rise (GMFR) and proportions with greater than or equal to 2- and 4-fold rises from baseline (Day 1) in plasma neutralization titers against an H3N2 M2SR-like virus for participants in Cohort 4 on approximately Day 57
- (Immunogenicity) The number and percentage of participants in Cohorts 1, 2, and 3 with putative seroprotection at baseline (Day 1) and on approximately Day 29, defined as a plasma HAI titer ≥1:40 against an H3N2 M2SR-like virus
- (Immunogenicity) The number and percentage of participants in Cohort 4 with putative seroprotection at baseline (Day 1) and on approximately Day 57, defined as a plasma HAI titer ≥1:40 against an H3N2 M2SR-like virus

- (Immunogenicity) The number and percentage of participants in Cohorts 1, 2, 3 with plasma neutralization titer ≥1:40 against an H3N2 M2SR-like virus at baseline (Day 1) and on approximately Day 29
- (Immunogenicity) The number and percentage of participants in Cohort 4 with plasma neutralization titer ≥1:40 against an H3N2 M2SR-like virus at baseline (Day 1) and on approximately Day 57
- (Immunogenicity) Geometric mean titers (GMTs) in secretory IgA (sIgA) endpoint titers, as measured by the enzyme-linked immunosorbent assay (ELISA) in nasal lavage specimens, against an H3N2 M2SR-like virus for participants in Cohorts 1, 2, and 3 at baseline (Day 1, before vaccination) and on approximately Day 29
- (Immunogenicity) Geometric mean titers (GMTs) in secretory IgA (sIgA) endpoint titers, as measured by the enzyme-linked immunosorbent assay (ELISA) in nasal lavage specimens, against an H3N2 M2SR-like virus for participants in Cohort 4 at baseline (Day 1, before vaccination) and on approximately Day 57
- (Immunogenicity) Geometric mean fold rise (GMFR) and proportions with greater than or equal to 2- and 4-fold rises from baseline (Day 1) in secretory IgA (sIgA) endpoint titers, as measured by the enzyme-linked immunosorbent assay (ELISA) in nasal lavage specimens, against an H3N2 M2SR-like virus for participants in Cohorts 1, 2, and 3 on approximately Day 29
- (Immunogenicity) Geometric mean fold rise (GMFR) and proportions with greater than or equal to 2- and 4-fold rises from baseline (Day 1) in secretory IgA (sIgA) endpoint titers, as measured by the enzyme-linked immunosorbent assay (ELISA) in nasal lavage specimens, against an H3N2 M2SR-like virus for participants in Cohort 4 on approximately Day 57
- (Immunogenicity) Mean total secretory IgA (sIgA), as measured by the enzyme-linked immunosorbent assay (ELISA) in nasal lavage specimens, against an H3N2 M2SR-like virus for participants in Cohorts 1, 2, and 3 at baseline (Day 1, before vaccination) and on approximately Day 29
- (Immunogenicity) Mean total secretory IgA (sIgA), as measured by the enzyme-linked immunosorbent assay (ELISA) in nasal lavage specimens, against an H3N2 M2SR-like virus for participants in Cohort 4 at baseline (Day 1, before vaccination) and on approximately Day 57
- (Immunogenicity) Mean change (difference) from baseline in total secretory IgA (sIgA), as measured by the enzyme-linked immunosorbent assay (ELISA) in nasal lavage specimens, against an H3N2 M2SR-like virus for participants in Cohorts 1, 2, and 3 on approximately Day 29
- (Immunogenicity) Mean change (difference) from baseline in total secretory IgA (sIgA), as measured by the enzyme-linked immunosorbent assay (ELISA) in nasal lavage specimens, against an H3N2 M2SR-like virus for participants in Cohort 4 on approximately Day 57
- (Immunogenicity) Mean normalized secretory IgA (sIgA), as measured by the enzyme-linked immunosorbent assay (ELISA) in nasal lavage specimens, against an H3N2 M2SR-like virus for participants in Cohorts 1, 2, and 3 at baseline (Day 1, before vaccination) and on approximately Day 29
- (Immunogenicity) Mean normalized secretory IgA (sIgA), as measured by the enzyme-linked immunosorbent assay (ELISA) in nasal lavage specimens, against an H3N2 M2SR-like virus for participants in Cohort 4 at baseline (Day 1, before vaccination) and on approximately Day 57

- (Immunogenicity) Mean change (difference) from baseline in normalized secretory IgA (sIgA), as measured by the enzyme-linked immunosorbent assay (ELISA) in nasal lavage specimens, against an H3N2 M2SR-like virus for participants in Cohorts 1, 2, and 3 on approximately Day 29
- (Immunogenicity) Mean change (difference) from baseline in normalized secretory IgA (sIgA), as measured by the enzyme-linked immunosorbent assay (ELISA) in nasal lavage specimens, against an H3N2 M2SR-like virus for participants in Cohort 4 on approximately Day 57
- (Immunogenicity) Geometric Mean Titers (GMTs) of plasma or serum NA antibodies against an H3N2 NA for participants in Cohorts 1, 2, and 3 at baseline (Day 1) and on approximately Day 29
- (Immunogenicity) Geometric Mean Titers (GMTs) of plasma or serum NA antibodies against an H3N2 NA for participants in Cohort 4 at baseline (Day 1) and on approximately Day 57
- (Immunogenicity) Geometric Mean Fold Rise (GMFR) and proportions with greater than or equal to 2- and 4-fold rises from baseline (Day 1) in plasma or serum NA antibodies against an H3N2 NA for participants in Cohorts 1, 2, and 3 on approximately Day 29
- (Immunogenicity) Geometric Mean Fold Rise (GMFR) and proportions with greater than or equal to 2- and 4-fold rises from baseline (Day 1) in plasma or serum NA antibodies against an H3N2 NA for participants in Cohort 4 on approximately Day 57
- (Immunogenicity) The number and percentage of participants in Cohorts 1, 2, and 3 with NA antibody titer ≥1:40 against an H3N2 NA at baseline (Day 1) and on approximately Day 29
- (Immunogenicity) The number and percentage of participants in Cohort 4 with NA antibody titer ≥1:40 against an H3N2 NA-like virus at baseline (Day 1) and on approximately Day 57

3.3. Study Definitions and Derived Variables

Baseline values for immunogenicity will be the last pre-vaccination results available.

Censored responses determined to be below the lower limit of detection (LOD) will be imputed as LOD/2 and censored responses determined to be above the upper limit of quantification (ULOQ) will be imputed as ULOQ. If lower limits of quantification (LLOQ) are known, responses above the LOD but below the LLOQ would be imputed by (LLOQ+LOD)/2. All imputations will be performed at the replicate level as applicable. Imputation may be differentially handled for assays pending final details regarding assay limits of detection as necessary.

Titers will be summarized using the geometric mean, first across replicates to compute one value for each individual sample and then applied again across participants within the same group as applicable. Non-titer data with replicates will be summarized using the arithmetic mean, first across replicates to compute one value for each individual sample and then applied again across participants within the same group as applicable.

The antigen specific electrochemiluminescence (ECL) signal will be calculated as the antigen specific non-dilution adjusted ECL signal times the dilution factor at the replicate level. sIgA specific activity against various influenza antigens as measured by the binding antibody multiplex assay (BAMA) will be calculated as the arithmetic mean of the antigen specific ECL signal replicates divided by the arithmetic mean of the total sIgA concentration replicates. If replicate data are unavailable, sIgA specific activity will be calculated as antigen specific non-dilution adjusted ECL signal times the dilution factor, divided by the total sIgA concentration.

Normalized secretory IgA (sIgA) as measured by the enzyme-linked immunosorbent assay (ELISA) will be calculated as the geometric mean of the sIgA titer replicates divided by the arithmetic mean of the total sIgA concentration replicates. For individual participants, fold-rise in titers will be calculated as the post-vaccination titer divided by the pre-vaccination titer and the mean difference in non-titer responses will be calculated as the post-vaccination response minus the pre-vaccination response.

Seroprotection for hemagglutination inhibition (HAI) will be defined as an HAI titer of at least 1:40 against an H3N2 M2SR-like virus (A/Singapore/INFIMH-16/0019/2016).

4. INVESTIGATIONAL PLAN

4.1. Overall Study Design and Plan

This is a Phase 1b, randomized, double-blind, dose-escalating, age de-escalating, placebo-controlled study of up to 200 children, who are in generally good health, ages 6 months to 17 years, to assess the safety, tolerability/reactogenicity, and immunogenicity of the Sing2016 M2SR H3N2 influenza vaccine. Participants within a cohort were randomly assigned, with randomization stratified by site and based on a blocked scheme to provide an approximate allocation to the vaccination group during the study, to receive either Sing2016 M2SR H3N2 vaccine or saline placebo at the specified randomization ratio. To allow for simultaneous enrollment at the four research sites, the number of children in each cohort and the total number of children in the entire study may slightly deviate from the targeted numbers mentioned throughout the protocol. Enrollment proceeded sequentially by cohort as progressions to sequential cohorts de-escalated the age of participants or escalated the dose within an age group. Blinded interim safety assessments by the Safety Review Committee (SRC) were conducted to determine if enrollment into a given cohort should continue and blinded and unblinded interim safety assessments by the Safety Monitoring Committee (SMC) were conducted to determine if enrollment into subsequent cohorts should begin as described in the protocol.

All participants received either vaccine or placebo at baseline (Day 1). Participants belonging to a cohort receiving two doses of the vaccine or placebo received the second dose at Day 29. During the Fall (September-November), all participants received the Center for Disease Control and Prevention (CDC) recommended seasonal inactivated influenza vaccine (IIV4) at least 28 days after receipt of the final investigational vaccine administration. The final study visit for each participant occurred in April of the following calendar year.

Solicited events were collected for 7 days following each dose; non-serious unsolicited adverse events (AEs) were collected for 28 days following each dose; and serious adverse events (SAEs), adverse events of special interest (AESIs, wheezing), and new onset chronic medical conditions (NOCMCs) were collected from Day 1 until the end of study follow-up. Participants were evaluated for wheezing episodes in 2 phases. For the day of each vaccination and the next 28 days, active surveillance occurred, and each episode required a standardized clinical evaluation as defined in the protocol (Appendix B – Evaluation Criteria for Acute Wheezing). After 28 days from the last receipt of investigational product, parents were instructed to notify the research team and recording of the relevant information may be completed by medical record review or parental reported outcomes. Blood draws were performed for immune responses and nasal washes were performed for mucosal immune responses on Day 1 (before vaccination), 28 days following last vaccination, and 28 days after receipt of IIV4.

The overall study design is presented below (Figure 1) for reference and is taken from Section 1.3 of the protocol.

Due to the limited availability of product, and funding to support additional years of enrollment into Cohorts 5, 6, and 7, the decision was made to stop enrollment after the final participant was enrolled into Cohort 4.

An unblinded interim immunogenicity analysis was conducted with analysis plans detailed in memorandums. Further details can be found in Section 5.6.1.

The Schedule of Activities is presented in Table 1 for reference and is taken from Section 1.2 of the protocol.

4.2. Discussion of Study Design, Including the Choice of Control Groups

Participants were randomized to receive either Sing 2016 M2SR H3N2 or placebo within each cohort. Participants received one or two doses depending upon the cohort into which they enrolled. The targeted number of participants randomized to receive either vaccine or placebo are given below (Table 2).

4.3. Selection of Study Population

The study population consists of male and female pediatric volunteers aged 6 months to 18 years, inclusive, and generally in good health. Participants 2-17 years should be "non-naïve," having been vaccinated against seasonal influenza in a prior season. Inclusion and exclusion criteria are presented in Sections 5.1 and 5.2 of the protocol, respectively.

4.4. Statistical Considerations for the Study Design

4.4.1. Sample Size Considerations

The probability of observing one or more safety events, such as a reactogenicity event or an adverse event of a particular classification, for varying sample sizes, given underlying true event probabilities is presented below (Table 3).

Among the 25 participants in each of Cohorts 1-2 considered for the safety reviews prior to enrolling the subsequent cohorts, there is a 22.2% chance of observing at least one uncommon event and a 92.8% chance of observing at least one common event (bolded and underlined in Table 3).

The primary objective of this study is to determine the safety and tolerability of the Sing2016 M2SR H3N2 influenza vaccine, which will be assessed via the incidence of adverse events of different types. While the study was not designed to achieve a pre-determined level of precision, confidence intervals (CIs) will be estimated for some of the binary endpoints. The exact 95% Clopper-Pearson CIs that would result from observing varying numbers of events in groups of possible interest is presented below (Table 4).

For illustration, if zero events of a certain type were observed in an individual vaccine group or in Cohorts 3-4 aggregate vaccine groups after one dose with N=30 participants, true event probabilities above 11.6% could be ruled out at the α=0.025 level, compared to 2.8% in the combined vaccine groups (N=132). Binomial CIs are widest at 50% events observed (the estimates associated with approximately [or exactly] 50% observed events are bolded in Table 4). Within an individual vaccine group or in Cohorts 3-4 aggregate vaccine groups after one dose with N=30 participants, the maximum half-width for a 95% CI would be 18.7%, compared to 10.7% across active vaccine groups in Cohorts 1-4. In the case of substantial loss to follow-up or missed visits, these estimates give an idea of the loss of precision due to decreasing the effective sample size.

4.4.2. Allocation of Subjects to Study Arms (Randomization)

Enrollment of participants was done online using the enrollment module of the Electronic Data Capture (EDC), maintained by the Statistical and Data Management Coordinating Center (SDMCC). Randomization to receive either Sing2016 M2SR H3N2 vaccine or saline placebo within each cohort was conducted via a randomization scheme that was stratified by site. Participants were assigned to receive either Sing2016 M2SR H3N2 vaccine or saline placebo at Day 1 (and Day 29, if applicable) after providing consent and confirmation of eligibility with the study inclusion and exclusion criteria.

4.5. Study Products

4.5.1. Study Products Administered

Participants in Cohorts 1-3 were administered 1 mL of Sing2016 M2SR H3N2 (diluted to the target dosing concentration) or placebo delivered intranasally via a disposable polypropylene syringes (Henke-Ject) with each syringe fitted with a MAD300™ nasal device (MAD300*; Teleflex, Morrisville, NC, USA)* on Day 1. Remaining participants received two vaccinations, one at Day 1 and one at Day 29, administered as noted above.

4.5.2. Identity of Investigational Product(s)

4.5.2.1. Product 1: Sing2016 M2SR H3N2 Intranasal Influenza Vaccine

The Sing2016 M2SR vaccine is provided as a frozen liquid formulation in 2 mL cryovials. Each vial contains ~0.6 mL of vaccine formulated to contain infectious viral particles of Sing2016 M2SR encoding the HA and NA of influenza virus strain A/Singapore/INFIMH-16-0019/2016 (H3N2). The virus is suspended in Sucrose Phosphate Glutamate with Sodium Chloride (SPG-NaCl) buffer comprised of 10% sucrose, 5 mM glutamic acid, 136.9 mM sodium chloride, 2.67 mM potassium chloride, 1.47 mM potassium dihydride phosphate and 8.1 mM disodium phosphate, at pH 7.2. The Sing2016 M2SR vaccine is clear to opalescent, colorless to slightly yellow suspension.

4.5.2.2. Product 2: SPG buffer to be used as the diluent for Product 1

The vaccine diluent, SPG-NaCl buffer (10% sucrose, 5 mM glutamic acid, 136.9 mM sodium chloride, 2.67 mM potassium chloride, 1.47 mM potassium dihydride phosphate and 8.1 mM disodium phosphate, at pH 7.2), is provided as a frozen, liquid formulation. It is a clear, colorless solution that is used to prepare dilutions of the investigational vaccine for the lower dose treatments.

4.5.2.3. Product 3: Placebo

The placebo consists of a commercially prepared 0.9% sodium chloride for injection, USP.

4.5.2.4. Product 4: Seasonal Inactivated Influenza Vaccine (IIV4)

All participants without contraindications will be given injectable IIV4 using a licensed product. All available IIV products licensed for children in the US are now quadrivalent.

4.5.2.5. Product 5: MAD300™ Sprayer Device

The intranasal delivery device, i.e., nasal spray device, is comprised of a MAD300™ mucosal atomization device and a 1 mL Henke-Ject (low dead space) syringe. The MAD300™ is made from radiation-stable medical-grade polycarbonate material and is compliant with USP Class VI and ISO 10993 requirements. It is manufactured by Teleflex Medical and is a conical shaped component with a Luer-lock feature for attachment to the filled syringe. For intranasal administration of the Sing2016 M2SR vaccine and placebo, the MAD300™ conical shape forms a plug in the nostril and rapid depression of the syringe plunger atomizes the liquid as it passes through the device nozzle into a fine mist.

4.5.3. Selection of Doses in the Study

Depending on the cohort, participants were randomized to receive either one or two doses of either Sing 2016 M2SR H3N2 (ranging from 10^7 $TCID_{50}$ to 10^9 $TCID_{50}$) or placebo. Justification for selection of these doses can be found in Section 4.3 of the protocol.

4.5.4. Selection and Timing of Dose for Each Subject

On Day 1, eligibility was reviewed. Participants in Cohorts 1-3 received Sing 2016 M2SR H3N2 or placebo intranasally on Day 1 if all eligibility criteria were met. All remaining participants received Sing 2016 M2SR H3N2 or placebo intranasally on Day 1 and Day 29 if eligibility were met on the day of vaccination.

4.5.5. Blinding

An unblinded interim immunogenicity analysis was performed (further details can be found in Section 5.6.1). These analyses were made available to the pharmaceutical partner for planning for future studies, with no public dissemination of results, and not used to make any decisions concerning the conduct of the trial. The SAP was finalized prior to unblinding of individual participants for the pharmaceutical partner and PI.

4.5.6. Prior and Concomitant Therapy

Details of prior and concomitant therapy can be found in Section 6.5 of the protocol.

4.5.7. Study Product Compliance

Participants were directly observed at the time of dosing by a member of the clinical research team who is licensed to administer the study product.

4.6. Efficacy, Immunogenicity, and Safety Variables

4.6.1. Safety Variables

Safety is assessed by the incidence, frequency, and severity of:

1. Solicited local reactogenicity events in the 7 days following administration of each dose of vaccine.
2. Solicited systemic reactogenicity events in the 7 days following administration of each dose of vaccine.
3. Unsolicited non-serious adverse events in the 28 days following administration of each dose of vaccine.
4. Adverse events of special interest (AESIs) from the time of first vaccination through the end of the study (in the month of April of the calendar year following enrollment)
5. Serious adverse events (SAEs) from the time of first vaccination through the end of the study (in the month of April of the calendar year following enrollment)
6. New-onset chronic medical conditions (NOCMCs) from the time of first vaccination through the end of the study (in the month of April of the calendar year following enrollment)

Additional details for data contributing to safety variables, including definitions, can be found in the protocol (Sections 8.3 and 8.4)

4.6.2. Immunogenicity Variables

Hemagglutination inhibition (HAI) and microneutralization (MN) antibody results as measured in serum will be reported by the research laboratory at Duke University. HAI, MN antibody titers and neuraminidase inhibition (NAI) titers as measured in plasma will be reported by the laboratory at VisMederi. Assay results for HAI and MN, as measured in serum and plasma, and NAI as measured in plasma, are reported as endpoint titers, with values of 10*2k, where k=0, 1, 2, etc., or are reported to be below the lower limit of detection (LOD). Antigen specific non-dilution adjusted ECL signals, dilution factors, and total sIgA concentrations, as measured by BAMA, will be reported by the research laboratory at Duke University. sIgA titers and total sIgA concentrations, as measured by ELISA, will be reported by the laboratory at FluGen, Inc. See Section 3.3 for definitions of derived variables for immunologic data.

All immunogenicity data will be uploaded into the SDMCC's electronic data capture system. Data for the remaining exploratory assays and corresponding analyses not covered in this document will be described in a separate analysis plan addendum(a).

5. GENERAL STATISTICAL CONSIDERATIONS

5.1. General Principles

For screening and baseline visits, the last assessment value obtained prior to the first vaccination/dose of study product will be used. If participants completed assessments at both scheduled and supplementary visits, the assessments from the scheduled visit will be considered in the statistical analyses, tabular summaries, and figures. However, if an assessment is completed only at supplementary visits, then the assessment from the earliest supplementary visit occurring after the scheduled visit will be included in the statistical analyses, tabular summaries, and figures. Results of all assessments, including those performed during supplementary visits, will be included in the listings.

Generally, summaries will be presented by cohort and vaccination group (i.e., 9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose; 9-17 yrs, Placebo, 1 Dose; 2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR, 1 Dose; etc., called "analysis group" throughout the SAP). Post-first dose safety results for participants in Cohorts 3 and 4 receiving active vaccine may be combined as both cohorts receive the same dose and belong to the same age group.

For descriptive analyses, continuous variables will be summarized by the non-missing sample size, mean, standard deviation (SD), and the minimum, median, and maximum. Categorical variables will be summarized by frequencies and percentages of observed levels, based on the non-missing sample size. When calculating incidence, or any sub-classification thereof (e.g., by study vaccination, time period, severity, relatedness, etc.) each participant will only be counted once at the maximum value of the respective variable (e.g., maximum severity, maximum relatedness, etc.), and any repetitions will be ignored. All tables will be annotated with the analysis population and the total population size relevant to that table, including any missing observations. Data listings will typically be sorted by cohort (even if not presented), vaccination group, site, participant, and visit number within participant, where appropriate.

For continuous variables, CIs will be computed based on the t-distribution, unless the data appear especially non-normal and the sample sizes for the analysis are insufficient to apply the central limit theorem. Bootstrap CIs may be calculated instead if the t-distribution is determined to be unsuitable. For binary variables, CIs will be computed using the exact Clopper-Pearson method.

For safety endpoints, summaries may also include a column for all participants receiving active study vaccination and all participants receiving placebo.

Subgroup analyses will be performed on a conditional basis for immunogenicity endpoints, as outlined in Section 7.2. Subgroups include age, dose level, sex, clinical site, prior receipt of IIV4, time between prior receipt of IIV4 and study vaccination, prior receipt of COVID-19 vaccination, time between prior receipt of COVID-19 vaccination and study vaccination, and seroprotection.

5.2. Timing of Analyses

The interim analysis was performed after all participants completed through 28 days post-first vaccination.

After clinical database lock and receipt of secondary immunogenicity data, a set of topline tables will be generated by the Statistical and Data Management Coordinating Center (SDMCC), including summaries of clinical safety and secondary immunogenicity data. These analyses will be considered final and will be included in the Clinical Study Report (CSR) as well. The CSR, comprised of the final analyses of safety and available immunological data, will be subsequently completed. Any available data from the exploratory endpoints may also be included. Additional exploratory endpoint data not available at the time of CSR

preparation may be included in one or more addenda to the CSR, manuscript(s), or other report. Plans for remaining analyses will included in an addendum to the SAP with results presented in an addendum to the CSR after those data are available.

5.3. Analysis Populations

Analyses will be conducted within one of the following populations.

5.3.1. Screened Populations

The Screened population will include all participants screened. This population will be used for summaries relating to screen failures.

5.3.2. Enrolled Population

The Enrolled population will include all participants enrolled and randomized. This population will be used for summaries of participant disposition as well as participant demographics and baseline characteristics.

5.3.3. Safety Population

The Safety population will include all participants who receive at least one study influenza vaccination. This population will be used for analyses of adverse events and reactogenicity.

5.3.4. Modified Intent to Treat (mITT) Population

The Modified Intent-to-Treat (mITT) population will consist of all participants who received study influenza vaccination and have a baseline and at least one post-baseline sample available. Immunogenicity analyses will be performed utilizing the mITT population.

5.3.5. Per-Protocol (PP) Population

The Per-Protocol (PP) population will include participants in the mITT population with the following exclusions of data:

- Data from participants determined to be ineligible at baseline (determined thereafter)
- Data from participants in Cohorts 4, 5, 6, and 7 subsequent to missed second study vaccinations
- Data from Visit 4 for Cohorts 1-3, from Visit 4C for remaining cohorts, and from Visit 6 for all cohorts if the corresponding visit occurred substantially out of window
- Data from all visits subsequent to major protocol deviations that could impact the validity of later data, such as:
  - Receipt of immunosuppression or any medications that may be associated with impaired responsiveness
  - Receipt of any non-study investigational drug/investigational vaccine/licensed vaccine outside of what is allowable per-protocol
  - Receipt of incorrect study influenza vaccination, including incorrect dosage

Visit 4, 4C, and 6 will be considered substantially out of window if they occur more than ±15 days from the target day (i.e., more than 500% of the half width of the visit window days from the target day).

If sufficient data (>10% of secondary analysis timepoints) would be excluded by the PP exclusions, sensitivity analyses will be performed utilizing the PP population for secondary immunogenicity analyses.

Sensitivity analyses will be performed according to the study influenza vaccination received if a sufficient number of participants receive the study influenza vaccination discrepant (e.g., the wrong vaccine or the wrong dose) from what was indicated per randomization.

5.4. Subgroups, Interactions and Covariates

The protocol does not define and is not powered for any formal subgroup analyses. Conditional post-hoc exploratory analyses will be performed for subgroups as outlined in Section 7.2.

5.5. Missing Data and Outliers

No imputation is planned for missing data.

Any data point that appears to be erroneous or inexplicable based on the observed data distribution and the statistical team's understanding of the analysis variables will be investigated as a possible outlier. If data points are identified as outliers, sensitivity analyses may be performed to examine the impact of including or excluding the outliers. Any substantive differences in these analyses will be reported.

5.6. Interim Analyses and Data Monitoring

5.6.1. Interim Analyses

An interim analysis focused primarily on immunogenicity was conducted while the study was ongoing. These analyses, including primary, secondary, and exploratory endpoints, were made available to the pharmaceutical partner for planning for future studies, with no public dissemination of results, and were not used to make any decisions concerning the conduct of this trial. Immunogenicity specimens (serum, plasma, nasal washes) collected through the Day 29 visit (Visit 4) for Cohorts 1 to 3 and through Day 57 visit (Visit 4C) for others were presented in aggregate by cohort and vaccine/placebo where data were available. Participant-level immunogenicity data were not presented to maintain the blind. Interim safety analyses through the Day 29 visit (Visit 4) for Cohorts 1 to 3 and through Day 57 visit (Visit 4C) for others were presented aggregated by cohort, to avoid the possibility of unblinding due to rare adverse events occurring only in active vaccine or placebo groups.

5.6.2. Data Monitoring Committee

Two safety committees were convened for this study: the Safety Review Committee (SRC) and the Safety Monitoring Committee (SMC).

The SRC reviewed blinded safety data to allow for progression through the cohorts as described in the protocol (Section 4.1). The SMC reviewed safety data if criteria for progression to enrollment of a subsequent cohort was not met, a halting rule (as outlined in the protocol, Section 1.1) occurred, or as regularly scheduled per the separate SMC charter.

SMC reviews were blinded to study assignment, with unblinded study assignments available upon SMC request. As an outcome of each SMC review, the SMC made a recommendation to continue, modify, or terminate the study.

Interim safety reviews included a summary of halting rules, demographic information, participant disposition, AEs, SAEs, AESIs, NOCMCs, and protocol deviations as per the mock TLF shells provided in a separate document.

5.7. Multicenter Studies

For most analyses, data will be pooled across all clinical sites. While the sites use standardized procedures and rely on central laboratories for the assessment of immunogenicity endpoints, exploratory subgroup analyses of immunogenicity endpoints will be conditionally conducted within site-specific subgroups as specified in Section 7.2.

5.8. Multiple Comparisons/Multiplicity

Analyses will be descriptive in nature. No adjustments for multiplicity are planned, but the number of comparisons made will be factored into the interpretation of results, as appropriate. No adjustment will be made for the interim analysis.

6. STUDY PARTICIPANTS

6.1. Demographic and Other Baseline Characteristics

Sex, race, ethnicity, age, prior receipt of seasonal influenza vaccination, and prior receipt of COVID-19 vaccination will be summarized by analysis group and site (Table 10 [categorical characteristics] and Table 11 [continuous characteristics]). Demographic characteristics will be detailed per participant (Listing 7).

6.2. Disposition of Participants

Screening failures will be listed (Listing 5) and summarized by reason and by cohort (Table 7). The disposition of participants in the study will be tabulated by analysis group. Disposition events to be summarized will be the total number of participants screened, enrolled/randomized, receiving at least 1 dose, receiving at least 2 doses (where applicable), completed safety follow-up for 7 days post-each dose, completed safety follow-up for 28 days post-each dose, completed safety follow-up through the end of the study, and terminated early from study (Table 8). A flowchart showing the disposition of study participants and the inclusion of participants in analyses, adapted from the Consort Statement, will be generated (Figure 2). This figure will present the number of participants screened, enrolled, randomized, receiving the protocol-defined number of study vaccinations, lost to follow-up, and analyzed, by analysis group.

The composition of analysis populations, including reasons for participant exclusion, will be presented by analysis group (Table 9).

The following participant listings will be generated:

- Listing of participants who received investigational product along with their intended randomized assignment, date of vaccine administration(s), and any relevant study product administration deviations (Listing 1).
- Listing of participants who discontinued dosing or terminated from study follow-up early along with the reason for early discontinuation/termination (Listing 2), including study terminations related to the COVID-19 pandemic as applicable.
- Listing of participants excluded from analysis populations (Listing 6).

6.3. Prior and Concurrent Medical Conditions

All current illnesses and past or pre-existing medical conditions will be coded using Medical Dictionary for Regulatory Activities (MedDRA®) version 26.1 or higher.

Summaries of participants' prior and concurrent medical conditions will be presented by analysis group and MedDRA® system organ class (SOC) for the Safety population (Table 12).

Individual participant listings will be presented for all reported medical history including prior and concurrent medical conditions (Listing 8).

6.4. Prior and Concomitant Medications

Prior (within 30 days of enrollment) and concomitant medications will be coded to the Anatomical Therapeutic Classification (ATC) using the WHO Drug Dictionary. The use of concomitant medications

during the study will be summarized by ATC1 and ATC2 code, as well as analysis group, for the Safety population (Table 114).

A listing of prior and concomitant medications by participant will be presented, with events corresponding to receipt of coronavirus 2019 (COVID-19) vaccine during the study period highlighted in green (Listing 15).

6.5. Prior Vaccinations

Vaccination history is obtained for all participants for the two years prior to enrollment. A listing of prior vaccinations will be presented, with events corresponding to seasonal influenza vaccine receipt and COVID-19 vaccine receipt highlighted in yellow and green, respectively (Listing 9).

6.6. Measurements of Study Product Compliance

Participants are directly observed at the time of dosing by a member of the clinical research team who is licensed to administer the study product. Participants in Cohorts 1, 2, and 3 receive one dose of study product and the remaining participants receive two doses of study product. The number of doses of study product administered to participants will be presented by analysis group as part of the participant disposition table (Table 8). Details of study product administration by participant will be provided (Listing 1).

6.7. Protocol Deviations

A summary of participant-specific protocol deviations will be presented by deviation category, deviation type, and analysis group for all enrolled participants (Table 5). A participant listing of all participant-specific protocol deviations and a listing of all non-participant specific protocol deviations will be generated (Listing 3 and Listing 4, respectively), including protocol deviations related to the COVID-19 pandemic as applicable.

7. IMMUNOGENICITY/IMMUNOLOGICAL EVALUATION

Immunogenicity analyses will be conducted in the modified intent-to-treat population. If sufficient data (>10% of secondary analysis timepoints) would be excluded by the PP exclusions, sensitivity analyses will be performed utilizing the PP population for secondary immunogenicity analyses.

Immunogenicity results will be listed with study days across columns (Listing 10).

7.1. Secondary Immunogenicity Analyses

Hemagglutination inhibition (HAI) and microneutralization (MN) antibody titers are measured in serum against A/Singapore/INFIMH-16-0019/2016. These antibody titers will be summarized by geometric mean titers (GMTs) and the percentage of participants reporting titers ≥ 1:40 (defined as seroprotection for HAI) and associated 95% CIs, presented by analysis group at baseline and 28 days post last vaccination (Day 29 for Cohorts 1-3, Day 57 for Cohort 4). Geometric mean fold-rise (GMFR) and the percentage of participants reporting a fold-rise ≥ 2 and ≥ 4 from baseline and associated 95% CIs will also be presented for visits post baseline (Table 13 and Table 14 for HAI and MN, respectively). Titers will be presented graphically over time via line graphs displaying the GMT and associated 95% CIs for each analysis group with individual trajectories presented at a decreased transparency (Figure 3 and Figure 4 for HAI and MN in serum, respectively).

ECL signal, total sIgA concentration, and specific activity (as defined in Section 3.3) are measured in NLF supernatant by BAMA will be summarized at baseline, 28 days post last study vaccination, and 28 days post IIV4 administration, separately for each antigen. Arithmetic means and associated 95% CIs will be presented for ECL signal, total sIgA concentration, and specific activity by analysis group at baseline and 28 days post last vaccination (Day 29 for Cohorts 1-3, Day 57 for Cohort 4). Arithmetic mean difference from baseline and associated 95% CIs for ECL signal, total sIgA concentration, and specific activity will also be presented for visits post baseline (Table 15 through Table 18). ECL signal, total sIgA concentration, and specific activity as measured by BAMA will be presented graphically over time, separately by antigen, via line graphs displaying the arithmetic mean and associated 95% CIs for each analysis group with individual trajectories presented at a decreased transparency (Figure 5 through Figure 7).

7.2. Exploratory Immunogenicity Analyses

Hemagglutination inhibition (HAI) and microneutralization (MN) antibody titers as measured in serum will be summarized 28 days post IIV4 administration as described for the secondary immunogenicity endpoints corresponding to baseline and 28 days post last vaccination (Table 13 and Table 14 for HAI and MN, respectively). Titers at the visit corresponding to 28 days post last vaccination will be presented in the line graphs for each analysis group (Figure 3 and Figure 4 for HAI and MN in serum, respectively).

Hemagglutination inhibition (HAI), microneutralization (MN) antibody titers and neuraminidase inhibition (NAI) titers are measured in plasma against A/Singapore/INFIMH-16-0019/2016. These titers will be summarized by GMTs and the percentage of participants reporting titers ≥ 1:40 (defined as seroprotection for HAI) and associated 95% CIs, presented by analysis group at baseline, 28 days post last vaccination (Day 29 for Cohorts 1-3, Day 57 for Cohort 4), and 28 days post IIV4 administration. GMFR and the percentage of participants reporting a fold-rise ≥ 2 and ≥ 4 from baseline and associated 95% CIs will also be presented for post baseline visits (Table 19 through Table 21). Titers will be presented graphically over time via line graphs displaying the geometric mean and associated 95% CIs for each analysis group with individual trajectories

presented at a decreased transparency (Figure 8, Figure 9, and Figure 10 for HAI, MN, and NAI in plasma, respectively).

sIgA titers, total sIgA concentration, and normalized sIgA in NLF supernatant against A/Singapore/INFIMH-16-0019/2016 as measured by ELISA (as defined in Section 3.3) will be summarized at baseline, 28 days post last study vaccination, and 28 days post IIV4 administration. Arithmetic means and associated 95% CIs for total sIgA concentration and normalized sIgA and GMTs and associated 95% CIs for sIgA titers will be presented by analysis group at baseline, 28 days post last vaccination (Day 29 for Cohorts 1-3, Day 57 for Cohort 4), and 28 days post IIV4 administration. Arithmetic mean difference from baseline and associated 95% CIs for total sIgA concentration and normalized sIgA, and GMFR and the percentage of participants reporting a fold-rise ≥ 2 and ≥ 4 from baseline and associated 95% CIs will be presented for visits post baseline (Table 22). sIgA titers, total sIgA concentration, and normalized sIgA as measured by ELISA will be presented graphically over time via line graphs displaying the (geometric or arithmetic, as appropriate) mean and associated 95% CIs for each analysis group with individual trajectories presented at a decreased transparency (Figure 11 through Figure 13).

The effects of age, dose level, sex, clinical site, prior receipt of seasonal influenza vaccine(s) within 2 years of first study vaccination, prior receipt of COVID-19 vaccine(s) within 2 years of first study vaccination, and seroprotection (i.e., HAI titer $\geq$ 1:40 against A/Singapore/INFIMH-16-0019/2016 [H3N2]) at baseline on humoral immunogenicity directed against homologous viral strains will be conditionally analyzed. Subgroup immunogenicity analyses may be performed if and only if, for at least one analysis group, the CIs of the change from baseline parameter (i.e., GMFR or mean difference from baseline) at the visit 28 days post-last vaccination do not overlap between the corresponding vaccine and placebo groups and sufficient data for each subgroup are available. If subgroup analyses are performed, each subgroup within an analysis group will be summarized separately (e.g., male participants receiving vaccine in Cohort 1, male participants age 9-17 receiving placebo in Cohort 1, female participants age receiving vaccine in Cohort 1, female participants receiving placebo in Cohort 1, etc.). Subgroups will be defined as the following:

- Age: 2-4 years old, 5-8 years old, and 9-17 years old
- Dose level: 10^8 $TCID_{50}$ and 10^9 $TCID_{50}$ (regardless of number of doses)
- Sex: male and female
- Clinical site: Duke University, University of Maryland, University of Maryland (Frederick), Vanderbilt University, and University of Iowa
- Prior receipt of seasonal influenza vaccine(s) within 2 years of first study vaccination: prior receipt of seasonal influenza vaccine(s) $\leq$ 1 year prior to first study vaccination,* prior receipt of seasonal influenza vaccine(s) 1-2 years prior to first study vaccination,* and no prior receipt of seasonal influenza vaccine(s)*
- Prior receipt of COVID-19 vaccine(s) within 2 years of first study vaccination: prior receipt of COVID-19 vaccine(s) $\leq$ 1 year prior to first study vaccination,* prior receipt of COVID-19 vaccine(s) 1-2 years prior to first study vaccination,* and no prior receipt of COVID-19 vaccine(s)*
- Seroprotection at baseline: plasma HAI titer $\geq$ 1:40 against A/Singapore/INFIMH-16-0019/2016 [H3N2]) at baseline and plasma HAI titer < 1:40 against A/Singapore/INFIMH-16-0019/2016 [H3N2]) at baseline

*Any prior receipt (limited to two years prior to enrollment) may be utilized as a subgroup if there are insufficient data for subgrouping by timing of receipt.

An example table shell for an age subgroup summary of HAI antibody titers in serum is presented in Table 23; additional subgroup analyses would follow a similar shell with the same variables presented as the corresponding shell from the secondary or exploratory endpoint. Figures will similarly present subgroups following the corresponding shell from the secondary or exploratory endpoint if such subgroup analyses are performed. Results from subgroup analyses, if performed, will be hypothesis generating.

Additional exploratory immunogenicity assessments include T-cell immune response, serum antibody response against homologous and heterologous viral strains, and additional humoral or mucosal immune responses, as described in Section 3.2. TFL shells for these endpoints will be included in an addendum to the SAP, after details for the data are finalized.

8. SAFETY EVALUATION

All summaries and analyses of safety data will be presented for the Safety population. Summaries of placebo groups will include all participants from applicable cohorts of the same age (i.e., placebo recipients in Cohorts 2, 3, and 4 will be combined) for post-first dose and overall analyses, unless otherwise specified. Solicited events occurring in the vaccine from Cohorts 3 and 4 will be combined for post-first dose analyses and summarized separately after the second dose in Cohort 4. The denominator for percentages will be based on the number of non-missing observations for an assessment or based on the number of participants in the Safety population, unless otherwise specified.

8.1. Adverse Events

Details of adverse events (AEs) and serious adverse events (SAEs) can be found in the protocol (Section 8.4.1 and Section 8.4.6, respectively). Adverse events of special interest (AESIs, wheezing) and new onset chronic medical conditions (NOCMCs) are reported and are defined in the protocol (Section 8.3.3 and Section 8.3.4, respectively). Adverse events will be coded according to the MedDRA® dictionary version 26.1 or higher.

Non-serious unsolicited AEs are reported for each participant from the time of first administration of study vaccine until 28 days post each study vaccination. SAEs, AESIs, and NOCMCs are reported for each participant from the time of first administration of study vaccine until the end of study follow-up (Section 8.4.8 of the protocol). Solicited events are reported 20 minutes after administration of the study vaccine and for 7 days post each study vaccination. Solicited AEs consist of local reactogenicity and systemic reactogenicity and assessments are based on age at enrollment (Appendix IV).

8.1.1. Primary Safety Analyses

8.1.1.1. Overall Summary

An overall summary of adverse events will be generated which includes the following participant-level count of participants reporting at least one of the following events by analysis group: local solicited AE, systemic solicited AE, unsolicited AE, related AE (by severity), SAE, related SAE, AE leading to early termination from the study, non-serious AE in the 28 days post-first dose, nonserious AE in the 28 days post-second dose, AESI, NOCMC, and AE classified as an unanticipated problem (Table 24).

Unsolicited and solicited AEs that were reported in at least 5% of participants in any analysis group will be summarized by MedDRA Preferred Term (PT), MedDRA SOC, and analysis group and for all participants by vaccination group (Table 25).

8.1.1.2. Solicited Events/Symptoms

Participant-level summaries of solicited AE data will be generated for solicited events applicable to each participant based on their age at enrollment. For summaries by severity, the maximum severity over 7 days post applicable vaccinations will be identified for each participant. For summaries independent of severity, a participant will be classified as reporting the event if their maximum severity for the event was classified as mild or worse. Denominators for percentages will be the number of participants with solicited data available for the given solicited event in the specified group for which the solicited event is applicable. All placebo participants ages 2-8 years old will be summarized together, except for events post dose 2, and solicited events of vaccine recipients post first study vaccination in Cohorts 3 and 4 will be summarized together.

The number and percentage of participants reporting any solicited event, any local event, any systemic event, and each applicable solicited adverse event individually will be summarized by maximum severity and vaccination group, separately for each vaccination and after any vaccination (Table 26 through Table 28) and presented graphically in a bar chart (Figure 14 through Figure 23).

The number of participants reporting a solicited adverse event will be summarized by day post vaccination for each vaccination and after any vaccination (Table 29 through Table 39) and presented graphically in a bar chart (Figure 24 through Figure 33).

All reported solicited events will be presented in participant listings separately for local events (Listing 11) and systemic events (Listing 12).

8.1.1.3. Unsolicited Adverse Events

When calculating the incidence of adverse events on the participant-level, each participant will only be counted once at the maximum value of the respective variable (e.g., maximum severity, maximum relatedness, etc.) and any repetitions of adverse events within a participant will be ignored. All adverse events reported will be included in the summaries and analyses.

The number and percentage of participants reporting at least one unsolicited adverse event will be summarized by MedDRA SOC and PT. Denominators for percentages are the number of participants who received the vaccination being summarized where applicable.

The following summaries of AEs will be provided:

- Incidence of the following by severity and relationship to study product
  - Non-serious unsolicited AEs in the 28 days following each study vaccination and across study vaccinations (Table 40 through Table 50)
  - AESIs (Table 51 through Table 58)
  - SAEs (Table 59 through Table 66)
  - NOCMCs (Table 67 through Table 74)
- Bar chart of the incidence of the following by severity of:
  - Non-serious unsolicited AEs in the 28 days following each study vaccination and across study vaccinations (Figure 34 through Figure 38)
  - AESIs (Figure 39 through Figure 41)
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  - NOCMCs (Figure 45 through Figure 47)
- Total frequency by severity, relationship to study product, and resolution of:
  - Non-serious unsolicited AEs in the 28 days following each study vaccination and across study vaccinations (Table 75 through Table 85)
  - AESIs (Table 86 through Table 93)
  - SAEs (Table 94 through Table 101)
  - NOCMCs (Table 102 through Table 109)

- Bar chart of frequency by severity of
  - Non-serious unsolicited AEs following each study vaccination and across study vaccinations (Figure 48 through Figure 52)
  - AESIs (Figure 53 through Figure 55)
  - SAEs (Figure 56 through Figure 58),
  - NOCMCs (Figure 59 through Figure 61)

Non-serious unsolicited AEs in the 28 days following study vaccination by participant will be presented (Listing 13). AESIs, SAEs, and NOCMCs occurring during the study period will also be presented (Table 110, Table 111, and Table 112, respectively). Additional information about wheezing events corresponding to vital signs and respiratory virus panels will be presented in Table 113.

8.2. Deaths, Serious Adverse Events, and other Significant Adverse Events

Listings of the following events will be presented:

- Adverse Events of Special Interest (Table 110);
- Serious Adverse Events (Table 111); and
- New Onset Chronic Medical Conditions (Table 112).

8.3. Clinical Laboratory Evaluations

Urine pregnancy tests were performed for females of childbearing potential, as defined in the eligibility criteria in Sections 5.1 and 5.2 of the protocol, and recorded negative within 24 hours prior to study product administration. No pregnancy tests were performed prior to seasonal influenza vaccine administration.

8.4. Vital Signs and Physical Evaluations

Vital signs including oral temperature, blood pressure, respiration, oxygen saturation, and inspiratory, and expiratory may be collected as part of a wheezing assessment. A participant listing of vital signs will be presented for wheezing events where data are available (Table 113).

Physical examinations are performed at Day 1 (or screening), Day 29, Day 57 (Cohort 4 participants only), at the IIV4 visit, and 28 days post IIV4. A participant listing of abnormal findings from physical examinations will be presented (Listing 14). The following body systems will be assessed: Abdomen, Cardiovascular/heart; Extremities; General Appearance; head, ears, eyes, nose, and throat (HEENT); Lymph nodes; Musculoskeletal; Neck; Neurological; Pulmonary/Chest; and Skin.

8.5. Pregnancies

For any participants in the Safety population who became pregnant during the study, every attempt will be made to follow these participants to completion of pregnancy to document the outcome, including information regarding any complications with pregnancy and/or delivery. Participant listings of pregnancies and pregnancy outcomes will be generated (Listing 16 through Listing 20).

9. REPORTING CONVENTIONS

The mean, standard deviation, and other summary statistics, except the minimum and maximum, will be reported to 1 decimal place greater than the original data. The minimum and maximum will use the same number of decimal places as the original data.

Percentages will be reported to the nearest whole number, unless otherwise specified. Values greater than zero and < 1% will be presented as "< 1", and values greater than 99% and less than 100% will be reported as "> 99". Zero counts will be displayed as "0" and percentages will not be reported to avoid redundancy, unless otherwise specified.

Estimated parameters, not on the same scale as raw observations (e.g., regression coefficients) will be reported to 3 significant figures.

Dashes ("-") will be used to denote cells that are not applicable, to denote cells displaying values that are structurally zero (i.e., values that will always be zero), or to denote cells that are missing values. "NE" (meaning Not Estimable) will be used for any summaries or statistics that could not be estimated or are undefined (e.g., due to dividing by zero). Missing values in listings will be blank.

10. TECHNICAL DETAILS

SAS version 9.4 or above, or R version 4.3.2 or above, will be used to generate all tables, figures and listings.

11. SUMMARY OF CHANGES IN THE CONDUCT OF THE STUDY OR PLANNED ANALYSES

Due to the limited availability of study product and funding to support additional years of enrollment into Cohorts 5, 6, and 7, the decision was made to stop enrollment after the final participant was enrolled into Cohort 4. This modification is reflected in protocol version 5.0. As such, results in the CSR will be provided only for Cohorts 1-4.

For descriptive analyses, continuous variables will not be summarized by first and third quartiles.

12. LISTING OF TABLES, FIGURES, AND LISTINGS

Table, figure, and listing shells are presented in Appendix 1 , Appendix 2 , and Appendix 3 .

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9.5.1 Immunogenicity and Safety Measurements Assessed and Flow Chart

Table 1: Schedule of Activities (SoA)

Visit number	*0[1]*	*1[1]*	*2*	*3*	*4*	*4A[2]*	*4B[2]*	*4C[2]*	*5*	*6*	*7*
Target day	*-*	*1*	*3*	*8*	*29*	*V4+3d*	*V4+7d*	*V4+28d*	*-*	*V5+28d*	*April*
First day of window	*-28*	*1*	*3*	*8*	*26*	*V4+3d*	*V4+7d*	*V4+25d*	*09.01*	*V5+25d*	*04.01*
Final day of window	*-1*	*1*	*4*	*11*	*32*	*V4+4d*	*V4+10d*	*V4+31d*	*11.30*	*V5+31d*	*04.30*
Visit Type	*Screen*	*Vaccine[1]*	*Follow*	*Follow*	*Vaccine/Follow*	*Follow*	*Follow*	*Follow*	*IIV4*	*Follow*	*Follow*
Visit Venue	*Clinic*	*Clinic*	*Phone*	*Phone*	*Clinic*	*Phone*	*Phone*	*Clinic*	*Clinic*	*Clinic*	*Phone*
Procedures											
Informed consent[3]											
Collect demographics[4]											
Medical history, eligibility[5]											
Concomitant med review[6]											
Physical exam[7]											
Pregnancy test[8]											
Randomization[9]											
Administer study product[10]											
Administer IIV4[11]											
Solicited AE[12]											
Non-serious unsolicited AEs[13]											
SAEs/AESIs/NOCMCs[14]											
Blood for immune response[15]											
Nasal wash immune response[16]											

Color legend: Gray= all cohorts, Orange = only Cohorts 1, 2, and 3 (cohorts receiving single dose of IP); Blue= only Cohorts 4, 5, 6, 7 (cohorts receiving 2 doses of IP); Green = only Cohort 1

[1]Screening and enrollment may occur on the same day (Day 1) or up to 28 days apart. Consent is obtained either on the screening day (when there is a separate screening day), or on the enrollment day (if there is no separate screening day). If there is a separate screening day, then all the procedures noted for that day will be performed on the screening day and the following will be done on the enrollment day (Day 1): update medical history and update concomitant medications. A physical will be performed either on the screening day or the enrollment day but is not required on both days. If performed on the screening day, a targeted physical exam may occur on the enrollment day, if needed, but is not required. Pregnancy test, final eligibility determination, randomization, and administration of study product occur on Day 1.

[2]Visits 4A, 4B, and 4C will not be done for Cohorts 1, 2, and 3 because participants in these cohorts receive a single dose of vaccine or placebo. Participants in Cohorts 4, 5, 6, and 7 are scheduled to receive 2 doses, but if they discontinue participation prior to the second dose, these participants will not complete Visits 4A, 4B, and 4C rather will follow the visit schedule of Cohort 1,2 and 3.

[3]Prior to any study related procedures, families will be provided information about the study and informed consent will be obtained from the parent/guardian and assent obtained from the participant, when required by the IRB. Note that the screening and enrollment may occur on the same day (Day 1) or up to 28 days apart. Consent is obtained either on the screening day (when there is a separate screening day), or on the enrollment day (if there is no separate screening day).

Table 1: Schedule of Activities (SoA) *(continued)*

[4]The investigator or appropriately delegated study staff will obtain demographic data.

[5]The investigator or appropriately delegated study staff will obtain medical history and information necessary to determine eligibility. Since screening may occur up to 28 days before enrollment, if eligibility and medical history are taken at a screening visit, they will be updated on the day of enrollment, before randomization. Demography will not be updated. Review of eligibility criteria will occur before second dose of the study product.

[6]Medications taken by the participant in the 30 days before enrollment will be recorded (while all medications taken from 30 days prior to screening, whether on the same day as enrollment or not, will be solicited). At subsequent visits, until Visit 4 (Day 29) for Cohorts 1, 2, and 3 and until Visit 4C (target Day 57, or 28 days after second dose), for Cohorts 4, 5, 6, and 7, updates to previous concomitant medications and additional medications taken in the interim will be recorded. No concomitant medications will be recorded after Day 57.

[7]Physical examination will occur for all participants at either Visit 0 or Visit 1. If they receive it at Visit 0, they may get a targeted physical exam on Visit 1 if necessary, to determine eligibility. Participants may receive an optional targeted physical exam at any other clinic visits at investigator discretion.

[8]Urine pregnancy test will be performed for females of childbearing potential and recorded negative within the 24 hours prior to each study product administration. No pregnancy test will be done before the seasonal influenza vaccine administration.

[9]Participants will be randomly allocated to receive either vaccine or placebo. For those receiving 2 doses (Cohorts 4, 5, 6, and 7), they will receive the same product (vaccine) at the specified dose or placebo, at both time points.

[10]Participants in Cohorts 1, 2, and 3 will be randomly allocated to receive on Day 1 a single dose of intranasal 2016 SingM2SR H3N2 vaccine or placebo. Participants in Cohorts 4, 5, 6, and 7 will be randomly allocated to receive 2 doses of intranasal 2016 SingM2SR H3N2 vaccine or placebo. The first dose will be given on Day 1 and the second, when applicable, on approximately Day 29. In order to receive the second dose, participants in Cohorts 4, 5, 6, and 7 must meet the eligibility requirements for subsequent dosing, as described in the protocol.

[11]All participants in Cohorts 1, 2, 3, and 4 (non-naives) will be provided a single injection of licensed, seasonal influenza vaccine (IIV4) in the period from September to November in the same year but at least 28 days after they receive the investigational vaccine or placebo. If vaccine is available earlier than September 1, and the participant is at least 28 days since the last intranasal vaccine, he/she may receive it earlier than September 1. Participants in Cohorts 5, 6, and 7 (naives) will receive 2 doses of IIV4, as currently recommended per standard of care. (Should the standard recommendations change, participants will receive the updated standard of care.) This vaccine will be given no earlier than 28 days following the final administration of the experimental vaccine or placebo. No safety or reactogenicity data related to IIV4 will be collected. Participants in Cohorts 1-3 (who receive a single dose of intranasal 2016 SingM2SR H3N2 vaccine or placebo) may receive their IIV4 at Visit 4 and participants in Cohorts 4-7 (who receive 2 doses of intranasal 2016 SingM2SR H3N2 vaccine or placebo) may receive their IIV4 at Visit 4C. IIV4 will not be given until after the completion of other study procedures. Participants may also receive their coronavirus disease 2019 (COVID-19) study product on the same day as their IIV4.

[12]Solicited AEs will first be collected 20 minutes after administration of vaccine or placebo (immediate reactogenicity). Additional solicited AEs will be collected by memory aid (eDiary) on Days 1-8 for participants in all cohorts and additionally on the 7 days following the second vaccination (e.g., Days 29-36 for those receiving the second vaccination on the target Day 29). Solicited AEs consist of immediate reactogenicity, local reactogenicity (upper respiratory symptoms as defined in the protocol) and systemic reactogenicity (constitutional signs and symptoms as defined in the protocol). Reactogenicity assessments are based on age at enrollment.

[13]Non-serious unsolicited AEs will be collected and recorded from Day 1 after administration of vaccine or placebo for all participants until Day 29 and for an additional 28 days after the second vaccination (Day 57 for those who receive the second vaccination on Day 29) for participants in Cohorts 4, 5, 6, and 7.

[14]SAEs, AESIs, and NOCMCs, as defined in the protocol, will be collected from Day 1, following vaccination, until the end of study follow-up, the date in April of the calendar year following enrollment at which Visit 7 occurs. The only AESI is wheezing. Participants will be evaluated for wheezing episodes in 2 phases. For the day of each vaccination and the next 28 days, active surveillance will occur, and each episode will require a standardized clinical evaluation as defined in Appendix B – Evaluation Criteria for Acute Wheezing. After 28 days from the last receipt of investigational product, parents will be instructed to notify the research team and recording of the relevant information may be completed by medical record review or parental reported outcomes.

[15]All participants will have blood drawn for immune responses at 3 times: on Day 1, before vaccination, for all participants; on Day 29, for participants in Cohorts 1, 2, and 3; 28 days after second vaccination (Day 57 for participants who receive their second vaccination on Day 29), for participants in Cohorts 4, 5, 6, and 7; and approximately 28 days after receipt of the licensed, seasonal influenza vaccine (IIV4), for all participants. The assays performed and blood volumes and tubes required are found in the protocol and MOP. The volumes and number of tubes collected are noted in Appendix A – Blood and Fluid Collection Volumes by age group.

[16]All participants will have nasal washes collected for mucosal immune responses at 3 times: on Day 1, before vaccination, for all participants; on Day 29, for participants in Cohorts 1, 2, and 3; approximately 28 days after second vaccination (Day 57 for participants who receive their second vaccination on Day 29), for participants in Cohorts 4, 5, 6, and 7; and approximately 28 days after receipt of the licensed, seasonal influenza vaccine (IIV4), for all participants. The assays performed and samples required are found in the protocol and MOP. The volumes and number of tubes collected are noted in Appendix A – Blood and Fluid Collection Volumes by age group.

Table 2: Cohorts

Cohort	Age	Experience	Vaccine	Dose	Doses	Participants
1	9-17 yrs.	Non-naive	Sing2016 M2SR H3N2	10^9 $TCID_{50}$	1	30
			Placebo	-	1	15
2	2-8 yrs.	Non-naive	Sing2016 M2SR H3N2	10^8 $TCID_{50}$	1	30
			Placebo	-	1	15
3	2-8 yrs.	Non-naive	Sing2016 M2SR H3N2	10^9 $TCID_{50}$	1	15
			Placebo	-	1	10
4	2-8 yrs.	Non-naive	Sing2016 M2SR H3N2	10^9 $TCID_{50}$	2	15
			Placebo	-	2	10
5	6-23 mo.	Naïve	Sing2016 M2SR H3N2	10^7 $TCID_{50}$	2	6
			Placebo		2	2
6	6-23 mo.	Naïve	Sing2016 M2SR H3N2	10^8 $TCID_{50}$	2	18
			Placebo	-	2	8
7	6-23 mo.	Naïve	Sing2016 M2SR H3N2	10^9 $TCID_{50}$	2	18
			Placebo	-	2	8
Total Sample size						200

9.7.1 Sample Size

Table 3: Probability (%) of observing at least one safety event, given varying underlying event probabilities and sample sizes

Group	Group Size	Underlying Event Probability			
		0.01% (Very Rare)	0.1% (Rare)	1% (Uncommon)	10% (Common)
Cohorts 5-6 lead-in safety review, Cohorts 6-7 placebo	N=8	0.08	0.797	7.73	57
Cohorts 3-4 placebo	N=10	0.1	1	9.6	65.1
Individual placebo group or Cohorts 3-4 vaccine group	N=15	0.15	1.5	14	79.4
Individual vaccine group in Cohorts 6-7	N=18	0.18	1.78	16.5	85
Cohorts 1-2 safety review	N=25	0.25	2.5	**22.2**	**92.8**
Individual vaccine group in Cohorts 1-2; Cohorts 3-4 aggregate vaccine groups, post first-dose	N=30	0.3	3	26	95.8
Any Sing2016 M2SR H3N2 Vaccine, Cohorts 1-4	N=90	0.9	8.6	59.5	>99.9
Any Sing2016 M2SR H3N2 Vaccine	N=132	1.31	12.4	73.5	>99.9

Table 4: Estimated event probabilities (%) and associated exact 95% Clopper-Pearson confidence intervals resulting from varying numbers of events observed in groups of different sizes.

Group Size	Number of Events Observed								
	0	**4**	**5**	**7**	**9**	**12**	**15**	**45**	**66**
Cohorts 5-6 lead-in safety review, Cohorts 6-7 placebo (N=8)	0 (0, 36.9)	**50 (15.7, 84.3)**	62.5 (24.5, 91.5)	87.5 (47.3, 99.7)	-	-	-	-	-
Cohorts 3-4 placebo (N=10)	0 (0, 30.8)	40 (12.2, 73.8)	**50 (18.7, 81.3)**	70 (34.8, 93.3)	90 (55.5, 99.7)	-	-	-	-
Individual placebo group or Cohorts 3-4 vaccine group (N=15)	0 (0, 21.8)	26.7 (7.8, 55.1)	33.3 (11.8, 61.6)	**46.7 (21.3, 73.4)**	60 (32.3, 83.7)	80 (51.9, 95.7)	100 (78.2, 100)	-	-
Individual vaccine group in Cohorts 6-7 (N=18)	0 (0, 18.5)	22.2 (6.4, 47.6)	27.8 (9.7, 53.5)	38.9 (17.3, 64.3)	**50 (26, 74)**	66.7 (41, 86.7)	83.3 (58.6, 96.4)	-	-
Cohorts 1-2 safety review (N=25)	0 (0, 13.7)	16 (4.5, 36.1)	20 (6.8, 40.7)	28 (12.1, 49.4)	36 (18, 57.5)	**48 (27.8, 68.7)**	60 (38.7, 78.9)	-	-
Individual vaccine group in Cohorts 1-2; Cohorts 3-4 aggregate vaccine groups, post first-dose (N=30)	0 (0, 11.6)	13.3 (3.8, 30.7)	16.7 (5.6, 34.7)	23.3 (9.9, 42.3)	30 (14.7, 49.4)	40 (22.7, 59.4)	**50 (31.3, 68.7)**	-	-
Any Sing2016 M2SR H3N2 Vaccine, Cohorts 1-4 (N=90)	0 (0, 4)	4.4 (1.2, 11)	5.6 (1.8, 12.5)	7.8 (3.2, 15.4)	10 (4.7, 18.1)	13.3 (7.1, 22.1)	16.7 (9.6, 26)	**50 (39.3, 60.7)**	73.3 (63, 82.1)
Any Sing2016 M2SR H3N2 Vaccine (N=132)	0 (0, 2.8)	3.0 (0.8, 7.6)	3.8 (1.2, 8.6)	5.3 (2.2, 10.6)	6.8 (3.2, 12.5)	9.1 (4.8, 15.3)	11.4 (6.5, 18)	-	**50.0 (41.2, 58.8)**

10.2 Protocol Deviations

Table 5: Summary of Protocol Deviations by Category, Type, Cohort, and Vaccination Group - Enrolled Population

Category	Deviation Type	9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 2 Doses (N=X)				All Participants (N=X)			
		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)	
		No. of Part.	No. of Dev.	No. of Part.	No. of Dev.	No. of Part.	No. of Dev.	No. of Part.	No. of Dev.	No. of Part.	No. of Dev.	No. of Part.	No. of Dev.	No. of Part.	No. of Dev.	No. of Part.	No. of Dev.	No. of Part.	No. of Dev.	No. of Part.	No. of Dev.
Eligibility/ enrollment	Any type	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Did not meet inclusion criterion	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Met exclusion criterion	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	ICF not signed prior to study procedures	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Assent not signed prior to study procedures	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Treatment administration schedule	Any type	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Missed treatment administration	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Delayed treatment administration	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Follow-up visit schedule	Any type	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x

Table 5: Summary of Protocol Deviations by Category, Type, Cohort, and Vaccination Group - Enrolled Population *(continued)*

Category	Deviation Type	9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 2 Doses (N=X)				All Participants (N=X)			
		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)	
		No. of Part.	No. of Dev.	No. of Part.	No. of Dev.	No. of Part.	No. of Dev.	No. of Part.	No. of Dev.	No. of Part.	No. of Dev.	No. of Part.	No. of Dev.	No. of Part.	No. of Dev.	No. of Part.	No. of Dev.	No. of Part.	No. of Dev.	No. of Part.	No. of Dev.
	Out of window visit	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Missed visit/visit not conducted	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Protocol procedure/ assessment	Any type	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Incorrect version of ICF signed	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Incorrect version of assent signed	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Blood not collected	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Urine not collected	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Nasal specimen not collected	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Other specimen not collected	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Too few aliquots obtained	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Specimen result not obtained	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Required procedure not conducted	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x

Table 5: Summary of Protocol Deviations by Category, Type, Cohort, and Vaccination Group - Enrolled Population *(continued)*

Category	Deviation Type	9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 2 Doses (N=X)				All Participants (N=X)			
		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)	
		No. of Part.	No. of Dev.	No. of Part.	No. of Dev.	No. of Part.	No. of Dev.	No. of Part.	No. of Dev.	No. of Part.	No. of Dev.	No. of Part.	No. of Dev.	No. of Part.	No. of Dev.	No. of Part.	No. of Dev.	No. of Part.	No. of Dev.	No. of Part.	No. of Dev.
	Required procedure done incorrectly	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Study product temperature excursion	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Specimen temperature excursion	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Treatment administration	Any type	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Required procedure done incorrectly	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Study product temperature excursion	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Blinding policy/procedure	Any type	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Treatment unblinded	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x

N = Number of participants in the enrolled population.

12.2 Adverse Events

Table 6: Grades of Local & Systemic Reactogenicity Assessments, By Age Group

Ages 9-17 Years

Symptoms	Grade 1	Grade 2	Grade 3
Local (Including Respiratory) Reactogenicity			
Rhinorrhea (Runny Nose)	Noticeable but does not interfere with daily activity	Moderate discomfort/interferes with daily activity	Significant discomfort/prevents daily activity or seeks medical encounter
Stuffy nose/congestion	Noticeable but does not interfere with daily activity	Moderate discomfort/interferes with breathing through the nose	Unable to breathe through the nose, or prevents daily activity or seeks medical encounter
Sneezing	Noticeable but does not interfere with daily activity	Moderate discomfort. Interferes with daily activity	Significant discomfort/prevents daily activity
Nasal pain/irritation	Noticeable but does not interfere with daily activity	Moderate discomfort/interferes with daily activity	Significant discomfort/prevents daily activity or seeks medical encounter
Nasal bleeding/ epistaxis	Total duration of all episodes in a 24-hour period ≤30 minutes	Total duration of all episodes in a 24-hour period > 30 minutes, but did not require a visit for a medical encounter	Any bleeding that required visit for medical encounter
Sinus pressure/pain	Noticeable but does not interfere with daily activity	Moderate discomfort. Interferes with daily activity	Significant discomfort/prevents daily activity
Sore throat (may include scratchy or painful throat)	Noticeable but does not interfere with eating and/or drinking	Moderate discomfort. Interferes with eating and/or drinking	Significant discomfort/prevents eating and/or drinking or seeks medical encounter
Cough	Noticeable but does not interfere with daily activity or sleeping	Moderate discomfort/interferes with daily activity or sleeping	Significant discomfort/prevents daily activity or seeks medical encounter
Trouble breathing or shortness of breath	Noticeable but does not interfere with daily activity or not troubled by breathlessness except on vigorous exercise	Moderate discomfort/interferes with daily activity or short of breath with regular movement activities such as when hurrying on a level surface or walking up a slight incline and need to stop	Significant discomfort/prevents daily activity or seeks medical encounter or too breathless to leave the house, or breathless when undressing, preventing normal activities
Systemic Reactogenicity			
Feverishness (may include chills or shivering)	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity
Fatigue (tiredness)	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity
Malaise (general unwell feeling)	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity
Myalgia (general body aches, general muscular pain)	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity
Arthralgia (general joint pains)	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity
Headache	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity and/or seeks medical encounter

Table 6: Grades of Local & Systemic Reactogenicity Assessments, By Age Group *(continued)*

Symptoms	Grade 1	Grade 2	Grade 3
Flushing	Asymptomatic flushing	Symptoms, some interference with daily activity	Symptomatic, significant interference, prevents daily activity
Decreased activity	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity
Decreased appetite	Loss of appetite without decrease in oral intake	Loss of appetite associated with decreased oral intake	Loss of appetite without oral intake, seek medical care
Abdominal pain	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity
Nausea	Transient (<24 hours) or intermittent and no or minimal interference with oral intake	Persistent nausea resulting in decreased oral intake for 24 to 48 hours	Persistent nausea resulting in minimal oral intake for > 48 hours, or rehydration indicated (e.g., IV fluids)
Vomiting	Transient or intermittent, and no interference with daily activity; minimal interference with oral intake	Frequent episodes with no dehydration and interferes with some daily activity	Persistent vomiting, resulting in orthostatic hypotension or aggressive rehydration (e.g., IV fluids) or prevents normal daily activity
Diarrhea	Transient or intermittent, and no interference with daily activity; minimal interference with oral intake	Frequent episodes with no dehydration and interferes with some daily activity	Persistent diarrhea, resulting in orthostatic hypotension or aggressive rehydration (e.g., IV fluids) or prevents normal daily activity
Eye pruritus	Transient of intermittent or minimal interference and no intervention	Persistent or frequent episodes, some interference with daily activity	Significant symptoms, prevents daily activity, or seeks medical attention
Eye redness	Asymptomatic eye redness	Symptomatic eye redness, some interference with daily activity	Eye redness prevents daily activity or seeks medical encounter
Allergic Skin Reaction	Pruritus with or without rash, no medical intervention	Localized urticaria, with intervention	Generalized urticaria, anaphylaxis, or angioedema
Fever* - oral or axillary†	38.0°C – 38.4°C (100.4°F – 101.1°F)	38.5°C – 38.9°C (101.2°F – 102.0°F)	>38.9°C (>102.0°F)

* A fever can be considered not related to the study product if an alternative etiology can be documented.
† Participants must not eat or drink anything hot or cold prior to taking oral temperature

Ages 4-8 Years

Symptoms	Grade 1	Grade 2	Grade 3
Local (Including Respiratory) Reactogenicity			
Rhinorrhea (Runny Nose)	Noticeable but does not interfere with daily activity	Moderate discomfort/interferes with daily activity	Significant discomfort/prevents daily activity or seeks medical encounter
Stuffy nose/congestion	Noticeable but does not interfere with daily activity	Moderate discomfort/interferes with breathing through nose	Unable to breathe through nose, or prevents daily activity or seeks medical encounter

Table 6: Grades of Local & Systemic Reactogenicity Assessments, By Age Group *(continued)*

Symptoms	Grade 1	Grade 2	Grade 3
Sneezing	Noticeable but does not interfere with daily activity	Moderate discomfort. Interferes with daily activity	Significant discomfort/prevents daily activity
Nasal pain/irritation	Noticeable but does not interfere with daily activity	Moderate discomfort/interferes with daily activity	Significant discomfort/prevents daily activity or seeks medical encounter
Nasal bleeding/ epistaxis	Total duration of all episodes in a 24-hour period ≤30 minutes	Total duration of all episodes in a 24-hour period > 30 minutes	Any bleeding that required visit for medical encounter
Facial Pain	Noticeable but does not interfere with daily activity	Moderate discomfort. Interferes with daily activity	Significant discomfort/prevents daily activity
Sore throat (may include scratchy or painful throat)	Noticeable but does not interfere with eating and/or drinking	Moderate discomfort. Interferes with eating and/or drinking	Significant discomfort/prevents eating and/or drinking or seeks medical encounter
Cough	Noticeable but does not interfere with daily activity or sleeping	Moderate discomfort/interferes with daily activity or sleeping	Significant discomfort/prevents daily activity or seeks medical encounter
Trouble breathing, shortness of breath	Noticeable but does not interfere with daily activity or not troubled by breathlessness except on vigorous exercise	Moderate discomfort/interferes with daily activity or short of breath with regular movement activities such as when hurrying on the level or walking up a slight incline and need to stop	Significant discomfort/prevents daily activity or seeks medical encounter or too breathless to leave the house, or breathless when undressing, preventing normal activities
Systemic Reactogenicity			
Feverishness (may include chills, shivering, sweating)	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity
Fatigue (tiredness)	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity
Malaise (general unwell feeling)	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity
Myalgia (general body aches/muscular pain)	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity
Arthralgia (general joint pains)	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity
Headache	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity and/or seeks medical encounter
Decreased activity	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity
Decreased appetite	Loss of appetite without decrease in oral intake	Loss of appetite associated with decreased oral intake	Loss of appetite without oral intake, seek medical care
Abdominal pain	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity
Nausea	Transient (<24 hours) or intermittent, and with no or minimal interference with oral intake	Persistent nausea resulting in decreased oral intake for 24 to 48 hours	Persistent nausea resulting in minimal oral intake for > 48 hours, or rehydration indicated (e.g., IV fluids)

Table 6: Grades of Local & Systemic Reactogenicity Assessments, By Age Group *(continued)*

Symptoms	Grade 1	Grade 2	Grade 3
Vomiting	Transient or intermittent AND no interference with daily activity; minimal interference with oral intake	Frequent episodes with no dehydration and interferes with some daily activity	Persistent vomiting, resulting in orthostatic hypotension or aggressive rehydration (e.g., IV fluids) or prevents normal daily activity
Diarrhea	Transient or intermittent AND no interference with daily activity; minimal interference with oral intake	Frequent episodes with no dehydration and interferes with some daily activity	Persistent diarrhea, resulting in orthostatic hypotension or aggressive rehydration (e.g., IV fluids) or prevents normal daily activity
Eye pruritus	Transient of intermittent or minimal interference and no intervention	Persistent or frequent episodes, some interference with daily activity	Significant symptoms, prevents daily activity, or seeks medical attention
Eye redness	Asymptomatic eye redness	Symptomatic eye redness, some interference with daily activity	Eye redness prevents daily activity or seeks medical encounter
Allergic Skin Reactions	Pruritus with or without rash, no medical intervention	Localized urticaria, with intervention	Generalized urticaria, anaphylaxis, or angioedema
Fever* - oral or axillary†	38.0°C – 38.4°C 100.4°F – 101.1°F	38.5°C – 38.9°C 101.2°F – 102.0°F	>38.9°C >102.0°F

* A fever can be considered not related to the study product if an alternative etiology can be documented.
† Participants must not eat or drink anything hot or cold prior to taking oral temperature

14.1.1 Disposition of Participants

Table 7: Ineligibility Summary of Screening Failures - Screened Population

[Implementation Note: All I/E criteria reported to not have been met by screen failures will be included.]

Inclusion/Exclusion Category	Inclusion/Exclusion Criterion	9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose n (%)	2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose n (%)	2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose n (%)	2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 2 Doses n (%)	All Participants n (%)
Inclusion and Exclusion	Number of participants failing any eligibility criterion	x (x)	x (x)	x (x)	x (x)	x (x)
Inclusion	Any inclusion criterion	x (x)	x (x)	x (x)	x (x)	x (x)
	[inclusion criterion 1]	x (x)	x (x)	x (x)	x (x)	x (x)
	[inclusion criterion 2]	x (x)	x (x)	x (x)	x (x)	x (x)
	[inclusion criterion 3]	x (x)	x (x)	x (x)	x (x)	x (x)
Exclusion	Any exclusion criterion	x (x)	x (x)	x (x)	x (x)	x (x)
	[exclusion criterion 1]	x (x)	x (x)	x (x)	x (x)	x (x)
	[exclusion criterion 2]	x (x)	x (x)	x (x)	x (x)	x (x)
	[exclusion criterion 3]	x (x)	x (x)	x (x)	x (x)	x (x)
Eligible but not Enrolled	Any reason	x (x)	x (x)	x (x)	x (x)	x (x)
	[reason 1]	x (x)	x (x)	x (x)	x (x)	x (x)
	[reason 2]	x (x)	x (x)	x (x)	x (x)	x (x)
	[reason 3]	x (x)	x (x)	x (x)	x (x)	x (x)

More than one criterion may be marked per participant. Denominator for percentages is the total number of screen failures.

Table 8: Participant Disposition by Cohort and Vaccination Group - Enrolled Population

Subject Disposition	9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 2 Doses (N=X)				All Participants[a] (N=X)			
	Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n/N*	%	n/N*	%
Screened[a]	x	-	x	-	x	-	x	-	x	-	x	-	x	-	x	-	x	-	x	-
Enrolled/Randomized	x	100	x	100	x	100	x	100	x	100	x	100	x	100	x	100	x/x	100	x/x	100
Received Dose 1 of Study Product	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x/x	x	x/x	x
Received Dose 2 of Study Product	-	-	-	-	-	-	-	-	-	-	-	-	x	x	x	x	x/x	x	x/x	x
Completed Safety Follow-up for 7 Days Post-Dose 1	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x/x	x	x/x	x
Completed Safety Follow-up for 7 Days Post-Dose 2	-	-	-	-	-	-	-	-	-	-	-	-	x	x	x	x	x/x	x	x/x	x
Completed Safety Follow-up for 28 Days Post-Dose 1	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x/x	x	x/x	x
Completed Safety Follow-up for 28 Days Post-Dose 2	-	-	-	-	-	-	-	-	-	-	-	-	x	x	x	x	x/x	x	x/x	x
Completed Safety Follow-up Through the End of the Study	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x/x	x	x/x	x
Early Termination	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x/x	x	x/x	x

N = Number of participants in the enrolled population. N*=Number and percent of participants in the enrolled population in the applicable cohorts
[a] Participants in the screened population will be included.

Table 9: Analysis Populations by Cohort and Vaccination Group - Enrolled Population

Analysis Populations	Reason Participants Excluded	9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 2 Doses (N=X)		All Participants[a] (N=X)	
		Vaccine (N=X)	Placebo (N=X)	Vaccine (N=X)	Placebo (N=X)	Vaccine (N=X)	Placebo (N=X)	Vaccine (N=X)	Placebo (N=X)	Vaccine (N=X)	Placebo (N=X)
		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n/N* (%)	n/N* (%)
Safety	No study product received	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x/x (x)	x/x (x)
mITT	Any reason	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x/x (x)	x/x (x)
	No study product received	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x/x (x)	x/x (x)
	No baseline immunogenicity result	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x/x (x)	x/x (x)
	No post-baseline immunogenicity results	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x/x (x)	x/x (x)
Per-Protocol, Visit 4/4C or 6	Any reason	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x/x (x)	x/x (x)
	No study product received	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x/x (x)	x/x (x)
	No baseline immunogenicity result	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x/x (x)	x/x (x)
	No post-baseline immunogenicity results	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x/x (x)	x/x (x)
	Ineligible at enrollment[a]	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x/x (x)	x/x (x)
	Visit 4 or 4C substantially out of window[b]	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x/x (x)	x/x (x)
	Visit 6 substantially out of window[b]	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x/x (x)	x/x (x)
	Receipt of immunosuppressive medication	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x/x (x)	x/x (x)
	Receipt of any non-study investigational drug/investigational vaccine/licensed vaccine[c]	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x/x (x)	x/x (x)

Table 9: Analysis Populations by Cohort and Vaccination Group - Enrolled Population *(continued)*

Analysis Populations	Reason Participants Excluded	9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 2 Doses (N=X)		All Participants[a] (N=X)	
		Vaccine (N=X)	Placebo (N=X)	Vaccine (N=X)	Placebo (N=X)	Vaccine (N=X)	Placebo (N=X)	Vaccine (N=X)	Placebo (N=X)	Vaccine (N=X)	Placebo (N=X)
		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n/N* (%)	n/N* (%)
	Receipt of incorrect study influenza vaccination[d]	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x (x)	x/x (x)	x/x (x)

N = Number of participants in the enrolled population. N*=Number and percent of participants in the enrolled population in the applicable cohorts
[a] Ineligible enrollment determined post-baseline
[b] Substantially out of window defined as occurring more than 500% of the half-width of the visit window days from the target day
[c] Outside of what is allowable per-protocol
[d] Includes incorrect dosage

14.1.2 Demographic Data

Table 10: Summary of Categorical Demographic and Baseline Characteristics by Site, Cohort, and Vaccination Group - Enrolled Population

[Implementation Note: Denominators for all variables will be the number of participants in the enrolled population for the given analysis group.]

		9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 2 Doses (N=X)				All Participants (N=X)			
		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)	
Variable	**Characteristic**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
All Sites																					
Sex	Male	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Female	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Ethnicity	Not Hispanic or Latino	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Hispanic or Latino	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Not Reported	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Unknown	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Race	American Indian or Alaska Native	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Asian	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Native Hawaiian or Other Pacific Islander	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Black or African American	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	White	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Multi-Racial	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Unknown	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Prior Receipt of Seasonal Vaccination	Prior Receipt within 2 Years of First Study Vaccination	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x

Table 10: Summary of Categorical Demographic and Baseline Characteristics by Site, Cohort, and Vaccination Group - Enrolled Population *(continued)*

Variable	Characteristic	9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 2 Doses (N=X)				All Participants (N=X)			
		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
	≤1 year from first study vaccination	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	1-2 years from first study vaccination	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	No Prior Receipt within 2 Years of First Study Vaccination	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Prior Receipt of COVID-19 Vaccination	Prior Receipt within 2 Years of First Study Vaccination	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	≤1 year from first study vaccination	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	1-2 years from first study vaccination	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	No Prior Receipt within 2 Years of First Study Vaccination	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Duke University																					
Sex	Male	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Female	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Ethnicity	Not Hispanic or Latino	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Hispanic or Latino	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Not Reported	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Unknown	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x

Table 10: Summary of Categorical Demographic and Baseline Characteristics by Site, Cohort, and Vaccination Group - Enrolled Population *(continued)*

Variable	Characteristic	9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 2 Doses (N=X)				All Participants (N=X)			
		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Race	American Indian or Alaska Native	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Asian	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Native Hawaiian or Other Pacific Islander	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Black or African American	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	White	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Multi-Racial	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Unknown	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Prior Receipt of Seasonal Influenza Vaccination	Prior Receipt within 2 Years of First Study Vaccination	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	≤1 year from first study vaccination	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	1-2 years from first study vaccination	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	No Prior Receipt within 2 Years of First Study Vaccination	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Prior Receipt of COVID-19 Vaccination	Prior Receipt within 2 Years of First Study Vaccination	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	≤1 year from first study vaccination	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x

Table 10: Summary of Categorical Demographic and Baseline Characteristics by Site, Cohort, and Vaccination Group - Enrolled Population *(continued)*

		9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 2 Doses (N=X)				All Participants (N=X)			
		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)	
Variable	**Characteristic**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
	1-2 years from first study vaccination	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	No Prior Receipt within 2 Years of First Study Vaccination	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Repeat for remaining sites																					

N = Number of participants in the enrolled population.

Table 11: Summary of Continuous Demographic Characteristics by Site, Cohort, and Vaccination Group - Enrolled Population

Variable	Characteristic	9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 2 Doses (N=X)		All Participants (N=X)	
		Vaccine (N=X)	Placebo (N=X)	Vaccine (N=X)	Placebo (N=X)	Vaccine (N=X)	Placebo (N=X)	Vaccine (N=X)	Placebo (N=X)	Vaccine (N=X)	Placebo (N=X)
All Sites											
Age (years)	n	x	x	x	x	x	x	x	x	x	x
	Mean	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Standard Deviation	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Median	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Minimum	x	x	x	x	x	x	x	x	x	x
	Maximum	x	x	x	x	x	x	x	x	x	x
Duke University											
Age (years)	n	x	x	x	x	x	x	x	x	x	x
	Mean	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Standard Deviation	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Median	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x	x.x
	Minimum	x	x	x	x	x	x	x	x	x	x
	Maximum	x	x	x	x	x	x	x	x	x	x
Repeat for remaining sites											

N = Number of participants in the enrolled population.

14.1.3 Prior and Concurrent Medical Conditions

Table 12: Number and Percent of Participants with Prior and Concurrent Medical Conditions by MedDRA SOC, Cohort, and Vaccination Group - Safety Population

[Implementation Note: SOCs will be sorted by frequency across all participants, most to least common.]

	9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose				2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose				2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose				2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 2 Doses				All Participants			
	Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)	
MedDRA SOC	**n**	%	**n**	%	**n**	%	**n**	%	**n**	%	**n**	%	**n**	%	**n**	%	**n**	%	**n**	%
Any SOC	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
[SOC 1]	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
[SOC 2]	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x

N = Number of participants in the safety population; n = Number of participants in the safety population reporting medical history within the specified SOC. A participant is only counted once per SOC.

14.2 Immunogenicity Data

14.2.1 Immunogenicity Data Summary Tables

Table 13: Summary of Hemagglutination Inhibition (HAI) Antibody Titers in Serum Against A/Singapore/INFIMH-16-0019/2016 by Cohort and Vaccination Group at Baseline, 28 Days after Last Vaccination, and 28 Days after IIV4 Administration - Modified Intent-to-Treat Population (N=X)

		9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 2 Doses (N=X)	
Study Day	**Statistic**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**
Baseline	n	x	x	x	x	x	x	x	x
	GMT (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Seroprotection - % (95% CI)[b,c]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Day 29	n	x	x	x	x	x	x	-	-
	GMT (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	-	-
	GMFR (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	-	-
	Fold-Rise ≥ 2 - % (95% CI)[b]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	-	-
	Fold-Rise ≥ 4 - % (95% CIb[c]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	-	-
	Seroprotection - % (95% CI)[b, c]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	-	-
Day 57	N	-	-	-	-	-	-	x	x
	GMT (95% CI)[a]	-	-	-	-	-	-	x.x (x.x, x.x)	x.x (x.x, x.x)
	GMFR (95% CI)[a]	-	-	-	-	-	-	x.x (x.x, x.x)	x.x (x.x, x.x)
	Fold-Rise ≥ 2 - % (95% CI)[b]	-	-	-	-	-	-	x.x (x.x, x.x)	x.x (x.x, x.x)
	Fold-Rise ≥ 4 - % (95% CI)[b]	-	-	-	-	-	-	x.x (x.x, x.x)	x.x (x.x, x.x)

Table 13: Summary of Hemagglutination Inhibition (HAI) Antibody Titers in Serum Against A/Singapore/INFIMH-16-0019/2016 by Cohort and Vaccination Group at Baseline, 28 Days after Last Vaccination, and 28 Days after IIV4 Administration - Modified Intent-to-Treat Population (N=X) *(continued)*

		9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 2 Doses (N=X)	
Study Day	**Statistic**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**
	Seroprotection - % (95% CI)[b, c]	-	-	-	-	-	-	x.x (x.x, x.x)	x.x (x.x, x.x)
28 Days Post IIV4 Administration	n	x	x	x	x	x	x	x	x
	GMT (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	GMFR (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Fold-Rise ≥ 2 - % (95% CI)[b]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Fold-Rise ≥ 4 - % (95% CI)[b]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Seroprotection - % (95% CI)[b, c]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)

N = Number of participants included in the modified intent-to-treat population, n=Number of participants with available results, GMT=Geometric Mean Titer, GMFR = Geometric Mean Fold-Rise.
[a] Confidence Interval calculated based on t-distribution or 10,000 bootstrap samples.
[b] Exact binomial confidence interval calculated using the Clopper-Pearson methodology.
[c] Seroprotection defined as HAI titer ≥ 1:40.

Table 14: Summary of Influenza Microneutralization (MN) Antibody Titers in Serum Against A/Singapore/INFIMH-16-0019/2016 by Cohort and Vaccination Group at Baseline, 28 Days after Last Vaccination, and 28 Days after IIV4 Administration - Modified Intent-to-Treat Population (N=X)

		9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 2 Doses (N=X)	
Study Day	**Statistic**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**
Baseline	n	x	x	x	x	x	x	x	x
	GMT (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Neutralization Titer ≥ 1:40 - % (95% CI)[b]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Day 29	n	x	x	x	x	x	x	-	-
	GMT (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	-	-
	GMFR (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	-	-
	Fold-Rise ≥ 2 - % (95% CI)[b]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	-	-
	Fold-Rise ≥ 4 - % (95% CI)[b]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	-	-
	Neutralization Titer ≥ 1:40 - % (95% CI)[b]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	-	-
Day 57	n	-	-	-	-	-	-	x	x
	GMT (95% CI)[a]	-	-	-	-	-	-	x.x (x.x, x.x)	x.x (x.x, x.x)
	GMFR (95% CI)[a]	-	-	-	-	-	-	x.x (x.x, x.x)	x.x (x.x, x.x)
	Fold-Rise ≥ 2 - % (95% CI)[b]	-	-	-	-	-	-	x.x (x.x, x.x)	x.x (x.x, x.x)
	Fold-Rise ≥ 4 - % (95% CI)[b]	-	-	-	-	-	-	x.x (x.x, x.x)	x.x (x.x, x.x)
	Neutralization Titer ≥ 1:40 - % (95% CI)[b]	-	-	-	-	-	-	x.x (x.x, x.x)	x.x (x.x, x.x)

Table 14: Summary of Influenza Microneutralization (MN) Antibody Titers in Serum Against A/Singapore/INFIMH-16-0019/2016 by Cohort and Vaccination Group at Baseline, 28 Days after Last Vaccination, and 28 Days after IIV4 Administration - Modified Intent-to-Treat Population (N=X) *(continued)*

		9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 2 Doses (N=X)	
Study Day	**Statistic**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**
28 Days Post IIV4 Administration	n	x	x	X	x	x	x	x	x
	GMT (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	GMFR (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Fold-Rise ≥ 2 - % (95% CI)[b]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Fold-Rise ≥ 4 - % (95% CI)[b]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Neutralization Titer ≥ 1:40 - % (95% CI)[b]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)

N = Number of participants included in the modified intent-to-treat population, n=Number of participants with available results, GMT=Geometric Mean Titer, GMFR = Geometric Mean Fold-Rise.
[a] Confidence Interval calculated based on t-distribution or 10,000 bootstrap samples.
[b] Exact binomial confidence interval calculated using the Clopper-Pearson methodology.

Table 15: Summary of Secretory IgA (sIgA) Against A/Singapore/INFIMH-16-0019/2016 as Measured by the Binding Antibody Multiplex Assay by Cohort and Vaccination Group at Baseline, 28 Days after Last Vaccination, and 28 Days after IIV4 Administration - Modified Intent-to-Treat Population (N=X)

		9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 2 Doses (N=X)	
Study Day	**Statistic**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**
ECL Signal against A/Singapore/INFIMH-16-0019/2016 (Non-Dilution Aadjusted ECL Signal against A/Singapore/INFIMH-16-0019/2016 * Dilution Factor)									
Day 1	N	x	x	x	x	x	x	x	x
	Mean (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Day 29	N	x	x	x	x	x	x	-	-
	Mean (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	-	-
	Mean Difference from Baseline (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	-	-
Day 57	N	-	-	-	-	-	-	x	x
	Mean (95% CI)[a]	-	-	-	-	-	-	x.x (x.x, x.x)	x.x (x.x, x.x)
	Mean Difference from Baseline (95% CI)[a]	-	-	-	-	-	-	x.x (x.x, x.x)	x.x (x.x, x.x)
28 Days Post IIV4 Administration	N	x	x	x	x	x	x	x	x
	Mean (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Mean Difference from Baseline (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Total sIgA Concentration (µg/ml)									
Day 1	N	x	x	x	x	x	x	x	x
	Mean (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Day 29	n	x	x	x	x	x	x	-	-
	Mean (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	-	-

Table 15: Summary of Secretory IgA (sIgA) Against A/Singapore/INFIMH-16-0019/2016 as Measured by the Binding Antibody Multiplex Assay by Cohort and Vaccination Group at Baseline, 28 Days after Last Vaccination, and 28 Days after IIV4 Administration - Modified Intent-to-Treat Population (N=X) *(continued)*

		9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 2 Doses (N=X)	
Study Day	**Statistic**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**
	Mean Difference from Baseline (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	-	-
Day 57	n	-	-	-	-	-	-	x	x
	Mean (95% CI)[a]	-	-	-	-	-	-	x.x (x.x, x.x)	x.x (x.x, x.x)
	Mean Difference from Baseline (95% CI)[a]	-	-	-	-	-	-	x.x (x.x, x.x)	x.x (x.x, x.x)
28 Days Post IIV4 Administration	n	x	x	x	x	x	x	x	x
	Mean (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Mean Difference from Baseline (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Specific Activity against A/Singapore/INFIMH-16-0019/2016 ([ECL Signal against A/Singapore/INFIMH-16-0019/2016] / µg/ml sIgA)									
Day 1	n	x	x	x	x	x	x	x	x
	Mean (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Day 29	n	x	x	x	x	x	x	-	-
	Mean (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	-	-
	Mean Difference from Baseline (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	-	-
Day 57	n	-	-	-	-	-	-	x	x
	Mean (95% CI)[a]	-	-	-	-	-	-	x.x (x.x, x.x)	x.x (x.x, x.x)
	Mean Difference from Baseline (95% CI)[a]	-	-	-	-	-	-	x.x (x.x, x.x)	x.x (x.x, x.x)

Table 15: Summary of Secretory IgA (sIgA) Against A/Singapore/INFIMH-16-0019/2016 as Measured by the Binding Antibody Multiplex Assay by Cohort and Vaccination Group at Baseline, 28 Days after Last Vaccination, and 28 Days after IIV4 Administration - Modified Intent-to-Treat Population (N=X) *(continued)*

		9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 2 Doses (N=X)	
Study Day	**Statistic**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**
28 Days Post IIV4 Administration	n	x	x	x	x	x	x	x	x
	Mean (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Mean Difference from Baseline (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)

Notes: N = Number of participants in modified intent-to-treat population; n = Number of participants with available results.
[a] Confidence interval calculated based on t-distribution or 10,000 bootstrap samples.

Similar Tables:

Table 16: Summary of Secretory IgA (sIgA) Against A/Texas/71/2017 as Measured by the Binding Antibody Multiplex Assay by Cohort and Vaccination Group at Baseline, 28 Days after Last Vaccination, and 28 Days after IIV4 Administration - Modified Intent-to-Treat Population (N=X)

Implementation Note: This table will be similar to Table 15.

Table 17: Summary of Secretory IgA (sIgA) Against A/Hong Kong/45/2019 as Measured by the Binding Antibody Multiplex Assay by Cohort and Vaccination Group at Baseline, 28 Days after Last Vaccination, and 28 Days after IIV4 Administration - Modified Intent-to-Treat Population (N=X)

Implementation Note: This table will be similar to Table 15.

Table 18: Summary of Secretory IgA (sIgA) Against A/Cambodia/e0826360/2020 as Measured by the Binding Antibody Multiplex Assay by Cohort and Vaccination Group at Baseline, 28 Days after Last Vaccination, and 28 Days after IIV4 Administration - Modified Intent-to-Treat Population (N=X)

Implementation Note: This table will be similar to Table 15.

Table 19: Summary of Hemagglutination Inhibition (HAI) Antibody Titers in Plasma Against A/Singapore/INFIMH-16-0019/2016 by Cohort and Vaccination Group at Baseline, 28 Days after Last Vaccination, and 28 Days after IIV4 Administration - Modified Intent-to-Treat Population (N=X)

Implementation Note: This table will be similar to Table 13. Participants will be included only if they have a sufficient number of aliquots at each visit of interest.

Table 20: Summary of Influenza Microneutralization (MN) Antibody Titers in Plasma Against A/Singapore/INFIMH-16-0019/2016 by Cohort and Vaccination Group at Baseline, 28 Days after Last Vaccination, and 28 Days after IIV4 Administration - Modified Intent-to-Treat Population (N=X)

Implementation Note: This table will be similar to Table 14. Participants will be included only if they have a sufficient number of aliquots at each visit of interest.

Table 21: Summary of Neuraminidase Inhibition (NAI) Titers in Plasma Against A/Singapore/INFIMH-16-0019/2016 by Cohort and Vaccination Group at Baseline, 28 Days after Last Vaccination, and 28 Days after IIV4 Administration - Modified Intent-to-Treat Population (N=X)

Implementation Note: This table will be similar to Table 14. "Titer ≥ 1:40" will be presented instead of "Neutralization Titer ≥ 1:40." Participants will be included only if they have a sufficient number of aliquots at each visit of interest.

Table 22: Summary of Secretory IgA (sIgA) as Measured by an Enzyme-Linked Immunosorbent Assay (ELISA) Against A/Singapore/INFIMH-16-0019/2016 by Cohort and Vaccination Group at Baseline, 28 Days after Last Vaccination, and 28 Days after IIV4 Administration - Modified Intent-to-Treat Population (N=X)

		9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 2 Doses (N=X)	
Study Day	**Statistic**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**
sIgA Titer Against A/Singapore/INFIMH-16-0019/2016 (H3N2)									
Day 1	N	x	x	x	X	x	x	x	x
	GMT (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Day 29	N	x	x	x	X	x	x	-	-
	GMT (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	-	-
	GMFR (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	-	-
	Fold-Rise ≥ 2 - % (95% CI)[b]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	-	-
	Fold-Rise ≥ 4 - % (95% CI)[b]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	-	-
Day 57	n	-	-	-	-	-	-	x	x
	GMT (95% CI)[a]	-	-	-	-	-	-	x.x (x.x, x.x)	x.x (x.x, x.x)
	GMFR (95% CI)[a]	-	-	-	-	-	-	x.x (x.x, x.x)	x.x (x.x, x.x)
	Fold-Rise ≥ 2 - % (95% CI)[b]	-	-	-	-	-	-	x.x (x.x, x.x)	x.x (x.x, x.x)
	Fold-Rise ≥ 4 - % (95% CI)[b]	-	-	-	-	-	-	x.x (x.x, x.x)	x.x (x.x, x.x)
28 Days Post IIV4 Administration	n	x	x	x	X	x	x	x	x
	GMT (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	GMFR (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Fold-Rise ≥ 2 - % (95% CI)[b]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Fold-Rise ≥ 4 - % (95% CI)[b]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)

Table 22: Summary of Secretory IgA (sIgA) as Measured by an Enzyme-Linked Immunosorbent Assay (ELISA) Against A/Singapore/INFIMH-16-0019/2016 by Cohort and Vaccination Group at Baseline, 28 Days after Last Vaccination, and 28 Days after IIV4 Administration - Modified Intent-to-Treat Population (N=X) *(continued)*

		9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 2 Doses (N=X)	
Study Day	**Statistic**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**
Total sIgA Concentration (µg/mL)									
Day 1	n	x	x	x	x	x	x	x	x
	Mean (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Day 29	n	x	x	x	x	x	x	-	-
	Mean (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	-	-
	Mean Difference from Baseline (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	-	-
Day 57	n	-	-	-	-	-	-	x	x
	Mean (95% CI)[a]	-	-	-	-	-	-	x.x (x.x, x.x)	x.x (x.x, x.x)
	Mean Difference from Baseline (95% CI)[a]	-	-	-	-	-	-	x.x (x.x, x.x)	x.x (x.x, x.x)
28 Days Post IIV4 Administration	n	x	x	x	x	x	x	x	x
	Mean (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Mean Difference from Baseline (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Normalized sIgA Against A/Singapore/INFIMH-16-0019/2016 (H3N2) (titer / µg/mL)									
Day 1	n	x	x	x	x	x	x	x	x
	Mean (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Day 29	n	x	x	x	x	x	x	-	-
	Mean (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	-	-

Table 22: Summary of Secretory IgA (sIgA) as Measured by an Enzyme-Linked Immunosorbent Assay (ELISA) Against A/Singapore/INFIMH-16-0019/2016 by Cohort and Vaccination Group at Baseline, 28 Days after Last Vaccination, and 28 Days after IIV4 Administration - Modified Intent-to-Treat Population (N=X) *(continued)*

		9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)		2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 2 Doses (N=X)	
Study Day	**Statistic**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**
	Mean Difference from Baseline (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	-	-
Day 57	n	-	-	-	-	-	-	x	x
	Mean (95% CI)[a]	-	-	-	-	-	-	x.x (x.x, x.x)	x.x (x.x, x.x)
	Mean Difference from Baseline (95% CI)[a]	-	-	-	-	-	-	x.x (x.x, x.x)	x.x (x.x, x.x)
28 Days Post IIV4 Administration	n	x	x	x	x	x	x	x	x
	Mean (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Mean Difference from Baseline (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)

N = Number of participants with a sufficient number of aliquots (5) at baseline, 28 days post-baseline, and 28 days post IIV4 administration each; n = Number of participants with available results; GMT = Geometric Mean Titer; GMFR = Geometric Mean Fold-Rise.
[a] Confidence interval calculated based on t-distribution or 10,000 bootstrap samples.
[b] Exact binomial confidence interval calculated using the Clopper-Pearson methodology.

Table 23: Exploratory Age Subgroup Summary of Hemagglutination Inhibition (HAI) Antibody Titers in Serum Against A/Singapore/INFIMH-16-0019/2016 by Cohort, and Vaccination Group, at Baseline, 28 Days after Last Vaccination, and 28 Days after IIV4 Administration - Modified Intent-to-Treat Population (N=X)

Implementation Note: Similar tables may be generated for additional subgroups as outlined in Section 7.2

		Cohort 1 (N=X)		Cohort 2 (N=X)				Cohort 3 (N=X)				Cohort 4 (N=X)			
		9–17-year-olds (N=X)		2–4-year-olds (N=X)		5–8-year-olds (N=X)		2–4-year-olds (N=X)		5–8-year-olds (N=X)		2–4-year-olds (N=X)		5–8-year-olds (N=X)	
Study Day	**Statistic**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**
Baseline	n	x	x	x	x	X	x	x	x	x	x	x	x	x	x
	GMT (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Seroprotection - % (95% CI)[b, c]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
Day 29	n	x	x	x	x	x	x	x	x	x	x	-	-	-	-
	GMT (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	-	-	-	-
	GMFR (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	-	-	-	-
	Fold-Rise ≥ 2 - % (95% CI)[b]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	-	-	-	-
	Fold-Rise ≥ 4 - % (95% CI)[b]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	-	-	-	-
	Seroprotection - % (95% CI)[b, c]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	-	-	-	-
Day 57	n	-	-	-	-	-	-	-	-	-	-	x	x	x	x
	GMT (95% CI)[a]	-	-	-	-	-	-	-	-	-	-	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	GMFR (95% CI)[a]	-	-	-	-	-	-	-	-	-	-	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)

Table 23: Exploratory Age Subgroup Summary of Hemagglutination Inhibition (HAI) Antibody Titers in Serum Against A/Singapore/INFIMH-16-0019/2016 by Cohort, and Vaccination Group, at Baseline, 28 Days after Last Vaccination, and 28 Days after IIV4 Administration - Modified Intent-to-Treat Population (N=X) *(continued)*

		Cohort 1 (N=X)		Cohort 2 (N=X)				Cohort 3 (N=X)				Cohort 4 (N=X)			
		9–17-year-olds (N=X)		2–4-year-olds (N=X)		5–8-year-olds (N=X)		2–4-year-olds (N=X)		5–8-year-olds (N=X)		2–4-year-olds (N=X)		5–8-year-olds (N=X)	
Study Day	**Statistic**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**	**Vaccine**	**Placebo**
	Fold-Rise ≥ 2 - % (95% CI)[b]	-	-	-	-	-	-	-	-	-	-	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Fold-Rise ≥ 4 - % (95% CI)[b]	-	-	-	-	-	-	-	-	-	-	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Seroprotection - % (95% CI)[b, c]	-	-	-	-	-	-	-	-	-	-	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
28 Days Post IIV4 Administration	n	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	GMT (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	GMFR (95% CI)[a]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Fold-Rise ≥ 2 - % (95% CI)[b]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Fold-Rise ≥ 4 - % (95% CI)[b]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Seroprotection - % (95% CI)[b, c]	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)

N = Number of participants included in the modified intent-to-treat population, n=Number of participants with available results, GMT=Geometric Mean Titer, GMFR = Geometric Mean Fold-Rise.
[a] Confidence Interval calculated based on t-distribution or 10,000 bootstrap samples.
[b] Exact binomial confidence interval calculated using the Clopper-Pearson methodology.
[c] Seroprotection defined as HAI titer ≥ 1:40.

14.3 Safety Data

14.3.1 Displays of Adverse Events

Table 24: Overall Summary of Adverse Events by Cohort and Vaccination Group - Safety Population

	9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 2 Doses (N=X)				All Participants (N=X)			
	Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)	
Participants with	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n/N***	**%**	**n/N***	**%**
At least one local solicited adverse event	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
At least one systemic solicited adverse event	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
At least one unsolicited adverse event	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
At least one related adverse event	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Mild (Grade 1)	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Moderate (Grade 2)	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Severe (Grade 3)	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
At least one serious adverse event	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
At least one related serious adverse event	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
At least one adverse event leading to early termination[a]	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
At least one non-serious adverse event in the 28 days post Dose 1	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
At least one non-serious adverse	-	-	-	-	-	-	-	-	-	-	-	-	x	x	x	x	x	x	x	x

Table 24: Overall Summary of Adverse Events by Cohort and Vaccination Group - Safety Population *(continued)*

	9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 2 Doses (N=X)				All Participants (N=X)			
	Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)	
Participants with	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n/N***	**%**	**n/N***	**%**
event in the 28 days post Dose 2																				
At least one adverse event of special interest (AESI)	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
At least one new-onset chronic medical condition (NOCMC)	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
At least one adverse event classified as an unanticipated problem[a]	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x

N = Number of participants in the safety population and is the denominator, unless otherwise specified.
N* = Number of participants in the safety population and is the denominator for which the specified event is applicable.
n = Number of participants in the safety population reporting the specified event type.
Non-serious adverse events are reported for the 28 days post dosing; serious adverse events (SAEs), adverse events of special interest (AESIs, wheezing) and new onset chronic medical conditions (NOCMCs) are reported from the time of the first study product administration until the end of the study period.
[a] As reported on the adverse event eCRF.

Table 25: Adverse Events Occurring in 5% of Participants in Any Group by MedDRA Preferred Term, System Organ Class, Cohort, and Vaccination Group - Safety Population

[Implementation Note: This table should include a row for any PT/SOC (solicited and unsolicited) reported by ≥5% participants in any group.]

		9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 2 Doses (N=X)				All Participants (N=X)			
MedDRA System Organ Class	Preferred Term	Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)	
		n (%)	# Events	n (%)	# Events	n (%)	# Events	n (%)	# Events	n (%)	# Events	n (%)	# Events	n (%)	# Events	n (%)	# Events	n (%)	# Events	n (%)	# Events
Serious Adverse Events																					
All	All																				
SOC1	PT1																				
Etc.	Etc.																				
Other (Non-Serious) Adverse Events																					
All	All																				
SOC1	PT1																				
Etc.	Etc.																				

N = Number of participants in the safety population.
n = Number of participants in the safety population reporting the specified adverse event.

14.3.1.1 Solicited Adverse Events

Table 26: Summary of Post-Dosing Solicited Adverse Events Through 7 Days Post Dose 1 by Cohort and Vaccination Group - Safety Population

Symptom	Severity	9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR, 1 Dose (N=X)		2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 or 2 Doses (N=X)		2-8 yrs, Placebo, 1 or 2 Doses (N=X)		All Participants (N=X)			
		Vaccine (N=X)		Placebo (N=X)								Vaccine (N=X)		Placebo (N=X)	
		n/N*	%	n/N*	%	n/N*	%	n/N*	%	n/N*	%	n/N*	%	n/N*	%
Any Solicited Event	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Local Solicited Events															
Any Local Solicited Event	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Rhinorrhea	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Stuffy Nose / Congestion	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Sneezing	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x

Table 26: Summary of Post-Dosing Solicited Adverse Events Through 7 Days Post Dose 1 by Cohort and Vaccination Group - Safety Population *(continued)*

Symptom	Severity	9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR, 1 Dose (N=X)		2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 or 2 Doses (N=X)		2-8 yrs, Placebo, 1 or 2 Doses (N=X)		All Participants (N=X)			
		Vaccine (N=X)		Placebo (N=X)								Vaccine (N=X)		Placebo (N=X)	
		n/N*	%	n/N*	%	n/N*	%	n/N*	%	n/N*	%	n/N*	%	n/N*	%
Nasal Pain / Irritation[a, b]	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Nasal Bleeding / Epistaxis	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Sinus Pressure / Pain[a]	None	x/x	x	x/x	x	-	-	-	-	-	-	-	-	-	-
	Mild	x/x	x	x/x	x	-	-	-	-	-	-	-	-	-	-
	Moderate	x/x	x	x/x	x	-	-	-	-	-	-	-	-	-	-
	Severe	x/x	x	x/x	x	-	-	-	-	-	-	-	-	-	-
Facial Pain[b]	None	-	-	-	-	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	-	-	-	-	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	-	-	-	-	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	-	-	-	-	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Sore Throat[a, b]	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Cough	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x

Table 26: Summary of Post-Dosing Solicited Adverse Events Through 7 Days Post Dose 1 by Cohort and Vaccination Group - Safety Population *(continued)*

Symptom	Severity	9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR, 1 Dose (N=X)		2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 or 2 Doses (N=X)		2-8 yrs, Placebo, 1 or 2 Doses (N=X)		All Participants (N=X)			
		Vaccine (N=X)		Placebo (N=X)								Vaccine (N=X)		Placebo (N=X)	
		n/N*	%	n/N*	%	n/N*	%	n/N*	%	n/N*	%	n/N*	%	n/N*	%
Trouble Breathing or Shortness of Breath	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Systemic Solicited Events															
Any Systemic Solicited Event	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Feverishness[a, b]	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Fatigue / Tiredness[a, b]	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Sleepiness[c]	None	-	-	-	-	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	-	-	-	-	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	-	-	-	-	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	-	-	-	-	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Malaise[a, b]	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x

Table 26: Summary of Post-Dosing Solicited Adverse Events Through 7 Days Post Dose 1 by Cohort and Vaccination Group - Safety Population *(continued)*

Symptom	Severity	9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR, 1 Dose (N=X)		2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 or 2 Doses (N=X)		2-8 yrs, Placebo, 1 or 2 Doses (N=X)		All Participants (N=X)			
		Vaccine (N=X)		Placebo (N=X)								Vaccine (N=X)		Placebo (N=X)	
		n/N*	%	n/N*	%	n/N*	%	n/N*	%	n/N*	%	n/N*	%	n/N*	%
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Myalgia[a, b]	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Arthralgia[a, b]	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Headache[a, b]	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Flushing[a]	None	x/x	x	x/x	x	-	-	-	-	-	-	-	-	-	-
	Mild	x/x	x	x/x	x	-	-	-	-	-	-	-	-	-	-
	Moderate	x/x	x	x/x	x	-	-	-	-	-	-	-	-	-	-
	Severe	x/x	x	x/x	x	-	-	-	-	-	-	-	-	-	-
Irritability / Fussiness[c]	None	-	-	-	-	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	-	-	-	-	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	-	-	-	-	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	-	-	-	-	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Decreased Activity	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x

Table 26: Summary of Post-Dosing Solicited Adverse Events Through 7 Days Post Dose 1 by Cohort and Vaccination Group - Safety Population *(continued)*

Symptom	Severity	9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR, 1 Dose (N=X)		2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 or 2 Doses (N=X)		2-8 yrs, Placebo, 1 or 2 Doses (N=X)		All Participants (N=X)			
		Vaccine (N=X)		Placebo (N=X)								Vaccine (N=X)		Placebo (N=X)	
		n/N*	%	n/N*	%	n/N*	%	n/N*	%	n/N*	%	n/N*	%	n/N*	%
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Decreased Appetite	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Abdominal Pain[a, b]	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Nausea[a, b]	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Vomiting	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Diarrhea	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Eye Pruritus	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x

Table 26: Summary of Post-Dosing Solicited Adverse Events Through 7 Days Post Dose 1 by Cohort and Vaccination Group - Safety Population *(continued)*

Symptom	Severity	9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR, 1 Dose (N=X)		2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 or 2 Doses (N=X)		2-8 yrs, Placebo, 1 or 2 Doses (N=X)		All Participants (N=X)			
		Vaccine (N=X)		Placebo (N=X)								Vaccine (N=X)		Placebo (N=X)	
		n/N*	%	n/N*	%	n/N*	%	n/N*	%	n/N*	%	n/N*	%	n/N*	%
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Eye Redness	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Allergic Skin Reaction	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Fever	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x

N = Number of participants in the safety population who received dose 1.
N* = Number of participants in the safety population with any solicited event data recorded post dose 1 and belonging to the respective age range for the specified event.
n = Number of participants in the safety population reporting the specified event type.
Participants are counted once at the highest severity reported post dose 1.
Events are reported for 7 days post dose 1.
Event applies to all age ranges, unless otherwise noted by [a], [b], or [c].
[a] Applicable for participants 9-17 years old.
[b] Applicable for participants 4-8 years old.
[c] Applicable for participants 2-3 years old.

Table 27: Summary of Post-Dosing Solicited Adverse Events Through 7 Days Post Dose 2 by Cohort and Vaccination Group – Safety Population

Symptom	Severity	2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 2 Doses (N=X)			
		Vaccine (N=X)		Placebo (N=X)	
		n/N*	%	n/N*	%
Any Solicited Event	None	x/x	x	x/x	x
	Mild	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x
	Severe	x/x	x	x/x	x
Local Solicited Events					
Any Local Solicited Event	None	x/x	x	x/x	x
	Mild	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x
	Severe	x/x	x	x/x	x
Rhinorrhea	None	x/x	x	x/x	x
	Mild	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x
	Severe	x/x	x	x/x	x
Stuffy Nose / Congestion	None	x/x	x	x/x	x
	Mild	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x
	Severe	x/x	x	x/x	x
Sneezing	None	x/x	x	x/x	x
	Mild	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x
	Severe	x/x	x	x/x	x

Table 27: Summary of Post-Dosing Solicited Adverse Events Through 7 Days Post Dose 2 by Cohort and Vaccination Group – Safety Population *(continued)*

Symptom	Severity	2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 2 Doses (N=X)			
		Vaccine (N=X)		Placebo (N=X)	
		n/N*	%	n/N*	%
Nasal Pain / Irritation[a]	None	x/x	x	x/x	x
	Mild	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x
	Severe	x/x	x	x/x	x
Nasal Bleeding / Epistaxis	None	x/x	x	x/x	x
	Mild	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x
	Severe	x/x	x	x/x	x
Facial Pain[a]	None	x/x	x	x/x	x
	Mild	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x
	Severe	x/x	x	x/x	x
Sore Throat[a]	None	x/x	x	x/x	x
	Mild	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x
	Severe	x/x	x	x/x	x
Cough	None	x/x	x	x/x	x
	Mild	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x
	Severe	x/x	x	x/x	x
Trouble Breathing or Shortness of Breath	None	x/x	x	x/x	x
	Mild	x/x	x	x/x	x

Table 27: Summary of Post-Dosing Solicited Adverse Events Through 7 Days Post Dose 2 by Cohort and Vaccination Group – Safety Population *(continued)*

Symptom	Severity	2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 2 Doses (N=X)			
		Vaccine (N=X)		Placebo (N=X)	
		n/N*	%	n/N*	%
	Moderate	x/x	x	x/x	x
	Severe	x/x	x	x/x	x
Systemic Solicited Events					
Any Systemic Solicited Event	None	x/x	x	x/x	x
	Mild	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x
	Severe	x/x	x	x/x	x
Feverishness[a]	None	x/x	x	x/x	x
	Mild	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x
	Severe	x/x	x	x/x	x
Fatigue / Tiredness[a]	None	x/x	x	x/x	x
	Mild	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x
	Severe	x/x	x	x/x	x
Sleepiness[b]	None	x/x	x	x/x	x
	Mild	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x
	Severe	x/x	x	x/x	x
Malaise[a]	None	x/x	x	x/x	x
	Mild	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x

Table 27: Summary of Post-Dosing Solicited Adverse Events Through 7 Days Post Dose 2 by Cohort and Vaccination Group – Safety Population *(continued)*

Symptom	Severity	2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 2 Doses (N=X)			
		Vaccine (N=X)		Placebo (N=X)	
		n/N*	%	n/N*	%
	Severe	x/x	x	x/x	x
Myalgia[a]	None	x/x	x	x/x	x
	Mild	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x
	Severe	x/x	x	x/x	x
Arthralgia[a]	None	x/x	x	x/x	x
	Mild	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x
	Severe	x/x	x	x/x	x
Headache[a]	None	x/x	x	x/x	x
	Mild	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x
	Severe	x/x	x	x/x	x
Irritability / Fussiness[b]	None	x/x	x	x/x	x
	Mild	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x
	Severe	x/x	x	x/x	x
Decreased Activity	None	x/x	x	x/x	x
	Mild	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x
	Severe	x/x	x	x/x	x
Decreased Appetite	None	x/x	x	x/x	x

Table 27: Summary of Post-Dosing Solicited Adverse Events Through 7 Days Post Dose 2 by Cohort and Vaccination Group – Safety Population *(continued)*

Symptom	Severity	2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 2 Doses (N=X)			
		Vaccine (N=X)		Placebo (N=X)	
		n/N*	%	n/N*	%
	Mild	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x
	Severe	x/x	x	x/x	x
Abdominal Pain[a]	None	x/x	x	x/x	x
	Mild	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x
	Severe	x/x	x	x/x	x
Nausea[a]	None	x/x	x	x/x	x
	Mild	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x
	Severe	x/x	x	x/x	x
Vomiting	None	x/x	x	x/x	x
	Mild	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x
	Severe	x/x	x	x/x	x
Diarrhea	None	x/x	x	x/x	x
	Mild	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x
	Severe	x/x	x	x/x	x
Eye Pruritus	None	x/x	x	x/x	x
	Mild	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x

Table 27: Summary of Post-Dosing Solicited Adverse Events Through 7 Days Post Dose 2 by Cohort and Vaccination Group – Safety Population *(continued)*

Symptom	Severity	2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 2 Doses (N=X)			
		Vaccine (N=X)		Placebo (N=X)	
		n/N*	%	n/N*	%
	Severe	x/x	x	x/x	x
Eye Redness	None	x/x	x	x/x	x
	Mild	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x
	Severe	x/x	x	x/x	x
Allergic Skin Reaction	None	x/x	x	x/x	x
	Mild	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x
	Severe	x/x	x	x/x	x
Fever	None	x/x	x	x/x	x
	Mild	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x
	Severe	x/x	x	x/x	x

N = Number of participants in the safety population who received dose 2.
N* = Number of participants in the safety population with any solicited event data recorded post dose 2 and belonging to the respective age range for the specified event.
n = Number of participants in the safety population reporting the specified event type.
Participants are counted once at the highest severity reported post dose 2.
Events are reported for the 7 days post dose 2.
Event applies to all age ranges, unless otherwise noted by [a] or [b].
[a] Applicable for participants 4-8 years old
[b] Applicable for participants 2-3 years old

Similar Tables:

Table 28: Summary of Post-Vaccination Solicited Adverse Events Through 7 Days Post Dosing by Cohort and Vaccination Group Following Any Dose - Safety Population

Implementation Note: This table will be similar to Table 27 with footnotes updated accordingly.

Table 29: Participant-Level Solicited Event Rate by Symptom, Severity, and Day Post Dosing – Participants 9-17 Years Old, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose - Safety Population (N=X)

		Post-Dose		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8+	
Symptom	**Severity**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**
Any Solicited Event	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild																		
	Moderate																		
	Severe																		
Local Solicited Events																			
Any Local Solicited Event	None																		
	Mild																		
	Moderate																		
	Severe																		
Rhinorrhea	None																		
	Mild																		
	Moderate																		
	Severe																		
Stuffy Nose / Congestion	None																		
	Mild																		
	Moderate																		
	Severe																		
Sneezing	None																		
	Mild																		
	Moderate																		
	Severe																		
Nasal Pain / Irritation	None																		
	Mild																		
	Moderate																		
	Severe																		

Table 29: Participant-Level Solicited Event Rate by Symptom, Severity, and Day Post Dosing – Participants 9-17 Years Old, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose - Safety Population (N=X) *(continued)*

		Post-Dose		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8+	
Symptom	**Severity**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**
Nasal Bleeding / Epistaxis	None																		
	Mild																		
	Moderate																		
	Severe																		
Sinus Pressure / Pain	None																		
	Mild																		
	Moderate																		
	Severe																		
Sore Throat	None																		
	Mild																		
	Moderate																		
	Severe																		
Cough	None																		
	Mild																		
	Moderate																		
	Severe																		
Trouble Breathing or Shortness of Breath	None																		
	Mild																		
	Moderate																		
	Severe																		
Systemic Solicited Events																			
Any Systemic Solicited Event	None																		
	Mild																		
	Moderate																		
	Severe																		

Table 29: Participant-Level Solicited Event Rate by Symptom, Severity, and Day Post Dosing – Participants 9-17 Years Old, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose - Safety Population (N=X) *(continued)*

		Post-Dose		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8+	
Symptom	**Severity**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**
Feverishness	None																		
	Mild																		
	Moderate																		
	Severe																		
Fatigue / Tiredness	None																		
	Mild																		
	Moderate																		
	Severe																		
Malaise	None																		
	Mild																		
	Moderate																		
	Severe																		
Myalgia	None																		
	Mild																		
	Moderate																		
	Severe																		
Arthralgia	None																		
	Mild																		
	Moderate																		
	Severe																		
Headache	None																		
	Mild																		
	Moderate																		
	Severe																		
Flushing	None																		
	Mild																		
	Moderate																		

Table 29: Participant-Level Solicited Event Rate by Symptom, Severity, and Day Post Dosing – Participants 9-17 Years Old, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose - Safety Population (N=X) *(continued)*

		Post-Dose		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8+	
Symptom	**Severity**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**
	Severe																		
Decreased Activity	None																		
	Mild																		
	Moderate																		
	Severe																		
Decreased Appetite	None																		
	Mild																		
	Moderate																		
	Severe																		
Abdominal Pain	None																		
	Mild																		
	Moderate																		
	Severe																		
Nausea	None																		
	Mild																		
	Moderate																		
	Severe																		
Vomiting	None																		
	Mild																		
	Moderate																		
	Severe																		
Diarrhea	None																		
	Mild																		
	Moderate																		
	Severe																		
Eye Pruritus	None																		
	Mild																		

Table 29: Participant-Level Solicited Event Rate by Symptom, Severity, and Day Post Dosing – Participants 9-17 Years Old, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose - Safety Population (N=X) *(continued)*

		Post-Dose		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8+	
Symptom	**Severity**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**
	Moderate																		
	Severe																		
Eye Redness	None																		
	Mild																		
	Moderate																		
	Severe																		
Allergic Skin Reaction	None																		
	Mild																		
	Moderate																		
	Severe																		
Fever	None																		
	Mild																		
	Moderate																		
	Severe																		

N = Number of participants in the safety population
N* = Number of participants in the safety population with any solicited event data recorded post dosing.
n = Number of participants in the safety population reporting the specified event type.
Participants are counted once at the highest severity reported at each day.

Similar Tables:

Table 30: Participant-Level Solicited Event Rate by Symptom, Severity, and Day Post Dosing – Participants 9-17 Years Old, Placebo, 1 Dose - Safety Population (N=X)

Implementation Note: This table will be similar to Table 29.

Table 31: Participant-Level Solicited Event Rate by Symptom, Severity, and Day Post Dose 1 – Participants 2-8 Years Old, 10^8 $TCID_{50}$ Sing2016 M2SR, 1 Dose - Safety Population (N=X)

		Post-Dose		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8+	
Symptom	**Severity**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**
Any Solicited Event	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild																		
	Moderate																		
	Severe																		
Local Solicited Events																			
Any Local Solicited Event	None																		
	Mild																		
	Moderate																		
	Severe																		
Rhinorrhea	None																		
	Mild																		
	Moderate																		
	Severe																		
Stuffy Nose / Congestion	None																		
	Mild																		
	Moderate																		
	Severe																		
Sneezing	None																		
	Mild																		
	Moderate																		
	Severe																		
Nasal Pain / Irritation[a]	None																		
	Mild																		

Table 31: Participant-Level Solicited Event Rate by Symptom, Severity, and Day Post Dose 1 – Participants 2-8 Years Old, 10^8 $TCID_{50}$ Sing2016 M2SR, 1 Dose - Safety Population (N=X) *(continued)*

		Post-Dose		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8+	
Symptom	**Severity**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**
	Moderate																		
	Severe																		
Nasal Bleeding / Epistaxis	None																		
	Mild																		
	Moderate																		
	Severe																		
Facial Pain[a]	None																		
	Mild																		
	Moderate																		
	Severe																		
Sore Throat[a]	None																		
	Mild																		
	Moderate																		
	Severe																		
Cough	None																		
	Mild																		
	Moderate																		
	Severe																		
Trouble Breathing or Shortness of Breath	None																		
	Mild																		
	Moderate																		
	Severe																		

Table 31: Participant-Level Solicited Event Rate by Symptom, Severity, and Day Post Dose 1 – Participants 2-8 Years Old, 10^8 $TCID_{50}$ Sing2016 M2SR, 1 Dose - Safety Population (N=X) *(continued)*

		Post-Dose		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8+	
Symptom	**Severity**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**
Systemic Solicited Events																			
Any Systemic Solicited Event	None																		
	Mild																		
	Moderate																		
	Severe																		
Feverishness[a]	None																		
	Mild																		
	Moderate																		
	Severe																		
Fatigue / Tiredness[a]	None																		
	Mild																		
	Moderate																		
	Severe																		
Sleepiness[b]	None																		
	Mild																		
	Moderate																		
	Severe																		
Malaise[a]	None																		
	Mild																		
	Moderate																		
	Severe																		
Myalgia[a]	None																		
	Mild																		

Table 31: Participant-Level Solicited Event Rate by Symptom, Severity, and Day Post Dose 1 – Participants 2-8 Years Old, 10^8 $TCID_{50}$ Sing2016 M2SR, 1 Dose - Safety Population (N=X) *(continued)*

		Post-Dose		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8+	
Symptom	**Severity**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**
	Moderate																		
	Severe																		
Arthralgia[a]	None																		
	Mild																		
	Moderate																		
	Severe																		
Headache[a]	None																		
	Mild																		
	Moderate																		
	Severe																		
Irritability / Fussiness[b]	None																		
	Mild																		
	Moderate																		
	Severe																		
Decreased Activity	None																		
	Mild																		
	Moderate																		
	Severe																		
Decreased Appetite	None																		
	Mild																		
	Moderate																		
	Severe																		
Abdominal Pain[a]	None																		
	Mild																		

Table 31: Participant-Level Solicited Event Rate by Symptom, Severity, and Day Post Dose 1 – Participants 2-8 Years Old, 10^8 $TCID_{50}$ Sing2016 M2SR, 1 Dose - Safety Population (N=X) *(continued)*

		Post-Dose		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8+	
Symptom	**Severity**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**
	Moderate																		
	Severe																		
Nausea[a]	None																		
	Mild																		
	Moderate																		
	Severe																		
Vomiting	None																		
	Mild																		
	Moderate																		
	Severe																		
Diarrhea	None																		
	Mild																		
	Moderate																		
	Severe																		
Eye Pruritus	None																		
	Mild																		
	Moderate																		
	Severe																		
Eye Redness	None																		
	Mild																		
	Moderate																		
	Severe																		
Allergic Skin Reaction	None																		
	Mild																		

Table 31: Participant-Level Solicited Event Rate by Symptom, Severity, and Day Post Dose 1 – Participants 2-8 Years Old, 10^8 $TCID_{50}$ Sing2016 M2SR, 1 Dose - Safety Population (N=X) *(continued)*

		Post-Dose		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8+	
Symptom	**Severity**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**
	Moderate																		
	Severe																		
Fever	None																		
	Mild																		
	Moderate																		
	Severe																		

N = Number of participants in the safety population.
N* = Number of participants in the safety population with any solicited event data recorded post dose 1 and belong to the respective age range for the specified event.
n = Number of participants in the safety population reporting the specified event type.
Participants are counted once at the highest severity reported at each day post dose 1.
Event applies to all age ranges, unless otherwise noted by [a] or [b].
[a] Applicable for participants 4-8 years old
[b] Applicable for participants 2-3 years old

Similar Tables:

Table 32: Participant-Level Solicited Event Rate by Symptom, Severity, and Day Post Dose 1 – Participants 2-8 Years Old, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 or 2 Doses - Safety Population (N=X)

Implementation Note: This table will be similar to Table 31.

Table 33: Participant-Level Solicited Event Rate by Symptom, Severity, and Day Post Dose 1 – Participants 2-8 Years Old, Placebo, 1 or 2 Doses - Safety Population (N=X)

Implementation Note: This table will be similar to Table 31.

Table 34: Participant-Level Solicited Event Rate by Symptom, Severity, and Day Post Dose 2 – Participants 2-8 Years Old, 10^9 $TCID_{50}$ Sing2016 M2SR, 2 Doses - Safety Population (N=X)

Implementation Note: This table will be similar to Table 31.

Table 35: Participant-Level Solicited Event Rate by Symptom, Severity, and Day Post Dose 2 – Participants 2-8 Years Old, Placebo, 2 Doses - Safety Population (N=X)

Implementation Note: This table will be similar to Table 31.

Table 36: Participant-Level Solicited Event Rate by Symptom, Severity, and Day Post Dosing Following Any Dose – Participants 2-8 Years Old, 10^9 $TCID_{50}$ Sing2016 M2SR, 2 Doses - Safety Population (N=X)

Implementation Note: This table will be similar to Table 31.

Table 37: Participant-Level Solicited Event Rate by Symptom, Severity, and Day Post Dosing Following Any Dose – Participants 2-8 Years Old, Placebo, 2 Doses - Safety Population (N=X)

Implementation Note: This table will be similar to Table 31.

Table 38: Participant-Level Solicited Event Rate by Symptom, Severity, and Day Post Dose 1 – All Vaccine Recipients - Safety Population (N=X)

		Post-Dose		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8+	
Symptom	**Severity**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**
Any Solicited Event	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Local Solicited Events																			
Any Local Solicited Event	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Rhinorrhea	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Stuffy Nose / Congestion	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Sneezing	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Nasal Pain / Irritation[a, b]	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x

Table 38: Participant-Level Solicited Event Rate by Symptom, Severity, and Day Post Dose 1 – All Vaccine Recipients - Safety Population (N=X) *(continued)*

		Post-Dose		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8+	
Symptom	**Severity**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Nasal Bleeding / Epistaxis	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Sinus Pressure / Pain[a]	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Facial Pain[b]	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Sore Throat[a, b]	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Cough	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x

Table 38: Participant-Level Solicited Event Rate by Symptom, Severity, and Day Post Dose 1 – All Vaccine Recipients - Safety Population (N=X) *(continued)*

		Post-Dose		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8+	
Symptom	**Severity**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**
Trouble Breathing or Shortness of Breath	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Systemic Solicited Events																			
Any Systemic Solicited Event	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Feverishness[a, b]	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Fatigue / Tiredness[a, b]	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Sleepiness[c]	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Malaise[a, b]	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x

Table 38: Participant-Level Solicited Event Rate by Symptom, Severity, and Day Post Dose 1 – All Vaccine Recipients - Safety Population (N=X) *(continued)*

		Post-Dose		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8+	
Symptom	**Severity**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Myalgia[a, b]	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Arthralgia[a, b]	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Headache[a, b]	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Flushing[a]	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Irritability / Fussiness[c]	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Decreased Activity	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x

Table 38: Participant-Level Solicited Event Rate by Symptom, Severity, and Day Post Dose 1 – All Vaccine Recipients - Safety Population (N=X) *(continued)*

		Post-Dose		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8+	
Symptom	**Severity**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Decreased Appetite	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Abdominal Pain[a, b]	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Nausea[a, b]	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Vomiting	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Diarrhea	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Eye Pruritus	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x

Table 38: Participant-Level Solicited Event Rate by Symptom, Severity, and Day Post Dose 1 – All Vaccine Recipients - Safety Population (N=X) *(continued)*

		Post-Dose		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8+	
Symptom	**Severity**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**	**n/N***	**%**
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Eye Redness	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Allergic Skin Reaction	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
Fever	None	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Mild	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Moderate	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x
	Severe	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x	x/x	x

N = Number of participants in the safety population.
N* = Number of participants in the safety population with any solicited event data recorded post dose 1 and belonging to the respective age range for the specified event.
n = Number of participants in the safety population reporting the specified event type.
Participants are counted once at the highest severity reported post dose 1.
Events are reported for 7 days post dose 1.
Event applies to all age ranges, unless otherwise noted by [a], [b], or [c].
[a] Applicable for participants 9-17 years old.
[b] Applicable for participants 4-8 years old.
[c] Applicable for participants 2-3 years old.

Table 39: Participant-Level Solicited Event Rate by Symptom, Severity, and Day Post Dose 1 – All Placebo Recipients - Safety Population (N=X)

Implementation Note: This table will be similar to Tables 38.

14.3.1.2 Unsolicited Adverse Events

Table 40: Number and Percentage of Participants Experiencing Non-Serious Unsolicited Adverse Events in the 28 Days Post Dosing by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 9-17 Years Old, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose - Safety Population (N=X)

MedDRA System Organ Class	MedDRA Preferred Term	Any Incidence			Severity						Relationship to Vaccination			
					Mild		Moderate		Severe		Not Related		Related	
		n	%	95% CI	n	%	n	%	n	%	n	%	n	%
Any SOC	Any PT	x	x	x.x, x.x	x	x	x	x	x	x	x	x	x	x
[SOC 1]	Any PT	x	x	x.x, x.x	x	x	x	x	x	x	x	x	x	x
	[PT 1]	x	x	x.x, x.x	x	x	x	x	x	x	x	x	x	x
	[PT 2]	x	x	x.x, x.x	x	x	x	x	x	x	x	x	x	x
[SOC 2]	Any PT	x	x	x.x, x.x	x	x	x	x	x	x	x	x	x	x
	[PT 1]	x	x	x.x, x.x	x	x	x	x	x	x	x	x	x	x
	[PT 2]	x	x	x.x, x.x	x	x	x	x	x	x	x	x	x	x

This table presents number and percentage of participants. A participant is only counted once per PT and is summarized according to their highest severity and closest relationship.

Similar Tables:

Table 41: Number and Percentage of Participants Experiencing Non-Serious Unsolicited Adverse Events in the 28 Days Post Dosing by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 9-17 Years Old, Placebo, 1 Dose - Safety Population (N=X)

Implementation Note: This table will be similar to Table 40.

Table 42: Number and Percentage of Participants Experiencing Non-Serious Unsolicited Adverse Events in the 28 Days Post Dose 1 by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 2-8 Years Old, 10^8 $TCID_{50}$ Sing2016 M2SR, 1 Dose - Safety Population (N=X)

Implementation Note: This table will be similar to Table 40.

Table 43: Number and Percentage of Participants Experiencing Non-Serious Unsolicited Adverse Events in the 28 Days Post Dose 1 by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 2-8 Years Old, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 or 2 Doses - Safety Population (N=X)

Implementation Note: This table will be similar to Table 40.

Table 44: Number and Percentage of Participants Experiencing Non-Serious Unsolicited Adverse Events in the 28 Days Post Dose 1 by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 2-8 Years Old, Placebo, 1 or 2 Doses - Safety Population (N=X)

Implementation Note: This table will be similar to Table 40.

Table 45: Number and Percentage of Participants Experiencing Non-Serious Unsolicited Adverse Events in the 28 Days Post Dose 2 by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 2-8 Years Old, 10^9 $TCID_{50}$ Sing2016 M2SR, 2 Doses - Safety Population (N=X)

Implementation Note: This table will be similar to Table 40.

Table 46: Number and Percentage of Participants Experiencing Non-Serious Unsolicited Adverse Events in the 28 Days Post Dose 2 by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 2-8 Years Old, Placebo, 2 Doses - Safety Population (N=X)

Implementation Note: This table will be similar to Table 40.

Table 47: Number and Percentage of Participants Experiencing Non-Serious Unsolicited Adverse Events in the 28 Days Post Dosing Following Any Dose by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 2-8 Years Old, 10^9 $TCID_{50}$ Sing2016 M2SR, 2 Doses - Safety Population (N=X)

Implementation Note: This table will be similar to Table 40.

Table 48: Number and Percentage of Participants Experiencing Non-Serious Unsolicited Adverse Events in the 28 Days Post Dosing Following Any Dose by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 2-8 Years Old, Placebo, 2 Doses - Safety Population (N=X)

Implementation Note: This table will be similar to Table 40.

Table 49: Number and Percentage of Participants Experiencing Non-Serious Unsolicited Adverse Events in the 28 Days Post Dose 1 by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – All Vaccine Recipients - Safety Population (N=X)

Implementation Note: This table will be similar to Table 40.

Table 50: Number and Percentage of Participants Experiencing Non-Serious Unsolicited Adverse Events in the 28 Days Post Dose 1 by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – All Placebo Recipients - Safety Population (N=X)

Implementation Note: This table will be similar to Table 40.

Table 51: Number and Percentage of Participants Experiencing Adverse Events of Special Interest by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 9-17 Years Old, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose - Safety Population (N=X)

Implementation Note: This table will be similar to Table 40.

Table 52: Number and Percentage of Participants Experiencing Adverse Events of Special Interest by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 9-17 Years Old, Placebo, 1 Dose - Safety Population (N=X)

Implementation Note: This table will be similar to Table 40.

Table 53: Number and Percentage of Participants Experiencing Adverse Events of Special Interest by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 2-8 Years Old, 10^8 $TCID_{50}$ Sing2016 M2SR, 1 Dose - Safety Population (N=X)

Implementation Note: This table will be similar to Table 40.

Table 54: Number and Percentage of Participants Experiencing Adverse Events of Special Interest by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 2-8 Years Old, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose - Safety Population (N=X)

Implementation Note: This table will be similar to Table 40.

Table 55: Number and Percentage of Participants Experiencing Adverse Events of Special Interest by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 2-8 Years Old, 10^9 $TCID_{50}$ Sing2016 M2SR, 2 Doses - Safety Population (N=X)

Implementation Note: This table will be similar to Table 40.

Table 56: Number and Percentage of Participants Experiencing Adverse Events of Special Interest by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 2-8 Years Old, Placebo, 1 or 2 Doses - Safety Population (N=X)

Implementation Note: This table will be similar to Table 40.

Table 57: Number and Percentage of Participants Experiencing Adverse Events of Special Interest by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – All Vaccine Recipients - Safety Population (N=X)

Implementation Note: This table will be similar to Table 40.

Table 58: Number and Percentage of Participants Experiencing Adverse Events of Special Interest by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – All Placebo Recipients - Safety Population (N=X)

Implementation Note: This table will be similar to Table 40.

Table 59: Number and Percentage of Participants Experiencing Serious Adverse Events by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 9-17 Years Old, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose - Safety Population (N=X)

Implementation Note: This table will be similar to Table 40.

Table 60: Number and Percentage of Participants Experiencing Serious Adverse Events by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 9-17 Years Old, Placebo, 1 Dose - Safety Population (N=X)

Implementation Note: This table will be similar to Table 40.

Table 61: Number and Percentage of Participants Experiencing Serious Adverse Events by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 2-8 Years Old, 10^8 $TCID_{50}$ Sing2016 M2SR, 1 Dose - Safety Population (N=X)

Implementation Note: This table will be similar to Table 40.

Table 62: Number and Percentage of Participants Experiencing Serious Adverse Events by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 2-8 Years Old, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose - Safety Population (N=X)

Implementation Note: This table will be similar to Table 40.

Table 63: Number and Percentage of Participants Experiencing Serious Adverse Events by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 2-8 Years Old, 10^9 $TCID_{50}$ Sing2016 M2SR, 2 Doses - Safety Population (N=X)

Implementation Note: This table will be similar to Table 40.

Table 64: Number and Percentage of Participants Experiencing Serious Adverse Events by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 2-8 Years Old, Placebo, 1 or 2 Doses - Safety Population (N=X)

Implementation Note: This table will be similar to Table 40.

Table 65: Number and Percentage of Participants Experiencing Serious Adverse Events by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – All Vaccine Recipients - Safety Population (N=X)

Implementation Note: This table will be similar to Table 40.

Table 66: Number and Percentage of Participants Experiencing Serious Adverse Events by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – All Placebo Recipients - Safety Population (N=X)

Implementation Note: This table will be similar to Table 40.

Table 67: Number and Percentage of Participants Experiencing New-Onset Chronic Medical Conditions by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 9-17 Years Old, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose - Safety Population (N=X)

Implementation Note: This table will be similar to Table 40.

Table 68: Number and Percentage of Participants Experiencing New-Onset Chronic Medical Conditions by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 9-17 Years Old, Placebo, 1 Dose - Safety Population (N=X)

Implementation Note: This table will be similar to Table 40.

Table 69: Number and Percentage of Participants Experiencing New-Onset Chronic Medical Conditions by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 2-8 Years Old, 10^8 $TCID_{50}$ Sing2016 M2SR, 1 Dose - Safety Population (N=X)

Implementation Note: This table will be similar to Table 40.

Table 70: Number and Percentage of Participants Experiencing New-Onset Chronic Medical Conditions by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 2-8 Years Old, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose - Safety Population (N=X)

Implementation Note: This table will be similar to Table 40.

Table 71: Number and Percentage of Participants Experiencing New-Onset Chronic Medical Conditions by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 2-8 Years Old, 10^9 $TCID_{50}$ Sing2016 M2SR, 2 Doses - Safety Population (N=X)

Implementation Note: This table will be similar to Table 40.

Table 72: Number and Percentage of Participants Experiencing New-Onset Chronic Medical Conditions by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 2-8 Years Old, Placebo, 1 or 2 Doses - Safety Population (N=X)

Implementation Note: This table will be similar to Table 40.

Table 73: Number and Percentage of Participants Experiencing New-Onset Chronic Medical Conditions by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – All Vaccine Recipients - Safety Population (N=X)

Implementation Note: This table will be similar to Table 40.

Table 74: Number and Percentage of Participants Experiencing New-Onset Chronic Medical Conditions by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – All Placebo Recipients - Safety Population (N=X)

Implementation Note: This table will be similar to Table 40.

Table 75: Summary of Non-Serious Unsolicited Adverse Events in the 28 Days Post Dosing by MedDRA® System Organ Class and Preferred Term, Severity, Relationship to Study Vaccination, and Resolution – Participants 9-17 Years Old, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose - Safety Population (N=X)

MedDRA Classification		Total Events	Severity				Relationship to Study Vaccination			Resolution	
			Mild	Moderate	Severe	Not Yet Determined	Not Related	Related	Not Yet Determined	Ongoing	Resolved
		n	n	n	n	n	n	n	n	n	n
System Organ Class	Preferred Term										
Any SOC	Any PT										
[SOC 1]	Any PT										
	[PT 1]										
	[PT 2]										
[SOC 2]	Any PT										
	[PT 1]										
	[PT 2]										

Similar Tables:

Table 76: Summary of Non-Serious Unsolicited Adverse Events in the 28 Days Post Dosing by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 9-17 Years Old, Placebo, 1 Dose - Safety Population (N=X)

Implementation Note: This table will be similar to Table 75.

Table 77: Summary of Non-Serious Unsolicited Adverse Events in the 28 Days Post Dose 1 by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 2-8 Years Old, 10^8 $TCID_{50}$ Sing2016 M2SR, 1 Dose - Safety Population (N=X)

Implementation Note: This table will be similar to Table 75.

Table 78: Summary of Non-Serious Unsolicited Adverse Events in the 28 Days Post Dose 1 by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 2-8 Years Old, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 or 2 Doses - Safety Population (N=X)

Implementation Note: This table will be similar to Table 75.

Table 79: Summary of Non-Serious Unsolicited Adverse Events in the 28 Days Post Dose 1 by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 2-8 Years Old, Placebo, 1 or 2 Doses - Safety Population (N=X)

Implementation Note: This table will be similar to Table 75.

Table 80: Summary of Non-Serious Unsolicited Adverse Events in the 28 Days Post Dose 2 by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 2-8 Years Old, 10^9 $TCID_{50}$ Sing2016 M2SR, 2 Doses - Safety Population (N=X)

Implementation Note: This table will be similar to Table 75.

Table 81: Summary of Non-Serious Unsolicited Adverse Events in the 28 Days Post Dose 2 by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 2-8 Years Old, Placebo, 2 Doses - Safety Population (N=X)

Implementation Note: This table will be similar to Table 75.

Table 82: Summary of Non-Serious Unsolicited Adverse Events in the 28 Days Post Dosing Following Any Dose by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 2-8 Years Old, 10^9 $TCID_{50}$ Sing2016 M2SR, 2 Doses - Safety Population (N=X)

Implementation Note: This table will be similar to Table 75.

Table 83: Summary of Non-Serious Unsolicited Adverse Events in the 28 Days Post Dosing Following Any Dose by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 2-8 Years Old, Placebo, 2 Dose - Safety Population (N=X)

Implementation Note: This table will be similar to Table 75.

Table 84: Summary of Non-Serious Unsolicited Adverse Events in the 28 Days Post Dose 1 by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – All Vaccine Recipients - Safety Population (N=X)

Implementation Note: This table will be similar to Table 75.

Table 85: Summary of Non-Serious Unsolicited Adverse Events in the 28 Days Post Dose 1 by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – All Placebo Recipients - Safety Population (N=X)

Implementation Note: This table will be similar to Table 75.

Table 86: Summary of Adverse Events of Special Interest by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 9-17 Years Old, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose - Safety Population (N=X)

Implementation Note: This table will be similar to Table 75.

Table 87: Summary of Adverse Events of Special Interest by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 9-17 Years Old, Placebo, 1 Dose - Safety Population (N=X)

Implementation Note: This table will be similar to Table 75.

Table 88: Summary of Adverse Events of Special Interest by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 2-8 Years Old, 10^8 $TCID_{50}$ Sing2016 M2SR, 1 Dose - Safety Population (N=X)

Implementation Note: This table will be similar to Table 75.

Table 89: Summary of Adverse Events of Special Interest by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 2-8 Years Old, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose - Safety Population (N=X)

Implementation Note: This table will be similar to Table 75.

Table 90: Summary of Adverse Events of Special Interest by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 2-8 Years Old, 10^9 $TCID_{50}$ Sing2016 M2SR, 2 Doses - Safety Population (N=X)

Implementation Note: This table will be similar to Table 75.

Table 91: Summary of Adverse Events of Special Interest by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 2-8 Years Old, Placebo, 1 or 2 Doses - Safety Population (N=X)

Implementation Note: This table will be similar to Table 75.

Table 92: Summary of Adverse Events of Special Interest by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – All Vaccine Recipients - Safety Population (N=X)

Implementation Note: This table will be similar to Table 75.

Table 93: Summary of Adverse Events of Special Interest by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – All Placebo Recipients - Safety Population (N=X)

Implementation Note: This table will be similar to Table 75.

Table 94: Summary of Serious Adverse Events by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 9-17 Years Old, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose - Safety Population (N=X)

Implementation Note: This table will be similar to Table 75.

Table 95: Summary of Serious Adverse Events by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 9-17 Years Old, Placebo, 1 Dose - Safety Population (N=X)

Implementation Note: This table will be similar to Table 75.

Table 96: Summary of Serious Adverse Events by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 2-8 Years Old, 10^8 $TCID_{50}$ Sing2016 M2SR, 1 Dose - Safety Population (N=X)

Implementation Note: This table will be similar to Table 75.

Table 97: Summary of Serious Adverse Events by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 2-8 Years Old, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose - Safety Population (N=X)

Implementation Note: This table will be similar to Table 75.

Table 98: Summary of Serious Adverse Events by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 2-8 Years Old, 10^9 $TCID_{50}$ Sing2016 M2SR, 2 Doses - Safety Population (N=X)

Implementation Note: This table will be similar to Table 75.

Table 99: Summary of Serious Adverse Events by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 2-8 Years Old, Placebo, 1 or 2 Doses - Safety Population (N=X)

Implementation Note: This table will be similar to Table 75.

Table 100: Summary of Serious Adverse Events by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – All Vaccine Recipients - Safety Population (N=X)

Implementation Note: This table will be similar to Table 75.

Table 101: Summary of Serious Adverse Events by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – All Placebo Recipients - Safety Population (N=X)

Implementation Note: This table will be similar to Table 75.

Table 102: Summary of New-Onset Chronic Medical Conditions by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 9-17 Years Old, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose - Safety Population (N=X)

Implementation Note: This table will be similar to Table 75.

Table 103: Summary of New-Onset Chronic Medical Conditions by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 9-17 Years Old, Placebo, 1 Dose - Safety Population (N=X)

Implementation Note: This table will be similar to Table 75.

Table 104: Summary of New-Onset Chronic Medical Conditions by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 2-8 Years Old, 10^8 $TCID_{50}$ Sing2016 M2SR, 1 Dose - Safety Population (N=X)

Implementation Note: This table will be similar to Table 75.

Table 105: Summary of New-Onset Chronic Medical Conditions by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 2-8 Years Old, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose - Safety Population (N=X)

Implementation Note: This table will be similar to Table 75.

Table 106: Summary of New-Onset Chronic Medical Conditions by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 2-8 Years Old, 10^9 $TCID_{50}$ Sing2016 M2SR, 2 Doses - Safety Population (N=X)

Implementation Note: This table will be similar to Table 75.

Table 107: Summary of New-Onset Chronic Medical Conditions by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – Participants 2-8 Years Old, Placebo, 1 or 2 Doses - Safety Population (N=X)

Implementation Note: This table will be similar to Table 75.

Table 108: Summary of New-Onset Chronic Medical Conditions by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – All Vaccine Recipients - Safety Population (N=X)

Implementation Note: This table will be similar to Table 75.

Table 109: Summary of New-Onset Chronic Medical Conditions by MedDRA® System Organ Class and Preferred Term, Severity, and Relationship to Study Vaccination – All Placebo Recipients - Safety Population (N=X)

Implementation Note: This table will be similar to Table 75.

14.3.2 Listings of Deaths, Other Serious and Significant Adverse Events

Table 110: Adverse Events of Special Interest

Part 1:											
Analysis Group	**Participant ID**	**AE Number**	**Adverse Event**	**Associated with Dose No.**	**No. of Days Post Associated Dose**	**Duration (Days)**	**MedDRA System Organ Class**	**MedDRA Preferred Term**	**Severity**	**SAE?**	
Part 2:											
Analysis Group	**Participant ID**	**AE Number**	**Adverse Event**	**Action Taken with Study Vaccination**	**Participant Discontinued Due to AE?**	**Relationship to Study Vaccination**	**If Not Related, Alternative Etiology**	**NOCMC?**	**Unanticipated Problem?**	**Outcome**	**Comments**

Similar Tables:

Table 111: Serious Adverse Events

Implementation Note: This will be similar to Table 110. This table will exclude the "SAE?" column, will have "Relationship to Study Vaccination" and "If Not Related, Alternative Etiology" as the last columns in Part 1, and will include an "AESI?" column to the left of the "NOCMC"?" column.

Table 112: New-Onset Chronic Medical Conditions

Implementation Note: This will be similar to Table 110. This table will replace the "NOCMC?" column with "AESI?".

Table 113: Listing of Wheezing Events and Corresponding Vital Signs and Respiratory Virus Panels

Part 1

Analysis Group	Participant ID	AE Number	Adverse Event	Study Day Event Started	Associated with Dose No.	No. of Days Post Associated Dose	Duration (Days)	# of Days Post Dose until Episode met Case Definition of Acute Wheeze	Severity	Relationship to Study Treatment	If Not Related, Alternate Etiology

Part 2

Analysis Group	Participant ID	AE Number	Adverse Event	Study Day Event Started	Participant Discontinued Due to AE?	Unanticipated Problem?	Outcome	MedDRA System Organ Class	MedDRA Preferred Term	Comments

Part 3

Analysis Group	Participant ID	AE Number	Adverse Event	Study Day Event Started	Study Day of Vital Signs	Temperature (°F)	Systolic Blood Pressure (mmHg)	Diastolic Blood Pressure (mmHg)	Respiratory Rate (breaths/min)	Oxygen Saturation (%)	Inspiratory: Expiratory (Ratio)

Part 4

Analysis Group	Participant ID	AE Number	Adverse Event	Study Day Event Started	Study Day of Virus Panel	Result of Qualitative RT-PCR Multiplex Respiratory Virus Assay	Positive or Equivocal Viruses from Qualitative RT-PCR Multiplex Respiratory Virus Assay	Name of Other Infectious Disease Diagnostic Test Performed	Results from Other Infectious Disease Diagnostic Test

14.4 Summary of Concomitant Medications

Table 114: Number and Percent of Participants Reporting Pre-Existing and Concomitant Medications by WHO Drug Classification, Cohort, and Vaccination Group - Safety Population

[Implementation Note: WHO Drug Code Level Codes will be sorted by frequency across all participants, most to least common.]

WHO Drug Code Level 1, Anatomic Group	WHO Drug Code Level 2, Therapeutic Subgroup	9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 1 Dose (N=X)				2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR or Placebo, 2 Doses (N=X)				All Participants[a] (N=X)			
		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)		Vaccine (N=X)		Placebo (N=X)	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Any Level 1 Codes	Any Level 2 Codes	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
[ATC Level 1 – 1]	Any [ATC 1 – 1]	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	[ATC 2 – 1]	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	[ATC 2 – 2]																				
	[ATC 2 – 3]																				
[ATC Level 1 – 2]	Any [ATC 1 – 2]	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	[ATC 2 – 1]																				
	[ATC 2 – 2]																				
	[ATC 2 – 3]																				

N = Number of participants in the safety population; n = Number of participants in the safety population reporting taking at least one medication in the specific WHO Drug Class.

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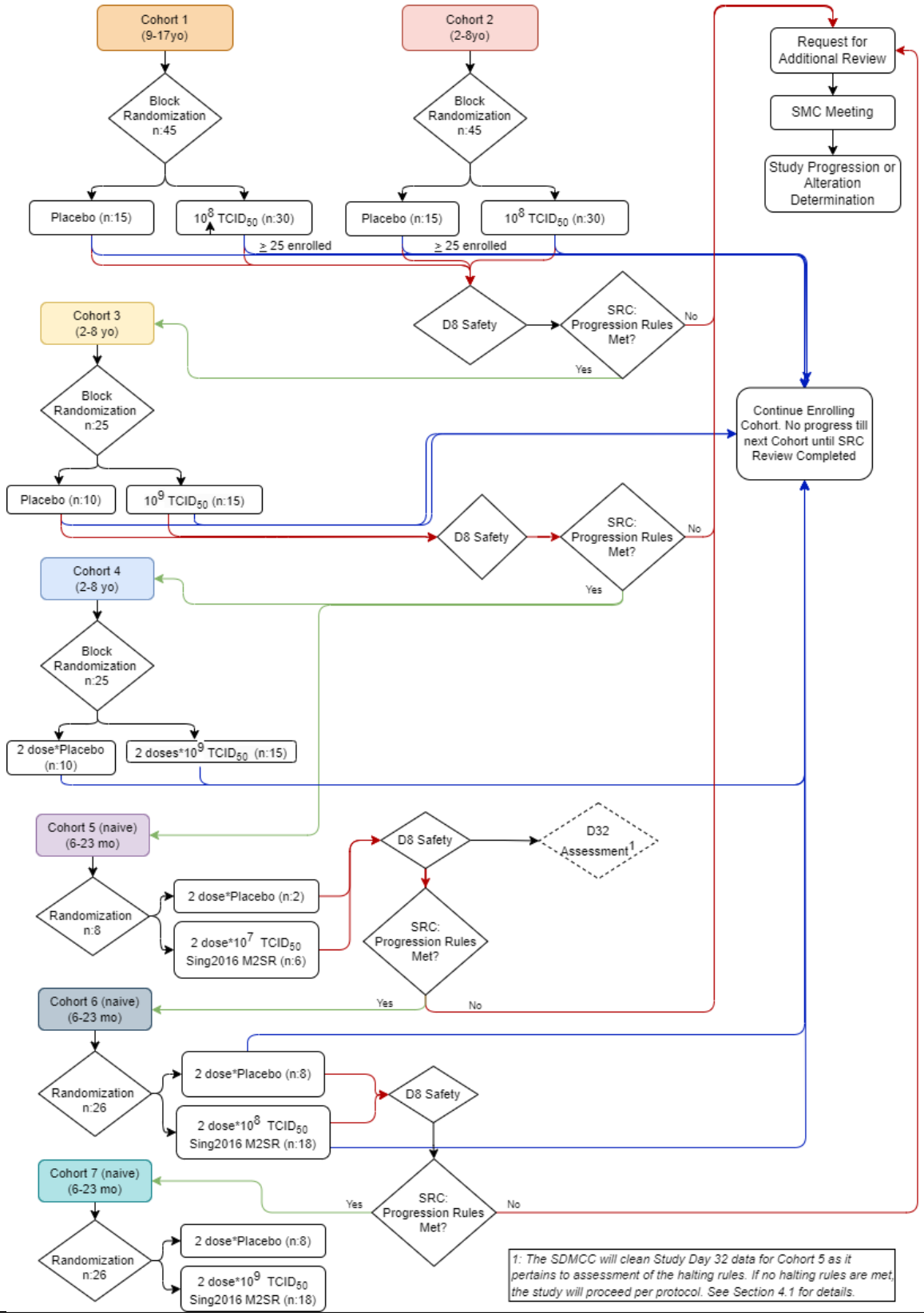
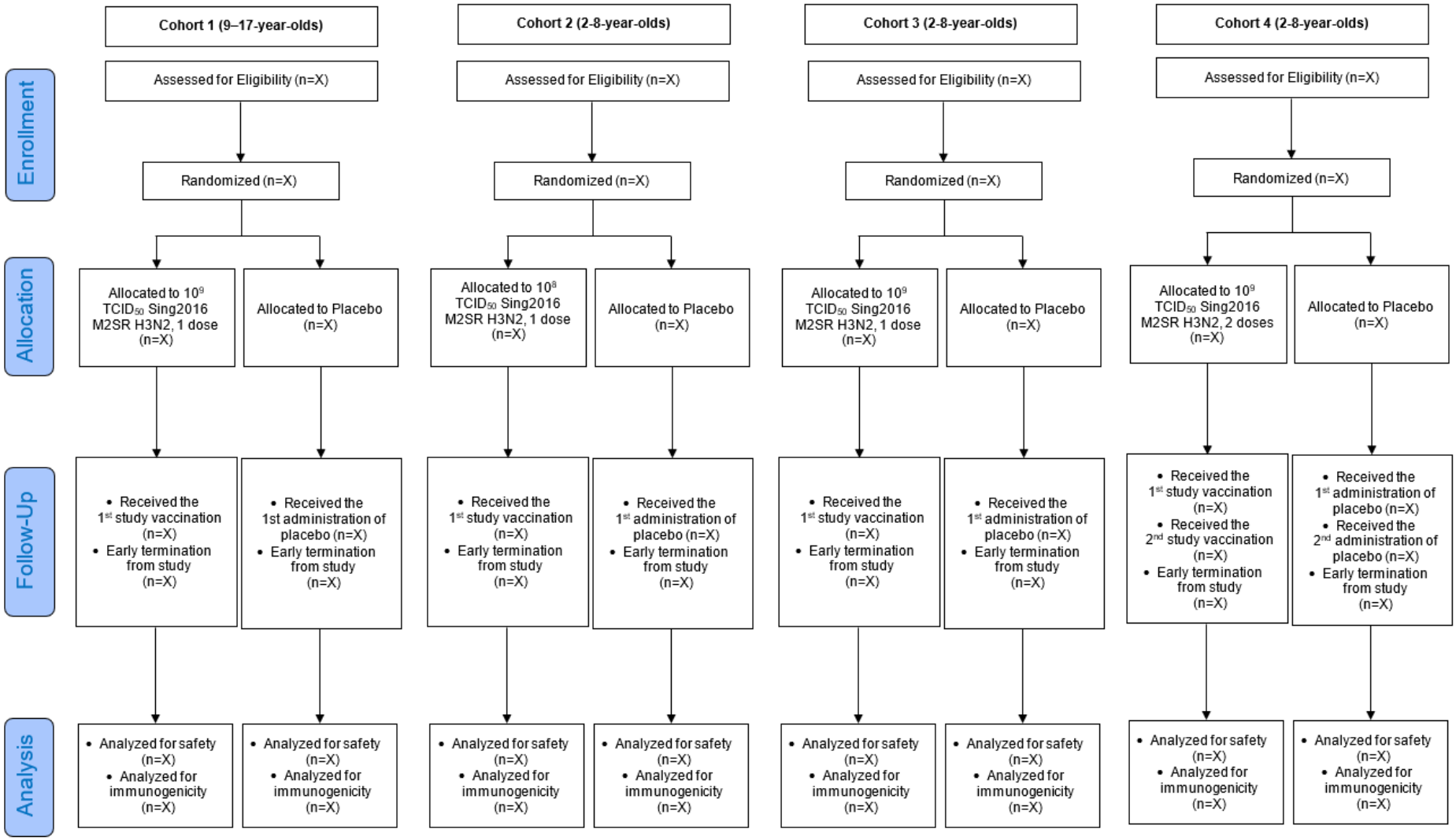
9.1 Overall Study Design and Plan Description

Figure 1: Study Schema



10.1 Disposition of Participants

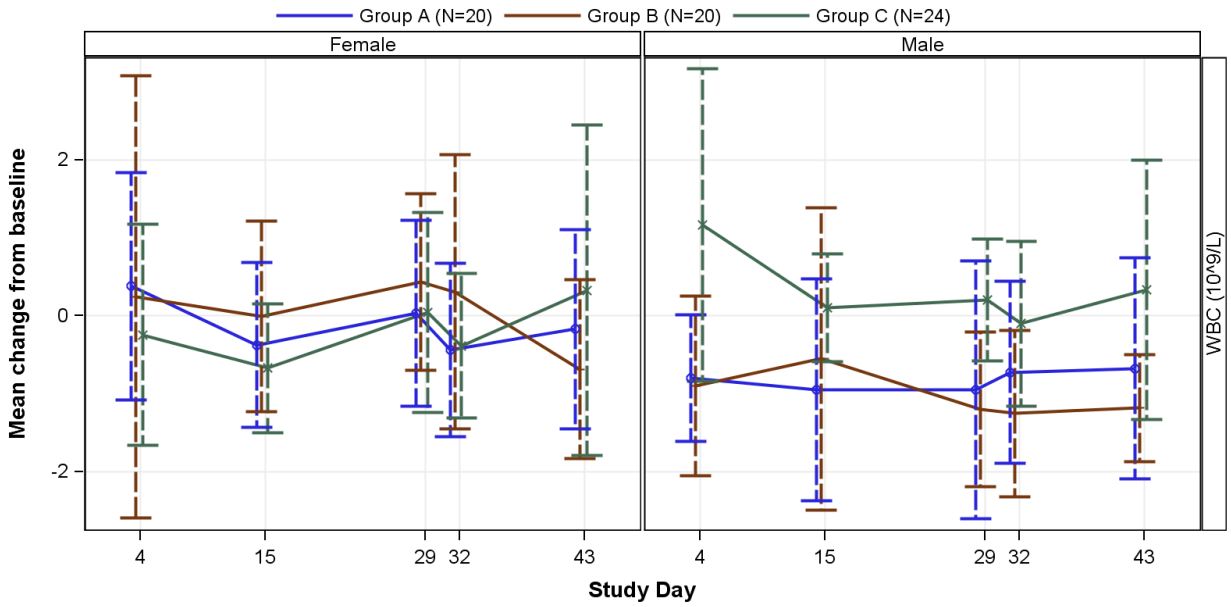
Figure 2: CONSORT Flow Diagram



14.2.1 Immunogenicity Response Figures

Figure 3: Geometric Mean Hemagglutination Inhibition (HAI) Antibody Titers in Serum Against A/Singapore/INFIMH-16-0019/2016 and Associated 95% Confidence Intervals by Cohort and Vaccination Group – Modified Intent-to-Treat Population

[Implementation note: The figure below is for reference only. This figure will display the geometric mean response with 95% CIs at each visit and individual participant trajectories at a decreased transparency. Immunogenicity results will be presented in three panels (9-17 year olds, 2-8 year olds, all participants) and different colors/markers to distinguish analysis groups. Groups include: 9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose; 9-17 yrs, Placebo, 1 Dose; 2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR, 1 Dose; 2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose; 2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 2 Doses; 2-8 yrs, Placebo, 1 Dose; 2-8 yrs, Placebo, 2 Doses; All Vaccine Recipients; All Placebo Participants]



Similar Figures:

Figure 4: Geometric Mean Influenza Microneutralization (MN) Antibody Titers in Serum against A/Singapore/INFIMH-16-0019/2016 and Associated 95% Confidence Intervals by Cohort and Vaccination Group – Modified Intent-to-Treat Population

Implementation Note: This will be similar to Figure 3.

Figure 5: Mean ECL Signal for sIgA as measured by the Binding Antibody Multiplex Assay and Associated 95% Confidence Intervals by Antigen, Cohort, and Vaccination Group – Modified Intent-to-Treat Population

Implementation Note: This will be similar to Figure 3. Antigens will be presented as panels. The figure will be split into different parts (e.g., Parts a, b, c, etc.) if all antigens are unable to be presented in a readable manner within one figure.

Figure 6: Mean Total IgA Concentration for sIgA as measured by the Binding Antibody Multiplex Assay and Associated 95% Confidence Intervals by Antigen, Cohort, and Vaccination Group – Modified Intent-to-Treat Population

Implementation Note: This will be similar to Figure 3. Antigens will be presented as panels. The figure will be split into different parts (e.g., Parts a, b, c, etc.) if all antigens are unable to be presented in a readable manner within one figure.

Figure 7: Mean Specific Activity for sIgA as measured by the Binding Antibody Multiplex Assay and Associated 95% Confidence Intervals by Antigen, Cohort, and Vaccination Group – Modified Intent-to-Treat Population

Implementation Note: This will be similar to Figure 3. Antigens will be presented as panels. The figure will be split into different parts (e.g., Parts a, b, c, etc.) if all antigens are unable to be presented in a readable manner within one figure.

Figure 8: Geometric Mean Hemagglutination Inhibition (HAI) Antibody Titers in Plasma Against A/Singapore/INFIMH-16-0019/2016 and Associated 95% Confidence Intervals by Cohort and Vaccination Group – Modified Intent-to-Treat Population

Implementation Note: This will be similar to Figure 3.

Figure 9: Geometric Mean Influenza Microneutralization (MN) Antibody Titers in Plasma Against A/Singapore/INFIMH-16-0019/2016 and Associated 95% Confidence Intervals by Cohort and Vaccination Group – Modified Intent-to-Treat Population

Implementation Note: This will be similar to Figure 3.

Figure 10: Geometric Mean Neuraminidase Inhibition (NAI) Titers in Plasma Against A/Singapore/INFIMH-16-0019/2016 and Associated 95% Confidence Intervals by Cohort and Vaccination Group – Modified Intent-to-Treat Population

Implementation Note: This will be similar to Figure 3.

Figure 11: Geometric Mean sIgA Titer Against A/Singapore/INFIMH-16-0019/2016 as Measured by the Enzyme Linked Immunosorbent Assays and Associated 95% Confidence Intervals by Cohort and Vaccination Group – Modified Intent-to-Treat Population

Implementation Note: This will be similar to Figure 3.

Figure 12: Mean Total sIgA Concentration Against A/Singapore/INFIMH-16-0019/2016 as Measured by the Enzyme Linked Immunosorbent Assays and Associated 95% Confidence Intervals by Cohort and Vaccination Group – Modified Intent-to-Treat Population

Implementation Note: This will be similar to Figure 3.

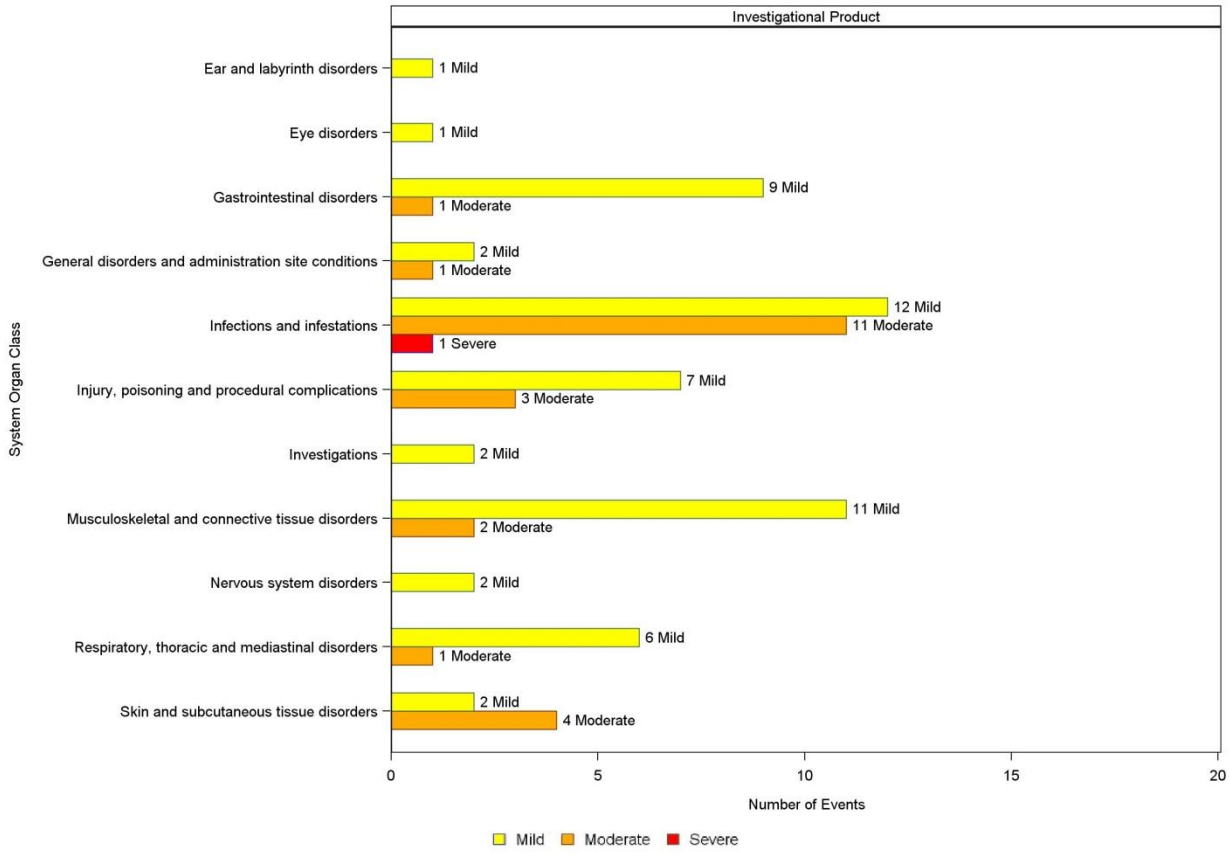
Figure 13: Mean Normalized sIgA Against A/Singapore/INFIMH-16-0019/2016 as Measured by the Enzyme Linked Immunosorbent Assays and Associated 95% Confidence Intervals by Cohort and Vaccination Group – Modified Intent-to-Treat Population

Implementation Note: This will be similar to Figure 3.

14.3.1.1 Solicited Adverse Events

Figure 14: Maximum Severity of Local Solicited Events Post Dose 1 by Symptom – Participants 9-17 Years Old – Safety Population

Implementation Note: This is an example figure. The y-axis label will be "Symptom" and each row on the y-axis will present all applicable local solicited events as well as a row for "Any Local Solicited Event". Panels will be included for each analysis group (9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose; 9-17 yrs, Placebo, 1 Dose)



Similar Figures:

Figure 15: Maximum Severity of Local Solicited Events Post Dose 1 by Symptom – Participants 2-8 Years Old – Safety Population

Implementation Note: This will be similar to Figure 14. Groups include: 2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 or 2 Doses; 2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR, 1 Dose; 2-8 yrs, Placebo, 1 or 2 Doses

Figure 16: Maximum Severity of Local Solicited Events Post Dose 1 by Symptom – All Participants – Safety Population

Implementation Note: This will be similar to Figure 14. Groups include: Vaccine Recipients, Placebo Recipients

Figure 17: Maximum Severity of Local Solicited Events Post Dose 2 by Symptom – Participants 2-8 Years Old – Safety Population

Implementation Note: This will be similar to Figure 14. Groups include: 2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 2 Doses; 2-8 yrs, Placebo, 2 Doses

Figure 18: Maximum Severity of Local Solicited Events Post Any Dose by Symptom, Participants 2-8 Years Old – Safety Population

Implementation Note: This will be similar to Figure 14. Groups include: 2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 2 Doses; 2-8 yrs, Placebo, 2 Doses

Figure 19: Maximum Severity of Systemic Solicited Events by Symptom – Participants 9-17 Years Old – Safety Population

Implementation Note This will be similar to Figure 14. Groups include: 9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose; 9-17 yrs, Placebo, 1 Dose

Figure 20: Maximum Severity of Systemic Solicited Events Post Dose 1 by Symptom – Participants 2-8 Years Old – Safety Population

Implementation Note: This will be similar to Figure 14. Groups include: 2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 or 2 Doses; 2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR, 1 Dose; 2-8 yrs, Placebo, 1 or 2 Doses

Figure 21: Maximum Severity of Systemic Solicited Events Post Dose 1 by Symptom – All Participants – Safety Population

Implementation Note: This will be similar to Figure 14. Groups include: Vaccine Recipients, Placebo Recipients

Figure 22: Maximum Severity of Systemic Solicited Events Post Dose 2 by Symptom – Participants 2-8 Years Old – Safety Population

Implementation Note: This will be similar to Figure 14. Groups include: 2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 2 Doses; 2-8 yrs, Placebo, 2 Doses

Figure 23: Maximum Severity of Systemic Solicited Events Post Any Dose by Symptom – Participants 2-8 Years Old – Safety Population

Implementation Note: This will be similar to Figure 14. Groups include: 2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 2 Doses; 2-8 yrs, Placebo, 2 Doses

Figure 24: Maximum Severity of Local Solicited Events by Days Post Dose 1 – Participants 9-17 Years Old – Safety Population

Implementation Note: This is an example figure. Panels will be included for each analysis group (9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose; 9-17 yrs, Placebo, 1 Dose). "Day 8" should be labeled as "Day 8+"

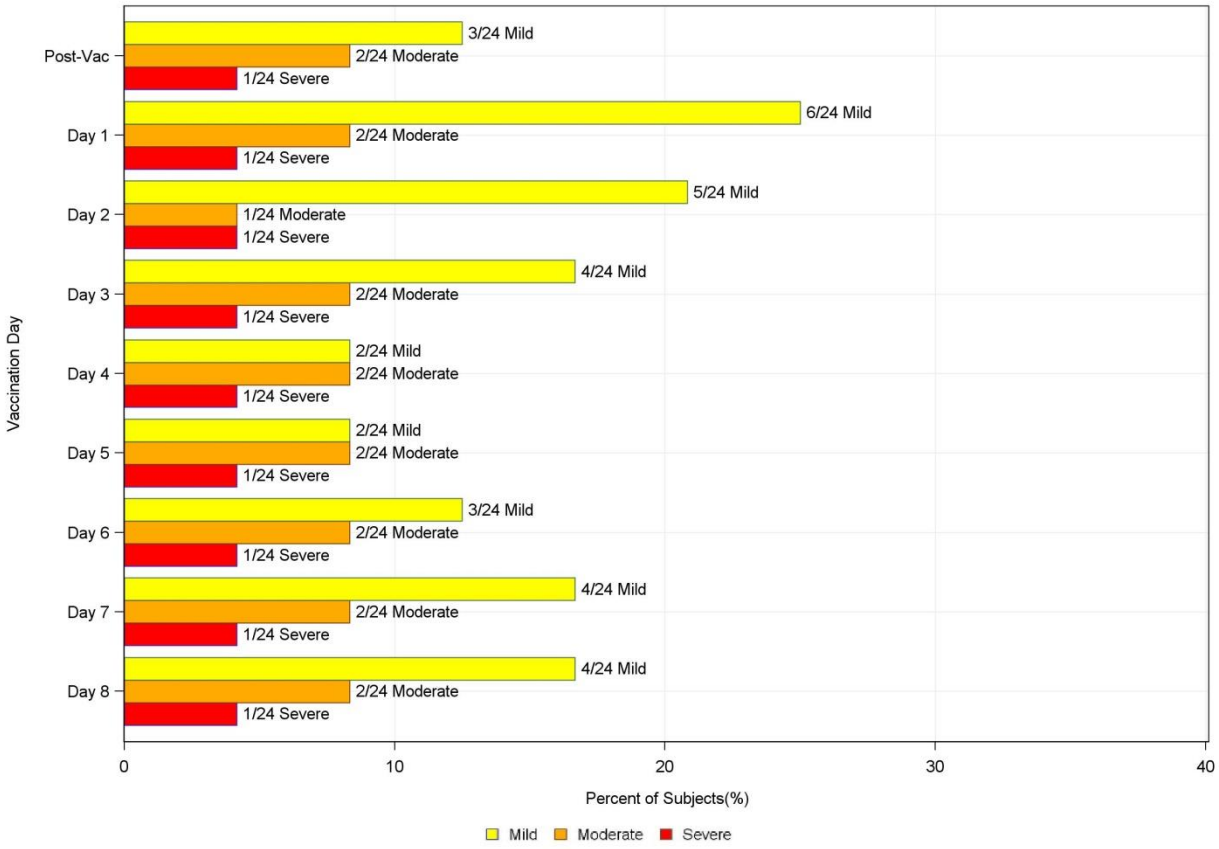


Figure 25: Maximum Severity of Local Solicited Events by Days Post Dose 1 – Participants 2-8 Years Old – Safety Population

Implementation Note: This will be similar to Figure 24. Groups include: 2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 or 2 Doses; 2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR, 1 Dose; 2-8 yrs, Placebo, 1 or 2 Doses

Figure 26: Maximum Severity of Local Solicited Events by Days Post Dose 1 – All Participants – Safety Population

Implementation Note: This will be similar to Figure 24. Groups include: Vaccine Recipients, Placebo Recipients

Figure 27: Maximum Severity of Local Solicited Events by Days Post Dose 2 – Participants 2-8 Years Old – Safety Population

Implementation Note: This will be similar to Figure 24. Groups include: 2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 2 Doses; 2-8 yrs, Placebo, 2 Doses

Figure 28: Maximum Severity of Local Solicited Events by Days Post Dose Following Any Dose – Participants 2-8 Years Old – Safety Population

Implementation Note: This will be similar to Figure 24. Groups include: 2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 2 Doses; 2-8 yrs, Placebo, 2 Doses

Figure 29: Maximum Severity of Systemic Solicited Events by Days Post Dose – Participants 9-17 Years Old – Safety Population

Implementation Note This will be similar to Figure 24. Groups include: 9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose; 9-17 yrs, Placebo, 1 Dose

Figure 30: Maximum Severity of Systemic Solicited Events by Days Post Dose 1 – Participants 2-8 Years Old – Safety Population

Implementation Note: This will be similar to Figure 24. Groups include: 2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 or 2 Doses; 2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR, 1 Dose; 2-8 yrs, Placebo, 1 or 2 Doses

Figure 31: Maximum Severity of Systemic Solicited Events by Days Post Dose 1 – All Participants – Safety Population

Implementation Note: This will be similar to Figure 24. Groups include: Vaccine Recipients, Placebo Recipients

Figure 32: Maximum Severity of Systemic Solicited Events by Days Post Dose 2 – Participants 2-8 Years Old – Safety Population

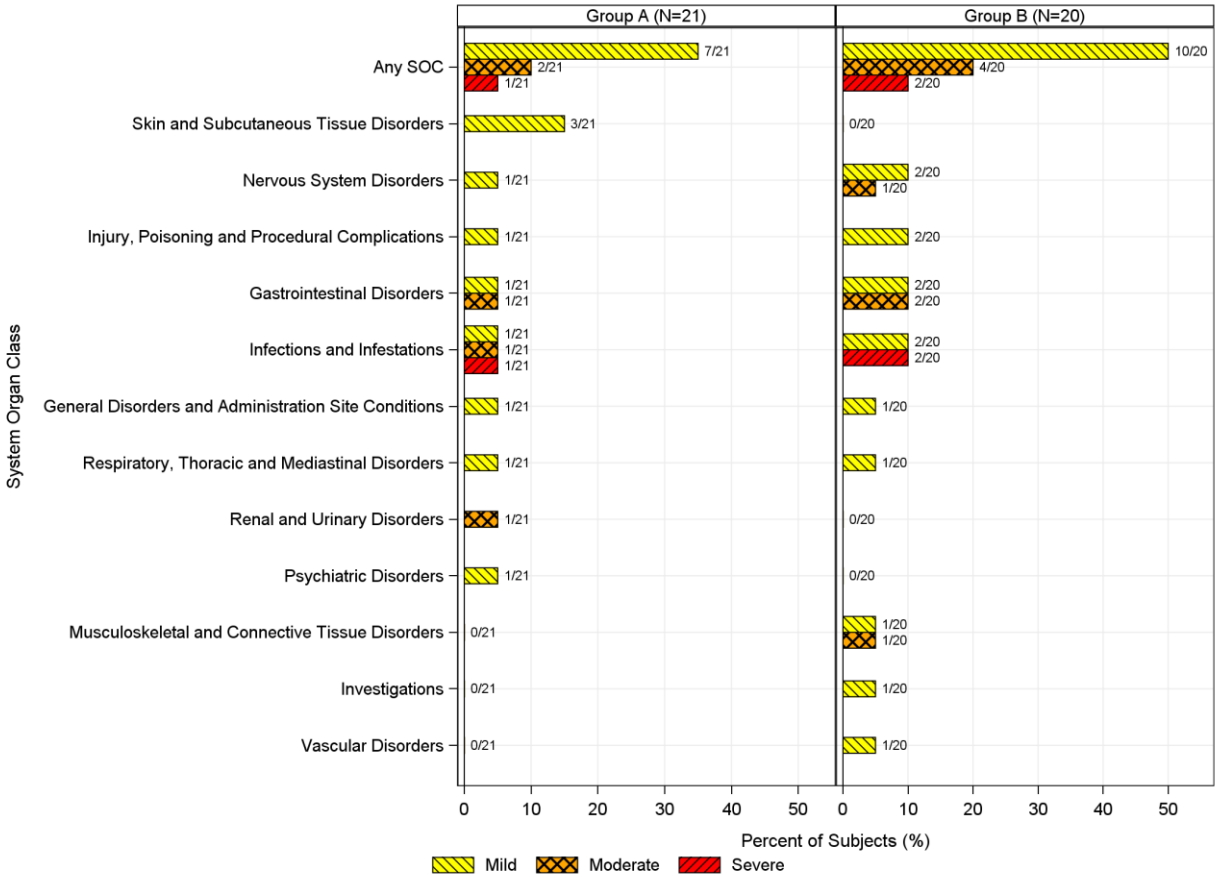
Implementation Note: This will be similar to Figure 24. Groups include: 2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 2 Doses; 2-8 yrs, Placebo, 2 Doses

Figure 33: Maximum Severity of Systemic Solicited Events by Days Post Dose Following Any Dose – Participants 2-8 Years Old – Safety Population

Implementation Note: This will be similar to Figure 24. Groups include: 2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 2 Doses; 2-8 yrs, Placebo, 2 Doses

14.3.1.2 Unsolicited Adverse Events

Figure 34: Participant-Level Incidence of Non-Serious Unsolicited Adverse Events in the 28 Days Post Dosing by MedDRA® System Organ Class and Maximum Severity – Participants 9-17 Years Old – Safety Population



Similar Figures:

Figure 35: Participant-Level Incidence of Non-Serious Unsolicited Adverse Events in the 28 Days Post Dose 1 by MedDRA® System Organ Class and Maximum Severity – Participants 2-8 Years Old – Safety Population

Implementation Note: This will be similar to Figure 34. Groups include: 2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 or 2 Doses; 2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR, 1 Dose; 2-8 yrs, Placebo, 1 or 2 Doses

Figure 36: Participant-Level Incidence of Non-Serious Unsolicited Adverse Events in the 28 Days Post Dose 1 by MedDRA® System Organ Class and Maximum Severity – All Participants – Safety Population

Implementation Note: This will be similar to Figure 34. Groups include: Vaccine Recipients, Placebo Recipients)

Figure 37: Participant-Level Incidence of Non-Serious Unsolicited Adverse Events in the 28 Days Post Dose 2 by MedDRA® System Organ Class and Maximum Severity – Participants 2-8 Years Old – Safety Population

Implementation Note: This will be similar to Figure 34. Groups include: 2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 2 Doses; 2-8 yrs, Placebo, 2 Doses

Figure 38: Participant-Level Incidence of Non-Serious Unsolicited Adverse Events in the 28 Days Post Any Dose by MedDRA® System Organ Class and Maximum Severity – Participants 2-8 Years Old – Safety Population

Implementation Note This will be similar to Figure 34. Groups include: 2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 2 Doses; 2-8 yrs, Placebo, 2 Doses

Figure 39: Participant-Level Incidence of Adverse Events of Special Interest by MedDRA® System Organ Class and Maximum Severity – Participants 9-17 Years Old – Safety Population

Implementation Note: This will be similar to Figure 34. Groups include: 9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose; 9-17 yrs, Placebo, 1 Dose

Figure 40: Participant-Level Incidence of Adverse Events of Special Interest by MedDRA® System Organ Class and Maximum Severity – Participants 2-8 Years Old – Safety Population

Implementation Note: This will be similar to Figure 34. Groups include: 2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR, 1 Dose; 2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose; 10^9 $TCID_{50}$ Sing2016 M2SR, 2 Doses; 2-8 yrs, Placebo, 1 or 2 Doses

Figure 41: Participant-Level Incidence of Adverse Events of Special Interest by MedDRA® System Organ Class and Maximum Severity – All Participants – Safety Population

Implementation Note: This will be similar to Figure 34. Groups include: Vaccine Recipients, Placebo Recipients

Figure 42: Participant-Level Incidence of Serious Adverse Events by MedDRA® System Organ Class and Maximum Severity – Participants 9-17 Years Old – Safety Population

Implementation Note: This will be similar to Figure 34. Groups include: 9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose; 9-17 yrs, Placebo, 1 Dose

Figure 43: Participant-Level Incidence of Serious Adverse Events by MedDRA® System Organ Class and Maximum Severity – Participants 2-8 Years Old – Safety Population

Implementation Note: This will be similar to Figure 34. Groups include: 2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR, 1 Dose; 2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose; 2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 2 Doses; 2-8 yrs, Placebo, 1 or 2 Doses

Figure 44: Participant-Level Incidence of Serious Adverse Events by MedDRA® System Organ Class and Maximum Severity – All Participants – Safety Population

Implementation Note: This will be similar to Figure 34. Groups include: Vaccine Recipients, Placebo Recipients

Figure 45: Participant-Level Incidence of New-Onset Chronic Medical Conditions by MedDRA® System Organ Class and Maximum Severity – Participants 9-17 Years Old – Safety Population

Implementation Note: This will be similar to Figure 34. Groups include: 9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose; 9-17 yrs, Placebo, 1 Dose

Figure 46: Participant-Level Incidence of New-Onset Chronic Medical Conditions by MedDRA® System Organ Class and Maximum Severity, Participants 2-8 Years Old – Safety Population

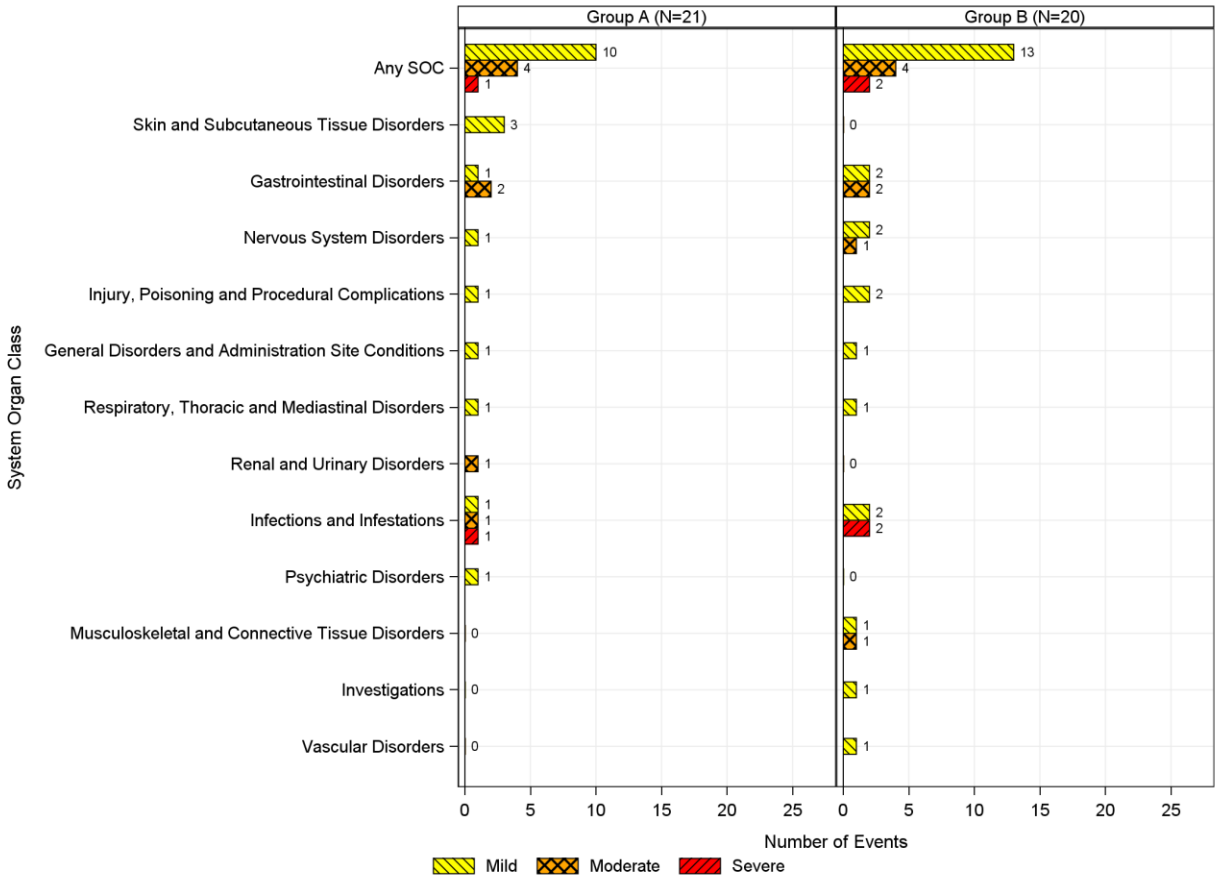
Implementation Note: This will be similar to Figure 34. Groups include: 2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR, 1 Dose; 2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose; 2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 2 Doses; 2-8 yrs, Placebo, 1 or 2 Doses

Figure 47: Participant-Level Incidence of New-Onset Chronic Medical Conditions by MedDRA® System Organ Class and Maximum Severity – All Participants – Safety Population

Implementation Note: This will be similar to Figure 34. Groups include: Vaccine Recipients, Placebo Recipients)

Figure 48: Frequency of Non-Serious Unsolicited Adverse Events in the 28 Days Post Dosing by MedDRA® System Organ Class and Severity – Participants 9-17 Years Old – Safety Population

Implementation Note: Panels will be included for each analysis group (9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose; 9-17 yrs, Placebo, 1 Dose)



Similar Figures:

Figure 49: Frequency of Non-Serious Unsolicited Adverse Events in the 28 Days Post Dose 1 by MedDRA® System Organ Class and Severity – Participants 2-8 Years Old – Safety Population

Implementation Note: This will be similar to Figure 48. Groups include: 2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 or 2 Doses; 2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR, 1 Dose; 2-8 yrs, Placebo, 1 or 2 Doses

Figure 50: Frequency of Non-Serious Unsolicited Adverse Events in the 28 Days Post Dose 2 by MedDRA® System Organ Class and Severity – Participants 2-8 Years Old – Safety Population

Implementation Note: This will be similar to Figure 48. Groups include: 2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 2 Doses; 2-8 yrs, Placebo, 2 Doses

Figure 51: Frequency of Non-Serious Unsolicited Adverse Events in the 28 Days Post Any Dose by MedDRA® System Organ Class and Severity – Participants 2-8 Years Old – Safety Population

Implementation Note This will be similar to Figure 48. Groups include: 2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 2 Doses; 2-8 yrs, Placebo, 2 Doses

Figure 52: Frequency of Non-Serious Unsolicited Adverse Events in the 28 Days Post Dose 1 by MedDRA® System Organ Class and Severity – All Participants – Safety Population

Implementation Note: This will be similar to Figure 48. Groups include: Vaccine Recipients, Placebo Recipients

Figure 53: Frequency of Adverse Events of Special Interest by MedDRA® System Organ Class and Severity – Participants 9-17 Years Old – Safety Population

Implementation Note: This will be similar to Figure 48. Groups include: 9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose; 9-17 yrs, Placebo, 1 Dose

Figure 54: Frequency of Adverse Events of Special Interest by MedDRA® System Organ Class and Severity – Participants 2-8 Years Old – Safety Population

Implementation Note: This will be similar to Figure 48. Groups include: 2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR, 1 Dose; 2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose; 2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 2 Doses; 2-8 yrs, Placebo, 1 or 2 Doses

Figure 55: Frequency of Adverse Events of Special Interest by MedDRA® System Organ Class and Severity – All Participants – Safety Population

Implementation Note: This will be similar to Figure 48. Groups include: Vaccine Recipients, Placebo Recipients

Figure 56: Frequency of Serious Adverse Events by MedDRA® System Organ Class and Severity – Participants 9-17 Years Old – Safety Population

Implementation Note: This will be similar to Figure 48. Groups include: 9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose; 9-17 yrs, Placebo, 1 Dose

Figure 57: Frequency of Serious Adverse Events by MedDRA® System Organ Class and Severity – Participants 2-8 Years Old – Safety Population

Implementation Note: This will be similar to Figure 48. Groups include: 2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR, 1 Dose; 2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose; 2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 2 Doses; 2-8 yrs, Placebo, 1 or 2 Doses

Figure 58: Frequency of Serious Adverse Events by MedDRA® System Organ Class and Severity – All Participants – Safety Population

Implementation Note: This will be similar to Figure 48. Groups include: Vaccine Recipients, Placebo Recipients

Figure 59: Frequency of New-Onset Chronic Medical Conditions by MedDRA® System Organ Class and Severity – Participants 9-17 Years Old – Safety Population

Implementation Note: This will be similar to Figure 48. Groups include: 9-17 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose; 9-17 yrs, Placebo, 1 Dose

Figure 60: Frequency of New-Onset Chronic Medical Conditions by MedDRA® System Organ Class and Severity, Participants 2-8 Years Old – Safety Population

Implementation Note: This will be similar to Figure 48. Groups include: 2-8 yrs, 10^8 $TCID_{50}$ Sing2016 M2SR, 1 Dose; 2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 1 Dose; 2-8 yrs, 10^9 $TCID_{50}$ Sing2016 M2SR, 2 Doses; 2-8 yrs, Placebo, 1 or 2 Doses

Figure 61: Frequency of New-Onset Chronic Medical Conditions by MedDRA® System Organ Class and Severity – All Participants – Safety Population

Implementation Note: This will be similar to Figure 48. Groups include: Vaccine Recipients, Placebo Recipients

APPENDIX 3. LISTINGS

General Listing Implementation Note: Participant ID should be USUBJID (not PATID) for purposes of de-identification.

LISTINGS

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16.1.6 Listing of Participants Receiving Investigational Product

Listing 1: Listing of Participants Receipt of Study Product

[Implementation Note: sorted by cohort, then date of first vaccine administration, then participant ID]

Cohort	Study Product Assigned per Randomization	Study Product Received	Participant ID	Study Product Administration Deviations[a]	Date(s) of Study Product Administration
[e.g., Cohort 1, 2, 3, or 4]	[10^8 TCID50 Sing2016 M2SR H3N2, 1 dose; 10^9 TCID50 Sing2016 M2SR H3N2, 1 dose; 10^9 TCID50 Sing2016 M2SR H3N2, 2 doses; Placebo]				[If one dose: DDMMMYYYY If two doses: DDMMMYYYY / DDMMMYYYY or DDMMMYYYY/ NA]

[a] Includes administration of incorrect study product (including incorrect dosing) and study product administration out of window.

16.2.1 Discontinued Participants

Listing 2: Discontinuations of Study Product or Early Terminated Participants

[Implementation Note: sorted by analysis group, then participant ID. Discontinued Study Product should be marked with "Yes" or "No" for participants in Cohort 4, and "N/A" otherwise. Terminated Early should be marked with either "Yes" or "No."]

			Study Product Discontinuation				Early Termination			
Analysis Group	**Participant ID**	**Enrollment Date**	**Discontinued Study Product?**	**Study Product Discontinuation Date**	**Study Day of Study Product Discontinuation**	**Reason for Discontinuation of Study Product**	**Terminated Early?**	**Early Termination Date**	**Study Day of Early Termination**	**Reason for Early Termination**

16.2.2 Protocol Deviations

Listing 3: Participant-Specific Protocol Deviations

[Implementation Note: sorted by analysis group, then participant ID, then deviation number. In the "Deviation" column, concatenate any and all "specify" fields (including visit number, etc.). If "Reason for Deviation" is "Other," concatenate "specify" field, separate by a colon, e.g., "Other: Participant refusal." If IRB reporting was required, display "Yes" with the study day the deviation was reported to the IRB in parentheses, e.g., "Yes (20)".]

Analysis Group	Participant ID	Deviation Number	Visit Number	Study Day	Deviation Category	Deviation Description	Reason for Deviation	Deviation Resolution	Deviation Resulted in AE?	Deviation Resulted in Participant Termination?	Deviation Affected Product Stability?	IRB Reporting Required? (Study Day Reported to IRB)	Comments

Listing 4: Non-Participant Specific Protocol Deviations

[Implementation Note: sorted by site, then deviation date. In the "Deviation" column, concatenate any and all "specify" fields (including visit number, etc.). If "Reason for Deviation" is "Other," concatenate "specify" field, separate by a colon, e.g., "Other: Participant refusal." If IRB reporting was required, display "Yes" with the date the deviation was reported to the IRB in parentheses, e.g., "Yes (01JAN2024)".]

Site	Deviation Date	Deviation Category	Deviation Description	Reason for Deviation	Deviation Resolution	Deviation Resulted in Participant Termination?	Deviation Affected Product Stability?	IRB Reporting Required? (Study Day Reported to IRB)	Comments

16.2.3 Participants Excluded from Analysis

Listing 5: Reason for Screen Failures

[Implementation Note: sorted by cohort, then date of screen failure. If multiple criteria/reasons are not met/met, criteria/reasons should be separated by a semi-colon.]

Cohort	Participant ID	Date of Screen Failure	Inclusion Criteria Not Met	Exclusion Criteria Met	Reason for Screen Failure if Eligible but not Enrolled

Listing 6: Participants Excluded from Analysis Populations

[Implementation Note: sorted by analysis group, then participant ID]

Analysis Group	Participant ID	Analyses in which Participant is Included	Analyses from which Participant is Excluded	Results Available?	Reason Participant Excluded
		[e.g., Safety; mITT; PP]	[e.g., Safety; mITT; PP, Day x]		

"Yes" in the "Results available" column indicates that available data were removed from the analysis. "No" indicates that no data were available for inclusion in the analysis.

16.2.4 Demographic Data

Listing 7: **Demographic Characteristics**

[Implementation Note: sorted by analysis group, then participant ID.]

Analysis Group	Participant ID	Sex	Age at Enrollment (years)	Ethnicity	Race

Listing 8: Prior and Concurrent Medical Conditions

[Implementation Note: sorted by analysis group, then participant ID, then medical history number. "Condition Start Day" and "Condition End Day" are relative to enrollment (which is Day 1, day before enrollment is Day -1). For medical conditions reported prior to enrollment, rather than using exact study days, categorize as follows: ">5 years prior to enrollment", "1-5 years prior to enrollment", "1-12 months prior to enrollment", "Within 1 month of enrollment". If ongoing, display "Ongoing" in the "Condition End Day" column.

Analysis Group	Participant ID	Medical History Number	Medical History Term	Condition Start Day	Condition End Day	MedDRA SOC	MedDRA PT

Listing 9: Prior Vaccinations

[Implementation Note: sorted by analysis group, then participant ID, then date of receipt. Date of receipt should be displayed to the highest level of specificity. For example, when both month and year are known, it should be displayed as "Month YYYY", if just year is known, it should be displayed as "YYYY". Seasonal influenza vaccine receipt events should be highlighted in yellow and COVID-19 vaccine receipt events should be highlighted in green.]

Analysis Group	Participant ID	Date of Receipt	Months Prior to First Study Vaccination	Product Received	Vaccine Type	Season of Vaccine[a]

[a] Applicable only for seasonal (influenza) vaccines.

16.2.6 Individual Immunological Response Data

Listing 10: Immunogenicity Response Data

[Implementation Note: Examples of assay include “HAI in serum, “MN in plasma,” “sIgA via ELISA,” etc. Examples of antigen include “A/Singapore/INFIMH-16-0019/2016”, “A/Texas/71/2017,” etc. Examples of measure include “Titer,” “Total sIgA concentration (µg/mL),” etc.]

Analysis Group	Participant ID	Assay	Antigen	Measure (units)	Result	Baseline	Day 29	Day 57	28 Days Post IIV4 Administration

16.2.7 Adverse Events

16.2.7.1 Solicited Adverse Events

Listing 11: Local Solicited Events

[Implementation Note: sort by analysis group, then participant ID, then dose number, then post dose day, then symptom]

Analysis Group	Participant ID	Dose Number	Post-Dose Day	Symptom	Severity

Similar Listings:

Listing 12: Systemic Solicited Events

[Implementation Note: This will be similar to Listing 11. It will include two additional columns: "Attributed to Alternate Etiology?" and "Alternate Etiology". Fever will be reported as the severity with the temperature in ºC in parentheses, e.g., "Mild (38.2)"]

16.2.7.3 Unsolicited Adverse Events

Listing 13: Non-Serious Unsolicited Adverse Events in the 28 Days Post Vaccination

Implementation Notes: Duration should be calculated as follows: End date – start date + 1

- If the event is ongoing (no stop date), indicate "Ongoing" in the "Duration" column.
- In the "If Not Related, Alternate Etiology" column, merge the 2 data fields for collecting alternate etiology, separate by a colon.
- If there are no comments for an event, populate "Comments" column with "None'"
- Sort order: Analysis Group, then Participant ID, then AE Number

Part 1:

Analysis Group	Participant ID	AE Number	Adverse Event	Associated with Dose No.	No. of Days Post Associated Dose	Duration (Days)	MedDRA System Organ Class	MedDRA Preferred Term	Severity	Relationship to Study Vaccination	If Not Related, Alternative Etiology

Part 2:

Analysis Group	Participant ID	AE Number	Adverse Event	Action Taken with Study Vaccination	Participant Discontinued Due to AE?	AESI?	NOCMC?	Unanticipated Problem?	Outcome	Comments	

For additional details about AESIs, see Table 110. For additional details about SAEs, see Table 111. For additional details about NOCMCs, see Table 112.

16.2.8.4 Physical Exam Findings

Listing 14: Abnormal Physical Examination Findings

[Implementation Note: sort by analysis group, then participant ID, then study day, then associated with dose number, then number of days post associated dose, then body system, then abnormal finding. Each abnormal finding should be one row.]

Analysis Group	Participant ID	Study Day	Associated with Dose No.	No. of Days Post Associated Dose	Body System	Abnormal Finding	Reported as Solicited AE?	Reported as Unsolicited AE?	Unsolicited AE Number

16.2.8.5 Concomitant Medications

Listing 15: Prior and Concomitant Medications

[Implementation Note: sorted by analysis group, then participant ID, then CM number. "Medication Start Day" and "Medication End Day" are relative to enrollment (which is Day 1, day before enrollment is Day -1). For medications reported prior to enrollment, rather than using exact study days, categorize as follows: ">5 years prior to enrollment", "1-5 years prior to enrollment", "1-12 months prior to enrollment", "Within 1 month of enrollment". If ongoing, display "Ongoing" in the "Medication End Day" column. If taken for an unsolicited AE or MH, display "Yes" with the description and AE or MH Number in parentheses, e.g., "Yes (COVID-19; 7)" in the appropriate column. If taken for a solicited AE, display "Yes" with the corresponding solicited event in parentheses, e.g., "Yes (Rhinorrhea)" in the appropriate column. Receipt of COVID-19 medications will be highlighted in green]

Analysis Group	Participant ID	CM Number	Medication	Medication Start Day	Medication End Day	Indication	Taken for an AE? (AE Description; Number)	Taken for a condition on MH? (MH Description; Number)	ATC Level 1 (ATC Level 2)
Medications relating to COVID-19 vaccine receipt are highlighted in green.									

16.2.8.6 Pregnancy Reports

Listing 16: Pregnancy Reports – Maternal Information

[Implementation Note: Only include the "Pregnancy Number" column if at least one participant has more than 1 pregnancy. Date of Conception will be calculated based on estimated delivery date. BMI will be calculated based on pre-pregnancy height and weight. Mother's weight gain will be calculated based on pre-pregnancy weight and end of pregnancy weight. If a major congenital anomaly with previous pregnancy, display "Yes" and the text from the "specify" field, separated by a colon. If any substance use is reported, include a listing of substance use. If autopsy revealed an alternate etiology, display "Yes" and the text from the "specify" field, separated by a colon. If abnormality in product of conception, display "Yes" and the text from the "specify" field, separated by a colon. Sort order: Analysis Group, Participant ID, Pregnancy Number.]

Analysis Group	Participant ID	Pregnancy Number	Date of Initial Report	Study Day Corresponding to Estimated Date of Conception	Source of Maternal Information	Pregnancy Status	Mother's Pre-Pregnancy BMI	Mother's Weight Gain During Pregnancy	Tobacco, Alcohol, or Drug Use During Pregnancy?	Medications During Pregnancy?	Maternal Complications During Pregnancy?	Maternal Complications During Labor, Delivery, or Post-Partum?
Maternal Complications are included in the Adverse Event listing. Medications taken during pregnancy are included in the Concomitant Medications Listing.												

Listing 17: Pregnancy Reports – Gravida and Para

[Implementation Note: Only include the "Pregnancy Number" column if at least one participant has more than 1 pregnancy. Sort order: Analysis Group, Participant ID, Pregnancy Number.]

			Live Births												
Participant ID	**Pregnancy Number**	**Gravida**	**Extremely PB[a]**	**Very PB[a]**	**Early PB[a]**	**Late PB[a]**	**Early TB[b]**	**Full TB[b]**	**Late TB[b]**	**Post TB[b]**	**Still Births[c]**	**Spontaneous Abortion/ Miscarriage[d]**	**Elective Abortions**	**Therapeutic Abortions**	**Major Congenital Anomaly with Previous Pregnancy?**

Gravida includes the current pregnancy, para events do not.
[a] Preterm birth
[b] Term birth
[c] ≥ 20 weeks
[d] < 20 weeks

Listing 18: Pregnancy Reports – Live Birth Outcomes

[Implementation Note: Only include the "Pregnancy Number" column if at least one participant has more than 1 pregnancy. Sort order: Analysis Group, Participant ID, Pregnancy Number.]

Analysis Group	Participant ID	Pregnancy Number	Fetus Number	Pregnancy Outcome (for this Fetus)	Fetal Distress During Labor and Delivery?	Delivery Method	Sex	Gestational Age at Live Birth	Size for Gestational Age	Apgar Score (1 minute; 5 minutes)	Cord pH	Congenital Anomalies?	Illnesses/ Hospitalizations within 1 Month of Birth?

Listing 19: Pregnancy Reports – Still Birth Outcomes

[Implementation Note: Only include the "Pregnancy Number" column if at least one participant has more than 1 pregnancy. Sort order: Analysis Group, Participant ID, Pregnancy Number, Fetus Number.]

Analysis Group	Participant ID	Pregnancy Number	Fetus Number	Pregnancy Outcome (for this Fetus)	Fetal Distress During Labor and Delivery?	Delivery Method	Sex	Gestational Age at Still Birth	Size for Gestational Age	Cord pH	Congenital Anomalies?	Autopsy Performed?	If Autopsy, Etiology for Still Birth Identified?

Listing 20: Spontaneous, Elective, or Therapeutic Abortion Outcomes

[Implementation Note: Only include the "Pregnancy Number" column if at least one participant has more than 1 pregnancy. Sort order: Analysis Group, Participant ID, Pregnancy Number.]

Analysis Group	Participant ID	Pregnancy Number	Fetus Number	Pregnancy Outcome (for this Fetus)	Gestational Age at Termination	Abnormality in Product of Conception?	Reason for Therapeutic Abortion