CLINICAL RESEARCH IN INFECTIOUS DISEASES

STATISTICAL ANALYSIS PLAN
for
DMID Protocol: 17-0012

Study Title:
A Phase I Trial to Evaluate the Safety and Immunogenicity of an Influenza Vaccination Strategy Including a H3N2 M2SR Prime followed by a Seasonal Quadrivalent Inactivated Vaccine Boost in a Pediatric Population 9-17 years old

NCT03553940

Version 1.0

DATE: June 17, 2019

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STUDY TITLE

Protocol Number Code:	**DMID Protocol: 17-0012**
Development Phase:	Phase I
Products:	1. Investigational Vaccine: A/Brisbane/10/2007 (H3N2) M2-deficient single replication (M2SR) manufactured by FluGen 2. Vaccine Diluent 3. Saline Placebo (0.9% sodium chloride) 4. Licensed Inactivated QIV: FLUCELVAX® QIV 5. VaxINator Device
Form/Route:	1. Investigational Vaccine and Placebo: Intranasal 2. Licensed Inactivated QIV: Intramuscular
Indication Studied:	Influenza
Sponsor:	Division of Microbiology and Infectious Diseases National Institute of Allergy and Infectious Diseases National Institutes of Health
Clinical Trial Initiation Date:	15 August 2018
Clinical Trial Completion Date:	Expected Summer 2020
Date of the Analysis Plan:	17 June 2019
Version Number:	1.0

This study was performed in compliance with Good Clinical Practice.

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LIST OF ABBREVIATIONS

AE	Adverse Event
ALT	Alanine Aminotransferase
aPTT	Activated Partial Thromboplastin Time
AST	Aspartate Aminotransferase
BP	Blood Pressure
C	Celsius
CI	Confidence Interval
CRF	Case Report Form
DMID	Division of Microbiology and Infectious Diseases
EDC	Electronic Data Capture
ELLA	Enzyme-linked Lectin Assay
ELISA	Enzyme-linked Immunosorbent Assay
ELISpot	Enzyme-linked Immunospot Assay
F	Fahrenheit
GMT	Geometric Mean Titer
GMFR	Geometric Mean Fold Rise
HAI	Hemagglutination Inhibition Assay
HGB	Hemoglobin
ICH	International Conference on Harmonisation
IRB	Institutional Review Board
L	Liter
LLN	Lower Limit of Normal
M2SR	M2 deleted Single Replication (influenza virus)
mcg	Microgram
MedDRA	Medical Dictionary for Regulatory Activities
mEq	Milliequivalent
mg	Milligram
mITT	Modified Intention to Treat
mL	Milliliter
N	Number (typically refers to subjects)

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List of Abbreviations *(continued)*

NIH	National Institutes of Health
PBMC	Peripheral Blood Mononuclear Cell
PI	Principal Investigator
PP	Per Protocol
PT	Preferred Term
PT	Prothrombin Time
QIV	Quadrivalent Influenza Vaccine
RBC	Red Blood Cell
RCD	Reverse Cumulative Distribution
SAE	Serious Adverse Event
SD	Standard Deviation
SDCC	Statistical and Data Coordinating Center
SMC	Safety Monitoring Committee
SOC	System Organ Class
SOP	Standard Operating Procedures
U	Units
ULN	Upper Limit of Normal
WBC	White Blood Cell

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1. PREFACE

The Statistical Analysis Plan (SAP) for "A Phase I Trial to Evaluate the Safety and Immunogenicity of an Influenza Vaccination Strategy Including a H3N2 M2SR Prime followed by a Seasonal Quadrivalent Inactivated Vaccine Boost in a Pediatric Population 9-17 years old" (DMID Protocol 17-0012) 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 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 four sections: (1) a review of the study design, (2) general statistical considerations, (3) comprehensive statistical analysis methods for efficacy and safety outcomes, and (4) a list of proposed tables and figures. Within the table, figure, and listing mock-ups (Appendices 1, 2, and 3), references to CSR sections are included. 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.

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2. INTRODUCTION

2.1. Purpose of the Analyses

These analyses will assess the immunogenicity and safety of H3N2 M2SR in comparison with saline placebo and will be included in the clinical study report.

3. STUDY OBJECTIVES AND ENDPOINTS

3.1. Study Objectives

3.1.1. Primary

Safety:

- To assess the safety and reactogenicity of a monovalent live attenuated influenza H3N2 M2SR vaccine.

3.1.2. Secondary

Immunogenicity:

- Identification of circulating and mucosal antibody responses induced by H3N2 M2SR vaccination.
- Identification of cellular immune responses induced by H3N2 M2SR vaccination.

3.1.3. Exploratory

Immunogenicity:

- Investigation of H3N2 M2SR priming effects on QIV-induced broadly neutralizing antibody responses to HA and NA.
- Investigation of H3N2 M2SR priming effects on QIV-induced influenza-specific secretory IgA (sIgA) responses.
- Investigation of H3N2 M2SR priming effects on QIV-induced influenza-specific CD4 and CD8 T cell lymphoproliferative and effector cytokine responses.

3.2. Endpoints

3.2.1. Primary

Safety:

- Frequency of solicited upper respiratory and systemic reactogenicity through approximately Day 8 after the first study vaccination.
- Frequency of unsolicited non-serious adverse events from the time of study vaccination through 21 days after the first study vaccination.
- Frequency of SAEs, regardless of seriousness or relationship to study vaccination, from receipt of the first vaccination throughout the entire study.
- Frequency of New Onset Chronic Medical Conditions (NOCMC) and AESIs that develop from receipt of vaccination through 3 months after first study vaccination.

3.2.2. Secondary

Immunogenicity:

- For HAI and Neutralizing antibody responses, percentage of subjects achieving seroconversion (defined as either a pre-vaccination titer <1:10 and a post-vaccination titer ≥1:40, or a pre-vaccination titer ≥1:10 and a minimum four-fold rise in post-vaccination antibody titer) against H3N2 M2SR-like and H3N2 QIV-like viruses at approximately 7, 21, and 56 days following receipt of the first study vaccination and immediately prior to and approximately 21 days following receipt of QIV.
- For HAI and Neutralizing antibody responses, percentage of subjects achieving a serum antibody titer of 1:40 or greater against the H3N2 M2SR-like virus and the H3N2 QIV-like virus at baseline and approximately 7, 21, and 56 days following receipt of the first study vaccination and immediately prior to and approximately 21 days following receipt of QIV.
- For HAI and Neutralizing antibody responses, the geometric mean titers (GMTs) and geometric mean fold rise (GMFR) to H3N2 M2SR-like virus and H3N2 QIV-like virus at baseline and approximately 7, 21, and 56 days following receipt of the first study vaccination and immediately prior to and approximately 21 days following receipt of QIV.
- GMT and GMFR of nasal sIgA responses directed against the H3N2 M2SR virus and the H3N2 QIV virus measured by EPT(ELISA) with and without normalization to total sIgA at baseline and approximately 7, 21, and 56 days following receipt of the first study vaccination and immediately prior to and approximately 21 days following receipt of QIV.
- Frequency of influenza H3 HA-specific (H3 M2SR-like and QIV-like viruses) and conserved internal viral protein-specific IFN-γ ELISPOT responses at baseline and approximately 7, 21, and 56 days following receipt of the first study vaccination and immediately prior to and approximately 21 days following receipt of QIV.

3.2.3. Exploratory

Immunogenicity:

- GMT and GMFR of serum chimeric HA ELISA reactivity with Groups 1 and 2 HA stem domains of the viral hemagglutinin at baseline and approximately 7, 21, and 56 days following receipt of the first study vaccination and immediately prior to and approximately 21 days following receipt of QIV. (Note: These studies will be contingent upon seeing increased seroconversion rates and/or 4-fold rise as measured by GMFR in either M2SR or QIV matched H3HA-specific HAI and/or MN assays induced by H3N2 M2SR vaccination.)
- GMT and GMFR of serum anti-NA antibody titers to N1 and N2 Neuraminidases as determined by NA ELLA or ELISA at baseline and approximately 7, 21, and 56 days following receipt of the first study vaccination and immediately prior to and approximately 21 days following receipt of QIV. (Note: These studies will be contingent upon seeing increased seroconversion rates and/or 4-fold rises in either M2SR or QIV matched H3N2-specific HAI and/or MN assays induced by H3N2 M2SR vaccination).
- GMT and GMFR of nasal wash sIgA chimeric HA ELISA to the HA stem domains of the viral hemagglutinin (Group 2 versus Group 1 viruses with and without normalization to total sIgA at

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baseline and approximately 7, 21, and 56 days following receipt of the first study vaccination and immediately prior to and approximately 21 days following receipt of QIV. (Note: These studies will be contingent upon seeing increased GMT and/or GMFR of sIgA reactive with M2SR matched H3HA induced by H3N2 M2SR vaccination).

- GMT and GMFR of sIgA anti-NA antibody titers to N1 and N2 Neuraminidases as determined by NA ELLA or ELISA at baseline and approximately 7, 21, and 56 days following receipt of the first study vaccination and immediately prior to and approximately 21 days following receipt of QIV. (Note: These studies will be contingent upon seeing increased GMT and/or GMFR of sIgA reactive with M2SR matched H3HA induced by H3N2 M2SR vaccination).
- CD4+ and CD8+ T cell responses to the H3HA present in the M2SR vaccine and pools of highly conserved Influenza A T cell epitopes by 7 day CFSE dilution/flow cytometry at baseline and approximately 7, 21, and 56 days following receipt of the first study vaccination and immediately prior to and approximately 21 days following receipt of QIV. (Note: These studies will be contingent upon seeing increased frequencies of H3HA-specific and/or conserved peptide epitope-specific IFN-gamma producing T cells induced by M2SR vaccination in ELISPOT assays).

3.3. Study Definitions and Derived Variables

Medically significant wheezing is defined as wheezing on physical exam, signs of respiratory distress (tachypnea, retractions, or dyspnea), hypoxemia (O_2 saturation < 95%), or new bronchodilator prescription, or use of daily bronchodilator therapy (not on an "as needed "basis) from receipt of the first vaccination through 3 months after the first vaccination. Wheezing experienced after first vaccination through Visit 02 is considered a solicited event. Wheezing recorded after Visit 02 is considered an AESI. For all wheezing events the following will be recorded: whether wheezing is diffuse or localized, respiratory rate, oxygen saturation, medications associated with wheezing, and physician's description on auscultation.

For laboratory and immunogenicity measures the baseline value will be defined as the last value obtained prior to the first vaccination/dose of study product.

Individual Hemagglutination inhibition (HAI) and neutralization results will be reported as a titer with values of $10*2^k$, where k=0, 1, 2, etc. The lower limit of detection for the HAI and neutralization assays is 1:10; values below the limit of detection will be reported as '<10'. Values used in analysis will be imputed as one-half the limit of detection (10/2 = 5). For analysis, the geometric mean of repeated HAI or neutralization results will for each subject and visit will be computed and used as the response for all subsequent calculations.

Individual nasal sIgA results will be reported as a titer with values of 2^k where k=0, 1, 2, etc. The lower limit of detection for the nasal sIgA results is 2; values below the limit of detection will be reported as <2. Values used in analysis will be imputed as one-half the limit of detection (2/2 = 1). For analysis, the geometric mean of repeated sIgA results for each subject and visit will be computed and used as the response for all subsequent calculations. Relative (normalized) strain-specific sIgA results will be calculated by dividing the strain-specific value by total sIgA at each time point for each subject.

The lower limit of detection for the frequency of conserved internal viral protein-specific IFN-γ T cells per million peripheral blood mononuclear cells (PBMC) as measured by ELISPOT assay is 0.

4. INVESTIGATIONAL PLAN

4.1. Overall Study Design and Plan

This is a Phase I double-blind, randomized, placebo-controlled study in 50 healthy adolescents and children, 9-17 years of age, who are in good health and meet all eligibility criteria. The study is designed to assess the safety and immunogenicity of a prime-boost regimen of H3N2 M2SR intranasal influenza vaccine followed by licensed inactivated QIV boost administered IM. Group A will receive one dose of M2SR intranasally on Day 1 and one dose of QIV on Day 92. Group B will receive one dose of saline intranasally on Day 1, and one dose of QIV on Day 92. See Table 1 for the randomization scheme for this trial.

The two study arms will be enrolled and vaccinated concurrently. Enrollment was paused in November 2018 until the spring of 2019 to ensure all subjects received seasonal QIV vaccine prior to the beginning of the influenza season. An interim analysis of safety and immunogenicity data through the Day 113 visit will be performed for all subjects enrolled in 2018. For details on changes to the study design and planned analyses see Section 12.

Reactogenicity will be measured by the occurrence of solicited upper respiratory (local) and systemic reactions from the time of the experimental (first) study vaccination through 7 days after vaccination and a respiratory tract assessment at 7 days post vaccination (Visit 02). Unsolicited non-serious AEs will be collected from the time of the first study vaccination through approximately 21 days after the first study vaccination. SAEs will be collected from the time of the first study vaccination throughout the entire study. AESIs (wheezing and otitis media) and NOCMC will be documented and reported from the time of first study vaccination through approximately 3months after first study vaccination.

Immunogenicity testing will include performing HAI, neutralization, and nasal secretory IgA (sIgA) assays for secondary endpoints. If significant responses are observed to be induced by H3N2 M2SR vaccination, then HA/NA ELISA, IFN-γ ELISPOT and CFSE dilution/ICS assays will also be performed (see Section 8.3 for further details). If performed, analyses for these assay results will be described in an addendum for this SAP.

Serum for HAI, HA/NA ELISA and neutralization assays will be obtained on Day 01 (pre-vaccination), Days 08, 22, and 57 after the first vaccination, immediately prior to the 2nd study vaccination (Day 92), and on Day 22 after the 2nd vaccination. Nasal swabs for sIgA will be collected on Day 01 (pre-vaccination), Days 08, 22, and 57 after the first vaccination, immediately prior to the 2nd vaccination (Day 92), and on Day 22 after the 2nd vaccination. PBMC for T cell functional assays (IFN-γ ELISPOT and CFSE dilution/ICS assays) will be harvested on Day 01 (pre-vaccination), Days 08, 22, and 57 after the first vaccination, immediately prior to 2nd vaccination (Day 92), and on Day 22 after the 2nd vaccination.

The duration of this study for each subject will be approximately 13 months.

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

This protocol follows double-blind, randomized, placebo concurrent control design. Subjects receive either H3N2 M2SR or saline placebo intranasally via VaxINator device as their first study vaccination. After approximately 3 months, all subjects receive licensed QIV administered intramuscularly (IM) as the second study vaccination.

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4.3. Selection of Study Population

The study population for this clinical trial is 50 male and non-pregnant female children and adolescents between the ages of 9 and 17 who are in good health and meet all eligibility criteria. Specific eligibility criteria can be found in the protocol sections 5.1 (Subject Inclusion Criteria) and 5.2 (Subject Exclusion Criteria). The subjects are recruited from the general population at the participating Vaccine Trial and Evaluation Unit (VTEU) site, Saint Louis University (SLU), which has substantial experience conducting influenza vaccine studies.

Following review of laboratory results for subjects enrolled through August 2018, it was identified that a significant portion had a drop in hemoglobin during the study. The protocol was amended to include screening for pre-existing iron deficiency anemia with ferritin and requiring both normal ferritin and HgB results for enrollment, to reduce the amount of blood collected overall, and to add a contingency regarding specimen collection. Subjects will be monitored after entry in the trial for drops in hemoglobin levels indicating anemia. If HgB levels are consistently low through the visit at approximately Day 57, the subject will no longer have PBMC samples collected at subsequent visits.

4.4. Treatments

4.4.1. Treatments Administered

H3N2 M2SR or saline placebo is administered intranasally using the VaxINator device as the first study vaccination. All subjects receive licensed seasonal QIV via IM injection as the second study vaccination.

4.4.2. Identity of Investigational Product(s)

See the study protocol section 6.1 for details of study product formulation.

4.4.3. Method of Assigning Subjects to Treatment Groups (Randomization)

Enrollment/randomization will be performed through the enrollment module in the electronic data capture system, maintained by the SDCC.

Eligible subjects will be randomized and assigned in a 1:1 ratio to receive intranasal H3N2 M2SR or saline placebo, with stratification by site. The randomization is based on a variable blocked scheme to provide an approximately balanced allocation to the treatment groups during the study.

4.4.4. Selection of Doses in the Study

A first-in-human dose escalation trial in healthy adults has already been conducted with doses up to $1x10^8$ $TCID_{50}$ of the experimental H3N2 M2SR vaccine without any safety issues. In addition, this highest dose resulted in the greatest immunogenicity for relevant serum antibody, mucosal antibody and T cell responses. Furthermore, the current study involves the oldest pediatric subjects (age 9-17 years old) and therefore the sponsor believed the maximum dose given in the first-in-human trial was appropriate for this study.

4.4.5. Selection and Timing of Dose for Each Subject

Each subject is randomly assigned to a study group which will define the product received for the first vaccination (H3N2 M2SR or placebo). The first vaccination takes place on the day of randomization. All subjects receive licensed QIV approximately 3 months after the first vaccination (protocol defined window of 77 to 105 days post first vaccination).

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4.4.6. Blinding

The first vaccination (H3N2 M2SR or saline placebo) will be prepared by the licensed pharmacist and administered by an unblinded study vaccine administrator. All follow-up safety and efficacy evaluations will be performed by blinded clinic staff.

The pharmacist at each site will refer to the Treatment Key provided for the trial by the SDCC to determine the treatment for the subjects. The pharmacist will maintain an open label code (provided by the SDCC) under locked/secured conditions and will follow the randomization code. The study products are identical in appearance.

The protocol contains no explicit provisions for emergency unblinding. According to DMID policy, the study medical monitor responds to requests for emergency unblinding and instructs the SDCC to release treatment codes only if necessary to ensure that the subject receives appropriate clinical care.

4.4.7. Prior and Concomitant Therapy

Concomitant medications will include all current medications and medications taken in the 30 days prior to signing the informed consent form through approximately 21 days after the first study vaccination, early termination or unscheduled visits (if prior to 21 days after the first study vaccination), whichever occurs first. Prescription and over-the-counter drugs will be included as well as herbals, vitamins, and supplements. In addition, receipt of non-study influenza vaccines will be solicited through approximately 21 days after the first study vaccination. The use of aspirin or salicylate containing products will be solicited from 30 days prior to the first vaccination through 21 days after the last vaccination.

4.4.8. Treatment Compliance

All subjects are to receive a single intranasal dose of either H3N2 M2SR or saline placebo administered in the clinic as the first vaccination. All subjects are to receive a single QIV vaccination approximately 3 months after the first vaccination.

4.5. Immunogenicity and Safety Variables

See Table 2 for a schedule of study procedures.

4.5.1. Immunogenicity Variables

Individual HAI and Neut titer results will be reported by the laboratory at St. Louis University for the H3N2 M2SR-like (A/Brisbane/10/2007) and H3N2 QIV-like viruses (A/Singapore/INFIMH-16-0019/2016 and cell culture-propagated A/North Carolina/04/2016 for 2018/2019 and any additional strains specific to the 2019/2020 QIV). The HAI assay for the A/North Carolina/04/2016 strain only will be tested using both turkey and guinea pig red blood cells (RBC) separately, both with and without oseltamivir. All other strains will be tested using turkey RBC without oseltamivir, and these results from these conditions will be used in grouped displays of QIV-like results. For analysis, the geometric mean (calculated on natural log scale) of repeated results for each subject at each visit will be computed and used as the response for all subsequent calculations. The variation arising from multiple measurements for an individual at a single time point is not used in subsequent calculations. See Section 3.3 for definitions of derived variables for the analysis of HAI and Neut data.

The laboratory at Saint Louis University will also provide individual titer results for nasal sIgA against the H3N2 M2SR-like and H3N2 QIV-like viruses and total sIgA, as well as individual H3 HA-specific (H3 M2SR-like and QIV-like viruses) For analysis, the geometric mean (calculated on natural log scale) of repeated results for each subject at each visit will be computed and used as the response for all subsequent calculations. The variation arising from multiple measurements for an individual at a single time point is not used in subsequent calculations. The frequency of conserved internal viral protein-specific (H3 M2SR-like and QIV-like viruses) IFN-γ T Cells per million PBMC as measured by ELISPOT will also be reported. See Section 3.3 for definitions of derived variables for the analysis of sIgA and IFN-γ T Cell results.

4.5.2. Safety Variables

Safety will be assessed by the frequency and severity of:

1. SAEs occurring from the time of the first study vaccination through 12 months after the first vaccination.
2. AESIs (wheezing, otitis media) and NOCMCs occurring from the time of the first study vaccination through 3 months after the first vaccination.
3. Solicited Adverse Events – reactogenicity events occurring from the time of experimental (first) study vaccination through 7 days after the first study vaccination.
4. Unsolicited Non-Serious Adverse Events –non-serious AEs occurring from the time of the first study vaccination through approximately 21 days after the first study vaccination.
5. Clinical safety laboratory AEs occurring at approximately 7 days after the first vaccination. Parameters to be evaluated include a WBC, HGB, Platelet Count, ALT, AST, Serum Creatinine, Ferritin level, PT and aPTT. HGB will also be repeated at Day 22 if there is a drop in HGB level from screen to Day 8 of > 0.5 g/dL or results are < lower limits of normal. If unable to collect at Day 22, collect at Day 57. If drawn at Day 22 and the results are still low, repeat at Day 57. If HGB results are still low at Day 57, no further PBMC collection will be done. HGB and Ferritin level will be drawn at Day 113. If the ferritin is < 15 ng/mL and/or the HGB is less than the lower limits of normal, will recommend follow-up with primary care provider for consideration of multivitamins with iron.

Grading scales for injection site and systemic solicited reactions, respiratory tract assessments, AESI, vital signs, and clinical laboratory parameters are provided in Table 6, Table 7, Table 8, Table 9, Table 10, and Table 11.

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5. SAMPLE SIZE CONSIDERATIONS

This study is planned to enroll approximately 25 subjects in each treatment arm (Table 1). The sample size for this study was selected to obtain preliminary estimates in a pediatric population. While this study is not designed to test any specific null hypothesis, the following tables illustrate the precision and power available for select estimates and comparisons of interest.

Table 3 indicates the probability of observing one or more safety events, such as solicited local or systemic reactogenicity events or an unsolicited AE of a particular type, for a single treatment arm (N=25), and for all enrolled subjects (N=50).

Table 4 illustrates the minimum detectable differences in the proportion of subjects responding (e.g., attaining seroconversion or a titer ≥1:40) between two treatment arms for a range of possible response rates in the comparator arm, using a Chi-Square Test and alpha = 0.05. In a Previous DMID trial (12-0016) in this population approximately 8% of subjects did not have available immunogenicity data at Day 42. Table 4 is presented for the planned enrollment (N = 25 per group) and accounting for 10% drop out (N = 22 per group).

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6. GENERAL STATISTICAL CONSIDERATIONS

6.1. General Principles

Unless otherwise specified, continuous variables will be summarized using the following descriptive statistics: n (non-missing sample size), mean, standard deviation, median, maximum and minimum. For post-baseline visits, fold rise from baseline will be calculated. Unless otherwise specified, confidence intervals for means (arithmetic or geometric) will be calculated using the student's t distribution with confidence level α=0.05 (95% confidence). P-values for spearman correlations will be calculated using the student's t distribution testing the hypothesis that the two variables tested are not correlated. The frequency and percentages (based on the non-missing sample size) of observed levels will be reported for all categorical measures. In general, all data will be listed, sorted by site, study group and subject, and when appropriate by visit number within subject. All summary tables will be structured with a column for each study group in the order presented in Table 1 and will be annotated with the total population size relevant to that table/treatment, including any missing observations.

6.2. Timing of Analyses

The interim analysis will be performed after all 19 subjects enrolled in 2018 have completed the Day 113 visit and HAI, MN, and sIgA data are available. The final analysis will be performed when all enrolled subjects have completed the Day 366 visit, the clinical database has been cleaned, monitored, and locked, and data is available for all secondary immunogenicity measures. Exploratory immunogenicity assays will be performed pending the results observed for the secondary outcome measures as described in Section 8.3. Analyses of the exploratory outcome measures will be described in addendum to this SAP.

6.3. Analysis Populations

Demographic and baseline characteristics will be presented for all enrolled subjects. All safety summaries will be presented for the safety population (Section 6.3.3). Secondary immunogenicity measures will be presented for the Per Protocol (PP) and modified intent-to-treat (mITT) populations.

A tabular listing of all subjects, visits, and observations excluded from analyses will be provided in the CSR (Listing 7).

6.3.1. Modified Intention-to-Treat (mITT) Population

The modified intent-to-treat (mITT) population includes all subjects who received at least one dose of study vaccine and contributed both pre- and at least one post-study vaccination sample for immunogenicity testing for which valid results were reported. Available valid results will be assessed separately for each assay (HAI, Neutralizing antibody, sIgA, frequency IFN-γ T-cells). For analyses using the mITT population, subjects will be grouped based on randomized treatment arm.

6.3.2. Per Protocol Population

The per protocol (PP) population includes all subjects in the mITT subset with the following exclusions:

- Data from all available visits for subjects found to be ineligible at baseline.
- Data from all visits subsequent to major protocol deviations, such as:
  - Second study vaccination not received,

- Second study vaccination received out of window,
- Receipt of non-study licensed live or inactivated vaccine within 30 days before or after each study vaccination.
- Receipt of influenza vaccine (live or inactivated) within 6 months prior to 30 days after for analyses using the PP population, subjects will be grouped based on study vaccinations received.

6.3.3. Safety Population

The Safety Analysis population includes all subjects who received one dose of M2SR vaccine. For analyses using the safety population, subjects will be grouped based on study vaccinations received.

6.4. Covariates and Subgroups

The protocol does not define any formal subgroup analyses, and the study is not adequately powered to perform subgroup analyses.

6.5. Missing Data

All attempts will be made to collect all data per protocol. As missing data are expected to be minimal, no imputation will be performed for missing values [2]. Any data point that appears to be erroneous or inexplicable based on clinical judgment will be investigated as a possible outlier. If such data points are identified as scientifically valid outliers, sensitivity analyses will be performed to examine the impact of including or excluding the outliers. Any substantive differences in these analyses will be reported.

6.6. Interim Analyses and Data Monitoring

Interim analyses will only be used to terminate this trial in the event that unanticipated safety events deemed to be of sufficient concern require such action by the sponsor. These assessments will not be made on the basis of testing a formal statistical hypothesis; therefore, p-value adjustment will not be made to any analyses. A DSMB will be convened by DMID to review study progress and participant, clinical, safety, and reactogenicity and immunogenicity data.

An interim analysis will be performed after the 19 subjects enrolled in 2018 have completed the Day 113 visit. The interim analysis will include summaries of MN results for the M2SR-like H3N2 strain and both 2018-2019 QIV-like H3N2 strains as well as safety and reactogenicity data. This streamlined report will be made available to the sponsor for planning subsequent trials. These analyses will not be used to make any decisions concerning the conduct of this trial. At the time of these analyses it is anticipated that subjects will remain in long term safety and immunogenicity follow-up and that enrollment will resume in 2019, so the presentation of these data will be in a format that prevents inadvertent unblinding of the sponsor or clinical investigators to any individual subject's treatment assignment. When it is not possible to display the data by treatment arm and maintain the blind for the investigators and sponsor, such as the presence of extreme values or noteworthy AEs, a presentation by treatment arm will not be provided until after the long-term safety follow-up is complete. No hypothesis testing will be included in the interim analysis. Tables to be generated in the interim analysis are marked with an asterisk (*).

6.7. Multicenter Studies

This study is conducted at a single clinical site.

6.8. Multiple Comparisons/Multiplicity

This study was designed to obtain preliminary estimates of the safety and immune response of one dose of M2SR followed by a dose of licensed QIV in a pediatric population. The study was not designed to test any specific null hypothesis, and as such no adjustment for multiple comparisons will be performed.

7. STUDY SUBJECTS

7.1. Disposition of Subjects

Table 16 will present a summary of the reasons that subjects were screened but not enrolled. A listing of all subjects that received study product is provided in Listing 1.

The composition of analysis populations, including reasons for subject exclusion, by treatment arm, is presented in Table 13.

The disposition of subjects in the study will be tabulated by study group (Table 12). The table shows the total number of subjects screened, enrolled, received at least one dose, discontinued dosing or terminated from study follow-up and the number completing the study.

A flowchart showing the disposition of study subjects, adapted from the Consort Statement [1] will be included (Figure 1). This figure will present the number of subjects screened, enrolled, lost to follow-up, and analyzed, by treatment arm.

A listing of subjects who discontinued dosing or terminated from study follow-up and the reason will be included in Listing 2.

7.2. Protocol Deviations

A summary of subject-specific protocol deviations will be presented by the reason for the deviation, the deviation category, and treatment group for all subjects (Table 5). Major deviations will be reviewed for possible subject exclusion from the per protocol population including deviations affecting eligibility at baseline, product administration deviations, primary endpoint missing data, and deviations relating to prohibited medications. See Section 6.3.2 for per protocol exclusion definitions. All subject-specific protocol deviations and non-subject specific protocol deviations will be included in Appendix 3 as data listings (Listing 3 and Listing 4, respectively).

8. IMMUNOGENICITY EVALUATION

This study was not designed to test a specific null hypothesis, rather the objective was to obtain preliminary estimates of immune response to the M2SR vaccine alone and after subsequent receipt of licensed seasonal QIV. Immunogenicity data summaries and analysis for secondary endpoints will be presented for the ITT and PP populations.

Immune responses for the M2SR strain (A/Brisbane/10/2007 (H3N2)) will be summarized at each time point presented overall and stratified by study arm. Immune responses for each QIV strain (egg-based A/Singapore/INFIMH-16-0019/2016 and cell culture-propagated A/North Carolina/04/2016 and any additional strains specific to the 2019/2020 QIV vaccine) will be summarized at each time point presented by stratified by study arm for each season and H3N2 QIV response overall. Descriptive summary statistics will be provided for all assays, strains, and time points.

HAI and MN serum antibody titer summaries will include GMT, the proportion of subjects with a titer ≥1:40, GMFR, and the proportion of subjects achieving seroconversion along with corresponding 95% confidence intervals for each measure. Exact (Blaker) confidence intervals will be presented for proportional endpoints [3]. Summaries of HAI and MN responses are presented in Table 20, Table 21, Table 22, Table 23, Table 24, Table 25, Table 26, Table 27, Table 28, and Table 29.

For nasal sIgA responses, the GMT with corresponding 95% CI visits strain-specific and relative sIgA (relative sIgA = strain-specific sIgA / total sIgA) results will be reported for the M2SR and QIV A/H3N2 strains. For post-baseline visits GMFR with corresponding 95% CI will also be calculated, as well as the proportion of subjects with ≥2-fold and ≥4-fold rise with corresponding 95% CI. Differences in GMT and GMFR between study groups will be presented at each time point. For QIV-like strains, differences will be calculated between overall response to the year-matched QIV strains. Summaries of nasal sIgA responses are presented in Table 30, Table 31, Table 32, and Table 33.

Summaries of the frequency of influenza H3 HA-specific (M2SR-like and QIV-like viruses) and conserved internal viral protein-specific IFN-γ producing T-cells will include the mean (or geometric mean if data are log-normally distributed) and corresponding 95% confidence interval as well as the median, minimum, and maximum values. Fold rise from baseline will be summarized by arithmetic or Williams mean [4] if data are approximately normally or log-normally distributed, respectively, or median if data are not approximately normally distributed by inspection. Differences in frequency between the study groups will be presented. Differences in QIV-like strains will be calculated based on results to the year-matched strain. Sum Test, as appropriate. Summaries of IFN-γ producing T cells are presented in Table 34, Table 35, Table 36, and Table 37.

Figures depicting the GMT (HAI, MN, sIgA) or frequency (IFN-γ producing T cells) for each strain and assay over time will be presented beginning with Figure 2 and continuing through Figure 13 (GMTs), and Figure 14, Figure 15, Figure 16, and Figure 17 (frequencies).

Reverse cumulative distribution (RCD) plots will be presented for each assay (HAI, MN, and sIgA) and strain generated with separate panels for each visit, and separate curves within each panel for each study arm and overall. HAI and MN antibody titers for the M2SR-like and QIV-like A/H3N2 strains are shown beginning with Figure 18 and continuing through Figure 29.

The spearman correlation and corresponding p-value between strains for each assay (HAI, MN, relative and specific sIgA, and IFN-γ T cell responses) will be calculated at each time point within each study arm and

overall. The correlations will be depicted in scatter plots as Figure 30, Figure 31, Figure 32, Figure 33, Figure 34, and Figure 35.

The spearman correlation and corresponding p-value between HAI and MN antibody titers for each strain (M2SR-like and QIV-like A/H3N2 (within and between strains)) will be calculated at each time point within each study arm and overall. The correlation will be depicted in scatter plots in Figure 36 and Figure 37. The spearman correlation of T cell responses between peptides tested will be presented for each strain as shown in Figure 38 and Figure 39.

The spearman correlation and corresponding p-value between HAI and MN antibody titers and relative and specific sIgA as well as between T cell responses and sIgA (relative and specific) will be calculated at each time point within each study arm and overall. The correlation will be depicted in scatter plots in Figure 40, Figure 41, Figure 42, Figure 43, Figure 44, Figure 45, Figure 46, Figure 47, Figure 48, and Figure 49.

Data listings of HAI and MN assay results, nasal sIgA assay results, and IFN-γ ELISpot assay results will be provided in Listing 8, Listing 9, and Listing 10, respectively. Listings will be sorted by study group, subject ID, and visit.

8.1. Primary Immunogenicity Analysis

This protocol does not define any primary immunogenicity objectives or outcome measures.

8.2. Secondary Immunogenicity Analyses

All secondary immunogenicity outcome measures will be summarized as described above.

8.3. Exploratory Immunogenicity Analyses

Completion of exploratory immunogenicity assays are contingent upon seeing scientifically relevant increased response in the M2SR-vaccinated group for the indicated assay, as determined by the scientific lead (SL) and principal investigator (PI) at the time of primary and secondary analyses.

HA ELISA reactivity with groups 1 and 2 HA stem domains of the viral hemagglutinin and serum anti-NA antibody titers to N1 and N2 neuraminidases measured by ELLA or ELISA will be completed if a scientifically relevant increase in rates of either seroconversion or 4-fold rise in either M2SR or QIV matched H3HA-specific HAI and/or MN assays in the M2SR vaccinated arm are observed after the H3N2 M2SR vaccination.

Anti-NA IgA responses to N1 and N2 neuraminidases will be assessed if a scientifically relevant increase in GMFR is observed for M2SR matched nasal sIgA is observed in the M2SR vaccinated arm after the H3N2 M2SR vaccination.

CD4+ and CD8+ T cell responses to the H3 HA present in the M2SR vaccine and pools of highly conserved Influenza A T cell epitopes will be assessed if a scientifically relevant increase in either H3 HA-specific or conserved peptide epitope-specific IFN-γ producing T cells is observed post M2SR vaccination for participants who received M2SR compared to participants who received placebo.

Planned analyses for any exploratory cellular immunology assays that are conducted based on the criteria above will be presented in an addendum to this SAP.

9. SAFETY EVALUATION

All summaries and analysis of safety data will be presented for the Safety Analysis Population. Safety summaries will be presented overall and stratified by study group. Note that solicited and unsolicited non-serious adverse events are reported following first vaccination only; as such displays are limited to first vaccination.

Listings will be sorted by study group subject ID, parameter (if applicable), and visit.

Continuous variables will be summarized using the following descriptive statistics: n (non-missing sample size), mean, standard deviation, median, maximum and minimum. All categorical measures will be summarized by the frequency and percentages (based on the non-missing sample size) of observed levels.

9.1. Demographic and Other Baseline Characteristics

Summaries of age, sex, ethnicity, and race will be presented by treatment group overall and by group for all enrolled subjects (Table 17 and Table 18). Ethnicity is categorized as Hispanic or Latino, or not Hispanic and not Latino. In accordance with NIH reporting policy, subjects may self-designate as belonging to more than one race or may refuse to identify a race, the latter reflected in the CRF as "No" to each racial option.

Individual subject listings will be presented for all demographics (Listing 6); pre-existing medical conditions (Listing 7); and concomitant medications (Listing 17).

9.1.1. Prior and Concurrent Medical Conditions

All current illnesses and past pre-existing medical conditions will be MedDRA® coded using MedDRA dictionary version 21.1 or higher.

Summaries of all enrolled subjects' pre-existing medical conditions will be presented by study group (Table 19).

Individual subject listings will be presented for all medical conditions (Listing 8).

9.1.2. Prior and Concomitant Medications

Summaries of medications that were started prior to dosing and continuing at the time of dosing will be presented by WHO Drug Terms 2 and 3 and study arm for subjects in the safety population (Table 68).

Individual subject listings will be presented for all concomitant medications (Listing 17).

9.2. Measurements of Treatment Compliance

The number of doses of study product administered to subjects will be presented by study group as part of the subject disposition table (Table 12).

Table 14 and Table 15 present the number of subjects who received first and second dose, respectively, by study arm.

9.3. Adverse Events

A summary of all adverse events is provided in Table 38. A summary of those events that occurred in ≥5% of subjects in any study group is provided in Table 39.

9.3.1. Solicited Events and Symptoms

Systemic and upper respiratory (local) solicited adverse events were collected pre-vaccination, and systemic and local solicited adverse events were collected 30 minutes post-vaccination and then daily for 7 days after first vaccination and graded on a scale of 0 (absent), 1 (mild), 2 (moderate) and 3 (severe). Systemic events include: fever, feverishness (chills/shivering/sweating), fatigue (tiredness), malaise (general unwell feeling), myalgia (body aches/muscular pain), arthralgia (joint pain), headache, flushing, decreased activity, decreased appetite, abdominal pain, nausea, vomiting, diarrhea, eye pruritus, eye redness (conjunctivitis), and allergy. Local events include: runny nose, stuffy nose/congestion, sneezing, nasal pain/irritation, nasal bleeding/epistaxis, sinus pressure/pain, sore throat/sore/scratchy/itchy or painful throat, cough, trouble breathing/shortness of breath. Wheezing experienced on or before Day 8 is considered a solicited event. The grading scales for solicited systemic and local (upper respiratory) adverse events are provided in Table 7 and Table 6 , respectively. Grading for wheezing events is provided in Table 9 .

The proportion of subjects reporting at least one solicited adverse event will be summarized for each solicited adverse event, any systemic symptom, any local symptom, and any symptoms. The 95% CI calculated using Blaker methodology from a binomial distribution (SAS Proc Freq with a binomial option) will be presented (Table 40).

For each systemic and local event, any systemic event, any local event, and any solicited event, the maximum severity over 7 days after first vaccination will be summarized for the Safety population. The number and percentage of subjects reporting each event will be summarized by the maximum severity and study group. For each event the denominator is the number of subjects with non-missing data for the specific event (Table 42).

The number of subjects reporting a solicited adverse event will be summarized for each day post vaccination in a summary table (Table 43 and Table 44) and graphically in a bar chart (Figure 50 and Figure 51). The difference proportion of subjects experiencing any individual symptom, any local or systemic symptom, and any symptom overall will be presented in Table 41.

Solicited adverse events by subject will be presented in Listing 11 and Listing 12.

9.3.2. Unsolicited Adverse Events

When calculating the incidence of unsolicited AEs (i.e., on a per subject basis), each subject will only be counted once at the highest severity and/or relationship, and any repetitions of AEs within a subject will be ignored; the denominator will be the total number of subjects in the safety population. All AEs reported will be included in the summaries and analyses.

The number and percentage of subjects reporting at least one unsolicited AE will be summarized by MedDRA system organ class and preferred term. Denominators for percentages are the number of subjects who received the study vaccination summarized. A 95% CI will be presented for the percentage of subjects reporting any unsolicited AE (serious or non-serious) for each MedDRA system organ class and preferred term

A listing of all reported AEs by subject will be presented in Listing 13, sorted by study group, subject ID, and AE Number.

The following summaries for unsolicited adverse events will be presented by MedDRA system organ class, preferred term, vaccination and study group:

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- Subject incidence and total frequency of adverse events over time with 95% CI (Days 1-8, Days > 8) (Table 45);
- Summary of severity and relationship to study product (Table 46);
- Subject incidence and total frequency of related adverse events over time (Days 1-8, Days > 8) (Table 47);
- Subject listing of non-serious adverse events of moderate or greater severity (Table 49);
- Bar charts of the frequency and incidence of non-serious adverse events by severity and MedDRA system organ class (Figure 52 and Figure 53);
- Bar charts of non-serious adverse events by relationship (Figure 54 and Figure 55).

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

The following listings will be presented including Subject ID, Age (years) AE Description, AE Onset Date/End Date, Last Vaccination Received/Days Post Vaccination, Reason Reported as an SAE, Relationship to Treatment, Alternate Etiology if not Related, Outcome, and Duration of Event (days):

- Deaths and Serious Adverse Events (Table 48);
- Adverse Events of Special Interest (Table 50);
- New Onset Chronic Medical Conditions (Table 51).

9.5. Pregnancies

For any subjects in the Safety population who became pregnant during the study, every attempt will be made to follow these subjects to completion of pregnancy to document the outcome, including information regarding any complications with pregnancy and/or delivery.

Listing 18, Listing 19, Listing 20, Listing 21, and Listing 22 will present any study pregnancies and their outcomes.

9.6. Clinical Laboratory Evaluations

Clinical laboratory parameters to be evaluated at the Screening Visit (Visit 00) and on Day 08 (Visit 02) will include a White Blood Cell Count (WC), HGB, HCT (only at Visit 00), Platelet Count, ALT, AST, Serum Creatinine, Ferritin (at Visit 00), Prothrombin Time (PT) and Activated Partial Thromboplastin Time (aPTT). The grading scales for clinical laboratory evaluations are presented in Table 11 and Table 10. Clinical laboratory evaluations assessed on Day 1 prior to the first study vaccination will be considered as baseline.

Subjects with HGB below the lower limit of normal (LLN) at Day 8, or subjects who experience a drop of ≥0.5 g/dL between screening and Day 8, will have HGB re-drawn at Day 22. If HBG remains low (result is less than LLN or ≥0.5 g/dL lower than screening levels) at Day 22, or if HGB is not collected at Day 22, hemoglobin labs will be re-drawn at Day 57. Any subject where HGB results remain low at Day 57 will have no further PBMC collected. HGB and Ferritin will be drawn for all subjects at Day 113 (approximately 22 days post QIV vaccination). Ferritin results taken at Day 57 will be used for clinical decision making only – values will not be graded or included in summaries of clinical laboratory data, but will be included in the listings of hematology results (Listing 15).

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The distribution of laboratory results by severity, study day and treatment group will be presented beginning with Table 54, and continuing through Table 65. Descriptive statistics including mean, standard deviation, median, minimum and maximum values and change from baseline by study day will be summarized for each parameter in Table 59 and Table 67. Box plots illustrating the change from baseline for each laboratory parameter will be presented in Figure 56, Figure 57, Figure 58, Figure 59, Figure 60, Figure 61, Figure 62, and Figure 63. Subject visits with abnormal laboratory results, Grade 1 severity or higher, will be presented in Table 52 and Table 53 for chemistry and hematology parameters, respectively. Abnormal results will be summarized by visit and study arm in Table 58 and Table 66 for chemistry and hematology parameters, respectively.

A complete listing of individual clinical laboratory results will be presented in Listing 14 and Listing 15 for chemistry and hematology, respectively, sorted by subject ID, parameter, and visit number.

9.7. Physical Evaluations

Physical examinations including skin, head and neck including upper respiratory tract (nares and nasopharynx), lungs including wheezing, heart, liver, spleen, extremities, lymph nodes, and nervous system will be performed at screening visit. Limited physical examinations to specifically include the nares (including edema), throat, and lungs (including evaluation for wheezing as well as other body systems if indicated based on review of medical history will be performed at the enrollment visit (Day 1) and approximately Day 8. The grading scale for erythema (redness) and induration (swelling or edema) detected in these exams are provided in Table 8. Targeted physical examinations may be performed at any other clinic visit if indicated based on review of medical history. Any changes in physical examination data from screening will be summarized for each visit by study arm for subjects in the Safety population (Listing 16).

9.8. Concomitant Medications

Concomitant medications will be collected in the database for the 30 days prior to the first study vaccination through 21 days after the second study vaccination. Concomitant medications will be coded to the Anatomical Therapeutic Classification using the WHO Drug Dictionary. The use of prior and concomitant medications taken during the study will be recorded on the CRFs. A by-subject listing of concomitant medication use will be presented (Listing 17). The use of concomitant medications during the study will be summarized by ATC1, ATC2 code and treatment group for the Safety population (Table 68).

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10. REPORTING CONVENTIONS

P-values ≥0.001 and ≤0.999 will be reported to 3 decimal places; p-values less than 0.001 will be reported as "<0.001" The mean, standard deviation, and other statistics 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. Proportions will be presented as 2 decimal places; values greater than zero but <0.01 will be presented as "<0.01". Percentages will be reported to the nearest whole number; values greater than zero but < 1% will be presented as "<1"; values greater than 99% but less than 100% will be reported as >99%. Estimated parameters, not on the same scale as raw observations (e.g. regression coefficients) will be reported to 3 significant figures.

11. TECHNICAL DETAILS

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

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

Enrollment into Protocol 17-0012 was paused in November 2018 for safety concerns and revision as follow:

- Subjects enrolled beyond early November would receive the protocol-provided QIV at an unacceptably late time in the 2018-2019 influenza season.
- Consistent drops in HGB post first vaccination had been noted among the subjects enrolled in 2018.

As a result, the protocol was updated to include additional blood draws past Visit 02 to confirm that low HGB values return to normal, or to implement a clinical plan for subjects who do not return to normal (see Section 9.6 for further details). Enrollment is to resume in 2019 to enroll the remaining 31 subjects, which will allow sufficient time to receive the QIV vaccination prior to the 2019-2020 influenza season. An interim analysis of the subjects enrolled in 2019 was added to the protocol at this time.

The plan to pursue exploratory anti-NA antibody assays was changed from being depending on observing increased sIgA response to the M2SR H3N2 strain in the M2SR vaccinated group, to being contingent on observing increased HAI or MN seroconversion or 4-fold rise rates in the M2SR vaccinated group compared to placebo post M2SR vaccination (see Section 8.3).

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13. REFERENCES

1. Drummond R. CONSORT Revised: Improving the Reporting of Randomized Clinical Trials. JAMA. 2001; 285(15):2006-2007.
2. The Prevention and Treatment of Missing Data in Clinical Trials. Washington, DC: The National Academies Press, 2010.
3. Blaker H. Confidence curves and improved exact confidence intervals for discrete distributions. The Canadian Journal of Statistics. 2000; 28:783-798.
4. Alexander, N. Review: analysis of parasite and other skewed counts. Tropical Medicine & International Health. 2012; 17:684-693.

14. LISTING OF TABLES, FIGURES, AND LISTINGS

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

APPENDICES

APPENDIX 1. TABLE MOCK-UPS

LIST OF TABLES

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9.1 Overall Study Design and Plan Description

Table 1: Study Design

Treatment Arm	Subjects	First Study Vaccination	Second Study Vaccination
Group A	25	M2SR	QIV
Group B	25	Placebo	QIV

9.5.1 Efficacy/Immunogenicity and Safety Measurements Assessed and Flow Chart

Table 2: Schedule of Study Procedures

Study Visit Number	**V00**	**V01**	**V02**	**V03**	**V04**	**V05**	**V06**	**V07**	**V08**	**Early Term**	**Unscheduled**
Study Day post first study vaccination	**Screen -28 to -1**	**Dose 1* D1**	**D8 ±1**	**D22 ±2**	**D57 ±3**	**Dose 2* D92 ±14**	**D113**	**D240**	**D366**		
Study Day post second study vaccination						**D1**	**D22 ±2**	**D149±14**	**D275±14**		
Obtain Informed Consent/Assent	X										
Collect Demographic Information	X										
Review Eligibility Criteria	X	X				X					
Medical History	X	X	X[1]	X[1]	X[1]	X	X	X	X	X	X
Concomitant Medications	X	X	X	X	X[2]	X[2]	X[2]			X[#3]	X[#3]
Counsel about avoidance of taking aspirin and salicylate containing products	X	X	X	X	X	X	X			X	X
Oral Temperature		X				X				X	X
Physical Examination	X										
Limited Physical Examination		X	X							X[@]	X[@]
Age and developmentally appropriate counseling about pregnancy prevention	X	X									
Targeted Physical Exam			{X}	{X}	{X}	{X}	{X}			X	X

Table 2: Schedule of Study Procedures (Continued)

Study Visit Number	V00	V01	V02	V03	V04	V05	V06	V07	V08	Early Term	Unscheduled
Study Day post first study vaccination	**Screen -28 to -1**	**Dose 1* D1**	**D8 ±1**	**D22 ±2**	**D57 ±3**	**Dose 2* D92 ±14**	**D113**	**D240**	**D366**		
Study Day post second study vaccination						**D1**	**D22 ±2**	**D149±14**	**D275±14**		
Urine Pregnancy Test	X^	X^				X^					
WBC, HGB, HCT, Platelet Count, ALT, AST, Serum Creatinine, PT, and aPTT	X		X	X[4,5]	X[4,6]		X				
Ferritin Level							X				
Serum (HAI, HA/NA ELISA, Neutralization Assays)		X	X	X	X	X	X			X	
Nasal Swab sIgA		X	X	X	X	X	X			X	
PBMC (IFN-γ ELISPOT and CFSE Dilution/ICS Assays)		X	X	X	X	X	X			X	
Whole Blood for Future Research		X	X	X							
Enrollment in AdvantageEDC[SM] and Randomization		X									
Pre-Administration Reactogenicity		X				X					
Study Vaccination		X				X					
30-minute Evaluation After Study Vaccination		X				X					
Distribute Memory Aid and Study-Related Materials		X									

Table 2: Schedule of Study Procedures (Continued)

Study Visit Number	V00	V01	V02	V03	V04	V05	V06	V07	V08	Early Term	Unscheduled
Study Day post first study vaccination	**Screen -28 to -1**	**Dose 1* D1**	**D8 ±1**	**D22 ±2**	**D57 ±3**	**Dose 2* D92 ±14**	**D113**	**D240**	**D366**		
Study Day post second study vaccination						**D1**	**D22 ±2**	**D149±14**	**D275±14**		
Review Memory Aid			X							X[@]	X[@]
AE Assessment		X	X	X						X[#]	X[#]
AESI + NOCMC Assessment			X	X	X	X				X[!]	X[!]
SAE Assessment		X	X	X	X	X	X	X	X	X	X
Phone Call								X	X		

{}Targeted physical examination if indicated based on review of complete or interim medical history
^Will be performed on all female adolescents of childbearing potential at screening and within 24 hours prior to each study vaccination and results must be negative and known prior to each study vaccination.

[#]If within 21 days post first study vaccination.

*On dose dates, samples must be collected pre-dose

[@]If within 8 days after 1st vaccination

[!]If within 3 months post first study vaccination

[1]Subject's parent(s)/legal guardian(s) will be asked if the subject had any additional blood taken for medical reasons.

[2]Concomitant medications will be limited to collecting aspirin and salicylate containing products

[3]Aspirin or salicylate containing products will be collected if within 30 days of the first vaccination through 21 days after the last vaccination

[4]Hemoglobin only

[5]Collect at Day 22 if Hgb results from screen to Day 8 drop $\geq$0.5 g/dL or < lower limits of normal

[6]If Hgb is not collected at Day 22 or low at Day 22, collect at Day 57

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9.7.1 Sample Size

Table 3: Power (%) to Detect Safety Events

Event Frequency	Single Treatment Arm N=25	All Enrolled Subjects N=50
10% Very Common	93	>99
1% Common	22	40
0.1% Uncommon	3	5
0.01% Rare	<1	<1

Table 4: Minimum Detectable Difference in Proportion Responders with 80% Power

Assumed Proportion of Responders in Comparator Arm	N = 25	N = 22
0.20	0.36	0.40
0.40	0.36	0.40
0.60	0.31	0.33
0.80	0.20	0.20

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10.2 Protocol Deviations

Table 5: Distribution of Protocol Deviations by Category, Type, and Treatment Group

Category	Deviation Type	M2SR (N=X)		Placebo (N=X)		All Subjects (N=X)	
		No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.
Eligibility/enrollment	Any type	x	x	x	x	x	x
	Did not meet inclusion criterion	x	x	x	x	x	x
	Met exclusion criterion	x	x	x	x	x	x
	ICF not signed prior to study procedures	x	x	x	x	x	x
	Other	x	x	x	x	x	x
Treatment administration schedule	Any type	x	x	x	x	x	x
	Out of window visit	x	x	x	x	x	x
	Missed visit/visit not conducted	x	x	x	x	x	x
	Missed treatment administration	x	x	x	x	x	x
	Delayed treatment administration	x	x	x	x	x	x
	Other	x	x	x	x	x	x
Follow-up visit schedule	Any type	x	x	x	x	x	x
	Out of window visit	x	x	x	x	x	x
	Missed visit/visit not conducted	x	x	x	x	x	x
	Other	x	x	x	x	x	x
Protocol procedure/assessment	Any type	x	x	x	x	x	x
	Incorrect version of ICF signed	x	x	x	x	x	x
	Blood not collected	x	x	x	x	x	x
	Nasal specimen not collected	x	x	x	x	x	x
	Too few aliquots obtained	x	x	x	x	x	x
	Specimen result not obtained	x	x	x	x	x	x
	Required procedure not conducted	x	x	x	x	x	x
	Required procedure done incorrectly	x	x	x	x	x	x
	Study product temperature excursion	x	x	x	x	x	x
	Specimen temperature excursion	x	x	x	x	x	x
	Other	x	x	x	x	x	x
Treatment administration	Any type	x	x	x	x	x	x
	Required procedure done incorrectly	x	x	x	x	x	x
	Study product temperature excursion	x	x	x	x	x	x

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Table 5: Distribution of Protocol Deviations by Category, Type, and Treatment Group (Continued)

Category	Deviation Type	M2SR (N=X)		Placebo (N=X)		All Subjects (N=X)	
		No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.
	Other	x	x	x	x	x	x
Blinding policy/procedure	Any type	x	x	x	x	x	x
	Treatment unblinded	x	x	x	x	x	x
	Other	x	x	x	x	x	x
Note: N= Number of enrolled subjects.							

12.2.2 Displays of Adverse Events

Table 6: Solicited Local (Upper Respiratory) Adverse Event Grading Scale

Local (Nasal) Reaction	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)
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 from nose	not being able to breath from 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 $\geq$ 30 minutes	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/Sore/Scratchy/ Itchy 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

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Table 7: Solicited Systemic Adverse Event Grading Scale

Systemic Reaction	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)
Subjective Systemic Reactions			
Feverishness (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 (Body Aches/Muscular Pain)	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity
Arthralgia (Joint Pain)	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
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

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Table 7: Solicited Systemic Adverse Event Grading Scale (Continued)

Systemic Reaction	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)
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 (Conjunctivitis)	Asymptomatic eye redness	Symptomatic eye redness, some interference with daily activity	Eye redness prevents daily activity or seeks medical encounter
Allergy	Pruritus with or without rash, no medical intervention	Localized urticaria, with intervention	Generalized Urticaria, Anaphylaxis, or Angioedema
Quantitative Systemic Reactions			
Fever* - oral[#†]	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

Oral temperature assessed on Day 1 prior to the first study vaccination will be considered as baseline.

* A fever can be considered not related to the study product if an alternative etiology can be documented.

† Subjects must not eat or drink anything hot or cold, or smoke within 10 minutes prior to taking oral temperature.

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Table 8: Respiratory Tract Assessment Grading Scale: Erythema and Induration

Parameter	Grade 1	Grade 2	Grade 3
Erythema (Redness)	Very slight or barely perceptible redness	Well defined redness	Moderate to severe beet redness to eschar
Induration (Swelling or edema)	Very slight or barely perceptible swelling	Slight swelling (edges of area well-defined by definite raising)	Moderate swelling (edges raised approximately 1 mm)

Table 9: Otitis Media and Wheezing Grading Scale

Symptom	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)
Otitis Media	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity
Wheezing	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity

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12.4.1 Individual Laboratory Measurements and Abnormal Laboratory Values

Table 10: Laboratory Adverse Event Grading Scale (Hematology)

Hematology Parameter	**Mild (Grade 1)**	**Moderate (Grade 2)**	**Severe (Grade 3)**
WBC cells/mm3; 103 cells/µL (Decrease)	2.0 – 2.4	1.50 – 1.0	<1.5
HgB g/dL 9-12 years of age	9.5-10.4	8.5-9.4	<8.5
HgB g/dL Males ≥ 13 years of age	10.0 – 10.9	9.0 - < 10.0	< 9.0
HgB g/dL Females ≥ 13 years of age	9.5 – 10.4	8.5 - < 9.5	< 8.5
Platelets cell/mm^3/UL	100- < 125	50- < 100	< 50
PT	1.1 - <1.25 x ULN	1.25 - < 1.50 x ULN	≥ 1.50 x ULN
aPTT	1.1 - < 1.66 x ULN	1.66 - <2.33 x ULN	≥ 2.33 x ULN

Table 11: Laboratory Adverse Event Grading Scale (Chemistry)

Chemistry Parameter	**Mild (Grade 1)**	**Moderate (Grade 2)**	**Severe (Grade 3)**
ALT	1.25 – < 2.5 x ULN	≥2.5 – <5.0 x ULN	≥5.0 x ULN
AST	1.25 – < 2.5 x ULN	≥2.5 – <5.0 x ULN	≥5.0 x ULN
Creatinine mg/dL	1.1 – 1.3 x ULN	>1.3 – 1.8 OR Increase to 1.3 to < 1.5 x subject's baseline	>1.8 x ULN OR Increase to ≥ 1.5 x subject's baseline

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14.1 Description of Study Subjects

14.1.1 Disposition of Subjects

Table 12: Subject Disposition by Treatment Group – All Enrolled Subjects*

Subject Disposition	M2SR (N=X)		Placebo (N=X)		All Subjects (N=X)	
	n	%	n	%	n	%
Screened	--	--	--	--	x	--
Enrolled/Randomized	x	100	x	100	x	100
Received First Vaccination	x	xx	x	xx	x	xx
Received Second Vaccination	x	xx	x	xx	x	xx
Received All Scheduled Vaccinations [a]	x	xx	x	xx	x	xx
Completed Final Blood Draw (Study Day 113)	x	xx	x	xx	x	xx
Completed Follow-up (Study Day 366)[a]	x	xx	x	xx	x	xx
Completed Per Protocol[b]						

Note: N=All Enrolled Subjects

[a] Refer to Listing 16.2.1 for reasons subjects discontinued or terminated early.

[b] Refer to Listing 16.2.3 for reasons subjects are excluded from the Analysis populations .

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Table 13: Analysis Populations by Study Group – All Enrolled Subjects

Analysis Populations	Reason Subjects Excluded	M2SR (N=X)		Placebo (N=X)		All Subjects (N=X)	
		n	%	n	%	%	n
Safety Population	Did not receive first study vaccination.	x	xx	x	xx	x	xx
Modified Intent-to-Treat Population	Any Reason						
	Did not receive first study vaccination.						
	No Baseline Sample						
	No Post-Baseline Sample						
	No Baseline HAI Results Reported						
	No Post-Baseline HAI Results Reported						
Per Protocol Population (All Visits)	Any Reason						
	Did not receive first study vaccination.						
	No Baseline Sample						
	No Post-Baseline Sample						
	No Baseline HAI Results Reported						
	No Post-Baseline HAI Results Reported						
	Ineligible at Baseline						
Per Protocol Population (Day 8)	Any Reason						
	Visit not conducted						
	Sample not collected						
	Result not reported						
	Receipt of live or inactivated vaccine						
	Receipt of immunosuppressive therapy						
	Visit Out of Window by >1 Day						
	Other reason						
Per Protocol Population (Day 22)	Any Reason						
	Sample not collected						
	Result not reported						
	Receipt of live or inactivated vaccine						
	Receipt of immunosuppressive therapy						
	Visit Out of Window by >1 Day						
	Other reason						

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Table 13: Analysis Populations by Study Group – All Enrolled Subjects (Continued)

Analysis Populations	Reason Subjects Excluded	M2SR (N=X)		Placebo (N=X)		All Subjects (N=X)	
		n	%	n	%	%	n
Per Protocol Population (Day 57)	Any Reason						
	Visit not conducted						
	Sample not collected						
	Result not reported						
	Receipt of live or inactivated vaccine						
	Receipt of immunosuppressive therapy						
	Visit Out of Window by >1 Day						
	Other reason						
Per Protocol Population (Day 92)	Any Reason						
	Visit not conducted						
	Sample not collected						
	Result not reported						
	Receipt of live or inactivated vaccine						
	Receipt of immunosuppressive therapy						
	Visit Out of Window by >1 Day						
	Other reason						
Per Protocol Population (Day 113)	Any Reason						
	Second vaccination not received						
	Second vaccination received out of window						
	Visit not conducted						
	Sample not collected						
	Result not reported						
	Receipt of live or inactivated vaccine						
	Receipt of immunosuppressive therapy						
	Visit Out of Window by >1 Day						
	Other reason						

Note: N= All enrolled subjects.

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Table 14: Dates of First Dose by Site and Study Group – All Vaccinated Subjects

[Implementation Note: Weeks between when enrollment was paused in September 2018 and when enrollment re-starts in 2019 will not be displayed.]

Dates of Dosing	M2SR (N=X)	Placebo (N=X)
Total (Entire period of enrollment)	x	x
DDMMMYYYY-DDMMMYYYY	x	x
DDMMMYYYY-DDMMMYYYY	x	x
DDMMMYYYY-DDMMMYYYY	x	x
DDMMMYYYY-DDMMMYYYY	x	x
Note: N= Number of subjects in the Safety Population		

Table with similar format:

Table 15: Dates of Second Dose by Site and Study Group – All Vaccinated Subjects

Table 16: Ineligibility Summary of Screen Failures

Category	Criterion	n[a]	%[b]
Inclusion and Exclusion	Number of subjects failing any eligibility criterion	x	100
Inclusion	Any inclusion criterion	x	xx
	[inclusion criterion 1]	x	xx
	[inclusion criterion 2]	x	xx
	[inclusion criterion 3]	x	xx
Exclusion	Any exclusion criterion	x	xx
	[exclusion criterion 1]	x	xx
	[exclusion criterion 2]	x	xx
	[exclusion criterion 3]	x	xx
Eligible but not enrolled	Any other reason	x	xx
	Time commitment	x	xx
	Concern of potential risks	x	xx
	Number of procedures/blood draws	x	xx
	Unable to contact subject	x	xx
	Other	x	xx

[a] More than one criterion may be marked per subject.
[b] Denominator for percentages is the total number of screen failures.

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14.1.2 Demographic Data by Study Group

Table 17: Summary of Categorical Demographic and Baseline Characteristics by Site

[Implementation Note: This table may include other categorical baseline characteristics]

Variable	Characteristic	M2SR (N=X)		Placebo (N=X)		All Subjects (N=X)	
		n	%	n	%	n	%
Sex	Male	x	xx	x	xx	x	xx
	Female						
Ethnicity	Not Hispanic or Latino	x	xx	x	xx	x	xx
	Hispanic or Latino						
	Not Reported						
	Unknown						
Race	American Indian or Alaska Native	x	xx	x	xx	x	xx
	Asian						
	Native Hawaiian or Other Pacific Islander						
	Black or African American						
	White						
	Multi-Racial						
	Unknown						
Note: N= Number of enrolled subjects							

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Table 18: Summary of Continuous Demographic and Baseline Characteristics by Site

Variable	Statistic	M2SR (N=X)	Placebo (N=X)	All Subjects (N=X)
Age (years)	Mean	xx	xx	xx
	Standard Deviation	xx	xx	xx
	Median	x	x	x
	Minimum	x	x	x
	Maximum	x	x	x
Note: N=Number of enrolled subjects				

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14.1.3 Prior and Concurrent Medical Conditions

Table 19: Summary of Subjects with Pre-Existing Medical Conditions by MedDRA System Organ Class and Treatment Group

MedDRA System Organ Class	M2SR (N=X)		Placebo (N=X)		All Subjects (N=X)	
	n	%	n	%	n	%
Any SOC	x	xx	x	xx	x	xx
[SOC 1]						
[SOC 2]						
[SOC 3]						
[SOC 4]						
Note: N=Number of subjects in the Safety Population; n = Number of subjects reporting medical history within the specified SOC. A subject is only counted once per SOC.						

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14.2 Efficacy/Immunogenicity Data

Table 20: Summaries of Hemagglutination Inhibition Antibody Against H3N2 M2SR-like Virus by Time Point and Study Group – mITT Population

Time Point	Statistic	M2SR (N=X)	Placebo (N=X)
Baseline	n	x	x
	GMT (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)
	% ≥ 40 (95% CI)	xx (xx, xx)	xx (xx, xx)
Day 8	n	x	x
	GMT (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)
	% ≥ 40 (95% CI)	xx (xx, xx)	xx (xx, xx)
	GMFR (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)
	% ≥ 4-Fold Rise (95% CI)	xx (xx, xx)	xx (xx, xx)
	Seroconversion (95% CI)	xx (xx, xx)	xx (xx, xx)
Day 22	n	x	x
	GMT (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)
	% ≥ 40 (95% CI)	xx (xx, xx)	xx (xx, xx)
	GMFR (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)
	% ≥ 4-Fold Rise (95% CI)	xx (xx, xx)	xx (xx, xx)
	Seroconversion (95% CI)	xx (xx, xx)	xx (xx, xx)
Day 57	n	x	x
	GMT (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)
	% ≥ 40 (95% CI)	xx (xx, xx)	xx (xx, xx)
	GMFR (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)
	% ≥ 4-Fold Rise (95% CI)	xx (xx, xx)	xx (xx, xx)
	Seroconversion (95% CI)	xx (xx, xx)	xx (xx, xx)
Day 92	n	x	x
	GMT (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)
	% ≥ 40 (95% CI)	xx (xx, xx)	xx (xx, xx)
	GMFR (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)
	% ≥ 4-Fold Rise (95% CI)	xx (xx, xx)	xx (xx, xx)
	Seroconversion (95% CI)	xx (xx, xx)	xx (xx, xx)
Day 113	n	x	x
	GMT (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)
	% ≥ 40 (95% CI)	xx (xx, xx)	xx (xx, xx)

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Table 20: Summaries of Hemagglutination Inhibition Antibody Against H3N2 M2SR-like Virus by Time Point and Study Group – mITT Population (Continued)

Time Point	Statistic	M2SR (N=X)	Placebo (N=X)
	GMFR (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)
	% ≥ 4-Fold Rise (95% CI) [a]	xx (xx, xx)	xx (xx, xx)
	Seroconversion (95% CI)[b]	xx (xx, xx)	xx (xx, xx)
Note: N= Number of subjects in the Modified Intent-to-Treat Population; n = Number of subjects with results reported.			

Tables with similar format:

Table 21: Summaries of Hemagglutination Inhibition Antibody Against H3N2 M2SR-like Virus by Time Point and Study Group – PP Population

Table 22: Summaries of Neutralizing Antibody Against H3N2 M2SR-like Virus by Time Point and Study Group – mITT Population*

Table 23: Summaries of Neutralizing Antibody Against H3N2 M2SR-like Virus by Time Point and Study Group – PP Population

Table 24: Summaries of Hemagglutination Inhibition Antibody Against A/NorthCarolina/04/2016 by Time Point and Study Group – mITT Population

[Implementation Note: Summaries will be repeated four times, displaying results obtained with Turkey and Guinea Pig red blood cells and both with and without oseltamivir.]

Table 25: Summaries of Hemagglutination Inhibition Against A/NorthCarolina/04/2016 by Time Point and Study Group – PP Population

[Implementation Note: Summaries will be repeated four times, displaying results obtained with Turkey and Guinea Pig red blood cells and both with and without oseltamivir.]

Table 26: Summaries of Hemagglutination Inhibition Antibody Against H3N2 QIV-like Virus by Time Point and Study Group – mITT Population

Time Point	Statistic	M2SR (N=X)			Placebo (N=X)		
		2018-2019 QIV	2019-2020 QIV	All QIV	2018-2019 QIV	2019-2020 QIV	All QIV
HA Glycosylation Site Retained (Cell-Based)							
Baseline	n	x	x	x	x	x	x
	GMT (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)
	% ≥ 40 (95% CI)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
Day 8	n	x	x	x	x	x	x
	GMT (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)
	% ≥ 40 (95% CI)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
	GMFR (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)
	% ≥ 4-Fold Rise (95% CI)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
	Seroconversion (95% CI)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
Day 22	n	x	x	x	x	x	x
	GMT (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)
	% ≥ 40 (95% CI)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
	GMFR (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)
	% ≥ 4-Fold Rise (95% CI)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
	Seroconversion (95% CI)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
Day 57	n	x	x	x	x	x	x
	GMT (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)
	% ≥ 40 (95% CI)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)

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Table 26: Summaries of Hemagglutination Inhibition Antibody Against H3N2 QIV-like Virus by Time Point and Study Group – mITT Population (Continued)

Time Point	Statistic	M2SR (N=X)			Placebo (N=X)		
		2018-2019 QIV	2019-2020 QIV	All QIV	2018-2019 QIV	2019-2020 QIV	All QIV
	GMFR (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)
	% ≥ 4-Fold Rise (95% CI)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
	Seroconversion (95% CI)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
Day 92	n	x	x	x	x	x	x
	GMT (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)
	% ≥ 40 (95% CI)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
	GMFR (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)
	% ≥ 4-Fold Rise (95% CI)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
	Seroconversion (95% CI)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
Day 113	n	x	x	x	x	x	x
	GMT (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)
	% ≥ 40 (95% CI)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
	GMFR (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)
	% ≥ 4-Fold Rise (95% CI) [a]	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
	Seroconversion (95% CI)[b]	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)	xx (xx, xx)
[Repeat for HA Glycosylation Site Missing (Egg-Based)]							

Note: N= Number of subjects in the Modified Intent-to-Treat Population; n = Number of subjects with results reported.

[Implementation Note: This table will be repeated for both the strain A/Singapore/INFIMH-16-0019/2016 (grown in eggs and missing HA glycosylation site) and A/NorthCarolina/04/2016 (grown only in cell lines and retains HA glycosylation site) and corresponding strain(s) for the 2019/2020 seasonal QIV. If strains do not change for the 2019/2020 seasonal QIV, display will be limited to the "All QIV" columns. For the A/North Carolina strain results obtained using Turkey RBC without oseltamivir will be used in this display.]

Tables with similar format:

Table 27: Summaries of Hemagglutination Inhibition Antibody Against H3N2 QIV-like Virus by Time Point and Study Group - PP Population

Table 28: Summaries of Neutralizing Antibody Against H3N2 QIV-like Virus by Time Point and Study Group - mITT Population*

[Implementation Note: This table will be repeated for both the strain A/Singapore/INFIMH-16-0019/2016 (grown in eggs and missing HA glycosylation site) and A/NorthCarolina/04/2016 (grown only in cell lines and retains HA glycosylation site. Only results for the A/NorthCarolina/04/2016 tested using Turkey RBC will be generated for the interim report.]

Table 29: Summaries of Neutralizing Antibody Against H3N2 QIV-like Virus by Time Point and Study Group - PP Population

Table 30: Summaries of Nasal sIgA Against M2SR-like H3 HA by Time Point and Study Group - mITT Population

Time Point	Statistic	Without Normalization		Normalized	
		M2SR (N=X)	Placebo (N=X)	M2SR (N=X)	Placebo (N=X)
Baseline	n	x	x	x	x
	GMT (95% CI)	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 8	n	x	x	x	x
	GMT (95% CI)	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)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)
	Any Fold Rise - % (95% CI)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)
	2-Fold Rise - % (95% CI)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)
	4-Fold Rise - % (95% CI)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)
Day 22	n	x	x	x	x
	GMT (95% CI)	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)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)
	Any Fold Rise - % (95% CI)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)
	2-Fold Rise - % (95% CI)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)
	4-Fold Rise - % (95% CI)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)
Day 57	n	x	x	x	x
	GMT (95% CI)	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)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)
	Any Fold Rise - % (95% CI)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)
	2-Fold Rise - % (95% CI)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)
	4-Fold Rise - % (95% CI)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)
Day 92	n	x	x	x	x
	GMT (95% CI)	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)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)
	Any Fold Rise - % (95% CI)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)
	2-Fold Rise - % (95% CI)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)

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Table 30: Summaries of Nasal sIgA Against M2SR-like H3 HA by Time Point and Study Group - mITT Population (Continued)

Time Point	Statistic	Without Normalization		Normalized	
		M2SR (N=X)	Placebo (N=X)	M2SR (N=X)	Placebo (N=X)
	4-Fold Rise - % (95% CI)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)
Day 113	n	x	x	x	x
	GMT (95% CI)	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)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)
	Any Fold Rise - % (95% CI)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)
	2-Fold Rise - % (95% CI)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)
	4-Fold Rise - % (95% CI)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)
Note: N= Number of subjects in the Modified Intent-to-Treat Population; n = Number of subjects with results reported.					

Table with similar format:

Table 31: Summaries of Nasal sIgA Against M2SR-like H3 HA by Time Point and Study Group - PP Population

Table 32: Summaries of Nasal sIgA Against QIV-like H3 HA by Time Point and Study Group - mITT Population

Time Point	Statistic	Without Normalization						With Normalization					
		M2SR (N=X)			Placebo (N=X)			M2SR (N=X)			Placebo (N=X)		
		2018-2019 QIV	2019-2020 QIV	All QIV	2018-2019 QIV	2019-2020 QIV	All QIV	2018-2019 QIV	2019-2020 QIV	All QIV	2018-2019 QIV	2019-2020 QIV	All QIV
HA Glycosylation Site Retained (Cell-Based)													
Baseline	n	x	x	x	x	x	x	x	x	x	x	x	x
	GMT (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	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 8	n	x	x	x	x	x	x	x	x	x	x	x	x
	GMT (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	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)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)
	Any Fold Rise - % (95% CI)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)
	2-Fold Rise - % (95% CI)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)
	4-Fold Rise - % (95% CI)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)
Day 22	n	x	x	x	x	x	x	x	x	x	x	x	x
	GMT (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)

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Table 32: Summaries of Nasal sIgA Against QIV-like H3 HA by Time Point and Study Group - mITT Population (Continued)

Time Point	Statistic	Without Normalization						With Normalization					
		M2SR (N=X)			Placebo (N=X)			M2SR (N=X)			Placebo (N=X)		
		2018-2019 QIV	2019-2020 QIV	All QIV	2018-2019 QIV	2019-2020 QIV	All QIV	2018-2019 QIV	2019-2020 QIV	All QIV	2018-2019 QIV	2019-2020 QIV	All QIV
	GMFR (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)
	Any Fold Rise - % (95% CI)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)
	2-Fold Rise - % (95% CI)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)
	4-Fold Rise - % (95% CI)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)
Day 57	n	x	x	x	x	x	x	x	x	x	x	x	x
	GMT (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	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)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)
	Any Fold Rise - % (95% CI)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)
	2-Fold Rise - % (95% CI)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)
	4-Fold Rise - % (95% CI)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)

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Table 32: Summaries of Nasal sIgA Against QIV-like H3 HA by Time Point and Study Group - mITT Population (Continued)

Time Point	Statistic	Without Normalization						With Normalization					
		M2SR (N=X)			Placebo (N=X)			M2SR (N=X)			Placebo (N=X)		
		2018-2019 QIV	2019-2020 QIV	All QIV	2018-2019 QIV	2019-2020 QIV	All QIV	2018-2019 QIV	2019-2020 QIV	All QIV	2018-2019 QIV	2019-2020 QIV	All QIV
Day 92	n	x	x	x	x	x	x	x	x	x	x	x	x
	GMT (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	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)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)
	Any Fold Rise - % (95% CI)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)
	2-Fold Rise - % (95% CI)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)
	4-Fold Rise - % (95% CI)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)
Day 113	n	x	x	x	x	x	x	x	x	x	x	x	x
	GMT (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	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)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)
	Any Fold Rise - % (95% CI)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)
	2-Fold Rise - % (95% CI)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)

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Table 32: Summaries of Nasal sIgA Against QIV-like H3 HA by Time Point and Study Group - mITT Population (Continued)

Time Point	Statistic	Without Normalization						With Normalization					
		M2SR (N=X)			Placebo (N=X)			M2SR (N=X)			Placebo (N=X)		
		2018-2019 QIV	2019-2020 QIV	All QIV	2018-2019 QIV	2019-2020 QIV	All QIV	2018-2019 QIV	2019-2020 QIV	All QIV	2018-2019 QIV	2019-2020 QIV	All QIV
	4-Fold Rise - % (95% CI)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)	xx (xx.x,xx.x)
Note: N= Number of subjects in the Modified Intent-to-Treat Population; n = Number of subjects with results reported.													

[Implementation Note: This table will be repeated for both the strain A/Singapore/INFIMH-16-0019/2016 (grown in eggs and missing HA glycosylation site) and A/NorthCarolina/04/2016 (grown only in cell lines and retains HA glycosylation site) and the corresponding 2019/2020 QIV strain(s). If strains do not change for the 2019/2020 seasonal QIV, display will be limited to the "All QIV" columns.]

Table with similar format:

Table 33: Summaries of Nasal sIgA Against QIV-like H3 HA by Time Point and Study Group - PP Population

Table 34: Summaries of IFN-γ T Cell Responses Against M2SR-like H3N2 by Peptide, Time Point and Study Group - mITT Population

[Implementation Note: This table will be repeated for all proteins/peptide pools tested.]

Time Point	Statistic	M2SR (N=X)	Placebo (N=X)
Baseline	n	x	x
	Mean Frequency (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)
	Median Frequency [Min, Max]	xx [xx,xx]	xx [xx,xx]
Day 8	n	x	x
	Mean Frequency (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)
	Median Frequency [Min, Max]	xx [xx,xx]	xx [xx,xx]
	Fold Rise (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)
Day 22	n	x	x
	Mean Frequency (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)
	Median Frequency [Min, Max]	xx [xx,xx]	xx [xx,xx]
	Fold Rise (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)
Day 57	n	x	x
	Mean Frequency (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)
	Median Frequency [Min, Max]	xx [xx,xx]	xx [xx,xx]
	Fold Rise (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)
Day 93	n	x	x
	Mean Frequency (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)
	Median Frequency [Min, Max]	xx [xx,xx]	xx [xx,xx]
	Fold Rise (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)
Day 113	n	x	x
	Mean Frequency (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)
	Median Frequency [Min, Max]	xx [xx,xx]	xx [xx,xx]
	Fold Rise (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)
Note: N= Number of subjects in the Modified Intent-to-Treat Population; n = Number of subjects with results reported.			

Table with similar format:

Table 35: Summaries of IFN-γ T Cell Responses Against M2SR-like H3N2 by Peptide, Time Point and Study Group - PP Population

Table 36: Summaries of IFN-γ T Cell Responses Against QIV-like H3N2 by Peptide, Time Point and Study Group - mITT Population

Time Point	Statistic	M2SR (N=X)			Placebo (N=X)		
		2018-2019 QIV	2019-2020 QIV	All QIV	2018-2019 QIV	2019-2020 QIV	All QIV
HA Glycosylation Site Retained (Cell-Based)							
Baseline	n	x	x	x	x	x	x
	Mean Frequency (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)
	Median Frequency [Min, Max]	xx [xx,xx]	xx [xx,xx]	xx [xx,xx]	xx [xx,xx]	xx [xx,xx]	xx [xx,xx]
Day 8	n	x	x	x	x	x	x
	Mean Frequency (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)
	Median Frequency [Min, Max]	xx [xx,xx]	xx [xx,xx]	xx [xx,xx]	xx [xx,xx]	xx [xx,xx]	xx [xx,xx]
	Fold Rise (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)	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 22	n	x	x	x	x	x	x
	Mean Frequency (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)
	Median Frequency [Min, Max]	xx [xx,xx]	xx [xx,xx]	xx [xx,xx]	xx [xx,xx]	xx [xx,xx]	xx [xx,xx]
	Fold Rise (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)	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	x	x
	Mean Frequency (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)
	Median Frequency [Min, Max]	xx [xx,xx]	xx [xx,xx]	xx [xx,xx]	xx [xx,xx]	xx [xx,xx]	xx [xx,xx]
	Fold Rise (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)	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 92	n	x	x	x	x	x	x
	Mean Frequency (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)
	Median Frequency [Min, Max]	xx [xx,xx]	xx [xx,xx]	xx [xx,xx]	xx [xx,xx]	xx [xx,xx]	xx [xx,xx]
	Fold Rise (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)

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Table 36: Summaries of IFN-γ T Cell Responses Against QIV-like H3N2 by Peptide, Time Point and Study Group - mITT Population (Continued)

Time Point	Statistic	M2SR (N=X)			Placebo (N=X)		
		2018-2019 QIV	2019-2020 QIV	All QIV	2018-2019 QIV	2019-2020 QIV	All QIV
Day 113	n	x	x	x	x	x	x
	Mean Frequency (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)
	Median Frequency [Min, Max]	xx [xx,xx]	xx [xx,xx]	xx [xx,xx]	xx [xx,xx]	xx [xx,xx]	xx [xx,xx]
	Fold Rise (95% CI)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)	x.x (x.x,x.x)
Note: N= Number of subjects in the Modified Intent-to-Treat Population; n = Number of subjects with results reported.							

[Implementation Note: This table will be repeated all proteins/peptide pools tested for both the strain A/Singapore/INFIMH-16-0019/2016 (grown in eggs and missing HA glycosylation site) and A/NorthCarolina/04/2016 (grown only in cell lines and retains HA glycosylation site) and the corresponding 2019/2020 QIV strain(s). If strains do not change for the 2019/2020 seasonal QIV, display will be limited to the "All QIV" columns.]

Table with similar format:

Table 37: Summaries of IFN-γ T Cell Responses Against QIV-like H3N2 by Peptide, Time Point and Study Group - PP Population

14.3 Safety Data

14.3.1 Displays of Adverse Events

Table 38: Overall Summary of Adverse Events – Safety Population*

	M2SR (N=X)		Placebo (N=X)		All Subjects (N=X)	
Subjects[a] with	**n**	**%**	**n**	**%**	**n**	**%**
At least one local solicited adverse event	x	x	x	x	x	x
Mild (Grade 1)	x	x	x	x	x	x
Moderate (Grade 2)	x	x	x	x	x	x
Severe (Grade 3)	x	x	x	x	x	x
At least one systemic solicited adverse event	x	x	x	x	x	x
Mild (Grade 1)	x	x	x	x	x	x
Moderate (Grade 2)	x	x	x	x	x	x
Severe (Grade 3)	x	x	x	x	x	x
At least one unsolicited adverse event	x	x	x	x	x	x
At least one related unsolicited adverse event	x	x	x	x	x	x
Mild (Grade 1)	x	x	x	x	x	x
Moderate (Grade 2)	x	x	x	x	x	x
Severe (Grade 3)	x	x	x	x	x	x
Not yet assessed						

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Table 38: Overall Summary of Adverse Events – Safety Population* (Continued)

	M2SR (N=X)		Placebo (N=X)		All Subjects (N=X)	
Subjects[a] with	**n**	**%**	**n**	**%**	**n**	**%**
At least one severe (Grade 3) unsolicited adverse event	x	x	x	x	x	x
Related	x	x	x	x	x	x
Unrelated	x	x	x	x	x	x
At least one serious adverse event[b]	x	x	x	x	x	x
At least one related, serious adverse event	x	x	x	x	x	x
At least one adverse event leading to early termination[c]	x	x	x	x	x	x
At least one adverse event of special interest	x	x	x	x	x	x
At least one new onset chronic medical condition	x	x	x	x	x	x

N = Number of subjects in the Safety Population

[a] Subjects are counted once for each category regardless of the number of events.

[b] A listing of Serious Adverse Events is included in Table X.

[c] As reported on the Adverse Event eCRF.

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Table 39: Adverse Events Occurring in 5% of Subjects in Any Study Group by MedDRA System Organ Class and Preferred Term, and Study Arm - Safety Population

Preferred Term	MedDRA System Organ Class	M2SR (N=X)			Placebo (N=X)			All Subjects (N=X)		
		n	%	Events	n	%	Events	n	%	Events
Serious Adverse Events										
All	All	x	x	x	x	x	x	x	x	x
PT1	SOC1	x	x	x	x	x	x	x	x	x
Etc.	Etc.									
Other (Non-serious) Adverse Events										
All	All	x	x	x	x	x	x	x	x	x
PT1	SOC1	x	x	x	x	x	x	x	x	x
Etc.	Etc.									

N = number of subjects in the Safety Population (number of subjects at risk).
n= number of subjects reporting event.
Events= total frequency of events reported.

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14.3.1.1 Solicited Adverse Events

Table 40: Number and Percentage of Subjects Experiencing Solicited Events Post First Vaccination with 95% Confidence Intervals by Symptom and Study Group – Safety Population

Symptom	M2SR (N=X)			Placebo (N=X)		
	n	%	95% CI	n	%	95% CI
Any Symptom	x	xx	x.x, x.x	x	xx	x.x, x.x
Systemic Symptoms						
Any Systemic Symptom	x	xx	x.x, x.x	x	xx	x.x, x.x
Feverishness (Chills/Shivering/Sweating)	x	xx	x.x, x.x	x	xx	x.x, x.x
Fatigue (Tiredness)	x	xx	x.x, x.x	x	xx	x.x, x.x
Malaise (General Unwell Feeling)	x	xx	x.x, x.x	x	xx	x.x, x.x
Myalgia (Body Aches/Muscular Pain)	x	xx	x.x, x.x	x	xx	x.x, x.x
Arthralgia (Joint Pain)	x	xx	x.x, x.x	x	xx	x.x, x.x
Headache	x	xx	x.x, x.x	x	xx	x.x, x.x
Flushing	x	xx	x.x, x.x	x	xx	x.x, x.x
Decreased Activity	x	xx	x.x, x.x	x	xx	x.x, x.x
Decreased Appetite	x	xx	x.x, x.x	x	xx	x.x, x.x
Abdominal Pain	x	xx	x.x, x.x	x	xx	x.x, x.x
Nausea	x	xx	x.x, x.x	x	xx	x.x, x.x
Vomiting	x	xx	x.x, x.x	x	xx	x.x, x.x
Diarrhea	x	xx	x.x, x.x	x	xx	x.x, x.x
Eye Pruritus	x	xx	x.x, x.x	x	xx	x.x, x.x
Eye Redness (Conjunctivitis)	x	xx	x.x, x.x	x	xx	x.x, x.x
Allergy	x	xx	x.x, x.x	x	xx	x.x, x.x
Wheezing	x	xx	x.x, x.x	x	xx	x.x, x.x

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Table 40: Number and Percentage of Subjects Experiencing Solicited Events Post First Vaccination with 95% Confidence Intervals by Symptom and Study Group – Safety Population (Continued)

Symptom	M2SR (N=X)			Placebo (N=X)		
	n	%	95% CI	n	%	95% CI
Local Symptoms						
Any Local Symptom	x	xx	x.x, x.x	x	xx	x.x, x.x
Runny Nose	x	xx	x.x, x.x	x	xx	x.x, x.x
Stuffy Nose/Congestion	x	xx	x.x, x.x	x	xx	x.x, x.x
Sneezing	x	xx	x.x, x.x	x	xx	x.x, x.x
Nasal Pain/Irritation	x	xx	x.x, x.x	x	xx	x.x, x.x
Nasal Bleeding/Epistaxis	x	xx	x.x, x.x	x	xx	x.x, x.x
Sinus Pressure/Pain	x	xx	x.x, x.x	x	xx	x.x, x.x
Sore Throat/Sore/Scratchy/Itchy or Painful Throat	x	xx	x.x, x.x	x	xx	x.x, x.x
Cough	x	xx	x.x, x.x	x	xx	x.x, x.x
Trouble Breathing/Shortness of Breath	x	xx	x.x, x.x	x	xx	x.x, x.x
Note: N= Number of subjects in the Safety Population						

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Table 41: Comparison of the Proportion of Subjects Experiencing Solicited Events by Study Group

Symptom	Proportion (95% CI)		Difference (95% CI)
	M2SR (N=X)	Placebo (N=X)	
Any Symptom	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Systemic Symptoms			
Any Systemic Symptom	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Feverishness (Chills/Shivering/Sweating)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Fatigue (Tiredness)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Malaise (General Unwell Feeling)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Myalgia (Body Aches/Muscular Pain)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Arthralgia (Joint Pain)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Headache	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Flushing	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Decreased Activity	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Decreased Appetite	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Abdominal Pain	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Nausea	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Vomiting	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Diarrhea	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Eye Pruritus	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Eye Redness (Conjunctivitis)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Allergy	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Wheezing	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)

PRIVILEGED AND CONFIDENTIAL COMMUNICATION

Table 41: Comparison of the Proportion of Subjects Experiencing Solicited Events by Study Group (Continued)

Symptom	Proportion (95% CI)		Difference (95% CI)
	M2SR (N=X)	Placebo (N=X)	
Local Symptoms			
Any Local Symptom	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Runny Nose	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Stuffy Nose/Congestion	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Sneezing	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Nasal Pain/Irritation	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Nasal Bleeding/Epistaxis	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Sinus Pressure/Pain	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Sore Throat/Sore/Scratchy/Itchy or Painful Throat	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Cough	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Trouble Breathing/Shortness of Breath	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
Note: N = Number of subjects in the Safety Population			

Table 42: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity, and Study Group - Safety Population

Symptom	Severity	M2SR (N=X)			Placebo (N=X)		
		n	%	95% CI	n	%	95% CI
Any Symptom	None	x	xx	x.x, x.x	x	xx	x.x, x.x
	Mild	x	xx	xx,xx	x	xx	xx,xx
	Moderate	x	xx	xx,xx	x	xx	xx,xx
	Severe	x	xx	xx,xx	x	xx	xx,xx
Systemic Symptoms							
Any Systemic Symptom	None	x	xx	xx,xx	x	xx	xx,xx
	Mild	x	xx	xx,xx	x	xx	xx,xx
	Moderate	x	xx	xx,xx	x	xx	xx,xx
	Severe	x	xx	xx,xx	x	xx	xx,xx
Feverishness (Chills/Shivering/Sweating)	None	x	xx	xx,xx	x	xx	xx,xx
	Mild	x	xx	xx,xx	x	xx	xx,xx
	Moderate	x	xx	xx,xx	x	xx	xx,xx
	Severe	x	xx	xx,xx	x	xx	xx,xx
Fatigue (Tiredness)	None	x	xx	xx,xx	x	xx	xx,xx
	Mild	x	xx	xx,xx	x	xx	xx,xx
	Moderate	x	xx	xx,xx	x	xx	xx,xx
	Severe	x	xx	xx,xx	x	xx	xx,xx
Malaise (General Unwell Feeling)	None	x	xx	xx,xx	x	xx	xx,xx
	Mild	x	xx	xx,xx	x	xx	xx,xx
	Moderate	x	xx	xx,xx	x	xx	xx,xx
	Severe	x	xx	xx,xx	x	xx	xx,xx

PRIVILEGED AND CONFIDENTIAL COMMUNICATION

Table 42: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity, and Study Group - Safety Population (Continued)

Symptom	Severity	M2SR (N=X)			Placebo (N=X)		
		n	%	95% CI	n	%	95% CI
Myalgia (Body Aches/Muscular Pain)	None	x	xx	xx,xx	x	xx	xx,xx
	Mild	x	xx	xx,xx	x	xx	xx,xx
	Moderate	x	xx	xx,xx	x	xx	xx,xx
	Severe	x	xx	xx,xx	x	xx	xx,xx
Arthralgia (Joint Pain)	None	x	xx	xx,xx	x	xx	xx,xx
	Mild	x	xx	xx,xx	x	xx	xx,xx
	Moderate	x	xx	xx,xx	x	xx	xx,xx
	Severe	x	xx	xx,xx	x	xx	xx,xx
Headache	None	x	xx	xx,xx	x	xx	xx,xx
	Mild	x	xx	xx,xx	x	xx	xx,xx
	Moderate	x	xx	xx,xx	x	xx	xx,xx
	Severe	x	xx	xx,xx	x	xx	xx,xx
Flushing	None	x	xx	xx,xx	x	xx	xx,xx
	Mild	x	xx	xx,xx	x	xx	xx,xx
	Moderate	x	xx	xx,xx	x	xx	xx,xx
	Severe	x	xx	xx,xx	x	xx	xx,xx
Decreased Activity	None	x	xx	xx,xx	x	xx	xx,xx
	Mild	x	xx	xx,xx	x	xx	xx,xx
	Moderate	x	xx	xx,xx	x	xx	xx,xx
	Severe	x	xx	xx,xx	x	xx	xx,xx
Decreased Appetite	None	x	xx	xx,xx	x	xx	xx,xx
	Mild	x	xx	xx,xx	x	xx	xx,xx

PRIVILEGED AND CONFIDENTIAL COMMUNICATION

Table 42: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity, and Study Group - Safety Population (Continued)

Symptom	Severity	M2SR (N=X)			Placebo (N=X)		
		n	%	95% CI	n	%	95% CI
	Moderate	x	xx	xx,xx	x	xx	xx,xx
	Severe	x	xx	xx,xx	x	xx	xx,xx
Abdominal Pain	None	x	xx	xx,xx	x	xx	xx,xx
	Mild	x	xx	xx,xx	x	xx	xx,xx
	Moderate	x	xx	xx,xx	x	xx	xx,xx
	Severe	x	xx	xx,xx	x	xx	xx,xx
Nausea	None	x	xx	xx,xx	x	xx	xx,xx
	Mild	x	xx	xx,xx	x	xx	xx,xx
	Moderate	x	xx	xx,xx	x	xx	xx,xx
	Severe	x	xx	xx,xx	x	xx	xx,xx
Vomiting	None	x	xx	xx,xx	x	xx	xx,xx
	Mild	x	xx	xx,xx	x	xx	xx,xx
	Moderate	x	xx	xx,xx	x	xx	xx,xx
	Severe	x	xx	xx,xx	x	xx	xx,xx
Diarrhea	None	x	xx	xx,xx	x	xx	xx,xx
	Mild	x	xx	xx,xx	x	xx	xx,xx
	Moderate	x	xx	xx,xx	x	xx	xx,xx
	Severe	x	xx	xx,xx	x	xx	xx,xx
Eye Pruritus	None	x	xx	xx,xx	x	xx	xx,xx
	Mild	x	xx	xx,xx	x	xx	xx,xx
	Moderate	x	xx	xx,xx	x	xx	xx,xx
	Severe	x	xx	xx,xx	x	xx	xx,xx

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Table 42: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity, and Study Group - Safety Population (Continued)

Symptom	Severity	M2SR (N=X)			Placebo (N=X)		
		n	%	95% CI	n	%	95% CI
Eye Redness (Conjunctivitis)	None	x	xx	xx,xx	x	xx	xx,xx
	Mild	x	xx	xx,xx	x	xx	xx,xx
	Moderate	x	xx	xx,xx	x	xx	xx,xx
	Severe	x	xx	xx,xx	x	xx	xx,xx
Allergy	None	x	xx	xx,xx	x	xx	xx,xx
	Mild	x	xx	xx,xx	x	xx	xx,xx
	Moderate	x	xx	xx,xx	x	xx	xx,xx
	Severe	x	xx	xx,xx	x	xx	xx,xx
Wheezing	None	x	xx	xx,xx	x	xx	xx,xx
	Mild	x	xx	xx,xx	x	xx	xx,xx
	Moderate	x	xx	xx,xx	x	xx	xx,xx
	Severe	x	xx	xx,xx	x	xx	xx,xx
Local Symptoms							
Any Local Symptom	None	x	xx	xx,xx	x	xx	xx,xx
	Mild	x	xx	xx,xx	x	xx	xx,xx
	Moderate	x	xx	xx,xx	x	xx	xx,xx
	Severe	x	xx	xx,xx	x	xx	xx,xx
Runny Nose	None	x	xx	xx,xx	x	xx	xx,xx
	Mild	x	xx	xx,xx	x	xx	xx,xx
	Moderate	x	xx	xx,xx	x	xx	xx,xx
	Severe	x	xx	xx,xx	x	xx	xx,xx

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Table 42: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity, and Study Group - Safety Population (Continued)

Symptom	Severity	M2SR (N=X)			Placebo (N=X)		
		n	%	95% CI	n	%	95% CI
Stuffy Nose/Congestion	None	x	xx	xx,xx	x	xx	xx,xx
	Mild	x	xx	xx,xx	x	xx	xx,xx
	Moderate	x	xx	xx,xx	x	xx	xx,xx
	Severe	x	xx	xx,xx	x	xx	xx,xx
Sneezing	None	x	xx	xx,xx	x	xx	xx,xx
	Mild	x	xx	xx,xx	x	xx	xx,xx
	Moderate	x	xx	xx,xx	x	xx	xx,xx
	Severe	x	xx	xx,xx	x	xx	xx,xx
Nasal Pain/Irritation	None	x	xx	xx,xx	x	xx	xx,xx
	Mild	x	xx	xx,xx	x	xx	xx,xx
	Moderate	x	xx	xx,xx	x	xx	xx,xx
	Severe	x	xx	xx,xx	x	xx	xx,xx
Nasal Bleeding/Epistaxis	None	x	xx	xx,xx	x	xx	xx,xx
	Mild	x	xx	xx,xx	x	xx	xx,xx
	Moderate	x	xx	xx,xx	x	xx	xx,xx
	Severe	x	xx	xx,xx	x	xx	xx,xx
Sinus Pressure/Pain	None	x	xx	xx,xx	x	xx	xx,xx
	Mild	x	xx	xx,xx	x	xx	xx,xx
	Moderate	x	xx	xx,xx	x	xx	xx,xx
	Severe	x	xx	xx,xx	x	xx	xx,xx

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Table 42: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity, and Study Group - Safety Population (Continued)

Symptom	Severity	M2SR (N=X)			Placebo (N=X)		
		n	%	95% CI	n	%	95% CI
Sore Throat/Sore/Scratchy/Itchy or Painful Throat	None	x	xx	xx,xx	x	xx	xx,xx
	Mild	x	xx	xx,xx	x	xx	xx,xx
	Moderate	x	xx	xx,xx	x	xx	xx,xx
	Severe	x	xx	xx,xx	x	xx	xx,xx
Cough	None	x	xx	xx,xx	x	xx	xx,xx
	Mild	x	xx	xx,xx	x	xx	xx,xx
	Moderate	x	xx	xx,xx	x	xx	xx,xx
	Severe	x	xx	xx,xx	x	xx	xx,xx
Trouble Breathing/Shortness of Breath	None	x	xx	xx,xx	x	xx	xx,xx
	Mild	x	xx	xx,xx	x	xx	xx,xx
	Moderate	x	xx	xx,xx	x	xx	xx,xx
	Severe	x	xx	xx,xx	x	xx	xx,xx
Note: N = Number of subjects in the Safety Population. Severity is the maximum severity reported over all solicited symptoms post dosing for each subject.							

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Table 43: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity and Day Post First Vaccination – M2SR Recipients, Safety Population

Symptom	Severity	Pre-Dose		Post-Dose		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8+	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Any Symptom	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Systemic Symptoms																					
Any Systemic Symptom	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Feverishness (Chills/Shivering/Sweating)	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Fatigue (Tiredness)	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx

PRIVILEGED AND CONFIDENTIAL COMMUNICATION

Table 43: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity and Day Post First Vaccination – M2SR Recipients, Safety Population (Continued)

Symptom	Severity	Pre-Dose		Post-Dose		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8+	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Malaise (General Unwell Feeling)	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Myalgia (Body Aches/Muscular Pain)	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Arthralgia (Joint Pain)	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Headache	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx

PRIVILEGED AND CONFIDENTIAL COMMUNICATION

Table 43: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity and Day Post First Vaccination – M2SR Recipients, Safety Population (Continued)

Symptom	Severity	Pre-Dose		Post-Dose		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8+	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Flushing	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Decreased Activity	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Decreased Appetite	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Abdominal Pain	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx

PRIVILEGED AND CONFIDENTIAL COMMUNICATION

Table 43: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity and Day Post First Vaccination – M2SR Recipients, Safety Population (Continued)

Symptom	Severity	Pre-Dose		Post-Dose		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8+	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Nausea	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Vomiting	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Diarrhea	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Eye Pruritus	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx

PRIVILEGED AND CONFIDENTIAL COMMUNICATION

Table 43: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity and Day Post First Vaccination – M2SR Recipients, Safety Population (Continued)

Symptom	Severity	Pre-Dose		Post-Dose		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8+	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Eye Redness (Conjunctivitis)	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Allergy	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Wheezing	None	x	xx	x	xx	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	x	xx
	Mild	x	xx	x	xx	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	x	xx
	Moderate	x	xx	x	xx	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	x	xx
	Severe	x	xx	x	xx	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	x	xx
	Not Reported	x	xx	x	xx	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	x	xx
Local Symptoms																					
Any Local Symptom	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx

PRIVILEGED AND CONFIDENTIAL COMMUNICATION

Table 43: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity and Day Post First Vaccination – M2SR Recipients, Safety Population (Continued)

Symptom	Severity	Pre-Dose		Post-Dose		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8+	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Runny Nose	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Stuffy Nose/Congestion	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Sneezing	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Nasal Pain/Irritation	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx

PRIVILEGED AND CONFIDENTIAL COMMUNICATION

Table 43: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity and Day Post First Vaccination – M2SR Recipients, Safety Population (Continued)

Symptom	Severity	Pre-Dose		Post-Dose		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8+	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Nasal Bleeding/Epistaxis	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Sinus Pressure/Pain	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Sore Throat/Sore/Scratchy/Itchy or Painful Throat	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Cough	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx

PRIVILEGED AND CONFIDENTIAL COMMUNICATION

Table 43: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity and Day Post First Vaccination – M2SR Recipients, Safety Population (Continued)

Symptom	Severity	Pre-Dose		Post-Dose		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8+	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Trouble Breathing/Shortness of Breath	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Not Reported	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx

Note: N = Number of subjects in the Safety Population who received the specified dose. Severity is the maximum severity reported post dosing for each subject for each day.

Table with similar formatting:

Table 44: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity and Day Post First Vaccination - Placebo Recipients, Safety Population

PRIVILEGED AND CONFIDENTIAL COMMUNICATION

14.3.1.2 Unsolicited Adverse Events

Table 45: Summary of Unsolicited Adverse Events by Study Group, MedDRA System Organ Class and Preferred Term – Safety Population

[Implementation Note: SOC and PT will be sorted by number of subjects. Any SOC that is in either group should be presented (i.e. if SOC1 has 1 event in M2SR but 0 in placebo, SOC1 will still be shown for placebo). For any SOC with a single PT the "Any PT" row will be omitted.]

			Day 1-7 Post Vaccination (N=X)				Day 8-21 Post Vaccination (N=X)				Any Time Post Vaccination (N=X)			
Study Arm	**MedDRA System Organ Class**	**MedDRA Preferred Term**	**n**	**%**	**95% CI**	**Events**	**n**	**%**	**95% CI**	**Events**	**n**	**%**	**95% CI**	**Events**
M2SR (N=X)	Any SOC	Any PT	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x
	[SOC 1]	Any PT												
		[PT 1]												
		[PT 2]												
	[SOC 2]	Any PT												
		[PT 1]												
		[PT 2]												
Placebo (N=X)	Any SOC	Any PT	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x
	[SOC 1]	Any PT												
		[PT 1]												
		[PT 2]												
	[SOC 2]	Any PT												
		[PT 1]												
		[PT 2]												

Note: N = number of subjects in the Safety Population. This table presents number and percentage of subjects. A subject is only counted once per PT/time point.

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Table 46: Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Maximum Severity, Relationship, and Study Group – Safety Population

[Implementation Note: SOC and PT will be sorted by the total number of subjects (any severity, any relationship, descending).]

MedDRA System Organ Class	Preferred Term	Severity	M2SR (N = X)						Placebo (N = X)						All Subjects (N = X)					
			Related		Not Related		Total		Related		Not Related		Total		Related		Not Related		Total	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Any SOC	Any PT	Any Severity	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
SOC 1	PT 1	Any Severity	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	PT 2	Any Severity	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Note: N = Number of subjects in the Safety Population.																				

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Table 47: Summary of Related Unsolicited Adverse Events by Study Group and MedDRA System Organ Class and Preferred Term – Safety Population

[Implementation Note: SOC and PT will be sorted by number of subjects. Any SOC that is in either group should be presented (i.e. if SOC1 has 1 event in M2SR but 0 in placebo, SOC1 will still be shown for placebo). For any SOC with a single PT the "Any PT" row will be omitted.]

			Day 1-7 Post Vaccination (N=X)				Day 8-21 Post Vaccination (N=X)				Any Time Post Vaccination (N=X)			
Study Group	**MedDRA System Organ Class**	**MedDRA Preferred Term**	**n**	**%**	**95% CI**	**Events**	**n**	**%**	**95% CI**	**Events**	**n**	**%**	**95% CI**	**Events**
M2SR (N=X)	Any SOC	Any PT	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x
	[SOC 1]	Any PT												
		[PT 1]												
		[PT 2]												
	[SOC 2]	Any PT												
		[PT 1]												
		[PT 2]												
Placebo (N=X)	Any SOC	Any PT	x	xx	xx, xx	x	x	xx	xx, xx	x	x	xx	xx, xx	x
	[SOC 1]	Any PT												
		[PT 1]												
		[PT 2]												
	[SOC 2]	Any PT												
		[PT 1]												
		[PT 2]												

Note: N = number of subjects in the Safety Population. This table presents number and percentage of subjects. A subject is only counted once per PT/time point.

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14.3.2 Listing of Deaths, Other Serious and Significant Adverse Events

Table 48: Listing of Serious Adverse Events - Safety Population*

Adverse Event	No. of Days Post Associated Dose (Duration)	No. of Days Post Dose the Event Became Serious	Reason Reported as an SAE	Severity	Relationship to Study Treatment	If Not Related, Alternative Etiology	Action Taken with Study Treatment	Subject Discontinued Due to AE	Outcome	AESI? NOCMC?	MedDRA System Organ Class	MedDRA Preferred Term
Subject ID: , Study Group: , AE Number: ,Associated with Dose No.:												
Comments:												
Subject ID: , Study Group: , AE Number: ,Associated with Dose No.:												
Comments:												

Table 49: Listing of Non-Serious, Unsolicited, Moderate or Severe Adverse Events – Safety Population

Adverse Event	No. of Days Post Associated Dose (Duration)	Severity	Relationship to Study Treatment	If Not Related, Alternative Etiology	Action Taken with Study Treatment	Subject Discontinued Due to AE	AESI? NOCMC?	Outcome	MedDRA System Organ Class	MedDRA Preferred Term
Subject ID: , Study Group: , AE Number: ,Associated with Dose No:										
Comments:										
Subject ID: , Study Group: , AE Number: ,Associated with Dose No:										
Comments:										

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Table 50: Listing of Adverse Events of Special Interest – Safety Population*

Adverse Event	Vaccination Received at Time of Event?	No. of Days Post Vaccination	Duration of Event	Severity	MedDRA System Organ Class	NOCMC?	Relationship	Outcome
Subject ID: , Study Group: , AE Number:								
Comments:								
Subject ID: , Study Group: , AE Number:								
Comments:								

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Table 51: Listing of New Onset Chronic Medical Conditions – Safety Population*

Adverse Event	Vaccination Received at Time of Event?	No. of Days Post Vaccination	Duration of Event	Severity	MedDRA System Organ Class	AESI?	Relationship	Outcome
Subject ID: , Study Group: , AE Number:								
Comments:								
Subject ID: , Study Group: , AE Number:								
Comments:								

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14.3.3 Narratives of Deaths, Other Serious and Significant Adverse Events

(not included in SAP, but this is a placeholder for the CSR)

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14.3.4 Abnormal Laboratory Value Listings (by Subject)

Table 52: Listing of Abnormal Chemistry Laboratory Results - Safety Population

Subject ID	Study Group	Sex	Age (years)	Planned Time Point	Actual Study Day	Laboratory Parameter (Units)	Result (Severity)	Relationship to Treatment	If Not Related, Alternate Etiology	Action Taken with Study Treatment	Subject Discontinued Due to Result?

Table with similar format:

Table 53: Listing of Abnormal Chemistry Laboratory Results - Safety Population

14.3.5 Displays of Laboratory Results

14.3.5.1 Chemistry Results

Table 54: Laboratory Results by Parameter, Maximum Severity, Time Point, and Study Group – Any Chemistry Parameter

Time Point	Study Group	N	None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Missing	
			n	%	n	%	n	%	n	%	n	%
Screening	M2SR	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo											
Day 8	M2SR											
	Placebo											
Max Severity Post Baseline	M2SR											
	Placebo											

Note: The "Max Post Baseline" rows indicate the maximum severity experienced by each subject at any time point post baseline, including unscheduled assessments.
N= Number of subjects in the Safety Population

Tables with similar format:

Table 55: Laboratory Results by Parameter, Maximum Severity, Time Point, and Study Group – Alanine Aminotransferase

Table 56: Laboratory Results by Parameter, Maximum Severity, Time Point, and Study Group – Aspartate Aminotransferase

Table 57: Laboratory Results by Parameter, Maximum Severity, Time Point, and Study Group – Creatinine

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Table 58: Abnormal Laboratory Results Related to Study Treatment by Parameter, Maximum Severity, Time Point, Study Group, and Chemistry Parameter – Safety Population

Laboratory Parameter	Time Point	Treatment Group	N	Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
				n	%	n	%	n	%
Any Chemistry Parameter	Day 8	M2SR	x	x	xx	x	xx	x	xx
		Placebo	x	x	xx	x	xx	x	xx
	Max Severity Post Baseline	M2SR	x	x	xx	x	xx	x	xx
		Placebo	x	x	xx	x	xx	x	xx
Alanine Aminotransferase	Day 8	M2SR	x	x	xx	x	xx	x	xx
		Placebo	x	x	xx	x	xx	x	xx
	Max Severity Post Baseline	M2SR	x	x	xx	x	xx	x	xx
		Placebo	x	x	xx	x	xx	x	xx
Aspartate Aminotransferase	Day 8	M2SR	x	x	xx	x	xx	x	xx
		Placebo	x	x	xx	x	xx	x	xx
	Max Severity Post Baseline	M2SR	x	x	xx	x	xx	x	xx
		Placebo	x	x	xx	x	xx	x	xx
Creatinine	Day 8	M2SR	x	x	xx	x	xx	x	xx
		Placebo	x	x	xx	x	xx	x	xx
	Max Severity Post Baseline	M2SR	x	x	xx	x	xx	x	xx
		Placebo	x	x	xx	x	xx	x	xx

Note: The "Max Post Baseline" rows indicate the maximum severity experienced by each subject at any time point post baseline, including unscheduled assessments.
N=Number of subjects in the Safety Population

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Table 59: Chemistry Summary Statistics by Parameter, Time Point, and Study Group

[Implementation Note: For calculated fields (Mean, SD, Median), decimal place should be the format in which the data were collected + 1 extra place. For Min, Max, decimal place should be in the same format in which the data were collected.]

Laboratory Parameter (Units)	Time Point	Study Group	N	n	Value				Change from Baseline			
					Mean	Standard Deviation	Median	Min, Max	Mean	Standard Deviation	Median	Min, Max
Alanine Aminotransferase (U/L)	Screening	M2SR	x	x	xx.x	xx.x	xx.x	xx.x, xx.x	NA	NA	NA	NA
		Placebo	x	x	xx.x	xx.x	xx.x	xx.x, xx.x	NA	NA	NA	NA
	Day 8	M2SR	x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x	xx.x	xx.x	xx.x, xx.x
		Placebo	x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x	xx.x	xx.x	xx.x, xx.x
Aspartate Aminotransferase (U/L)	Screening	M2SR	x	x	xx.x	xx.x	xx.x	xx.x, xx.x	NA	NA	NA	NA
		Placebo	x	x	xx.x	xx.x	xx.x	xx.x, xx.x	NA	NA	NA	NA
	Day 8	M2SR	x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x	xx.x	xx.x	xx.x, xx.x
		Placebo	x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x	xx.x	xx.x	xx.x, xx.x
Creatinine (mg/dL)	Screening	M2SR	x	x	xx.x	xx.x	xx.x	xx.x, xx.x	NA	NA	NA	NA
		Placebo	x	x	xx.x	xx.x	xx.x	xx.x, xx.x	NA	NA	NA	NA
	Day 8	M2SR	x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x	xx.x	xx.x	xx.x, xx.x
		Placebo	x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x	xx.x	xx.x	xx.x, xx.x

Note: N= Number of subjects in the Safety Population; n= Number of subjects with results reported.

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14.3.5.2 Hematology Results

Table 60: Laboratory Results by Parameter, Maximum Severity, Time Point, and Study Group – Any Hematology Parameter, Safety Population

Time Point	Study Group	N	None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Missing		Not Applicable	
			n	%	n	%	n	%	n	%	n	%	n	%
Screening	M2SR	x	x	xx	x	xx	x	xx	x	xx	x	xx	NA	NA
	Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	NA	NA
Day 8	M2SR	x	x	xx	x	xx	x	xx	x	xx	x	xx	NA	NA
	Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	NA	NA
Day 22[a]	M2SR	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	x
	Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	x
Day 57[b]	M2SR	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	x
	Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	x
Max Severity Post Baseline	M2SR	x	x	xx	x	xx	x	xx	x	xx	x	xx	NA	NA
	Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	NA	NA

Note: The "Max Post Baseline" rows indicate the maximum severity experienced by each subject at any time point post baseline, including unscheduled assessments.
N = Number of subjects in the Safety Population
[a] Any subject with either a drop of > 0.5 g/dL or results less than the lower limit of normal (based on age and gender) at Day 8 will have hemoglobin only re-drawn at Day 22
[b] Any subject with either a drop of > 0.5 g/dL or results less than the lower limit of normal (based on age and gender) at Day 22 will have hemoglobin only re-drawn at Day 57

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Table 61: Laboratory Results by Parameter, Maximum Severity, Time Point, and Study Group – Hemoglobin, Safety Population

Time Point	Study Group	N	None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Missing		Not Applicable	
			n	%	n	%	n	%	n	%	n	%	n	%
Screening	M2SR	x	x	xx	x	xx	x	xx	x	xx	x	xx	NA	NA
	Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	NA	NA
Day 8	M2SR	x	x	xx	x	xx	x	xx	x	xx	x	xx	NA	NA
	Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	NA	NA
Day 22[a]	M2SR	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	x
	Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	x
Day 57[b]	M2SR	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	x
	Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	x
Max Severity Post Baseline	M2SR	x	x	xx	x	xx	x	xx	x	xx	x	xx	NA	NA
	Placebo	x	x	xx	x	xx	x	xx	x	xx	x	xx	NA	NA

Note: The "Max Post Baseline" rows indicate the maximum severity experienced by each subject at any time point post baseline, including unscheduled assessments.
N = Number of subjects in the Safety Population
[a] Any subject with either a drop of > 0.5 g/dL or results less than the lower limit of normal (based on age and gender) at Day 8 will have hemoglobin re-drawn at Day 22
[b] Any subject with either a drop of > 0.5 g/dL or results less than the lower limit of normal (based on age and gender) at Day 22 will have hemoglobin re-drawn at Day 57

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Table 62: Laboratory Results by Parameter, Maximum Severity, Time Point, and Study Group – White Blood Cells, Safety Population

Time Point	Study Group	N	None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Missing	
			n	%	n	%	n	%	n	%	n	%
Screening	M2SR	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Placebo											
Day 8	M2SR											
	Placebo											
Max Severity Post Baseline	M2SR											
	Placebo											

Note: The "Max Post Baseline" rows indicate the maximum severity experienced by each subject at any time point post baseline, including unscheduled assessments.
N = Number of subjects in the Safety Population

Tables with similar format:

Table 63: Laboratory Results by Parameter, Maximum Severity, Time Point, and Study Group – Platelets, Safety Population

Table 64: Laboratory Results by Parameter, Maximum Severity, Time Point, and Study Group – Prothrombin Time, Safety Population

Table 65: Laboratory Results by Parameter, Maximum Severity, Time Point, and Study Group – Activated Partial Thromboplastin Time, Safety Population

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Table 66: Abnormal Laboratory Results Related to Study Treatment by Parameter, Maximum Severity, Time Point, and Treatment Group – Any Hematology Parameter

Hematology Parameter	Time Point	Study Group	N	N*	Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
					n	%	n	%	n	%
Any Hematology Parameter	Day 8	M2SR	x	x	x	xx	x	xx	x	xx
		Placebo	x	x	x	xx	x	xx	x	xx
	Max Severity Post Baseline	M2SR	x	x	x	xx	x	xx	x	xx
		Placebo	x	x	x	xx	x	xx	x	xx
Hemoglobin	Day 8	M2SR	x	x	x	xx	x	xx	x	xx
		Placebo	x	x	x	xx	x	xx	x	xx
	Day 22[a]	M2SR	x	x	x	xx	x	xx	x	xx
		Placebo	x	x	x	xx	x	xx	x	xx
	Day 57[b]	M2SR	x	x	x	xx	x	xx	x	xx
		Placebo	x	x	x	xx	x	xx	x	xx
	Max Severity Post Baseline	M2SR	x	x	x	xx	x	xx	x	xx
		Placebo	x	x	x	xx	x	xx	x	xx
White Blood Cells	Day 8	M2SR	x	x	x	xx	x	xx	x	xx
		Placebo	x	x	x	xx	x	xx	x	xx
	Max Severity Post Baseline	M2SR	x	x	x	xx	x	xx	x	xx
		Placebo	x	x	x	xx	x	xx	x	xx
Platelets	Day 8	M2SR	x	x	x	xx	x	xx	x	xx
		Placebo	x	x	x	xx	x	xx	x	xx

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Table 66: Abnormal Laboratory Results Related to Study Treatment by Parameter, Maximum Severity, Time Point, and Treatment Group – Any Hematology Parameter (Continued)

Hematology Parameter	Time Point	Study Group	N	N*	Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
					n	%	n	%	n	%
	Max Severity Post Baseline	M2SR	x	x	x	xx	x	xx	x	xx
		Placebo	x	x	x	xx	x	xx	x	xx
Prothrombin Time	Day 8	M2SR	x	x	x	xx	x	xx	x	xx
		Placebo	x	x	x	xx	x	xx	x	xx
	Max Severity Post Baseline	M2SR	x	x	x	xx	x	xx	x	xx
		Placebo	x	x	x	xx	x	xx	x	xx
Activated Partial Thromboplastin Time	Day 8	M2SR	x	x	x	xx	x	xx	x	xx
		Placebo	x	x	x	xx	x	xx	x	xx
	Max Severity Post Baseline	M2SR	x	x	x	xx	x	xx	x	xx
		Placebo	x	x	x	xx	x	xx	x	xx

Note: The "Max Post Baseline" rows indicate the maximum severity experienced by each subject at any time point post baseline, including unscheduled assessments.
N = Number of subjects in the Safety Population; N* = Number of subjects in the Safety Population expected for the test at the listed time point (see [a] and [b] below for a description of eligibility for HGB at Day 22 and Day 57).

[a] Any subject with either a drop of > 0.5 g/dL or results less than the lower limit of normal (based on age and gender) at Day 8 will have hemoglobin re-drawn at Day 22

[b] Any subject with either a drop of > 0.5 g/dL or results less than the lower limit of normal (based on age and gender) at Day 22 will have hemoglobin re-drawn at Day 57

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Table 67: Hematology Summary Statistics by Parameter, Time Point, and Study Group – Safety Population

Laboratory Parameter (Unit)	Time Point	Study Group	N	N*	n	Value				Change from Screening			
						Mean	Standard Deviation	Median	Min, Max	Mean	Standard Deviation	Median	Min, Max
Hemoglobin (g/dL)	Screening	M2SR	x	x	x	xx.x	xx.x	xx.x	xx.x, xx.x	NA	NA	NA	NA
		Placebo	x	x	x	xx.x	xx.x	xx.x	xx.x, xx.x	NA	NA	NA	NA
	Day 8	M2SR	x	x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x	xx.x	xx.x	xx.x, xx.x
		Placebo	x	x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x	xx.x	xx.x	xx.x, xx.x
	Day 22[a]	M2SR	x	x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x	xx.x	xx.x	xx.x, xx.x
		Placebo	x	x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x	xx.x	xx.x	xx.x, xx.x
	Day 57[b]	M2SR	x	x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x	xx.x	xx.x	xx.x, xx.x
		Placebo	x	x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x	xx.x	xx.x	xx.x, xx.x
White Blood Cells (cells/µL)	Screening	M2SR	x	x	x	xx.x	xx.x	xx.x	xx.x, xx.x	NA	NA	NA	NA
		Placebo	x	x	x	xx.x	xx.x	xx.x	xx.x, xx.x	NA	NA	NA	NA
	Day 8	M2SR	x	x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x	xx.x	xx.x	xx.x, xx.x
		Placebo	x	x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x	xx.x	xx.x	xx.x, xx.x
Platelets (cells/µL)	Screening	M2SR	x	x	x	xx.x	xx.x	xx.x	xx.x, xx.x	NA	NA	NA	NA
		Placebo	x	x	x	xx.x	xx.x	xx.x	xx.x, xx.x	NA	NA	NA	NA
	Day 8	M2SR	x	x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x	xx.x	xx.x	xx.x, xx.x
		Placebo	x	x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x	xx.x	xx.x	xx.x, xx.x
Prothrombin Time (sec)	Screening	M2SR	x	x	x	xx.x	xx.x	xx.x	xx.x, xx.x	NA	NA	NA	NA
		Placebo	x	x	x	xx.x	xx.x	xx.x	xx.x, xx.x	NA	NA	NA	NA
	Day 8	M2SR	x	x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x	xx.x	xx.x	xx.x, xx.x
		Placebo	x	x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x	xx.x	xx.x	xx.x, xx.x

Table 67: Hematology Summary Statistics by Parameter, Time Point, and Study Group – Safety Population (Continued)

Laboratory Parameter (Unit)	Time Point	Study Group	N	N*	n	Value				Change from Screening			
						Mean	Standard Deviation	Median	Min, Max	Mean	Standard Deviation	Median	Min, Max
Activated Partial Thromboplastin Time (sec)	Screening	M2SR	x	x	x	xx.x	xx.x	xx.x	xx.x, xx.x	NA	NA	NA	NA
		Placebo	x	x	x	xx.x	xx.x	xx.x	xx.x, xx.x	NA	NA	NA	NA
	Day 8	M2SR	x	x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x	xx.x	xx.x	xx.x, xx.x
		Placebo	x	x	x	xx.x	xx.x	xx.x	xx.x, xx.x	xx.x	xx.x	xx.x	xx.x, xx.x

Note: N = Number of subjects in the Safety Population; N* = Number of subjects in the Safety Population expected for the test at the listed time point (see [a] and [b] below for a description of eligibility for HGB at Day 22 and Day 57); n = Number of subjects with results reported.

[a] Any subject with either a drop of > 0.5 g/dL or results less than the lower limit of normal (based on age and gender) at Day 8 will have hemoglobin re-drawn at Day 22

[b] Any subject with either a drop of > 0.5 g/dL or results less than the lower limit of normal (based on age and gender) at Day 22 will have hemoglobin re-drawn at Day 57

14.4 Summary of Concomitant Medications

Table 68: Number and Percentage of Subjects with Prior and Concurrent Medications by WHO Drug Classification and Study Group – Safety Population

WHO Drug Code Level 1, Anatomic Group	WHO Drug Code Level 2, Therapeutic Subgroup	M2SR (N=X)		Placebo (N=X)		All Subjects (N=X)	
		n	%	n	%	n	%
Any Level 1 Codes	Any Level 2 Codes	x	xx	x	xx	x	xx
[ATC Level 1 - 1]	Any [ATC 1 – 1]						
	[ATC 2 - 1]						
	[ATC 2 - 2]						
	[ATC 2 - 3]						
[ATC Level 1 – 2]	[ATC 2 - 1]						
	[ATC 2 - 2]						
	[ATC 2 - 3]						

N = Number of subjects in the Safety Population; n=Number of subjects reporting taking at least one medication in the specific WHO Drug Class.

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APPENDIX 2. FIGURE MOCK-UPS

LIST OF FIGURES

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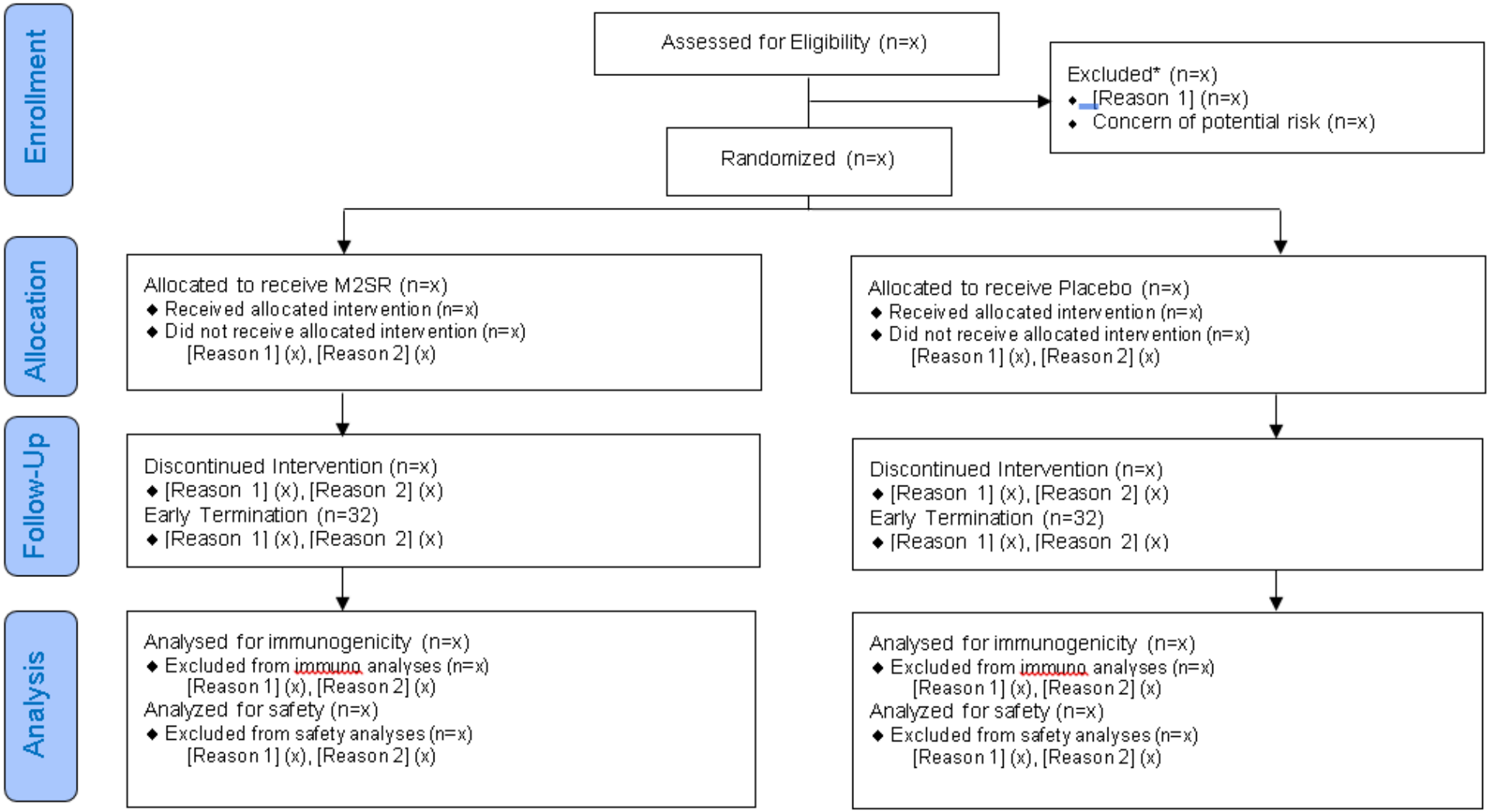
10.1 Disposition of Subjects

Figure 1: CONSORT Flow Diagram



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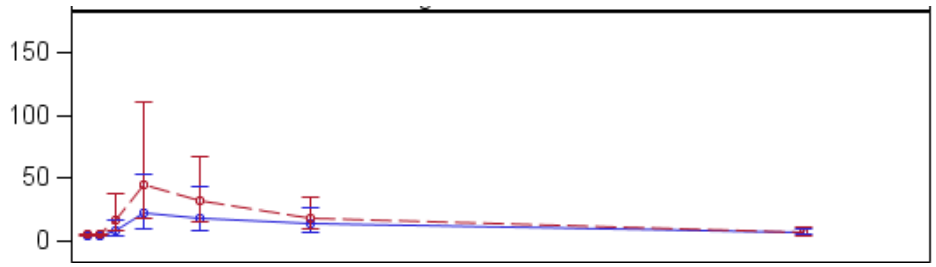
14.2.2 Efficacy/Immunogenicity Response Figures by Measure, Treatment/Vaccination, and Time Point

Figure 2: Geometric Mean Titers of Hemagglutination Inhibition Antibody Against M2SR-like H3N2 by Study Day and Study Group, mITT Population

[Implementation Note: A generic sample figure is shown below. Planned study day is plotted along the x-axis, with visit labels as tick labels. Titer/frequency is plotted on the y-axis (on the log scale for HAI/MN; scale will be determined for sIgA and IFN-γ T cells based on the distribution of the data received). GMT/frequency will be plotted at each visit with upper and lower error bars for the 95% CI for each study arm with different marker shapes/colors for each study arm.]



Figures with similar format:

Figure 3: Geometric Mean Titers of Hemagglutination Inhibition Antibody Against M2SR-like H3N2 by Study Day and Study Group, PP Population

Figure 4: Geometric Mean Titers of Hemagglutination Inhibition Antibody Against QIV-like H3N2 by Study Day and Study Group - mITT Population

[Implementation Note for GMT Figures QIV strains: Planned study day is plotted along the x-axis, with visit labels as tick labels. Titer/frequency is plotted on the y-axis on the log scale. GMT/frequency will be plotted at each visit with upper and lower error bars for the 95% CI for each study arm and strain with different marker colors/shapes for each study arm. Results for 2018/2019 and 2019/2020 QIV strains will be plotted with different line types and fill (i.e. dashed with empty markers for 2018/2019, solid with filled markers for 2019/2020). This figure will be repeated for strains with the HA Glycosylation Site retained (cell-based, A/North Carolina for 2018/2019, Turkey and Guinea pig RBC, with and without oseltamivir) and missing (egg-based, A/Singapore for 2018/2019).]

Figure 5: Geometric Mean Titers of Hemagglutination Inhibition Antibody Against QIV-like H3N2 by Study Day and Study Group - PP Population

Figure 6: Geometric Mean Titers of Neutralizing Antibody Against M2SR-like H3N2 by Study Day and Study Group, mITT Population

[Implementation Note: A generic sample figure is shown below. Planned study day is plotted along the x-axis, with visit labels as tick labels. Titer/frequency is plotted on the y-axis (on the log scale for HAI/MN; scale will be determined for sIgA and IFN-γ T cells based on the distribution of the data received). GMT/frequency will be plotted at each visit with upper and lower error bars for the 95% CI for each study arm with different marker shapes/colors for each study arm.]

Figure 7: Geometric Mean Titers of Neutralizing Antibody Against M2SR-like H3N2 by Study Day and Study Group, PP Population

Figure 8: Geometric Mean Titers of Neutralizing Antibody Against QIV-like H3N2 by Study Day and Study Group - mITT Population

[Implementation Note for GMT Figures QIV strains: Planned study day is plotted along the x-axis, with visit labels as tick labels. Titer/frequency is plotted on the y-axis on the log scale. GMT/frequency will be plotted at each visit with upper and lower error bars for the 95% CI for each study arm and strain with different marker colors/shapes for each study arm. Results for 2018/2019 and 2019/2020 QIV strains will be plotted with different line types and fill (i.e. dashed with empty markers for 2018/2019, solid with filled markers for 2019/2020). This figure will be repeated for strains with the HA Glycosylation Site retained (cell-based, A/North Carolina for 2018/2019, Turkey and Guinea pig RBC, with and without oseltamivir) and missing (egg-based, A/Singapore for 2018/2019).]

Figure 9: Geometric Mean Titers of Neutralizing Antibody Against QIV-like H3N2 by Study Day and Study Group – PP Population

Figure 10: Geometric Mean Titers of Nasal sIgA Against M2SR-like H3N2 by Study Day and Study Group - mITT Population

[Implementation Note for sIgA Figures, M2SR strain: Planned study day is plotted along the x-axis, with visit labels as tick labels. Titer is plotted on the y-axis (scale will be determined based on the distribution of the data received). GMT will be plotted at each visit with upper and lower error bars for the 95% CI for each study arm with different marker shapes/colors for each study arm. There will be two panels (rows) – one for non-normalized sIgA, one for normalized sIgA.]

Figure 11: Geometric Mean Titers of Nasal sIgA Against M2SR-like H3N2 by Study Day and Study Group - PP Population

Figure 12: Geometric Mean Titers of Nasal sIgA Against QIV-like H3N2 by Study Day and Study Group - mITT Population

[Implementation Note for sIgA Figures, QIV strain: Planned study day is plotted along the x-axis, with visit labels as tick labels. Titer is plotted on the y-axis (scale will be determined based on the distribution of the data received). GMT will be plotted at each visit with upper and lower error bars for the 95% CI for each study arm with different marker shapes/colors for each study arm. Results for 2018/2019 and 2019/2020 QIV strains will be plotted with different line types and fill (i.e. dashed with empty markers for 2018/2019, solid with filled markers for 2019/2020). There will be two panels (rows) – one for non-normalized sIgA, one for normalized sIgA. This figure will be repeated for strains with the HA Glycosylation Site retained (cell-based, A/North Carolina for 2018/2019, Turkey and Guinea pig RBC, with and without oseltamivir) and missing (egg-based, A/Singapore for 2018/2019).]

Figure 13: Geometric Mean Titers of Nasal sIgA Against QIV-like H3N2 by Study Day and Study Group – PP Population

Figure 14: Frequency of IFN-γ T Cells Expressing Against M2SR-like H3N2 Peptides by Study Day and Study Group – mITT Population

[Implementation Note for T Cell Figures: Planned study day is plotted along the x-axis, with visit labels as tick labels. Frequency is plotted on the y-axis (scale will be determined based on the distribution of the data received). Frequency will be plotted at each visit with upper and lower error bars for the 95% CI for each study arm with different marker shapes/colors for each study arm. There will be multiple panels (rows), one for each peptide panel (H3 HA, other peptides).]

Figure 15: Frequency of IFN-γ T Cells Expressing Against M2SR-like H3N2 Peptides by Study Day and Study Group – PP Population

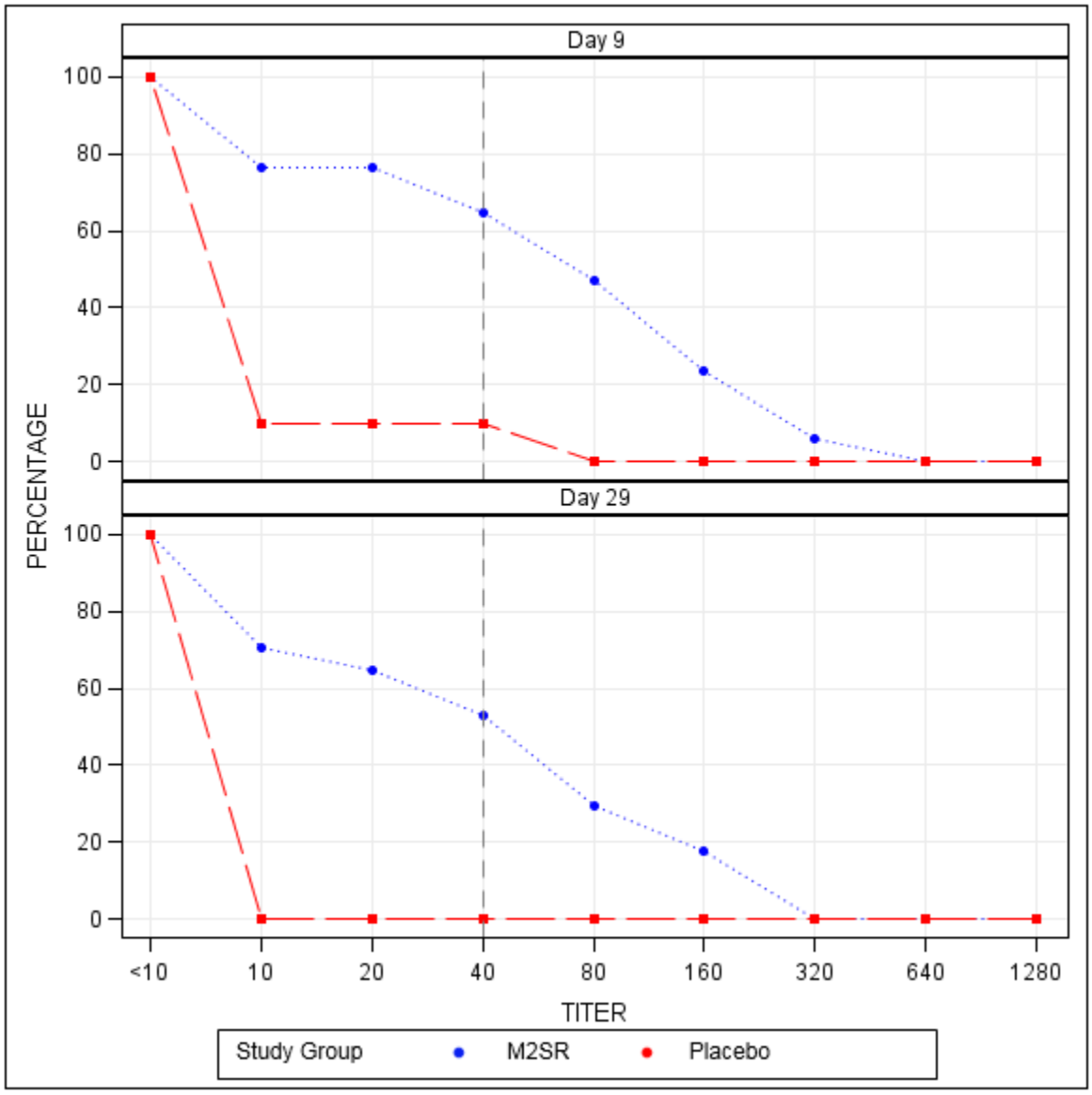
Figure 16: Frequency of IFN-γ T Cells Expressing Against QIV-like H3N2 Peptides by Study Day and Study Group - mITT Population

[Implementation Note for T Cell Figures: Planned study day is plotted along the x-axis, with visit labels as tick labels. Frequency is plotted on the y-axis (scale will be determined based on the distribution of the data received). Frequency will be plotted at each visit with upper and lower error bars for the 95% CI for each study arm with different marker shapes/colors for each study arm. Results for 2018/2019 and 2019/2020 QIV strains will be plotted with different line types and fill (i.e. dashed with empty markers for 2018/2019, solid with filled markers for 2019/2020). There will be multiple panels (rows), one for each peptide panel (H3 HA, other peptides). This figure will be repeated for strains with the HA Glycosylation Site retained (cell-based, A/North Carolina for 2018/2019, Turkey and Guinea pig RBC, with and without oseltamivir) and missing (egg-based, A/Singapore for 2018/2019).]

Figure 17: Frequency of IFN-γ T Cells Expressing Against QIV-like H3N2 Peptides by Study Day and Study Group - PP Population

Figure 18: Reverse Cumulative Distribution of Hemagglutination Inhibition Antibody Against M2SR-like H3N2 by Time Point and Study Group – mITT Population

[Implementation Note: An example figure is shown below. The figures for HAI and MN will have one panel (row) for each post-baseline time point (Day 8, Day 22, Day 57, Day 113). Study arms will be plotted with different marker/line colors.]



Figures with similar format:

Figure 19: Reverse Cumulative Distribution of Hemagglutination Inhibition Antibody Against M2SR-like H3N2 by Time Point and Study Group – PP Population

Figure 20: Reverse Cumulative Distribution of Hemagglutination Inhibition Antibody Against QIV-like H3N2 by Time Point and Study Group – mITT Population

[Implementation Note: An example figure is shown below. The figures for HAI and MN will have one panel (row) for each post-baseline time point (Day 8, Day 22, Day 57, Day 113). Study arms will be plotted with different marker/line colors. Different strains will be plotted with different line patterns (solid vs dashed).

This figure will be repeated for strains with the HA Glycosylation Site retained (cell-based, A/North Carolina for 2018/2019, Turkey and Guinea pig RBC, with and without oseltamivir) and missing (egg-based, A/Singapore for 2018/2019).]

Figure 21: Reverse Cumulative Distribution of Hemagglutination Inhibition Antibody Against QIV-like H3N2 by Time Point and Study Group – PP Population

Figure 22: Reverse Cumulative Distribution of Neutralizing Antibody Against M2SR-like H3N2 by Time Point and Study Group – mITT Population

Figure 23: Reverse Cumulative Distribution of Neutralizing Antibody Against M2SR-like H3N2 by Time Point and Study Group – PP Population

Figure 24: Reverse Cumulative Distribution of Neutralizing Antibody Against QIV-like H3N2 by Time Point and Study Group – mITT Population

Figure 25: Reverse Cumulative Distribution of Neutralizing Antibody Against QIV-like H3N2 by Time Point and Study Group – PP Population

Figure 26: Reverse Cumulative Distribution of Nasal sIgA Against M2SR-like H3N2 by Time Point and Study Group – mITT Population

[Implementation Note for sIgA Figures: Figures for sIgA will be paneled with two columns – one depicting RCD for non-normalized results, one for normalized results and four rows (Day 8, Day 22, Day 57, Day 113). Study arms will be plotted with different marker/line colors.]

Figure 27: Reverse Cumulative Distribution of Nasal sIgA Against M2SR-like H3N2 by Time Point and Study Group – PP Population

Figure 28: Reverse Cumulative Distribution of Nasal sIgA Against QIV-like H3N2 by Time Point and Study Group – mITT Population

[Implementation Note for sIgA Figures: Figures for sIgA will be paneled with two columns – one depicting RCD for non-normalized results, one for normalized results and four rows (Day 8, Day 22, Day 57, Day 113). Study arms will be plotted with different marker/line colors. Different strains will be plotted with different line patterns (solid vs dashed). This figure will be repeated for strains with the HA Glycosylation Site retained (cell-based, A/North Carolina for 2018/2019, Turkey and Guinea pig RBC, with and without oseltamivir) and missing (egg-based, A/Singapore for 2018/2019).]

Figure 29: Reverse Cumulative Distribution of Nasal sIgA Against QIV-like H3N2 by Time Point and Study Group – PP Population

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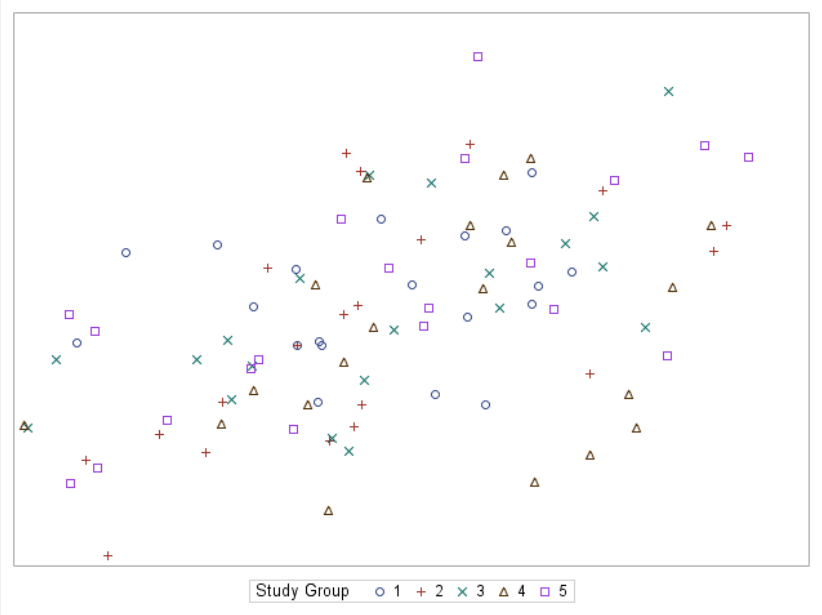
Figure 30: Correlation of Serum Antibody Responses Against M2SR-like versus QIV-like H3N2 Viruses by Study Day and Study Group, mITT Population

[Implementation Note: A generic sample figure is shown below. The scatter plots will be presented in a single figure with separate panels (rows) for each visit (baseline and 8, 22, 57, and 113 days post dose 1) and two columns (HAI and MN). M2SR-like antibody will be the X-axis; QIV-like antibody will be the Y-axis. Visit labels should be included in the panel header. Within each panel distinct marker types and colors should be used to indicate the study arms, with labels included in a legend. Use filled/unfilled markers to indicate the 2018/2019 versus 2019/2020 QIV strains. The spearman correlation should be calculated over all subjects and annotated within each panel as:

"Spearman Correlation:
All Subjects (r=0.xx, p=0.xx)
M2SR (r=0.xx, p=0.xx)
Placebo (r=0.xx, p=0.xx)"

This figure will be repeated for QIV strains with the HA Glycosylation Site retained (cell-based, A/North Carolina for 2018/2019, Turkey and Guinea pig RBC, with and without oseltamivir) and missing (egg-based, A/Singapore for 2018/2019).]



Figures with similar format:

Figure 31: Correlation of Serum Antibody Responses Against M2SR-like versus QIV-like H3N2 Viruses by Study Day and Study Group, PP Population

Figure 32: Correlation of Serum Antibody Responses Against QIV-like H3N2 Viruses by Study Day and Study Group, PP Population

[Implementation Note: The scatter plots will be presented in a single figure with separate panels (rows) for each visit (baseline and 8, 22, 57, and 113 days post dose 1) and two columns (HAI and MN). Egg-based strains (A/Singapore for 2018/2019 QIV) will be the X-axis, cell-based strains (A/North Carolina for 2018/2019 QIV) will be the Y-axis . Visit labels should be included in the panel header. Within each panel distinct marker types and colors should be used to indicate the study arms, with labels included in a legend.

Use filled/unfilled markers to indicate the 2018/2019 versus 2019/2020 QIV strains. The spearman correlation should be calculated over all subjects and annotated within each panel as:

"Spearman Correlation:
All Subjects (r=0.xx, p=0.xx)
M2SR (r=0.xx, p=0.xx)
Placebo (r=0.xx, p=0.xx)"

This figure will be repeated for A/North Carolina tested with Turkey and Guinea pig RBC, with and without oseltamivir]

Figure 33: Correlation of Serum Antibody Responses Against QIV-like H3N2 Viruses by Study Day and Study Group, PP Population

Figure 34: Correlation of Nasal Antibody Responses Against M2SR-like versus QIV-like H3N2 Viruses by Study Day and Study Group, mITT Population

Figure 35: Correlation of Nasal Antibody Responses Against M2SR-like versus QIV-like H3N2 Viruses by Study Day and Study Group, PP Population

Figure 36: Correlation of IFN-γ T Cell Responses Against M2SR-like versus QIV-like H3N2 Viruses by Study Day and Study Group, mITT Population

Figure 37: Correlation of IFN-γ T Cell Responses Against M2SR-like versus QIV-like H3N2 Viruses by Study Day and Study Group, PP Population

Figure 38: Correlation of Hemagglutination Inhibition Antibody and Neutralizing Antibody Against H3N2 Viruses by Study Day and Study Group, mITT Population

Figure 39: Correlation of Hemagglutination Inhibition Antibody and Neutralizing Antibody Against H3N2 Viruses by Study Day and Study Group, PP Population

Figure 40: Correlation of the Frequency of T-cells Expressing H3 HA and Other Peptides by Study Day and Study Group, mITT Population

Figure 41: Correlation of the Frequency of T-cells Expressing H3 HA and Other Peptides by Study Day and Study Group, PP Population

Figure 42: Correlation of Strain-Specific sIgA and Serum Antibody Responses Against H3N2 Viruses by Study Day and Study Group, mITT Population

Figure 43: Correlation of Strain-Specific sIgA and Serum Antibody Responses Against H3N2 Viruses by Study Day and Study Group, PP Population

Figure 44: Correlation of Relative sIgA and Serum Antibody Responses Against H3N2 Viruses by Study Day and Study Group, mITT Population

Figure 45: Correlation of Relative sIgA and Serum Antibody Responses Against H3N2 Viruses by Study Day and Study Group, PP Population

Figure 46: Correlation of Strain-Specific sIgA and T Cell Responses Against H3N2 Viruses by Study Day and Study Group, mITT Population

Figure 47: Correlation of Strain-Specific sIgA and TCell Responses Against H3N2 Viruses by Study Day and Study Group, PP Population

Figure 48: Correlation of Relative sIgA and T Cell Responses Against H3N2 Viruses by Study Day and Study Group, mITT Population

Figure 49: Correlation of Relative sIgA and T Cell Responses Against H3N2 Viruses by Study Day and Study Group, PP Population

14.3.1.1 Solicited Adverse Events

Figure 50: Maximum Severity of Solicited Systemic Symptoms per Subject by Day Post Vaccination

[Implementation Note: A Generic figure is shown below. A horizontal bar chart should be presented in 1 image file with separate panels for each study arm and dose (2 rows (study arms) x 1 columns). Axes should be labeled as follows: y-axis label: Study Day, x-axis label: Percentage of Subjects (%). The study arm should be indicated in the panel header including "(N=X)", where N = the number of subjects in the in the Safety Population who received the first vaccination. Subjects are counted at most once at the maximum severity across all systemic events reported]

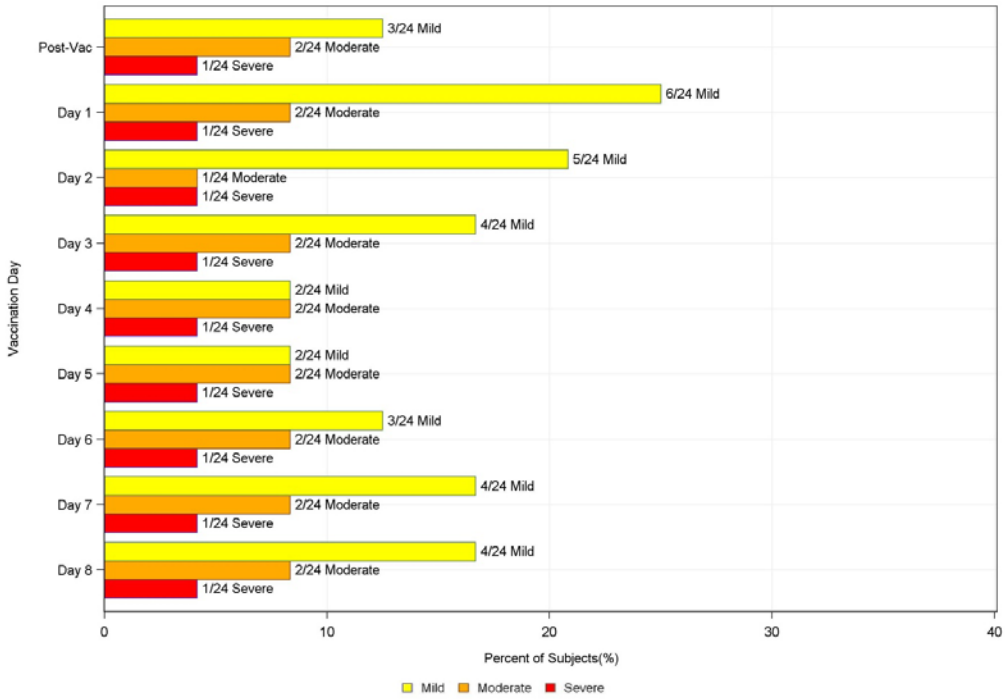


Figure with similar format:

Figure 51: Maximum Severity of Solicited Local Symptoms per Subject by Day Post Vaccination

14.3.1.2 Unsolicited Adverse Events

Figure 52: Frequency of Unsolicited Adverse Events by MedDRA® System Organ Class and Severity

[Implementation Note: A Generic figure is shown below. This figure includes all unsolicited events across all doses. A horizontal bar chart should be presented in separate panels for each study arm (2 columns (treatment groups)). Axes should be labeled as follows: y-axis label: System Organ Class, x-axis label: Number of Events. The study arm should be indicated in the panel headers including "(N=X)", where N = the number of subjects in the in the Safety Population. The y-axis should present all SOCs reported by at least 1 subject and an "All Events" category. Y-axis should be sorted with "All Events first, then in decreasing order of total frequency.]

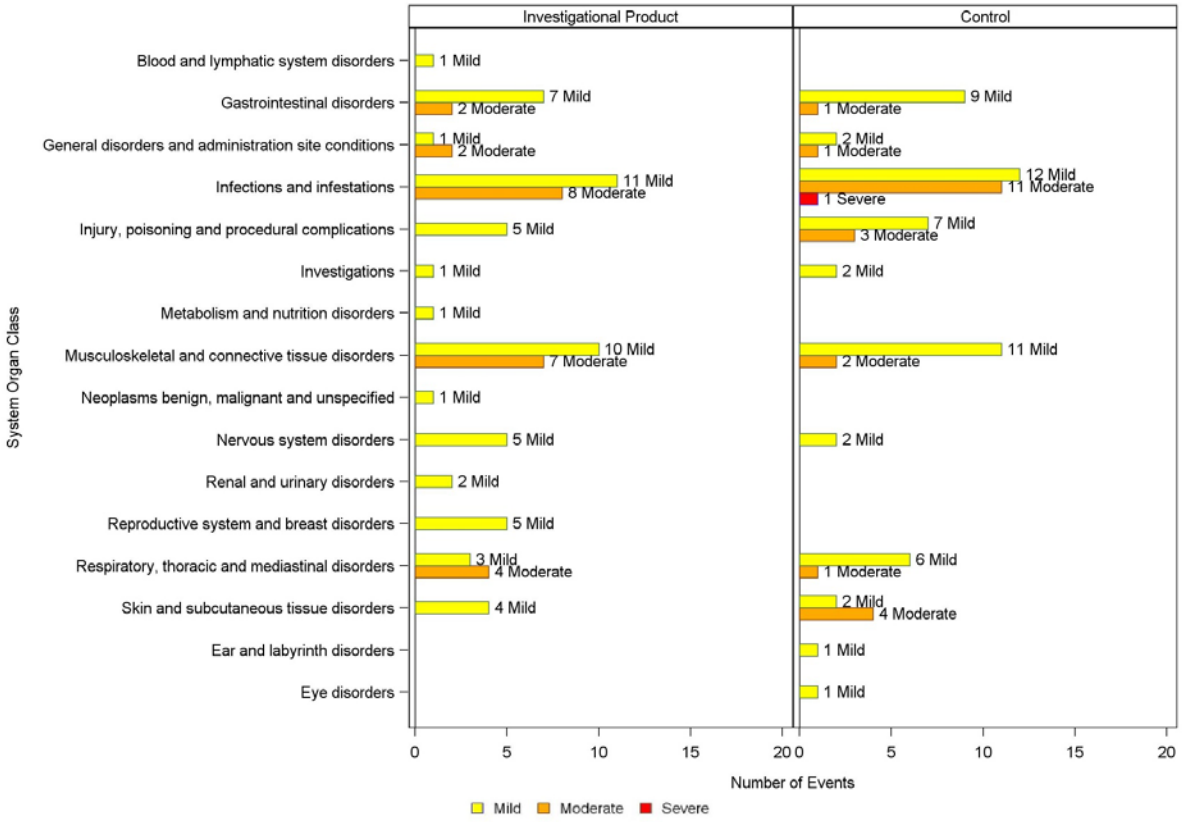


Figure 53: Incidence of Unsolicited Adverse Events by MedDRA® System Organ Class and Severity

[Implementation Note: A Generic figure is shown below. This figure includes all unsolicited events across all doses. A horizontal bar chart should be presented in 1 image file with separate panels for each study arm (2 columns). Axes should be labeled as follows: y-axis label: System Organ Class, x-axis label: Percentage of Subjects (%). The treatment groups should be indicated in the panel headers including "(N=X)", where N = the number of subjects in the in the Safety Population. Subjects are counted at most once at the maximum severity across for any events in the applicable SOC. The y-axis should present all SOCs reported by at least 1 subject and an "All Events" category. Y-axis should be sorted with "All Events" first then in decreasing order of total incidence]

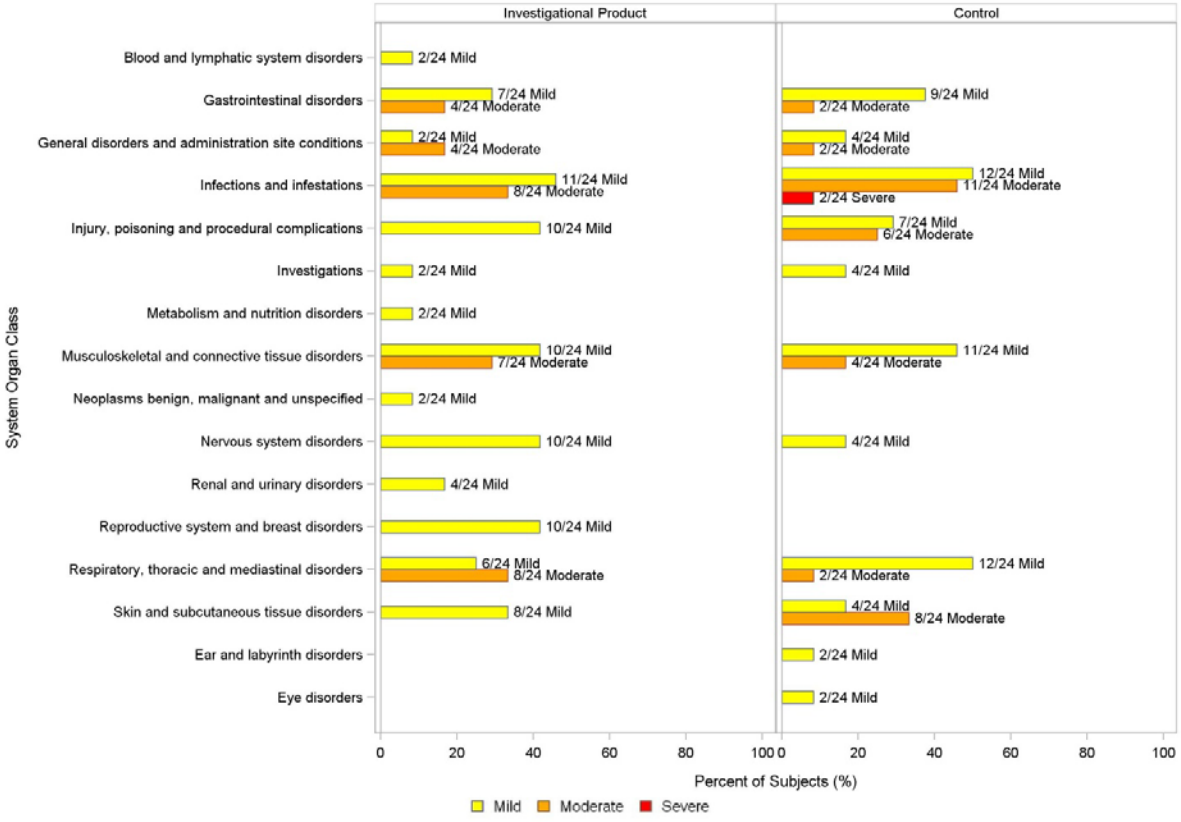


Figure 54: Frequency of Unsolicited Adverse Events by MedDRA® System Organ Class and Relationship to Treatment

[Implementation Note: A generic sample figure is shown below. This figure includes all unsolicited events across all doses. A horizontal bar chart should be presented in 1 image file with separate panels for each study arm (2 columns (study arms) x 1 row). Axes should be labeled as follows: y-axis label: System Organ Class, x-axis label: Number of Events. The treatment groups should be indicated in the panel headers including "(N=X)", where N = the number of subjects in the in the Safety Population. The y-axis should present all SOCs reported by at least 1 subject and an "All Events" category. Y-axis should be sorted with "All Events first then in decreasing order of total frequency]

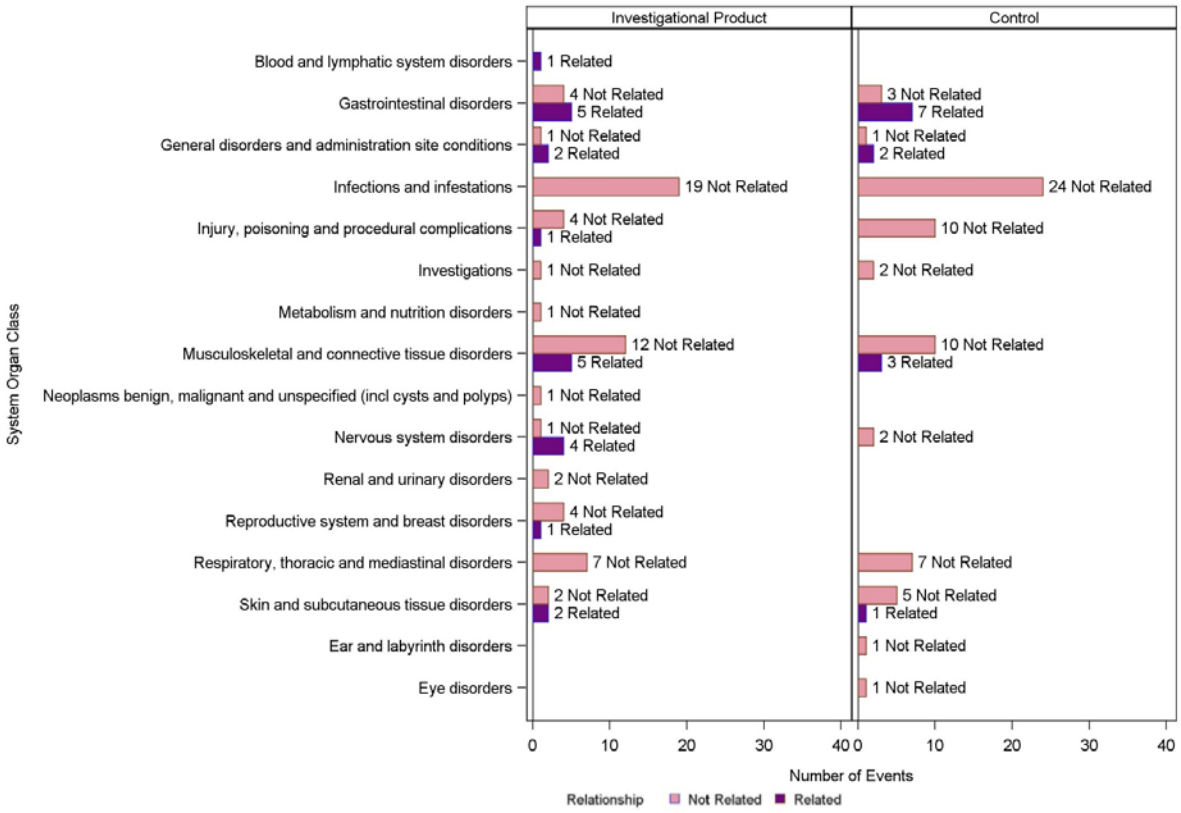
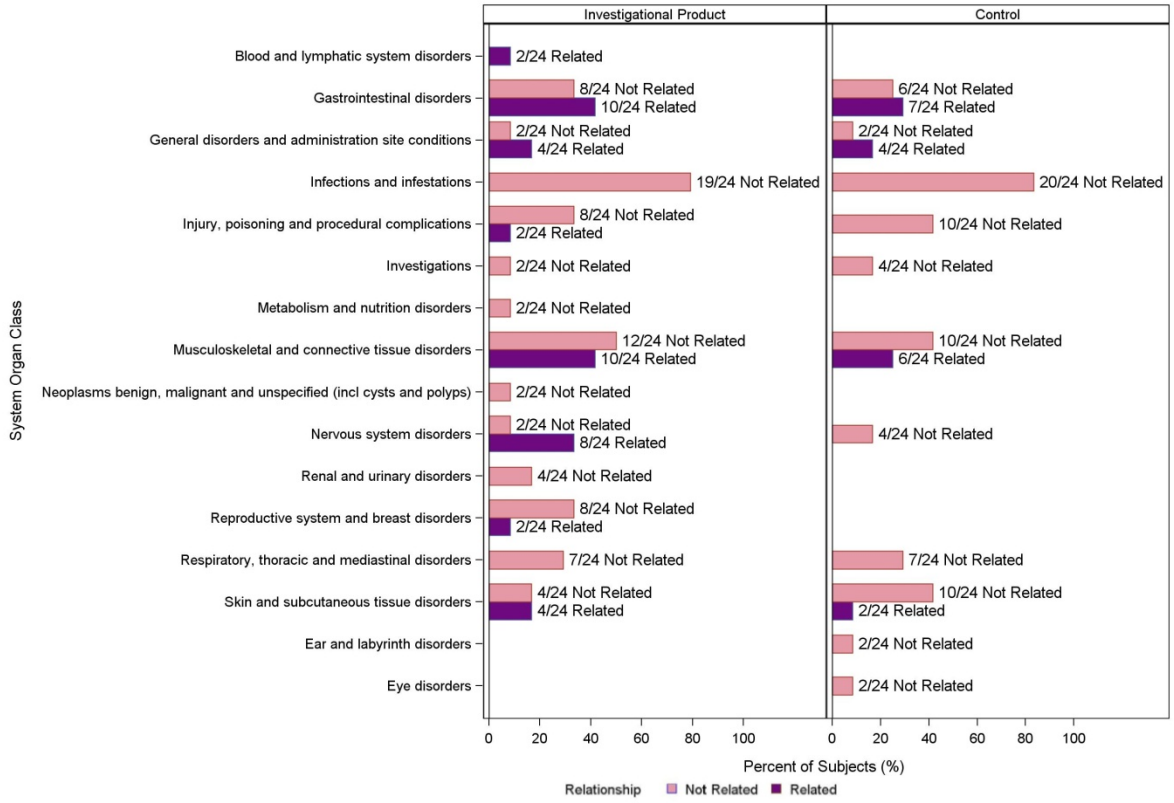


Figure 55: Incidence of Unsolicited Adverse Events by MedDRA® System Organ Class and Relationship to Treatment

[Implementation Note: A Generic figure is shown below. This figure includes all unsolicited events across all doses. A horizontal bar chart should be presented in a 1 image file with separate panels for each study arm (2 columns (treatment groups)). Axes should be labeled as follows: y-axis label: System Organ Class, x-axis label: Percentage of Subjects (%). The treatment groups should be indicated in the panel headers including "(N=X)", where N = the number of subjects in the in the Safety Population. Subjects are counted at most once at the maximum relationship (related > not-related) across for any events in the applicable SOC. The y-axis should present all SOCs reported by at least 1 subject and an "All Events" category. Y-axis should be sorted with "All Events" first, then in decreasing order of total incidence.]



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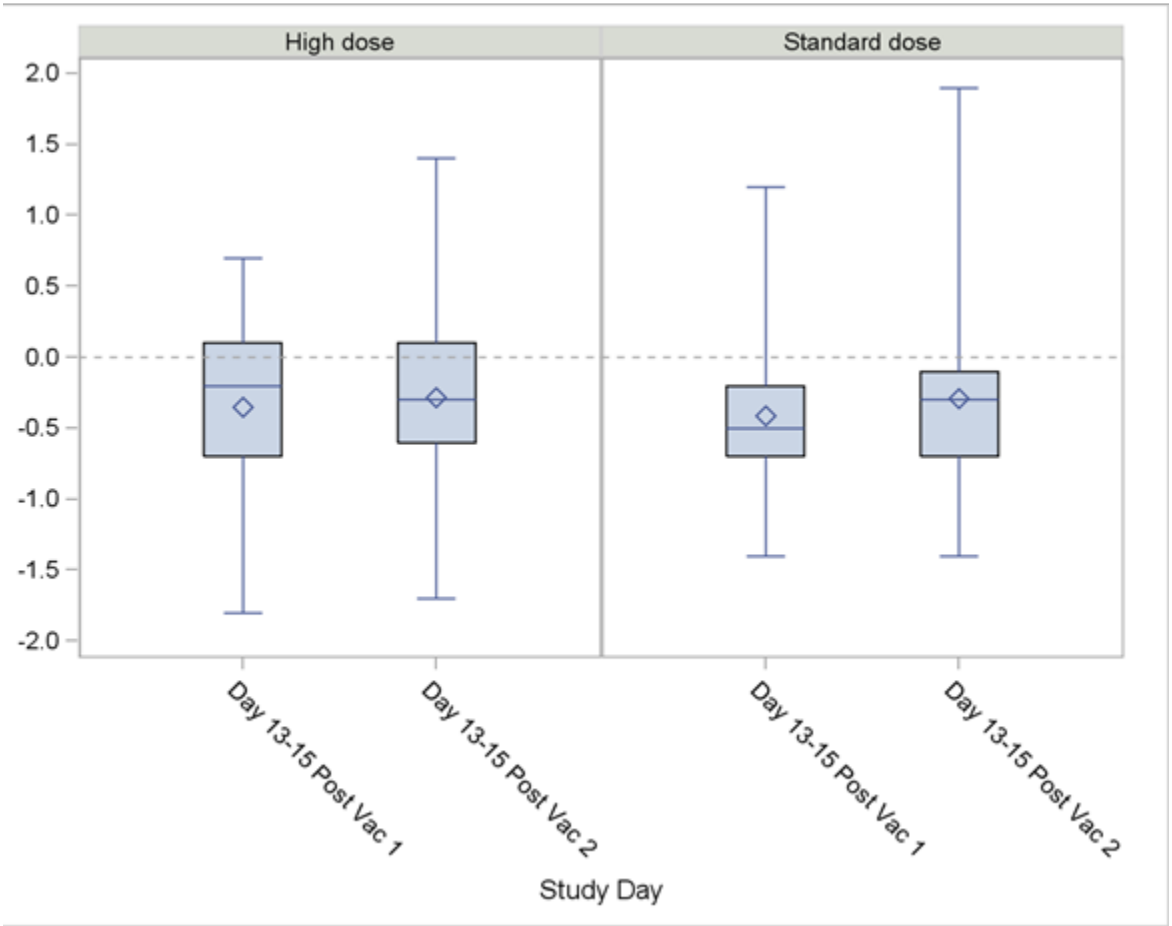
14.3.5 Displays of Laboratory Results

Figure 56: Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter and Study Group – Alanine Aminotransferase

[Implementation Note: An example figure is shown below. Change from baseline will be displayed for each group following the first vaccination (Day 8) in a single panel.]



Figures with similar format:

Figure 57: Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter and Study Group – Aspartate Aminotransferase

Figure 58: Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter and Study Group – Creatinine

Figure 59: Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter and Study Group – Hemoglobin

Figure 60: Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter and Study Group – White Blood Cells

Figure 61: Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter and Study Group – Platelets

APPENDIX 3. LISTINGS MOCK-UPS

LISTINGS

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Listing 1: 16.1.6 Listing of Subjects Receiving Investigational Product

Subject ID	Randomized Study Group	Product Received Study Vaccination 1	Product Received Study Vaccination 2

16.2 Database Listings by Subject

16.2.1 Discontinued Subjects

Listing 2: 16.2.1 Early Terminations or Discontinued Subjects

[Implementation Note: Category will be either "Early Termination" or "Treatment Discontinuation." In the "Reason" column, concatenate any "specify" fields, including AE number and DV number. In the CSR, Subject ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Treatment Group, Subject ID, alphabetically by Category (in the case a subject both terminates early and discontinues treatment).]

Study Group	Subject ID	Category	Reason for Early Termination or Treatment Discontinuation	Study Day

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16.2.2 Protocol Deviations

Listing 3: 16.2.2.1 Subject-Specific Protocol Deviations

[Implementation Note: 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: Subject refusal." In the CSR, Subject ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Treatment Group, Subject ID, DV Number.]

Study Group	Subject ID	DV Number	Deviation	Deviation Category	Study Day	Reason for Deviation	Deviation Resulted in AE?	Deviation Resulted in Subject Termination?	Deviation Affected Product Stability?	Deviation Resolution	Comments

Listing 4: 16.2.2.2 Non-Subject-Specific Protocol Deviations

[Implementation Note: 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: Subject refusal." Sort order: Site, Start Date.]

Start Date	Deviation	End Date	Reason for Deviation	Deviation Resulted in Subject Termination?	Deviation Affected Product Stability?	Deviation Category	Deviation Resolution	Comments

16.2.3 Subjects Excluded from the Efficacy Analysis

Listing 5: 16.2.3 Subjects Excluded from Analysis Populations

[Implementation Note: In the CSR, Subject ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Treatment Group, Subject ID.]

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

Note: "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.

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16.2.4 Demographic Data

Listing 6: 16.2.4.1 Demographic Data

[Implementation Note: If a subject is multi-racial, in "Race" column, note "Multiple: (list races, separated by a comma)." In the CSR, Subject ID should be USUBJID (not PATID) for purposes of de-identification.] Sort order: Treatment Group, Subject ID.]

Study Group	Subject ID	Sex	Age at Enrollment (years)	Ethnicity	Race

Listing 7: 16.2.4.2 Pre-Existing and Concurrent Medical Conditions

[Implementation Note: "Condition Start Day" and "Condition End Day" are relative to enrollment (which is Day 1, day before enrollment is Day -1). In the CSR, Subject ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Treatment Group, Subject ID, MH Number.]

Study Group	Subject ID	MH Number	Medical History Term	Condition Start Day	Condition End Day	MedDRA System Organ Class	MedDRA Preferred Term

16.2.6 Individual Efficacy/Immunogenicity Response Data

Listing 8: 16.2.6.1 Individual Immunogenicity Response Data – Serum Assays

Study Group	Subject ID	Planned Time Point	Actual Study Day	H3N2 M2SR[1] Titer	H3N2 QIV[2] Titer

[1] [Insert M2SR Strain here]
[2] [Insert QIV Strain here]

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Listing 9: 16.2.6.2 Individual Immunogenicity Response Data – Nasal Assays

Study Group	Subject ID	Planned Time Point	Actual Study Day	H3N2 M2SR[1] Titer (Not normalized)	H3N2 M2SR[1] Titer (Normalized)	H3N2 QIV[2] Titer (Not normalized)	H3N2 QIV[2] Titer (Normalized)

[1] [Insert M2SR Strain here]
[2] [Insert QIV Strain here]

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Listing 10: 16.2.6.3 Individual Immunogenicity Response Data – IFN-γ T Cell Responses

Study Group	Subject ID	Planned Time Point	Actual Study Day	H3 HA (H3N2 M2SR[1])	Conserved Internal Proteins (H3N2 M2SR[1])	H3 HA (H3N2 QIV[2])	Conserved Internal Proteins (H3N2 QIV[2])

[1] [Insert M2SR Strain here]
[2] [Insert QIV Strain here]

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16.2.7 Adverse Events

Listing 11: 16.2.7.1 Solicited Events – Systemic Symptoms

[Implementation Note: To indicate severity for quantitative symptoms (e.g., temperature, measurements), include the grade in parentheses after the number, e.g., 100.7 (Mild). This listing includes baseline assessments in addition to post-treatment assessments. In the CSR, Subject ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Subject ID, Dose Number, Post Dose Day, Symptom.]

Study Group	Subject ID	Vaccination Number	Post Vac Day	Assessment[a]	Symptom	Severity	Attributed to Alternate Etiology?[b]	Alternate Etiology
				MA				
				Clinic				

[a] MA = Data reported by subject on the Memory Aid and reviewed by clinic staff and reported in Solicited Events eCRF.
[b] Grade 3 events only.
Note: Clinic = Data collected by clinic staff during physical exam or symptom assessment (treatment administration record, in-clinic assessment, etc.)

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Listing 12: 16.2.7.2 Solicited Events – Local Symptoms

[Implementation Note: To indicate severity for quantitative symptoms (e.g., temperature, measurements), include the grade in parentheses after the number, e.g., 100.7 (Mild). This listing includes baseline assessments in addition to post-treatment assessments. In the CSR, Subject ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Subject ID, Dose Number, Post Dose Day, Symptom.]

Study Group	Subject ID	Vaccination Number	Post Vac Day	Assessment[a]	Symptom	Severity
				MA		
				Clinic		

[a] MA = Data reported by subject on the Memory Aid and reviewed by clinic staff and reported in Solicited Events eCRF.
Note: Clinic = Data collected by clinic staff during physical exam or symptom assessment (treatment administration record, in-clinic assessment, etc.)

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Listing 13: 16.2.7.3 Unsolicited Adverse Events

[Implementation Note: 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. This listing includes all unsolicited adverse events. If there are no comments for an event, populate 'Comments' row with 'None'. In the CSR, Subject ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Treatment Group, Subject ID, Associated with Dose No., No. of Days Post Associated Dose.]

Adverse Event	Associated with Vac No.	No. of Days Post Associated Vaccination (Duration)	Severity	SAE? AESI? NOCMC?	Relationship to Study Treatment	In Not Related, Alternative Etiology	Action Taken with Study Treatment	Subject Discontinued Due to AE	Outcome	MedDRA System Organ Class	MedDRA Preferred Term
Study Group: , Subject ID: , AE Number:											
Comments:											
Study Group: , Subject ID: , AE Number:											
Comments:											
Note: For additional details about SAEs, see Table: xx.											

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16.2.8 Individual Laboratory Measurements

Listing 14: 16.2.8.1 Clinical Laboratory Results – Chemistry

[Implementation Note: This listing includes all laboratory results, scheduled and unscheduled. The severity should be included in parentheses after the result for abnormal results, e.g., 16.2 (Mild). In the CSR, Subject ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Treatment Group, Subject ID, and Planned Time Point.]

Study Group	Subject ID	Planned Time Point	Actual Study Day	Sex	Age (years)	Laboratory Parameter (Units)	Result (Severity Grade)	Reference Range Low	Reference Range High

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Listing 15: 16.2.8.2 Clinical Laboratory Results – Hematology

[Implementation Note: This listing includes all laboratory results, scheduled and unscheduled. The severity should be included in parentheses after the result for abnormal results, e.g., 16.2 (Mild). In the CSR, Subject ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Treatment Group, Subject ID, and Planned Time Point.]

Study Group	Subject ID	Planned Time Point	Actual Study Day	Sex	Age (years)	Laboratory Parameter (Units)	Result (Severity Grade)	Reference Range Low	Reference Range High

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16.2.9 Vital Signs and Physical Exam Findings

Listing 16: 16.2.9.1 Physical Exam Findings

[Implementation Note: This listing includes all physical exam findings, scheduled and unscheduled. If a subject does not have any findings upon examination, they will not be included in this listing. If reported as an AE, display "Yes" with the AE Number in parentheses, e.g., "Yes (7)". In the CSR, Subject ID should be USUBJID (not PATID) for purposes of de-identification.] Sort order: Treatment Group, Subject ID, Planned Time Point.]

Study Group	Subject ID	Planned Time Point	Actual Study Day	Body System	Abnormal Finding	Reported as an AE? (AE Description; Number)

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16.2.10 Concomitant Medications

Listing 17: 16.2.10 Concomitant Medications

[Implementation Note: "Medication Start Day" and "Medication End Day" are relative to enrollment (which is Day 1, day before enrollment is Day -1). For medication start dates that are > 30 days prior to enrollment, rather than use exact study days, categorize as follows:

- >5 years prior to enrollment
- 1-5 years prior to enrollment
- <1 year prior to enrollment

If ongoing, display "Ongoing" in the "Medication End Day" column. If taken for an AE or MH, display "Yes" with the AE or MH Number in parentheses, e.g., "Yes (7)". In the CSR, Subject ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Treatment Group, Subject ID, and CM Number.]

Study Group	Subject ID	CM Number	Medication	Medication Start Day	Medication End Day	Indication	Taken for an AE? (AE Description; Number)	Taken for a condition on Medical History? (MH Description; Number)	ATC Level 1 (ATC Level 2)

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16.2.11 Pregnancy Reports

Listing 18: 16.2.11.1: Pregnancy Reports – Maternal Information

Study Group	Subject ID	Pregnancy Number	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?

Note: Maternal Complications are included in the Adverse Event listing. Medications taken during pregnancy are included in the Concomitant Medications Listing.

Listing 19: 16.2.11.2: Pregnancy Reports – Gravida and Para

			Live Births												
Subject ID	Pregnancy Number	Gravida	Extremely PB[a]Error! Reference source not found.	Very Early PB[a]Error! Reference source not found.	Early PB[a]Error! Reference source not found.	Late PB[a]	Early TB[b]	Full TB[b]	Late TB[b]	Post TB[b]Error! Reference source not found.	Still Births	Spontaneous Abortion/ Miscarriage	Elective Abortions	Therapeutic Abortions	Major Congenital Anomaly with Previous Pregnancy?

Note: Gravida includes the current pregnancy, para events do not.

[a] Preterm Birth
[b] Term Birth

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Listing 20: 16.2.11.3: Pregnancy Reports – Live Birth Outcomes

Subject ID	Pregnancy Number	Fetus Number	Pregnancy Outcome (for this Fetus)	Fetal Distress During Labor and Delivery?	Delivery Method	Gestational Age at Live Birth	Size for Gestational Age	Apgar Score, 1 minute	Apgar Score, 5 minutes	Cord pH	Congenital Anomalies?	Illnesses/ Hospitalizations within 1 Month of Birth?
Note: Congenital Anomalies are included in the Adverse Event listing.												

Listing 21: 16.2.11.4: Pregnancy Reports – Still Birth Outcomes

Subject ID	Date of Initial Report	Fetus Number	Pregnancy Outcome (for this Fetus)	Fetal Distress During Labor and Delivery?	Delivery Method	Gestational Age at Still Birth	Size for Gestational Age	Cord pH	Congenital Anomalies?	Autopsy Performed?	If Autopsy, Etiology for Still Birth Identified?

Listing 22: 16.2.11.5: Pregnancy Reports – Spontaneous, Elective, or Therapeutic Abortion Outcomes

Subject ID	Date of Initial Report	Fetus Number	Pregnancy Outcome (for this Fetus)	Gestational Age at Termination	Abnormality in Product of Conception?	Reason for Therapeutic Abortion

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