Collaborative Influenza Vaccine Innovation Centers

STATISTICAL ANALYSIS PLAN
for
DMID Protocol: 21-0010

Study Title:

A Phase 1 Open label, Comparator-Controlled, Dose-Escalation Study to Evaluate the Safety and Immunogenicity of a Single Dose of VRC H1ssF_3928 mRNA-LNP in Healthy Adults

NCT05755620

Version 1.0

DATE: 10 December 2025

RESTRICTED

STUDY TITLE

Protocol Number Code:	**DMID Protocol: 21-0010**
Development Phase:	Phase 1
Products:	H1ssF_3928 mRNA-LNP Vaccine, seasonal inactivated influenza vaccine (IIV4)
Form/Route:	Intramuscular (IM)
Indication Studied:	Influenza
Sponsor:	Division of Microbiology and Infectious Diseases Division of Allergy, Immunology, and Transplantation National Institute of Allergy and Infectious Diseases National Institutes of Health
Clinical Trial Initiation Date:	March 27, 2023
Clinical Trial Completion Date:	October 3, 2025
Date of the Analysis Plan:	December 10, 2025
Version Number:	1.0

This study was performed in compliance with Good Clinical Practice.

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LIST OF ABBREVIATIONS

AE	Adverse Event
AESI	Adverse Event of Special Interest
AUC	Area Under the Curve
C	Celsius
CI	Confidence Interval
COVID-19	Coronavirus Disease 2019
CSR	Clinical Study Report
DMID	Division of Microbiology and Infectious Diseases
EDC	Electronic Data Capture
ELISA	Enzyme-linked Immunosorbent Assay
EU	ELISA Units
F	Fahrenheit
FDA	Food and Drug Administration
GMT	Geometric Mean Titer
GMFR	Geometric Mean Fold-Rise
HAI	Hemagglutination Inhibition
HEENT	Head, Eyes, Ears, Nose, and Throat
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
ID50	Median Infectious Dose
IIV4	Inactivated Influenza Vaccine Quadrivalent
IND	Investigational New Drug
IRB	Institutional Review Board
ITT	Intention to Treat
L	Liter
LNP	Lipid Nanoparticle
LOD	Lower Limit of Detection
LLOQ	Lower Limit of Quantitation
MAAE	Medically Attended Adverse Event

List of Abbreviations *(continued)*

MedDRA	Medical Dictionary for Regulatory Activities
MFI	Median Fluorescence Intensity
mL	Milliliter
MN	Microneutralization
NOCMC	New-Onset Chronic Medical Condition
OD_{450}	Optical Density at 450nm
N	Number (typically refers to Participants)
PBMC	Peripheral Blood Mononuclear Cells
PI	Principal Investigator
PP	Per Protocol
PT	Preferred Term
RMN	Reporter Microneutralization
Q-Q	Quantile-Quantile
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SDMCC	Statistical, Data Management, and Coordination Center
SDTM	Study Data Tabulation Model
SMC	Safety Monitoring Committee
SOC	System Organ Class
SRC	Safety Review Committee
Tfh	T-Follicular Helper
ULOD	Upper Limit of Detection
ULOQ	Upper Limit of Quantitation
WHO	World Health Organization

1. PREFACE

The Statistical Analysis Plan (SAP) for "A Phase 1 Open label, Comparator-Controlled, Dose-Escalation Study to Evaluate the Safety and Immunogenicity of a Single Dose of VRC H1ssF_3928 mRNA-LNP in Healthy Adults" (Division of Microbiology and Infectious Diseases [DMID] Protocol 21-0010) describes and expands upon the statistical information presented in the protocol (version 7.0).

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

This document contains five broad sections: (1) a description of the purpose of analyses; (2) a description of the study design, its objectives; and the variables collected/assessed to be used in analyses; (3) general statistical principles and considerations; (4) comprehensive statistical analysis methods for study outcomes, and (5) a list of proposed tables, figures, and listings along with mock-ups (Appendices 1, 2, and 3). The past tense will be utilized to describe objective descriptions of the study and its related design features or elements of the study that have already been completed (e.g., the interim analyses); the subjunctive mood will be utilized to describe design elements of the study that could deviate depending on actual study conduct; and the future tense will be utilized to describe planned statistical analyses. Any deviation from this SAP will be described and justified in the CSR, as appropriate. The reader of this SAP is encouraged to also review the study protocol for details on the conduct of the study and the operational aspects of clinical assessments.

2. INTRODUCTION

Influenza has been recognized as a global health threat since the 1918 influenza pandemic that caused an estimated 50 million deaths globally. Over 100 years of research on influenza has resulted in the availability of preventative vaccines, but seasonal vaccines remain only partially effective. The vaccine product evaluated in this study is a modified messenger ribonucleic acid (mRNA) encoding a headless HA stabilized stem construct, derived from influenza A/New Caledonia/20/1999 (H1N1) and covalently linked to *Helicobacter pylori (H. pylori)* ferritin. The mRNA is encapsulated in a lipid nanoparticle (LNP) for delivery. This formulation is being tested as a proof-of-concept for a universal influenza vaccine approach, leveraging an immunogen that is designed to elicit universally protective responses.

2.1. Purpose of the Analyses

Final analyses will assess the safety, reactogenicity, and immunogenicity of the VRC H1ssF_3928 mRNA-LNP vaccine at doses of 10, 25 and 50 mcg in adults aged 18 to 49 years.

This analysis plan covers all primary, secondary, and exploratory objectives. The CSR will be generated after all primary and secondary endpoint data are available and clinical and relevant non-clinical data have been cleaned and locked. Exploratory endpoints may be included in the primary CSR if data are available. Any exploratory endpoints not available for inclusion in the primary CSR will be presented in one or more addenda to the CSR, manuscript(s), or other report as data are available.

The protocol for DMID 21-0010 called for planned interim safety analyses and a planned interim immunogenicity analysis. The planned interim safety analyses were performed to assess safety prior to progressing to subsequent dose groups, and to select the optimal dose. The purpose of the planned interim immunogenicity analysis was to present immunological response results to aid with planning of future studies. Additional details about these interim analyses, including timing, can be found in Section 5.6.1. The analysis plan for the interim immunogenicity analysis was defined in a memorandum.

3. STUDY OBJECTIVES AND ENDPOINTS

3.1. Study Objectives

Primary

- (Safety) To assess the safety of a single dose of VRC H1ssF_3928 mRNA-LNP vaccine administered IM in healthy adults (18-49 yrs.) at doses of 10 mcg, 25 mcg, and 50 mcg.

Secondary

- (Immunogenicity) To assess serum antibody response to a single dose of VRC H1ssF_3928 mRNA-LNP vaccine administered IM in healthy adults at doses of 10 mcg, 25 mcg, and 50 mcg in comparison to a standard dose of inactivated influenza vaccine quadrivalent (IIV4).

Exploratory

- (Immunogenicity) To assess the anti-ferritin antibody response (to human and *H. pylori* ferritin) to a single dose of VRC H1ssF_3928 mRNA-LNP vaccine administered IM in healthy adults at doses of 10 mcg, 25 mcg, and 50 mcg.
- (Immunogenicity) To assess the durability of the immune response to a single dose of VRC H1ssF_3928 mRNA-LNP vaccine administered IM in healthy adults at doses of 10 mcg, 25 mcg, and 50 mcg in comparison to a standard dose of IIV4.
- (Immunogenicity) To assess antibody breadth to a single dose of VRC H1ssF_3928 mRNA-LNP vaccine administered IM in healthy adults at doses of 10 mcg, 25 mcg, and 50 mcg in comparison to a standard dose of IIV4.
- (Immunogenicity) To assess the B cell and/or T cell, including T follicular helper cell, responses to a single dose of VRC H1ssF_3928 mRNA-LNP vaccine administered IM in healthy adults at doses of 10 mcg, 25 mcg, and 50 mcg in comparison to a standard dose of IIV4.

3.2. Endpoints

Primary

- (Safety) Number and percentage of participants experiencing solicited local and systemic reactogenicity adverse events (AEs) through 14 days.
- (Safety) Number and percentage of participants experiencing any unsolicited AEs through 28 days.
- (Safety) Number and percentage of participants experiencing any medically attended adverse events (MAAEs), new-onset chronic medical conditions (NOCMCs), adverse events of special interest (AESIs) corresponding to Grade 2 or greater decrease in lymphocyte or neutrophil count, influenza-like illnesses (ILIs), and serious adverse events (SAEs) through one year (Day 366) and AESIs corresponding to myocarditis, pericarditis, or myopericarditis through 57 days (Day 57).
- (Safety) Number and percentage of participants experiencing clinical laboratory AEs through 57 days (Day 57).

Secondary

- (Immunogenicity) Geometric mean titer (GMT) of homologous H1-specific neutralizing antibodies in a reporter microneutralization assay at Days 1, 8, 15, 29, and 57 by dose group and stratified by prior season's receipt of seasonal influenza vaccine within each analysis group.
- (Immunogenicity) Geometric mean fold rise (GMFR) from baseline (Day 1) of homologous H1-specific neutralizing antibodies in a reporter microneutralization assay at Days 8, 15, 29, and 57 by dose group and stratified by prior season's receipt of seasonal influenza vaccine within each analysis group.
- (Immunogenicity) GMT of homologous H1-specific neutralizing antibodies in a viral microneutralization assay at Days 1, 8, 15, 29, and 57 by dose group and stratified by prior season's receipt of seasonal influenza vaccine within each analysis group.
- (Immunogenicity) GMFR from baseline (Day 1) of homologous H1-specific neutralizing antibodies in a viral microneutralization assay at Days 8, 15, 29, and 57 by dose group and stratified by prior season's receipt of seasonal influenza vaccine within each analysis group.
- (Immunogenicity) GMT of anti-stalk serum antibodies, measured by enzyme linked immunosorbent assay (ELISA) at Days 1, 8, 15, 29, and 57 by dose group and stratified by prior season's receipt of seasonal influenza vaccine within each analysis group.
- (Immunogenicity) GMFR from baseline (Day 1) of anti-stalk serum antibodies, measured by ELISA, at Days 8, 15, 29, and 57 by dose group and stratified by prior season's receipt of seasonal influenza vaccine within each analysis group.

Exploratory

- (Immunogenicity) Measures of anti-ferritin antibody response (to human and *H. pylori* ferritin) to a single dose of VRC H1ssF_3928 mRNA-LNP vaccine administered IM in healthy adults at doses of 10 mcg, 25 mcg, and 50 mcg at Days 1, 29, and 181 by dose group and stratified by prior season's receipt and/or subsequent receipt (where applicable) of seasonal influenza vaccine within each analysis group.
- (Immunogenicity) GMT of homologous H1-specific neutralizing antibodies in a reporter microneutralization assay at Days 85, 181, and 366 by dose group and stratified by prior season's receipt of seasonal influenza vaccine within each analysis group.
- (Immunogenicity) GMT of homologous H1-specific neutralizing antibodies in a viral microneutralization assay at Days 85, 181, and 366 by dose group and stratified by prior season's receipt and/or subsequent receipt of seasonal influenza vaccine within each analysis group.
- (Immunogenicity) GMT of anti-stalk serum antibodies, measured by ELISA, at Days 85, 181, and 366 by dose group and stratified by prior season's receipt and/or subsequent receipt of seasonal influenza vaccine within each analysis group.
- (Immunogenicity) Neutralizing antibody response to divergent H1 influenza virus isolates and other Group 1 non-H1 influenza virus isolates at Day 1 and 29 by dose group and stratified by prior season's receipt of seasonal influenza vaccine within each analysis group.

- (Immunogenicity) Anti-stalk serum antibody response to divergent H1 influenza virus isolates and other Group 1 non-H1 influenza virus isolates at Day 1 and 29 by dose group and stratified by prior season's receipt of seasonal influenza vaccine within each analysis group.
- (Immunogenicity) B cell assays, T cell assays, and T follicular helper cell assays at selected time points in the entire study population or subsets of participants by dose group and stratified by prior season's receipt and/or subsequent receipt (where applicable) of seasonal influenza vaccine within each analysis group.

3.3. Study Definitions and Derived Variables

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

End point titer replicates will be reported with values of $10*2^k$, where k=0, 1, 2, etc.

Assay results determined to be below the lower limit of detection (LOD) will be imputed as LOD/2. If the lower limit of quantification (LLOQ) exists and is distinct from the LOD, responses above the LOD but below the LLOQ will be imputed by (LLOQ+LOD)/2. If the LLOQ exists and is not distinct from the LOD or the LOD does not exist, responses below the LLOQ will be imputed as LLOQ/2. If the upper limit of quantification (ULOQ) exists, responses above the ULOQ will be imputed as the ULOQ. All imputations will be performed at the replicate level as applicable. See Section 7.1.3 for a sensitivity analysis utilizing an alternative imputation method for assay results falling below the LLOQ.

Titers will be summarized using the geometric mean, first across replicates to compute one value for each individual sample (as applicable) and then applied again across participants within the same group as applicable. Fold-rise will be calculated as the post-baseline result divided by the baseline result. Non-titer data will be summarized using the arithmetic mean, first across replicates to compute one value for each individual sample (as applicable) and then applied again across participants within the same group as applicable.

Prior season's receipt of seasonal influenza vaccine will be defined as receipt of a seasonal influenza vaccine less than 12 months (365 days) from study vaccination. If the exact year of a prior seasonal influenza vaccination is unknown, the year will be taken as the year of study vaccination. If the exact month is unknown, the month will be taken as December if receipt was reported in a year different from study vaccination; otherwise, the month will be taken such that the vaccination occurred three months prior to enrollment. The day of receipt will be taken as the 15th of the month.

Subsequent receipt of seasonal influenza vaccine will be defined as receipt of a seasonal influenza vaccine during a participant's time on study, collected as concomitant medications. If the exact month is unknown, the month will be taken as the month of reporting. If the exact day is unknown and the reported month and year is the same as the study vaccination, the day will be taken as one day after study vaccination; otherwise, the day will be taken as the 15th of the month.

All other dates were imputed, as necessary, during data entry according to the convention described in the Manual of Procedures.

4. INVESTIGATIONAL PLAN

4.1. Overall Study Design and Plan

This is a Phase 1 open label, comparator-controlled, dose escalation study of an intramuscularly (IM) administered mRNA-LNP vaccine encoding for VRC H1ssF_3928, including up to 50 healthy adult volunteers aged 18 to 49 years, designed to assess vaccine safety, reactogenicity, and immunogenicity at varying doses.

Enrollment into dosing groups (Low Dose [10 mcg], Medium Dose [25 mcg], High Dose [50 mcg], and selected optimal dose) of the VRC H1ssF_3928 mRNA-LNP vaccine was to be performed sequentially starting with the Low Dose group 10 mcg. Up to 10 participants were to be enrolled per dosing group. The Safety Review Committee (SRC) reviewed reactogenicity and safety data collected through Day 3 for the first 2 participants enrolled in each dosing group (termed the sentinel subgroup) prior to proceeding with enrollment of the remaining 8 participants (termed the expanded subgroup) in the respective dosing group. After review of reactogenicity and safety data through Day 7 and clinical laboratory results through Day 8 for all 10 enrolled participants in the preceding dose and confirming no safety issues were identified, enrollment into the next highest dose proceeded. The optimal dosing group, consisting of 10 participants, was selected based on reactogenicity and safety data through Day 7 and clinical laboratory results through Day 8 from the three dosing levels (see Section 5.6) and was chosen to be the High Dose group (50 mcg).

Ten separate participants were to be enrolled to receive standard quadrivalent inactivated influenza vaccine (IIV4) as an immunogenicity comparator group. Due to the logistical challenges of concurrently enrolling the immunogenicity comparator group and sequential investigational vaccine dose groups in a seasonal influenza vaccine season, randomization and blinding was infeasible. Therefore, the study was not randomized and was open label.

An overview of the dosing groups is presented in the study schema (Table 1, taken from Section 1.1 of the protocol).

Participants were to receive either VRC H1ssF_3928 mRNA-LNP or IIV4 at baseline (Day 1) and to be followed for one year. The final study visit for the last participant occurred on October 3, 2025.

Solicited local and systemic events were to be collected through a memory aid through 14 days after study vaccination; unsolicited, non-serious AEs were to be collected through 28 days after study vaccination; and MAAEs, NOCMCs, AESIs corresponding to Grade 2 or greater decrease in lymphocyte or neutrophil count, ILIs, and SAEs were to be collected from the time of vaccination throughout the study period. AESIs corresponding to myocarditis, pericarditis and myopericarditis were to be collected from the time of vaccination through Day 57.

Serum blood draws for immunologic assessments were to be performed at all scheduled study visits except screening. PBMC, plasma collection, and whole blood PAXgene were to be performed at select study visits for exploratory and secondary research.

The Schedule of Activities, taken from Section 1.2 of the protocol, is presented in Table 2 for reference.

An interim immunogenicity analysis was planned and conducted while the study was ongoing; the analysis plan for the interim analysis was detailed in a memorandum. Further details can be found in Section 5.6.1.

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

Participants to have received one dose of IIV4 were enrolled first, prior to the seasonal flu vaccine expiring for the year of enrollment. After enrollment of IIV4 participants, participants were enrolled to receive one dose of VRC H1ssF_3928 mRNA-LNP at the dosing level that was active at the time of enrollment. The study was not randomized and was open label.

4.3. Selection of Study Population

The study population consisted of healthy male and female adult volunteers aged 18 to 49 years, inclusive, at time of screening and enrollment. Inclusion and exclusion criteria are presented in Sections 5.1 and 5.2 of the protocol, respectively.

4.4. Statistical Considerations for the Study Design

The study was not designed to achieve pre-determined levels of power or precision to address the primary, secondary, or exploratory objectives. However, the implications of the chosen sample size on the probability of observing events and the level of precision are given below.

4.4.1. Sample Size Considerations

The primary objective of this study is to determine the safety of the VRC H1ssF_3928 mRNA-LNP vaccine. This will be assessed by the number and percentage of participants experiencing solicited reactogenicity events, unsolicited AEs, MAAEs, NOCMCs, AESIs, ILIs, SAEs, and clinical laboratory AEs after vaccination for the given time period of interest (see Section 4.6.2 for further details).

The probability of observing at least one safety event, given various underlying event probabilities and sample sizes, is presented in Table 7. Among the 2 participants in each dose group considered for the safety reviews prior to enrolling the expanded dose group, there was a 2.0% chance of observing at least one uncommon event and a 19% chance of observing at least one common event. When assessing a sentinel + expanded dose group (N=10) as well as the optimal dose group (N=20), there was a 9.6% and 18.2% chance of observing at least one uncommon event, respectively, and a 65.1% and 87.8% chance of observing at least one common event, respectively.

While the study was not designed to achieve a pre-determined level of precision, confidence intervals (CIs) will be estimated for some of the binary endpoints. Table 8 presents the exact 95% Clopper-Pearson confidence intervals that would result from observing varying numbers of events in groups of possible interest.

For illustration, if zero events of a certain type were observed in an individual sentinel lead-in group with N=2 participants, true event probabilities above 84.2% could be ruled out at the 95% confidence level, compared to 30.8% in a sentinel + expanded dose group (N=10) and 16.8% in the optimal dose group (N=20). Binomial CIs are widest at 50% events observed; the estimates associated with 50% observed events are bolded in Table 8. Within a sentinel lead in group with N=2 participants, the maximum half-width for a 95% CI would be 48.7%, compared to 31.3% in a sentinel + expanded dose group (N=10) and 22.8% in the optimal dose group (N=20). In the case of substantial loss to follow-up or missed visits, these estimates give an idea of the loss of precision due to decreasing the effective sample size.

4.4.2. Allocation of Participants to Study Arms

The study was not randomized; participants were sequentially enrolled with the first 10 participants enrolled to receive one dose of IIV4 and the remaining 40 participants sequentially enrolled to receive one vaccination at an increasing dose of VRC H1ssF_3928 mRNA-LNP. Enrollment of participants was done online using the enrollment module of the Electronic Data Capture (EDC), maintained by the Statistical, Data Management, and Coordination Center (SDMCC).

4.5. Study Products

4.5.1. Study Products Administered

Participants were to be administered either one dose of VRC H1ssF_3928 mRNA-LNP vaccine (0.5 mL of H1ssF_3928 mRNA [0.5 mg/mL] diluted in normal saline to achieve 0.5 mL doses of 10 mcg, 25 mcg, or 50 mcg, depending on the dose group) or 60 mcg (15 mcg per antigen) of IIV4 (Fluzone Quadrivalent). All vaccines were to be administered IM.

4.5.2. Identity of Investigational Product(s)

4.5.2.1. Product 1: VRC H1ssF_3928 mRNA-LNP Vaccine

The investigational vaccine consisted of modified nucleoside mRNA encapsulated in LNP, comprised of four lipid components: (Bis(2-butyloctyl) 10-(N-3-(pyrrolidin-1-yl) propyl) nonanamido) nonadecanedioate [ionizable lipid], DSPC, cholesterol, and PEG lipid). These lipid components are similar to those used in the Moderna and Pfizer SARS-CoV-2 vaccines, except the novel ionizable cationic lipid, for which there is not yet clinical experience. The VRC H1ssF_3928 mRNA vaccine was supplied in one single-dose 2 mL Type 1 glass vials, with each vial containing 0.7 mL of the vaccine, 0.5 mg/mL diluted in normal saline to achieve the targeted dose.

The VRC H1ssF_3928 mRNA vaccine was administered by two manufacturers: The Duke Human Vaccine Institute GMP Program (Durham, NC) manufactured the Good Manufacturing Practice-grade mRNA and provided it to Evonik Canada (Burnaby, BC, Canada) for the formulation into a lipid nanoparticle. Lipids were provided by Avanti Polar Lipids in Birmingham, Alabama. Each vial was individually labeled with the product name, description, and caution statement. The investigational drug batch was ECI20211117.

4.5.2.2. Product 2: Diluent for Product 1

The diluent for the VRC H1ssF_3928 mRNA vaccine was sterile 0.9% sodium chloride for injection, USP, supplied as single-use vials.

4.5.2.3. Product 3: Seasonal Influenza Vaccine (IIV4) Immunogenicity Comparator: Fluzone Quadrivalent

Fluzone Quadrivalent, manufactured by (Sanofi Pasteur Inc.), was utilized as the IIV4 vaccine.

Fluzone Quadrivalent is a vaccine indicated for active immunization for the prevention of influenza disease caused by influenza A subtype viruses and type B viruses contained in the vaccine. It is an inactivated influenza vaccine, prepared from influenza viruses propagated in embryonated chicken eggs.

4.5.3. Selection of Doses in the Study

Selected dosage levels of 10 mcg, 25 mcg and 50 mcg of the VRC H1ssF_3928 mRNA vaccine were based on clinical experience with other mRNA-LNP investigational, authorized, and approved vaccines. A study of influenza A/H10N8 mRNA vaccines determined that 400 mcg doses were not well tolerated while doses of 100 mcg or less were acceptable. Participants were to be enrolled at the lowest dose (10 mcg) first, with dose escalation occurring only after approval from the SRC.

4.5.4. Selection and Timing of Dose for Each Subject

One dose of VRC H1ssF_3928 mRNA-LNP vaccine (10 mcg, 25 mcg, or 50 mcg) or IIV4 was to be administered IM on Day 1 if all eligibility criteria were met.

4.5.5. Blinding

This is an open-label study. As such, blinding was not applicable.

4.5.6. Prior and Concomitant Therapy

All concomitant medications taken within 90 days prior to signing the informed consent form (ICF) were to be reviewed with participants to determine stability of chronic diseases and eligibility and recorded on the data collection forms/source documentation. Medications reported in the eCRF from the paper CRFs were to be limited to those taken within 30 days prior to receipt of study product. Concomitant medications were to be reviewed at every study visit through the end of the study.

Participants should not have received seasonal influenza vaccine within 90 days prior to enrollment or within 60 days post-study vaccination. Participants should not have received any approved or authorized vaccines within 60 days prior to study enrollment or 60 days post-study vaccination.

Receipt of any influenza vaccine prior to study vaccination for the 2021/2022, 2022/2023, and 2023/2024 influenza vaccine seasons was to be documented. Participants should not have received influenza vaccine three months (90 days) prior to receipt of study product but should have received at least one seasonal influenza vaccine during the past 5 seasons. Receipt of seasonal influenza vaccine subsequent to study vaccination was to be documented throughout the study.

For participant receipt of non-seasonal influenza vaccine (including those that are experimental) product type, vaccine virus strains, and approximate date was to be documented. Note that participants should not have received an investigational H1 influenza vaccine within the past 10 years. Prior participation in any influenza challenge study was to be documented and captured in the clinical database. Previous participation in DMID Protocol No. 18-0010 human influenza challenge study was considered an exclusion. Additionally, participants should not have received an H5 influenza vaccine at any point. Example DMID studies where participation involved H5 influenza vaccination include Protocol Nos. 05-0127, 07-0022, 08-0013, and 15-0066.

Additional details of allowable and prohibited prior and concomitant therapy can be found in Section 6.5 of the protocol and in the inclusion and exclusion criteria defined in Section 5.1 and Section 5.2 of protocol.

4.5.7. Study Product Compliance

Participants were to be directly observed at the time of dosing, with the vaccination being administered by a member of the clinical research team who was licensed to administer the study product.

4.6. Immunogenicity and Safety Variables

4.6.1. Immunogenicity Variables

Neutralizing antibodies measured by a reporter microneutralization (RMN) assay and a viral microneutralization (MN) assay as well as T-cell and T-follicular helper (Tfh) cell assays will be reported by the research laboratory at Duke University. Anti-HA stalk serum antibodies measured by enzyme-linked immunosorbent assay (ELISA) and will be reported by the research laboratory at the University of Maryland - Baltimore. H. Pylori ferritin binding, human ferritin light chain binding, and human ferritin heavy chain binding from the anti-ferritin assay and B-cell assays will be reported by the research laboratory at the Vaccine Research Center Vaccine Immunology Program. RMN, MN, anti-HA stalk, and anti-ferritin antibodies will be measured in serum. T-cell, Tfh cell, and B-cell assays will be measured in peripheral blood mononuclear cells (PBMC).

Assay results for RMN will be reported as median infectious dose (ID_{50}) titers. Assay results for MN will be reported as endpoint titers. Assay results for anti-HA stalk serum antibodies, as measured by ELISA, will be reported as titers in ELISA units (EU) per mL whereby the response of an individual replicate is the interpolated antibody concentrations for the observed optical density 450 (OD_{450}) multiplied by the applicable dilution, and the individual assay result is the arithmetic mean of applicable replicates. Assay results for anti-ferritin will be reported as the area under the curve (AUC). Assay results for T-cell, Tfh cell, and B-cell assays will be reported as the percent of expressed cells and number of cells in the parent population, or the median fluorescence intensity (MFI) for each marker, as applicable.

Values for all immunogenicity data are reported i) as estimated, ii) as below the lower limit of detection (LOD), or iii) as above the upper limit of quantitation (ULOQ). See Section 3.3 for definitions of derived variables for immunologic data.

All immunogenicity data will be uploaded into the SDMCC's electronic data capture system.

4.6.2. Safety Variables

Safety will be assessed by the incidence and severity of:

1. Solicited local reactogenicity events through 13 days post-vaccination (Day 14).
2. Solicited systemic reactogenicity events through 13 days post-vaccination (Day 14).
3. Unsolicited AEs through 28 days post-vaccination (Day 29).
4. MAAEs from vaccine administration through one year post-vaccination (Day 366)
5. NOCMCs from vaccine administration through one year post-vaccination (Day 366).
6. AESIs corresponding to a Grade 2 or greater decrease in lymphocyte or neutrophil count from vaccine administration through one year post-vaccination (Day 366).
7. ILIs from vaccine administration through one year post-vaccination (Day 366).
8. SAEs from vaccine administration through one year post-vaccination (Day 366).

9. AESIs corresponding to myocarditis, pericarditis, or myopericarditis from vaccine administration through 56 days post-vaccination (Day 57).
10. Clinical laboratory AEs from vaccine administration through 56 days post-vaccination (Day 57).

Solicited adverse events were to be graded as per Table 3.

Myocarditis, pericarditis, or myopericarditis were to be confirmed (defined in Table 6) to contribute as an AESI.

Clinical laboratory AEs were defined as laboratory abnormalities with a grade level increase from baseline in clinical laboratory values (with laboratory values graded as per Table 4). For hemoglobin, only raw hemoglobin values that worsened by grade from baseline will be considered laboratory AEs; hemoglobin values gradable based on change from baseline alone will not be included as laboratory AEs as no baseline grade will be available. The resolution date of a clinical laboratory abnormality will be unknown as laboratory values were to only be attained at in-clinic visits, as indicated in the Schedule of Activities. Therefore, the incidence of such clinical laboratory AEs will be reported with each participant counting at most once towards a given laboratory AE at the maximum severity for the corresponding time period, with repetitions ignored.

Additional details for data contributing to safety variables, including additional definitions, can be found in the protocol (Section 8.4).

5. GENERAL STATISTICAL CONSIDERATIONS

5.1. General Principles

If participants completed assessments at both scheduled and supplementary visits for a post-baseline visit with no issues (e.g., technical problems) identified for the scheduled visit, the assessments from the scheduled visit will be considered in the statistical analyses, tabular summaries, and figures. If participants completed assessments at both scheduled and supplementary visits for a post-baseline visit with issues identified for the scheduled visit, the assessments from the supplementary visit with no identified issues occurring in closest succession to the scheduled visit will be considered in the statistical analyses, tabular summaries, and figures. If an assessment is completed only at supplementary visits for post-baseline visits, then the assessment from the earliest supplementary visit occurring after the scheduled visit with no identified issues will be included in the statistical analyses, tabular summaries, and figures. Results of all assessments, including those completed at supplementary visits, will be included in the listings.

Continuous demographic and baseline characteristics will be summarized by the non-missing sample size (denoted as "n"), mean, standard deviation (SD), minimum, and maximum. Immunological data will be summarized by "n," the arithmetic or geometric mean (depending on the distribution of the data), and the corresponding 95% CI. The preferred approach for computing CIs for continuous variables will be based on the t-distribution with n-1 degrees of freedom, where n denotes the number of observations. If the data are found to be non-normal (by visual inspection of histograms and quantile-quantile [Q-Q] plots), and the sample size is insufficient for application of the central limit theorem, nonparametric bootstrap confidence intervals may be calculated instead.

Categorical variables will be descriptively summarized by frequencies and percentages of observed levels, based on the non-missing sample size. Exact Clopper-Pearson CIs will be computed for binary variables, where required. When calculating incidence, or any sub-classification thereof (e.g., severity, relatedness, etc.) each participant will only be counted at most once at the maximum value of the respective variable (e.g., maximum severity, maximum relatedness, etc.), and any repetitions will be ignored.

In general, summaries will be presented by dose group (interchangeable with "analysis group"). Dose groups will include sentinel and expanded participants, and the High Dose group will include a total of 20 participants: the 10 participants originally enrolled into the High Dose group and the 10 participants enrolled into the High Dose group after it was chosen as the optimal dose. All tables will be annotated with the total population size relevant to that table, including any missing observations. The analysis population for each exhibit will be clearly indicated.

Data listings will typically be sorted by ascending dose group with the IIV4 group last (i.e., Low Dose, then Medium Dose, then High Dose, then IIV4), participant, and visit number within participant, where appropriate. In the CSR, participant identifiers assigned by the site staff will be replaced with the Study Data Tabulation Model (SDTM) variable USUBJID in all data listings to protect the confidentiality of participants. USUBJID will be a composite of the 3-letter EDC platform code followed by a numeric identifier assigned chronologically to enrolled participants and individuals screened but not enrolled in the EDC platform.

5.2. Timing of Analyses

A review of safety data was completed and approval was provided from the SRC prior to enrolling expanded participants within each dose group (review of data through Day 3) and prior to enrolling participants in the next highest dose group (review of data through the Day 8 visit).

An interim immunogenicity analysis through Day 57 presented a high-level overview of interim participant disposition, demographics and baseline characteristics, and primary safety data, as well as summaries of secondary immunogenicity data.

The CSR will be completed after all primary and secondary endpoint data are available and clinical and relevant non-clinical data have been cleaned and locked. Any available data from exploratory endpoints may also be included. Additional exploratory endpoint data not available at the time of the CSR would be included in one or more addenda to the CSR, manuscript(s), or other report.

5.3. Analysis Populations

Analyses will be conducted within one of the following populations.

5.3.1. Screened Population

The Screened population will include all individuals screened. This population will be used for summaries relating to reasons for not enrolling and participant disposition.

5.3.2. Intent-to-Treat (ITT) Population

The Intent-to-Treat (ITT) population will include all enrolled participants who received the study vaccination. This population will be used for summaries of participant demographics and baseline characteristics, and immunogenicity assessments. All participants will be summarized according to the dose group to which they were enrolled. If all participants receive the assigned dose, the ITT population will be the same as the safety population.

5.3.3. Safety Population

The Safety population will include all participants who received the study vaccination. This population will be used for analyses of reactogenicity and adverse events. All participants will be summarized according to the dose received. If all participants receive the assigned dose, the safety population will be the same as the ITT population.

5.3.4. Per-Protocol (PP) Population

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

- Data from participants ineligible at baseline (determined thereafter).
- Data from any post-baseline visit that occurs substantially out of window, defined as occurring out of the specified visit window.
- Data from any post-baseline visit occurring less than 28 days after an AE in the PT “Influenza”.
- Data from all visits subsequent to events that could impact the validity of later data, such as:
    - Receipt of the incorrect study vaccination dose.
    - Receipt of the following, with exclusion determined by the Sponsor, or other concomitant medications with exclusions determined by the Sponsor:
        - Immunosuppressives or other immune-modifying drugs. Low dose topical and intranasal steroid preparations were to be permitted.

- Anticancer chemotherapy or radiation therapy (cytotoxic).
- Oral or parenteral (including intra-articular) corticosteroids.
- High-dose inhaled or nebulized corticosteroids.
- Seasonal influenza vaccine prior to the Day 57 visit.
- Investigational H1 or H5 influenza vaccine.
- Ferritin-based vaccine.
- Immunoglobulin and/or any blood products (except Rho D immunoglobulin).
- An experimental agent, other than those administered as per protocol.
- Interventional agents, including licensed or unlicensed vaccine, drug, biologic device, blood product, or medication.

The PP population will be used for sensitivity analyses of secondary endpoints if more than 10% of secondary endpoint observations across Days 1, 8, 15, 29 and 57 are excluded by the PP exclusions. All participants will be summarized according to the dose group to which they were enrolled.

5.4. Subgroups, Interactions and Covariates

The study is not powered for any formal subgroup analyses, but exploratory subgroup analyses will be conducted.

Participants were allowed to receive the seasonal influenza vaccine more than 90 days before enrollment and after 60 days post-study vaccination. Therefore, to control for this potential confounding, immunologic endpoints assessed prior to Day 60 will be stratified by receipt of the prior season's influenza vaccine within a dose group. Immunologic endpoints assessed after Day 60 will be separately stratified by receipt of the subsequent receipt of the current season's influenza vaccine within a dose group. Stratified summaries will only be presented if there are at least three participants in each subgroup, for a given dose group. Additional details of these stratified analyses are outlined in Section 7.1 and 7.2.

All planned analyses that include covariates or interactions are exploratory in nature and are meant to supplement the main analyses.

5.5. Missing Data and Outliers

All attempts were to be made to collect all data per protocol during the study. No imputation is planned for missing data apart from what is described in Section 3.3.

Any data point that, in the opinion of the statistical team, appears to be erroneous or inexplicable based on the observed data distribution will be investigated as a possible outlier. If any data points are identified as possible outliers (via visual inspection of histograms, Q-Q plots, and further investigation of observations that appear to fall outside of the range of the other observed values), sensitivity analyses may be performed by examining the impact of their exclusion on the results. Any substantive differences between the analysis results will be reported.

5.6. Interim Analyses and Data Monitoring

5.6.1. Interim Analyses

An interim analysis, focused primarily on secondary immunogenicity endpoints, was conducted while the study was ongoing. The results of this analysis were made available to aid with planning of future studies. There was not public dissemination of results and the results were not used to make any decisions concerning the conduct of the trial.

The interim analysis included a high-level overview of interim participant disposition, demographics and baseline characteristics, and primary safety data, as well as secondary immunogenicity data (e.g., RMN, MN, and anti-HA stalk in serum) collected through Day 57. Immunogenicity data were aggregated by dose group and participant-level immunogenicity data were not presented to avoid inadvertent impact on future results or data collection.

5.6.2. Data Monitoring Committee

Two safety committees were convened for this study: the SRC and the Safety Monitoring Committee (SMC). Refer to Section 10.1.6 of the protocol for more details.

The SRC reviewed safety data to allow for progression through the dose groups as described in Section 4.1. The SMC had an organizational meeting and planned to conduct reviews of safety data if i) a halting rule was met (refer to Section 7.1.1 of the protocol), ii) the SRC requested a review of the data, iii) as regularly scheduled per the SMC charter, and iv) ad hoc when requested by the sponsor, investigators or SMC. The SMC will also review the safety and tolerability at the conclusion of the trial.

Interim safety reviews included enrollment and demographic information, clinical laboratory tests, and unsolicited AEs. During SMC reviews, additional data may have been requested by the SMC.

5.7. Multiple Comparisons/Multiplicity

Analyses are mostly descriptive in nature. No adjustments for multiplicity are planned, but the number of comparisons made will be factored into the interpretation of results, as appropriate. No adjustment will be made for the interim analysis as the results did not affect the conduct of the trial.

6. STUDY PARTICIPANTS

6.1. Disposition of Participants

Disposition of participants will be tabulated by dose group. Disposition events to be summarized will be the total number of individuals screened, and the number of participants enrolled, received study vaccination, completed at least one post-baseline secondary endpoint visit (Day 8, 15, 29 or 57), completed follow-up through the end of the study, completed all post-baseline visits, completed the study per-protocol, and terminated early from the study (Table 10). A flowchart showing the disposition of study participants and the inclusion of participants in analyses will be generated (Figure 1). This figure will present by dose group the number of individuals screened, the number of individuals not enrolled, and the number of participants enrolled, vaccinated, completed the study, terminated early, and analyzed.

Reasons for individuals not enrolling will be listed (Listing 2) and summarized by reason and by dose group (Table 11).

Dates of first and last study product administration by dose group will also be presented (Table 12).

A summary of the reasons for exclusion from analysis populations will be presented by dose group (Table 13).

The following participant listings will be generated:

- Listing of participants who received study product along with their dose assignment, date of vaccine administration, and any relevant study product administration deviations (Listing 1).
- Listing of participants who terminated early from the study along with the reason for early termination (Listing 3).
- Listing of participants excluded from any analysis population (Listing 6).

6.2. Demographic and Other Baseline Characteristics

Demographic and baseline characteristics including age, sex, ethnicity, race, and receipt of the prior season's seasonal influenza vaccination will be summarized by dose group (Table 14). Demographic and baseline characteristics will be detailed per participant (Listing 7).

6.3. Prior and Concurrent Medical Conditions

All current illnesses and past or pre-existing medical conditions will be coded using the Medical Dictionary for Regulatory Activities (MedDRA®) version 28.0 or higher.

Summaries of participants' prior and concurrent medical conditions will be presented by dose group and MedDRA® system organ class (SOC) for the Safety population (Table 15).

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

6.4. Prior and Concomitant Medications

Prior (within 30 days of receipt of study product) and concomitant medications, excluding influenza viral challenges and vaccinations, will be coded to the Anatomical Therapeutic Classification (ATC) using the World Health Organization (WHO) Drug Dictionary. The use of prior and concomitant medications during the study will be summarized by ATC1 and ATC2 code, as well as dose group, for the Safety population (Table 66).

A listing of prior and concomitant medications by participant will be presented (Listing 18).

6.5. Prior Influenza Viral Challenges and Vaccinations

All prior influenza viral challenges and vaccinations will be presented in (Listing 9). Seasonal influenza vaccination history from the 2021/2022, 2022/2023, and 2023/2024 seasons was to be obtained and will be presented.

6.6. Measurements of Study Product Compliance

Participants were to be directly observed at the time of dosing by a member of the clinical research team who was licensed to administer the study product. Participants were to have received one dose of study product. The number of participants receiving the study product will be presented by dose group as part of the participant disposition table (Table 10). Details of study product administration by participant will be provided (Listing 1).

6.7. Protocol Deviations

A summary of participant-specific protocol deviations will be presented by deviation classification (major or minor), deviation category, deviation type and dose group for all enrolled participants (Table 9). A participant listing of all participant-specific protocol deviations and a listing of all non-participant-specific protocol deviations will be generated (Listing 4 and Listing 5, respectively).

7. IMMUNOGENICITY EVALUATION

Immunogenicity analyses will be conducted in the ITT population. Immunogenicity results will be listed (Listing 10).

7.1. Analyses Supporting Secondary Immunogenicity Objectives

7.1.1. Endpoints and Estimands

Secondary immunogenicity endpoints include: i) GMT of homologous H1-specific neutralizing antibodies in a reporter microneutralization assay at Days 1, 8, 15, 29, and 57 by analysis group and stratified by prior season's receipt of seasonal influenza vaccine within each analysis group; ii) GMFR from baseline (Day 1) of homologous H1-specific neutralizing antibodies in a reporter microneutralization assay at Days 8, 15, 29, and 57 by analysis group and stratified by prior season's receipt of seasonal influenza vaccine within each analysis group; iii) GMT of homologous H1-specific neutralizing antibodies in a viral microneutralization assay at Days 1, 8, 15, 29, and 57 by analysis group and stratified by prior season's receipt of seasonal influenza vaccine within each analysis group; iv) GMFR from baseline (Day 1) of homologous H1-specific neutralizing antibodies in a viral microneutralization assay at Days 8, 15, 29, and 57 by analysis group and stratified by prior season's receipt of seasonal influenza vaccine within each analysis group; v) GMT of anti-stalk serum antibodies, measured by ELISA at Days 1, 8, 15, 29, and 57 by analysis group and stratified by prior season's receipt of seasonal influenza vaccine within each analysis group; vi) GMFR from baseline (Day 1) of anti-stalk serum antibodies, measured by ELISA, at Days 8, 15, 29, and 57 by analysis group and stratified by prior season's receipt of seasonal influenza vaccine within each analysis group.

Vaccination conditions, target populations, intercurrent events, and population-level summaries for secondary immunogenicity objectives are described below:

Vaccination conditions: 10 mcg VRC H1ssF_3928 mRNA-LNP (Low Dose); 25 mcg VRC H1ssF_3928 mRNA-LNP (Medium Dose); 50 mcg VRC H1ssF_3928 mRNA-LNP (High Dose); 60 mcg IIV4.

Target population: Healthy adult volunteers 18 through 49 years of age meeting the protocol defined eligibility criteria.

Intercurrent events: Any intercurrent events, such as events that impact the validity of later data, will be handled with the while-on-treatment strategy in sensitivity analyses if needed (see Section 5.3.4).

Population-level summary: GMT and GMFR at each available timepoint under each vaccination condition for each assay (i.e., homologous H1-specific neutralizing antibody titers in a RMN assay, homologous H1-specific neutralizing antibody titers in a viral MN assay, and anti-HA stalk antibody titers measured by ELISA).

7.1.2. Main Analysis

Homologous H1-specific neutralizing antibody titers in a RMN assay and a viral MN assay are measured in serum against A/New Caledonia/20/1999 (H1N1). Anti-HA stalk antibody titers measured by ELISA are measured in serum against A/New Caledonia/20/1999 (H1N1). Results will be summarized by dose group. GMTs and associated 95% CIs will be presented for baseline (Day 1) and Days 8, 15, 29 and 57, and GMFR and associated 95% CIs will also be presented for visits post-baseline (Table 16, Table 20, and Table 24 for RMN, MN, and anti-HA stalk, respectively). Results will be similarly summarized, stratified by receipt of the

prior season's influenza vaccine within each dose group (Table 17, Table 21, and Table 25 for RMN, MN, and anti-HA stalk, respectively).

Titers will be presented graphically over time via line graphs displaying the GMT and associated 95% CIs, and GMFR and associated 95% CIs for post-baseline time points, for each dose group (Figure 2, Figure 8, and Figure 14 for RMN, MN, and anti-HA stalk, respectively) and stratified by prior season's receipt of seasonal influenza vaccine within each dose group (Figure 3, Figure 9, and Figure 15 for RMN, MN, and anti-HA stalk, respectively).

7.1.3. Sensitivity Analysis

If sufficient data (>10% of secondary immunologic endpoint observations across Days 8, 15, 29 and 57) would be excluded by the PP exclusions, sensitivity analyses will be performed utilizing the PP population for the main secondary immunogenicity analyses.

For secondary immunogenicity assays with an LLOQ that is distinct from the LOD, a sensitivity analysis will be performed imputing values below LLOQ as LLOQ/2 for the main secondary immunogenicity analyses, instead of the derivation in Section 3.3; applicable tables from Section 7.1.2 will be regenerated with this alternative imputation approach.

7.1.4. Supplementary Analyses

To supplement the primary analyses of GMFR for secondary immunogenicity assays, a generalized estimating equations (GEE) analysis with robust standard errors will be conducted. (Log-transformed) Fold-rise will be analyzed as the outcome and robust standard errors will be utilized. The following covariates will be included: dose group; post-baseline study visits (as a categorical variable, including exploratory immunogenicity timepoints at Days 85, 181, and 366); an interaction between dose group and post-baseline study visit; (log base 2-transformed) baseline titer for the applicable assay; participant's sex; participant's age at the time of enrollment (in years); and previous seasonal influenza receipt (yes or no, defined in Section 3.2) will be included to adjust for potential confounding. The unstructured correlation structure will be preferred. If the model fails to converge with an unstructured correlation structure, the compound symmetric correlation structure will be utilized. If convergence challenges persist, forward model selection may be considered.

The ratio of GMFRs between each pair of dose groups, and associated Wald 95% CI and p-values, after adjusting for the other covariates included in the model, will be presented for each post-baseline study visit (Table 18, Table 22, and Table 26 for RMN, MN, and anti-HA stalk, respectively) and will be presented graphically (Figure 5, Figure 11, and Figure 17 for RMN, MN, and anti-HA stalk, respectively). Also presented will be the estimated ratio of GMFRs, associated 95% CIs, and associated p-values from a 2-fold increase in baseline titer, between males and females, from an increase in participants' age at the time of enrollment of 5 years, and between those with and without previous seasonal influenza receipt (Table 18, Table 22, and Table 26 for RMN, MN, and anti-HA stalk, respectively).

The duration and period of enrollment for each dose group (Table 12) will be taken into consideration when interpreting results.

7.2. Analyses Supporting Exploratory Immunogenicity Objectives

Homologous H1-specific neutralizing antibody titers in a RMN and MN assay, and anti-HA stalk antibody titers measured by ELISA will be summarized at Days 85, 181, and 366 by dose group (Table 16, Table 20, and Table 24, respectively) and separately stratified by receipt of the prior season's influenza vaccine and by

subsequent receipt of a seasonal influenza vaccine (Table 17, Table 21, and Table 25, respectively). Titers will be presented graphically over time via line graphs displaying the GMT and associated 95% CIs, and GMFR and associated 95% CIs for post-baseline time points, for each dose group and stratified by prior (Figure 3, Figure 9, and Figure 15 for RMN, MN, and anti-HA stalk, respectively) and subsequent (Figure 4, Figure 10, and Figure 16 for RMN, MN, and anti-HA stalk, respectively) receipt of a seasonal influenza vaccine within each dose group. Figures stratified by subsequent receipt will only present baseline and Days 85, 181, and 366.

Neutralizing antibody responses and anti-stalk serum antibody responses to divergent H1 influenza virus isolates and other Group 1 non-H1 influenza virus isolates at Day 1 and 29 will be analyzed in a similar manner to the secondary immunogenicity analyses (Table 19, Figure 6, and Figure 7 for RMN, Table 23, Figure 12, and Figure 13 for MN, and Table 27, Figure 18, and Figure 19 for anti-HA stalk).

H. Pylori ferritin binding, human ferritin light chain binding, and human ferritin heavy chain binding will be reported from the anti-ferritin assay as the AUC. Mean AUC and associated 95% CIs will be presented for each dose group (Table 28, Table 30, and Table 32 for binding, light chain binding, and heavy chain binding, respectively), and stratified by prior receipt of seasonal influenza vaccination, and, where applicable, stratified by subsequent receipt of seasonal influenza vaccination (Table 29, Table 31, and Table 33 for binding, light chain binding, and heavy chain binding, respectively). Arithmetic mean and arithmetic mean change from baseline, and associated 95% CIs, of AUC will also be presented graphically over time, stratified as applicable (Figure 20-Figure 28).

B-cells, T-cells, and Tfh cells will be summarized by parent population and stimulation, unstratified and stratified by prior season's receipt and subsequent receipt of seasonal influenza vaccine as applicable. For each parent population and stimulation combination, the percent of cells expressing a given marker or the MFI for each marker, as applicable, will be summarized along with the total number of cells in the parent population (unstratified in Table 34, Table 36, and Table 38 and stratified in Table 35, Table 37, and Table 39 for B-cells, T-cells, and Tfh cells, respectively). For markers where the percentage of cells expressed is reported, the mean percentage of cells and mean difference from baseline and associated 95% CIs for post-baseline time points for each dose group (Figure 29), and further stratified by prior (Figure 30) and subsequent (Figure 31) receipt of a seasonal influenza vaccine within each dose group, will be presented for each cell marker and will exclude presentation of the overall parent population. Similar figures will be generated for markers where MFI is reported (Figure 32, Figure 33, and Figure 34). Figures stratified by subsequent receipt will only present baseline and Days 85, 181, and 366.

Results from exploratory immunogenicity objectives will be included in one or more CSR addenda, manuscript(s), or other report as data are available if data are unavailable at the time of the CSR.

8. SAFETY EVALUATION

All summaries and analyses of safety data will be presented for the Safety population. The denominator for percentages will be based on the number of participants in the Safety population, unless otherwise specified. Summaries will be presented by dose group, as well as for all participants receiving the mRNA-LNP vaccine (i.e., "Any Non-IIV4 Dose").

8.1. Analyses Supporting Primary Objective

8.1.1. Endpoints and Estimands

Safety endpoints include: i) number and percentage of participants experiencing solicited local and systemic reactogenicity AEs through 14 days; ii) number and percentage of participants experiencing any unsolicited AEs through 28 days; iii) number and percentage of participants experiencing any MAAEs, NOCMCs, AESIs corresponding to Grade 2 or greater decrease in lymphocyte or neutrophil count, ILIs, and SAEs through one year (Day 366) and myocarditis, pericarditis, or myopericarditis as AESIs, through Day 57; and iv) number and percentage of participants experiencing clinical laboratory AEs through 57 days (Day 57).

Vaccination conditions, target populations, and population-level summaries are the same across all primary safety endpoints and are described below:

Vaccination conditions: 10 mcg VRC H1ssF_3928 mRNA-LNP (Low Dose); 25 mcg VRC H1ssF_3928 mRNA-LNP (Medium Dose); 50 mcg VRC H1ssF_3928 mRNA-LNP (High Dose); 60 mcg IIV4.

Target population: Healthy adult volunteers 18 through 49 years of age who received study product.

Population-level summary: Number and percentage of participants under each vaccination condition, calculated by severity where applicable.

8.2. Adverse Events

Details of AEs and SAEs can be found in the protocol (Section 8.4.1 and Section 8.4.2, respectively). AESIs were defined as post-vaccination myocarditis, pericarditis, or myopericarditis (through Day 57), or as a Grade 2 or greater decrease in lymphocyte or neutrophil count as described in the protocol (Section 8.4.8). ILIs, SAEs, MAAEs and NOCMCs were defined in the protocol (Section 8.3.4, Section 8.4.2, Section 8.4.9, and Section 8.4.10, respectively). Adverse events will be coded according to the MedDRA® dictionary version 28.0 or higher.

Solicited AEs were to be collected through an electronic memory aid in Advantage eClinical℠ (Electronic Data Capture System) or through a paper memory aid through Day 14. Solicited AEs consisted of local reactogenicity and systemic reactogenicity (graded as per Table 3). Unsolicited AEs were to be reported for each participant from administration of study vaccine through Day 29. AESIs corresponding to myocarditis, pericarditis or myopericarditis and clinical laboratory AEs were to be reported through Day 57. AESIs corresponding to Grade 2 or greater decrease in lymphocyte or neutrophil count, MAAEs, NOCMCs, ILIs, and SAEs were to be reported through the participants' time on study.

8.2.1. Overall Summary

An overall summary of adverse events will be generated which includes the percent of participants reporting at least one of the following events, by dose group: local solicited AE, systemic solicited AE, unsolicited AE, related unsolicited AE (by severity), severe unsolicited AE (by relatedness), unsolicited AE through Day 29,

SAE, related SAE, MAAE, NOCMC, AESI corresponding to a Grade 2 or greater decrease in lymphocyte or neutrophil count; AESI corresponding to myocarditis, pericarditis, or myopericarditis (through Day 57); ILI, clinical laboratory AE (by type, through Day 57); AE leading to early termination, and AE classified as an unanticipated problem (Table 40).

Unsolicited, solicited, and laboratory AEs reported in at least 5% of participants in any dose group will be summarized by MedDRA preferred term (PT) and MedDRA SOC (Table 41).

8.2.2. Solicited Events/Symptoms

Summaries of solicited (local and systemic) AE data through Day 14 will be generated for the safety population. For summaries by severity, the maximum severity post-vaccination will be identified for each participant. For summaries independent of severity, a participant will be classified as reporting the event if their maximum severity for the event was classified as mild or worse. Denominators for percentages will be the number of participants with any solicited data available. Analyses of solicited AEs will be descriptive in nature and any intercurrent events will not be accounted for in summaries.

The number and percentage of participants reporting any solicited event, any local event, any systemic event, and each applicable solicited adverse event individually will be summarized by maximum severity with 95% exact Clopper-Pearson CIs (Table 42) and presented graphically in a bar chart (Figure 35 for local events and Figure 36 for systemic events).

The number of participants reporting a solicited adverse event by day post-dosing will be presented graphically in a bar chart (Figure 37 for local events and Figure 38 for systemic events).

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

8.2.3. Unsolicited Adverse Events

All unsolicited AEs through Day 29 will be summarized by MedDRA SOC, MedDRA PT, severity, and relation to study vaccination.

Each summary table will present the frequency and percentage of participants reporting at least one unsolicited adverse event, as well as the number of events reported. Denominators for percentages will be the number of participants in the safety population (i.e., received study product). Analyses of unsolicited AEs will be descriptive in nature and any intercurrent events will not be accounted for in summaries.

The following summaries of unsolicited AEs through Day 29 will be provided:

- Incidence with 95% CI, and total frequency of events over time (Table 43).
- Summary of events by severity (Table 44).
- Summary of related events by severity (Table 45).
- Bar chart of the frequency of events by severity (Figure 39).
- Bar chart of the incidence of events by severity (Figure 40).

If at least five related unsolicited AEs through Day 29 were reported, a table summarizing the incidence with 95% CI, and total frequency of related events over time (similar to Table 43) will be presented, as well as bar charts of frequency (similar to Figure 39) and incidence (similar to Figure 40).

All unsolicited AEs that occurred through Day 29 will be presented by participant (Listing 13).

8.2.4. Clinical Laboratory Adverse Events

Chemistry parameters assessed as part of clinical safety evaluations include creatinine, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), bilirubin, and lipase. Troponin, iron, total iron binding capacity, and ferritin were to also be collected, but not assessed for severity. Hematology parameters to be assessed included hemoglobin (Hgb), white blood cells (WBC), lymphocyte count, neutrophil count, platelet count, prothrombin time, activated partial thromboplastin time, and fibrinogen. Analyses of clinical laboratory AEs will be descriptive in nature and any intercurrent events will not be accounted for in summaries.

The laboratory AE summary table will present the frequency and percentage of participants reporting at least one laboratory AE through Day 57, as well as the number of events reported (Table 46). Denominators for percentages will be the number of participants in the safety population (i.e., received study product).

The number and percentage of participants reporting laboratory AEs overall, and by type (e.g., chemistry or hematology) will also be presented, as well as the number of percentage of participants reporting laboratory AESIs (Grade 2 [moderate] or greater decrease in lymphocyte or neutrophil count), in Table 40. The reporting of a laboratory AE by at least one participant in a given dose group will result in at least 5% of participants having reported the specified laboratory event in the given dose group. As such, the incidence and frequency of clinical laboratory AEs, as defined in Section 4.6.2 and graded as per Table 4, will be summarized by laboratory parameter in Table 41.

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

Analyses of MAAEs, NOCMCs, non-laboratory AESIs, ILIs, and SAEs will be descriptive in nature and any intercurrent events will not be accounted for in summaries. Similar presentations to those described in Section 8.2.3 will be provided for the following events not included in protocol halting rules, if at least five events of the given event type are reported:

- MAAEs
  - Incidence with 95% CI, and total frequency of events over time (Table 47).
  - Summary of events by severity (Table 48).
  - Summary of related events by severity (Table 49).
  - Bar chart of the frequency of events by severity (Figure 41).
  - Bar chart of the incidence of events by severity (Figure 42).
- NOCMCs
  - Incidence with 95% CI, and total frequency of events over time (Table 50).
  - Summary of events by severity (Table 51).
  - Summary of related events by severity (Table 52).
  - Bar chart of the frequency of events by severity (Figure 43).
  - Bar chart of the incidence of events by severity (Figure 44).
- ILIs
  - Incidence with 95% CI, and total frequency of events over time (Table 53).

- Summary of events by severity (Table 54).
- Summary of related events by severity (Table 55).
- Bar chart of the frequency of events by severity (Figure 45).
- Bar chart of the incidence of events by severity (Figure 46).

Participant listings will be provided for SAEs (Table 56); as well as non-serious, unsolicited, moderate or severe adverse events (Table 57); and other significant adverse events (e.g., MAAEs; NOCMCs; AESIs corresponding to myocarditis, pericarditis or myopericarditis [through Day 57]; and ILIs, Table 58).

8.4. Clinical Laboratory Evaluations

Scheduled clinical laboratory assessments were to be performed at screening, prior to vaccination on Day 1 (baseline), and on Days 8, 29, and 57. Screening results will be excluded from summary tables but included in listings.

Chemistry parameters assessed as part of clinical safety evaluations include creatinine, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), bilirubin, and lipase. Troponin, iron, total iron binding capacity, and ferritin were also to be collected, but not assessed for severity. Hematology parameters to be assessed included hemoglobin (Hgb), white blood cells (WBC), lymphocyte count, neutrophil count, platelet count, prothrombin time, partial thromboplastin time, and fibrinogen. Urinalysis parameters were to be assessed as negative or positive for screening purposes and include human chorionic gonadotropin, amphetamine, cocaine, opiate, and cannabinoids; these will not be presented or analyzed in the final CSR.

Laboratory values were to be graded, if applicable, according to the protocol-defined toxicity table (Table 4). Abnormal values will be listed for chemistry parameters (Table 59) and hematology parameters (Table 60). Clinical laboratory assessments will be listed in full for chemistry parameters (Listing 14) and hematology parameters (Listing 15).

The incidence of graded values, including those at screening and baseline and those not deemed laboratory AEs (see Section 8.2.4), for chemistry laboratory parameters (Figure 47, Figure 48, Figure 49, and Figure 50 for Low Dose, Medium Dose, High Dose, and IIV4, respectively) and hematology laboratory parameters (Figure 51, Figure 52, Figure 53, and Figure 54 for Low Dose, Medium Dose, High Dose, and IIV4, respectively) by severity and time point will also be presented graphically, separately for each dose group.

8.5. Vital Signs and Physical Evaluations

Vital signs, including oral temperature, heart rate, and blood pressure (systolic and diastolic), were to be assessed at screening, baseline (Day 1) and Days 3, 8, 15 and 29. Vital signs were to be graded according to the protocol (Table 5). Data may have been collected at other visits at the discretion of the investigator. Vital signs will be summarized by maximum severity and time point in Table 61 - Table 65 A participant listing of vital signs will be presented (Listing 16).

A full physical examination was to be performed at screening, and a targeted physical exam may have been performed at any other visit. A participant listing of physical examination findings will be presented (Listing 17). The following body systems will be assessed: Abdomen; Cardiovascular/Heart; Extremities; General Appearance; Head, Eyes, Ears, Nose, and Throat (HEENT): Lymph Nodes; Musculoskeletal; Neck; Neurological; Pulmonary/Chest; and Skin.

8.6. Pregnancies

For any participants in the Safety population who became pregnant during the study, every attempt will be made to follow these participants to completion of pregnancy to document the outcome, including information regarding any complications with pregnancy and/or delivery. Participant listings of pregnancies and pregnancy outcomes will be generated (Listings 19-23).

9. REPORTING CONVENTIONS

The mean, SD, other summary statistics, except the minimum and maximum, and results derived from statistical models will be reported to 1 decimal place greater than the original data. The minimum and maximum will use the same number of decimal places as the original data.

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

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

10. TECHNICAL DETAILS

SAS version 9.4 or above, or R version 4.5.1 or above, will be used to generate all tables, figures and listings.

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

There are no changes in the conduct of the study or planned analyses.

12. LISTING OF TABLES, FIGURES, AND LISTINGS

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

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Table 1: Study Schema

Group/Dose Group	Subgroup	VRC H1ssF_3928 mRNA LNP Dose[1]	Number of Participants
Low Dose	Sentinel[2]	10 mcg VRC H1ssF_3928 mRNA-LNP	2
	Expanded[3]	10 mcg VRC H1ssF_3928 mRNA-LNP	8
Medium Dose	Sentinel[2]	25 mcg VRC H1ssF_3928 mRNA-LNP	2
	Expanded[3]	25 mcg VRC H1ssF_3928 mRNA-LNP	8
High Dose[5]	Sentinel[2]	50 mcg VRC H1ssF_3928 mRNA-LNP	2
	Expanded[3]	50 mcg VRC H1ssF_3928 mRNA-LNP	18
	Subgroup	**IIV4 Dose[4]**	
IIV4	Immunogenicity Comparator	60 mcg (15 mcg / antigen)	10
Total			50

[1] VRC H1ssF_3928 VRC H1ssF_3928 mRNA-LNP given as an IM injection on Day 1.
[2] SRC review of the reactogenicity and AE data available from enrollment through Day 3 for the first 2 sentinel participants (VRC H1ssF_3928 mRNA- LNP) was conducted prior to initiation of enrollment of the remaining participants in the Group. If deemed necessary by the SRC, the Safety Monitoring Committee (SMC) would also review the safety data.
[3] SRC review of the reactogenicity and AE data available from enrollment through the post vaccination Day 7 visit and clinical laboratory results through Day 8 for the Group were conducted prior to initiation of enrollment in the next highest dosing group. If deemed necessary by the SRC, the SMC would also review the safety data.
[4] Licensed quadrivalent inactivated influenza vaccine (IIV4) given as an IM injection at Day 1.
[5] High dose includes 10 participants enrolled into the optimal dose group.

Table 2: Schedule of Activities

Procedures	Study Visit 0 Screening Day -14 to -1	Enrollment/Baseline Visit 1, Day 1	Study Visit 2 Day 3 +/- 1 day	Study Visit 3 Day 8 +/- 2 days	Study Visit 4 Day 15 +/- 2 days	Study Visit 5 Day 29 +/- 3 days	Study Visit 6 Day 57 +/- 3 days	Study Visit 7 Day 85 +/- 7 days	Study Visit 8 Day 181 +/- 7 days	Study Visit 9 Day 366 +/- 7 days	Unscheduled Visit[21]	Early Termination Visit
Type of Visit	**Clinic**	**Clinic**	**Clinic**	**Clinic**	**Clinic**	**Clinic**	**Clinic**	**Clinic**	**Clinic**	**Clinic**	**Clinic**	**Clinic**
Informed consent[1]	X											
Review / Confirm Eligibility Criteria	X	X										
Abstinence and contraception counseling[16]	X	X	X	X	X	X	X					X
Demographics[2]	X											
Medical history[3]	X	X										X
Influenza vaccination history[3]	X	X	X	X	X	X	X	X	X	X	X	X
Concomitant medication review[4]	X	X	X	X	X	X	X	X	X	X	X	X
Complete physical exam (including height and weight)[5]	X											
Targeted physical exam[5]		X	X	X	X	X	X	X	X	X	X	X
ECG (12-lead)	X		X	X[17]	X[17]	X[17]	X[17]	X[17]	X[17]	X[17]	X[17]	X[17]
Vital signs[6]	X	X	X	X	X	X	X[17]	X[17]	X[17]	X[17]	X[17]	X[17]
Hematology[7]	X	X		X		X	X				X[17]	X[17]
Coagulation studies[8]	X	X		X		X	X				X[17]	X[17]
Serum chemistry[9]	X	X		X		X	X				X[17]	X[17]
Troponin	X	X[18]	X[18]	X[17]	X[17]	X[17]	X[17]	X[17]	X[17]	X[17]	X[17]	X[17]
Blood for HIV 1 and 2 antigen/antibody, HBV, and HCV	X											
Serum HCG	X											
Urine Toxicology Screen[10]	X											
Urine HCG[11]		X										

Table 2: Schedule of Activities *(continued)*

Procedures	Study Visit 0 Screening Day -14 to -1	Enrollment/Baseline Visit 1, Day 1	Study Visit 2 Day 3 +/- 1 day	Study Visit 3 Day 8 +/- 2 days	Study Visit 4 Day 15 +/- 2 days	Study Visit 5 Day 29 +/- 3 days	Study Visit 6 Day 57 +/- 3 days	Study Visit 7 Day 85 +/- 7 days	Study Visit 8 Day 181 +/- 7 days	Study Visit 9 Day 366 +/- 7 days	Unscheduled Visit[21]	Early Termination Visit
Administer study product		X										
Solicited AEs[12]		X	X	X	X							
Non-serious unsolicited AEs[13]		X	X	X	X	X						
MAAEs, NOCMCs, AESIs, SAEs[14]		X	X	X	X	X	X	X	X	X	X	X
Nasal absorptive matrix for secondary research		X[19]	X	X	X	X	X				X[17]	X[17]
Serum for immunologic assessments (e.g., MN, Stalk, Breadth)		X[19, 20]	X	X	X	X[20]	X	X	X[20]	X	X[17]	X[17]
PBMC and plasma collection for exploratory and secondary research		X[19]		X	X	X	X	X	X	X	X[17]	X[17]
Whole blood PAXgene tube for secondary research		X[19]	X	X							X[17]	X[17]
ILI Visit (e.g., nasopharyngeal swab for influenza virus RT-PCR testing)[15]											X	

Prior to any study related procedures, participants will be provided information about the study and informed consent will be obtained from the participant.
The investigator or appropriately delegated study staff will obtain demographic data.
The investigator or appropriately delegated study staff will obtain medical history, influenza vaccination history and information necessary to determine eligibility. Since screening may occur up to 14 days before enrollment, if eligibility and medical history are taken at a screening visit, they will be updated on the day of enrollment, before administration of study product. Demography will not be updated.
Medications taken by the participant in the 30 days before enrollment will be recorded (while all medications taken from 90 days prior to screening, whether on the same day as enrollment or not, will be solicited). At subsequent visits, until Visit 9 (Day 366) updates to previous concomitant medications and additional medications taken in the interim will be recorded.
Physical examination will occur for all participants at Visit 0. Participants may receive an optional targeted physical exam at any other clinic visits at investigator discretion.
Vital signs include oral temperature, heart rate, and blood pressure
Hematology includes white blood cell count with differential, hemoglobin and platelet count. If low levels of Hb are found, it will be under the PI's discretion to decide the amount of blood, if any, that can be withdrawn in the following visit
Coagulation studies includes prothrombin time (PT), activated partial thromboplastin time (APTT) and fibrinogen. If abnormal levels are found, it will be under the PI's discretion to continue with protocol procedures such as blood withdrawn at the following visit.
Serum chemistry includes creatinine, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, total bilirubin, lipase, total iron binding capacity, serum iron, and ferritin
Negative drug urine toxicology result (amphetamines, cocaine, and opiates) required at screening.
Urine pregnancy test will be performed for females of childbearing potential within the 24 hours prior to study product administration. Result must be negative before study product can be administered.

Table 2: Schedule of Activities *(continued)*

Procedures	Study Visit 0 Screening Day -14 to -1	Enrollment/Baseline Visit 1, Day 1	Study Visit 2 Day 3 +/- 1 day	Study Visit 3 Day 8 +/- 2 days	Study Visit 4 Day 15 +/- 2 days	Study Visit 5 Day 29 +/- 3 days	Study Visit 6 Day 57 +/- 3 days	Study Visit 7 Day 85 +/- 7 days	Study Visit 8 Day 181 +/- 7 days	Study Visit 9 Day 366 +/- 7 days	Unscheduled Visit[21]	Early Termination Visit

Solicited AEs will first be collected 30 minutes after administration of vaccine (immediate reactogenicity). Additional solicited AEs will be collected by memory aid (eDiary) on Days 1-14 for all participants. Solicited AEs consist of immediate reactogenicity, local reactogenicity and systemic reactogenicity (constitutional signs and symptoms as defined in the protocol).
Non-serious unsolicited AEs will be collected and recorded from Day 1 after administration of vaccine for all participants until Day 28
MAAEs, NOCMCs, and SAEs as defined in the protocol, will be collected from Day 1, following vaccination, until the end of study follow-up (Day 366). AESIs corresponding to myocarditis, pericarditis, and myopericarditis will be collected from Day 1, following vaccination, until Day 57. AESIs, corresponding to any Grade 2 or greater decrease in lymphocyte or neutrophil count will be collected from Day 1, following vaccination, until the end of study follow up (Day 366).
Participants will be required to report influenza-like illness starting from enrollment through day 366. Participants will have the ability to notify the study team through a weekly electronic memory aid starting on Day 7. Participants experiencing an influenza-like illness will have an unscheduled visit and a nasopharyngeal (NP) swab will be obtained for influenza virus testing by RT-PCR. ILI symptoms will be collected from the day of enrollment through Day 366.
Screening will include counseling women of childbearing potential and sexually active men on abstinence or approved contraceptive methods. If an early termination visit is performed before Day 30 for a woman of childbearing potential, or before Day 60 for a sexually active man, contraceptive counseling will be performed.
Evaluation performed at the discretion of the investigator
Blood sample for troponin measurements will be collected, stored, and tested at the discretion of the PI and will not be included in the participant's electronic medical record.
Sample collection will occur prior to vaccination.
Exploratory anti-ferritin antibody assays.
Unscheduled visits may be conducted by phone or IRB-approved telehealth means if in-person visits are not feasible. If an unscheduled visit is performed to evaluate, in the judgment of the site investigator, a case of suspected myocarditis and/or pericarditis, the site will coordinate an appropriate diagnostic workup to make a determination of probable or confirmed myocarditis and/or pericarditis. The suspected myocarditis and/or pericarditis case should be reported to the DMID Pharmacovigilance Group within 24 hours of site awareness.

Table 3: Solicited Reactogenicity Assessments

	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)
Local Reaction to Injectable Product			
Pain	Does not interfere with activity	Use of non-narcotic pain reliever or interferes withactivity	Any use of narcotic pain reliever or prevents dailyactivity
Tenderness	Mild discomfort totouch	Discomfort withmovement	Significant discomfort at rest
Erythema/Redness *	2.5 – 5 cm	5.1 – 10 cm	> 10 cm
Erythema/Redness Functional*	Does not interfere with activity	Interferes with activity	Prevents daily activity
Induration/Hardness **	2.5 – 5 cm	5.1 – 10 cm	> 10 cm
Induration/Hardness Functional**	Does not interfere with activity	Interferes with activity	Prevents daily activity
Axillary lymph node swelling on same arm as injection	Does not interfere with activity	Interferes with activity	Prevents daily activity
Systemic (General)			
Oral Temperature (°C) *** (°F) ***	38.0 – 38.4 100.4 – 101.1	38.5 – 38.9 101.2 – 102.0	≥39.0 >102.0
Nausea	Does not interfere with activity	Interferes with activity	Prevents daily activity
Vomiting	No interference with activity or 1 – 2episodes/24 hours	Some interference with activity or > 2 episodes/24 hours	Prevents daily activity, requires outpatient IVhydration
Diarrhea	No interference with activity or 2 – 3 loose stools /24 hours	Some interference with activity or 4 – 5 stools/24hours	Prevents daily activity, 6 or more watery stools or /24 hours or requires outpatient IV hydration
Headache	No interference withactivity	Use of non-narcotic pain reliever or some interferencewith activity	Anyuse of narcotic pain reliever or prevents dailyactivity
Chills	No interference withactivity	Some interferencewith activity	Prevents dailyactivity
Fatigue	No interference withactivity	Some interferencewith activity	Prevents dailyactivity
Myalgia (muscle pain other than injection site)	No interference withactivity	Some interferencewith activity	Significant; prevents daily activity
Arthralgia (joint ache)	No interference withactivity	Some interferencewith activity	Significant; prevents daily activity

* For each day measured, the greatest diameter of local reactions including erythema and induration should be recorded.
** Induration/Hardness and Erythema/Redness should be evaluated and graded using the functional scale as well as the actual measurement
*** Oral temperature; no recent hot or cold beverages or smoking

Table 4: Clinical Laboratory Abnormalities Grades

	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)
Serum *			
Creatinine – mg/dL± (Male) (Female)	1.4 – 1.7 1.1 - 1.5	1.8 – 2.0 1.6 - 2.0	>2.0 >2.0
Alanine aminotransferase (ALT) (increase by factor)	1.01 – 2.5 x ULN	2.6 – 5.0 x ULN	> 5.0 x ULN
Aspartate aminotransferase (AST) (increase by factor)	1.01 – 2.5 x ULN	2.6 – 5.0 x ULN	> 5.0 x ULN
Alkaline phosphatase (increase by factor)	1.01 – 2.0 x ULN	2.1 – 3.0 x ULN	> 3.0 x ULN
Bilirubin – when accompanied by any increase in AST or ALT (increase by factor)	1.01 – 1.25 x ULN	1.26 – 1.5 x ULN	> 1.5 x ULN
Bilirubin – when AST and ALT are normal; increase by factor	1.01 – 1.5 x ULN	1.6 – 2.0 x ULN	> 2.0 x ULN
Lipase	1.1 – 1.5 x ULN	1.6 – 2.0 x ULN	> 2.0 x ULN
Troponin (hsTnI)	Severity will not be assessed. Normal range (Male ≤ 20 ng/L) Normal range (Female ≤ 14 ng/L)		
Iron	Severity will not be assessed. Normal range (Male 50 - 160 µg/dL) Normal range (Female 45- 150 µg/dL)		
Hematology *			
Hemoglobin (Female) - gm/dL±	11.0 – 11.9	9.5 – 10.9	<9.5
Hemoglobin (Female) change from baseline value - gm/dL	Any decrease – 1.5	1.6 – 2.0	>2.0
Hemoglobin (Male) - gm/dL±	12.5 – 13.6	10.5 – 12.4	<10.5
Hemoglobin (Male) change from baseline value – gm/dL	Any decrease – 1.5	1.6 – 2.0	>2.0
WBC Increase - cell/mm^{3}±	9,900 – 15,000	15,001 – 20,000	>20,000
WBC Decrease - cell/mm^{3}	2,500 – 3,100	1,500 – 2,499	<1,500
Lymphocytes Decrease – cells/mm^{3}	500 – 599	400 – 499	<400

Table 4: Clinical Laboratory Abnormalities Grades *(continued)*

Neutrophils Decrease – cell/mm^3	1,500 – 1,999	1,000 – 1,499	<999
Platelets Decreased - cell/mm$^{3\pm}$	125,000 – 149,000	100,000 – 124,000	<100,000
PT – increase by factor (prothrombin time)	>1.0 – 1.10 x ULN**	1.11 – 1.20 x ULN	>1.20 x ULN
PTT – increase by factor (partial thromboplastin time)	>1.0 – 1.2 x ULN	1.21 – 1.4 x ULN	>1.40 x ULN
Fibrinogen increase - mg/dL$^{\pm}$	436 – 500	501 – 600	>600
Fibrinogen decrease - mg/dL$^{\pm}$	150 – 212	125 – 149	< 125

* The laboratory values provided in the tables serve as guidelines and are dependent upon institutional normal parameters. Institutional normal reference ranges will be provided to the SDMCC to demonstrate that they are appropriate.
± Modified to correspond to normal institutional laboratory ranges
**ULN" is the upper limit of the normal range.

Table 5: Vital Signs Grades

Vital Signs *	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)
Oral Temperature (°C) ** (°F) **	38.0 – 38.4 100.4 – 101.1	38.5 – 38.9 101.2 – 102.0	≥39.0 >102.0
Tachycardia - beats perminute	101 – 115	116 – 130	> 130
Bradycardia - beats perminute	50-54	45-49	< 45
Hypertension (systolic) -mm Hg	141 – 150	151 – 155	> 155
Hypertension (diastolic) -mm Hg	91 – 95	96 – 100	> 100
Hypotension (systolic) –mm Hg	85 – 89	80 – 84	< 80

* Participant should be at rest for all vital sign measurements.
** Oral temperature; no recent hot or cold beverages or smoking.

Table 6: Case definitions of probable and confirmed myocarditis, pericarditis, and myopericarditis

Condition	**Definition**	
Acute myocarditis	**Probable case**	**Confirmed case**
	Presence of ≥ 1 new or worsening of the following clinical symptoms:*	Presence of ≥ 1 new or worsening of the following clinical symptoms:*
	chest pain, pressure, or discomfort	chest pain, pressure, or discomfort
	dyspnea, shortness of breath, or pain with breathing	dyspnea, shortness of breath, or pain with breathing
	palpitations	palpitations
	syncope	syncope
	OR, infants and children aged < 12 years might instead have ≥ 2 of the following symptoms:	OR, infants and children aged < 12 years might instead have ≥ 2 of the following symptoms:
	irritability	irritability
	vomiting	vomiting
	poor feeding	poor feeding
	tachypnea	tachypnea
	lethargy	lethargy
	AND ≥ 1 new finding of	AND ≥ 1 new finding of
	troponin level above upper limit of normal (any type of troponin)	Histopathologic confirmation of myocarditis†
	abnormal electrocardiogram (ECG or EKG) or rhythm monitoring findings consistent with myocarditis§	cMRI findings consistent with myocarditis¶ in the presence of troponin level above upper limit of normal (any type of troponin)
	abnormal cardiac function or wall motion abnormalities on echocardiogram	
	cMRI findings consistent with myocarditis¶	
	AND	AND

Table 6: Case definitions of probable and confirmed myocarditis, pericarditis, and myopericarditis *(continued)*

	No other identifiable cause of the symptoms and findings	No other identifiable cause of the symptoms and findings
Acute pericarditis**	Presence of ≥ 2 new or worsening of the following clinical features:	
	acute chest pain††	
	pericardial rub on exam	
	new ST-elevation or PR-depression on EKG	
	new or worsening pericardial effusion on echocardiogram or MRI	
Myopericarditis	This term may be used for patients who meet criteria for both myocarditis and pericarditis.	

Abbreviations: AV = atrioventricular; cMRI = cardiac magnetic resonance imaging; ECG or EKG = electrocardiogram.
* Persons who lack the listed symptoms but who meet other criteria may be classified as subclinical myocarditis (probable or confirmed).
† Using the Dallas criteria (Aretz HT, Billingham ME, Edwards WD, et al. Myocarditis. A histopathologic definition and classification. Am J Cardiovasc Pathol 1987; 1:3–14). Autopsy cases may be classified as confirmed clinical myocarditis on the basis of meeting histopathologic criteria if no other identifiable cause.
§ To meet the ECG or rhythm monitoring criterion, a probable case must include at least one of 1) ST-segment or T-wave abnormalities; 2) Paroxysmal or sustained atrial, supraventricular, or ventricular arrhythmias; or 3) AV nodal conduction delays or intraventricular conduction defects.
¶ Using either the original or the revised Lake Louise criteria. https://www.sciencedirect.com/science/article/pii/S0735109718388430?via%3Dihub
** https://academic.oup.com/eurheartj/article/36/42/2921/2293375
†† Typically described as pain made worse by lying down, deep inspiration, or cough, and relieved by sitting up or leaning forward, although other types of chest pain might occur.

Table 7: Probability (%) of observing at least one safety event, given varying underlying event probabilities and sample sizes.

True Event Probability	Individual Dose Groups		
	Sentinel Lead-In N=2	Sentinel + Expanded Dose Group N=10	Optimal Dose Dose Group N=20
0.01% (Very rare)	<0.1	0.1	0.2
0.1% (Rare)	0.2	1	2
1% (Uncommon)	2	9.6	18.2
10% (Common)	19	65.1	87.8
30% (Very common)	51	97.2	99.9

Table 8: Estimated event probabilities (%) and associated exact 95% Clopper-Pearson confidence intervals resulting from varying numbers of events observed in groups of different sizes.

Number of Observed Events	Individual Dose Groups		
	Sentinel Lead-In N=2	Sentinel + Expanded Dose Group N=10	Optimal Dose Dose Group N=20
0	0 (0, 84.2)	0 (0, 30.8)	0 (0, 16.8)
1	**50 (1.3, 98.7)**	10 (0.3, 44.5)	5 (0.1, 24.9)
2	100 (15.8, 100)	20 (2.5, 55.6)	10 (1.2, 31.7)
5	-	**50 (18.7, 81.3)**	25 (8.7, 49.1)
6	-	60 (26.2, 87.8)	30 (11.9, 54.3)
10	-	100 (69.2, 100)	**50 (27.2, 72.8)**
12	-	-	60 (36.1, 80.9)
16	-	-	80 (56.3, 94.3)
20	-	-	100 (83.2, 100)

Table 9: Distribution of Protocol Deviations by Category, Type and Dose Group - Enrolled Population

[Implementation Note: Include all categories but only include deviation types that were reported within the respective deviation classification (major or minor, or all). Sort alphabetically by category, then deviation type within a category with "Any type" presented first and "Other" presented last.]

		Low Dose (10 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)		Medium Dose (25 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)		High Dose (50 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)		IIV4 (60 mcg) (N=X)		All Participants (N=X)	
Category	**Deviation Type**	**No. of Part.**	**No. of Dev.**	**No. of Part.**	**No. of Dev.**	**No. of Part.**	**No. of Dev.**	**No. of Part.**	**No. of Dev.**	**No. of Part.**	**No. of Dev.**
Major Deviations											
Eligibility / enrollment	Any type	x	x	x	x	x	x	x	x	x	x
	Did not meet inclusion criterion										
	…										
	Other										
Follow-up visit schedule	Any type										
	Missed visit/visit not conducted										
	…										
	Other										
Protocol procedure/ assessment	Any type										
	Blood not collected										
	…										
	Other										
Treatment administration	Any type										
	Missed treatment administration										
	…										
	Other										
Repeat for Minor Deviations											
Repeat for All Deviations											

Note: N = Number of participants enrolled.

Table 10: Participant Disposition by Dose Group – Screened Population

Participant Disposition	Low Dose (10 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)		Medium Dose (25 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)		High Dose (50 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)		IIV4 (60 mcg) (N=X)		All Participants (N=X)	
	n	%	n	%	n	%	n	%	n	%
Screened	x	-	x	-	x	-	x	-	x	-
Enrolled	x	100	x	100	x	100	x	100	x	100
Received Study Product (Safety Population)	x	x	x	x	x	x	x	x	x	x
Completed at Least One Post-Baseline Secondary Endpoint Visit (Day 8, 15, 29, or 57)	x	x	x	x	x	x	x	x	x	x
Completed Follow-up Through End of Study (Day 366)[a]	x	x	x	x	x	x	x	x	x	x
Completed all Post-Baseline Visits	x	x	x	x	x	x	x	x	x	x
Completed Study Per-Protocol[b]	x	x	x	x	x	x	x	x	x	x
Early Termination	x	x	x	x	x	x	x	x	x	x

Notes: N = Number of participants enrolled and is the denominator for percentages.
[a] Refer to "Early Terminations" listing for reasons participants terminated early.
[b] Refer to "Participants Excluded from Analysis Populations" listing for reasons participants are excluded from the Per-Protocol analysis population.

Table 11: Summary of Reasons for Not Enrolling - Screened Population

[Implementation Note: Only I/E criteria reported to not have been met by screen failures and reported reasons for individuals eligible but not enrolled will be included.]

Reason for Not Enrolling Category	Reason for Not Enrolling Criterion	Low Dose (10 mcg VRC H1ssF_3928 mRNA-LNP)	Medium Dose (25 mcg VRC H1ssF_3928 mRNA-LNP)	High Dose (50 mcg VRC H1ssF_3928 mRNA-LNP)	IIV4 (60 mcg)	All Individuals
		n (%)	n (%)	n (%)	n (%)	n (%)
Any Reason	Any Reason	x	x	x	x	x
Inclusion and Exclusion						
Inclusion and Exclusion	Failing any eligibility criterion	x (x)	x (x)	x (x)	x (x)	x (x)
Inclusion	Any inclusion criterion	x (x)	x (x)	x (x)	x (x)	x (x)
	[inclusion criterion 1]	x (x)	x (x)	x (x)	x (x)	x (x)
	[inclusion criterion 2]	x (x)	x (x)	x (x)	x (x)	x (x)
	[inclusion criterion 3]	x (x)	x (x)	x (x)	x (x)	x (x)
Exclusion	Any exclusion criterion	x (x)	x (x)	x (x)	x (x)	x (x)
	[exclusion criterion 1]	x (x)	x (x)	x (x)	x (x)	x (x)
	[exclusion criterion 2]	x (x)	x (x)	x (x)	x (x)	x (x)
	[exclusion criterion 3]	x (x)	x (x)	x (x)	x (x)	x (x)
Eligible but not Enrolled						
Eligible but not Enrolled	Any reason	x (x)	x (x)	x (x)	x (x)	x (x)
	[reason 1]	x (x)	x (x)	x (x)	x (x)	x (x)
	[reason 2]	x (x)	x (x)	x (x)	x (x)	x (x)
	[reason 3]	x (x)	x (x)	x (x)	x (x)	x (x)

Notes: More than one criterion may be marked per individual. Denominator for percentages is the total number of individuals not enrolled.

Table 12: Dates of First and Last Study Product Administration by Dose Group – Safety Population

Dose Group	Date of First Study Product Administration	Date of Last Study Product Administration
Low Dose (10 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)	Month DD, YYYY	Month DD, YYYY
Medium Dose (25 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)	Month DD, YYYY	Month DD, YYYY
High Dose (50 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)	Month DD, YYYY	Month DD, YYYY
IIV4 (60 mcg) (N=X)	Month DD, YYYY	Month DD, YYYY

Note: N = Number of participants receiving study product.

Table 13: Analysis Population Exclusions by Dose Group – Enrolled Participants

[Implementation Note: If at least one participant did not receive the study vaccination, a "Modified Intent-to-Treat" row will be added, mimicking the "Safety Population" row. Updates to the footnotes will be implemented as needed.]

Analysis Populations	Reason Excluded	Low Dose (10 mcg VRC H1ssF_3928 mRNA-LNP) (N=X) n (%)	Medium Dose (25 mcg VRC H1ssF_3928 mRNA-LNP) (N=X) n (%)	High Dose (50 mcg VRC H1ssF_3928 mRNA-LNP) (N=X) n (%)	IIV4 (60 mcg) (N=X) n (%)	All Participants (N=X) n (%)
Intent-to-Treat	No study product received	x (x)	x (x)	x (x)	x (x)	x (x)
Safety	No study product received	x (x)	x (x)	x (x)	x (x)	x (x)
Per-Protocol, Day 1	Ineligible at enrollment[a]	x (x)	x (x)	x (x)	x (x)	x (x)
Per-Protocol, Day 8	Any reason	x (x)	x (x)	x (x)	x (x)	x (x)
	Ineligible at enrollment[a]	x (x)	x (x)	x (x)	x (x)	x (x)
	Visit substantially out of window[b]	x (x)	x (x)	x (x)	x (x)	x (x)
	Visit less than 28 days after onset of Influenza infection[c]	x (x)	x (x)	x (x)	x (x)	x (x)
	Receipt of incorrect study vaccination dose	x (x)	x (x)	x (x)	x (x)	x (x)
	Receipt of exclusionary medication or vaccine[d]	x (x)	x (x)	x (x)	x (x)	x (x)
Repeat Per-Protocol, Day 8 for:						
Per-Protocol, Day 15						
Per-Protocol, Day 29						
Per-Protocol, Day 57						

Notes: N = Number of participants enrolled and is the denominator for percentages.
[a] Ineligibility at enrollment determined post-baseline.
[b] Substantially out of window defined as occurring out of the specified visit window.
[c] Defined as an adverse event in the MedDRA Preferred Term "Influenza".
[d] May include immunosuppressives or other immune-modifying drugs (low dose topical and intranasal steroid preparations were to be permitted); anticancer chemotherapy or radiation therapy (cytotoxic); oral or parenteral (including intra-articular) corticosteroids, high-dose inhaled or nebulized corticosteroids; seasonal influenza vaccine prior to the Day 57 visit; investigational H1 or H5 influenza vaccine; ferritin-based vaccine; immunoglobulin and/or any blood products (except Rho D immunoglobulin); an experimental agent, other than those administered as per protocol; or interventional agents, including licensed or unlicensed vaccine, drug, biologic device, blood product, or medication. Exclusions determined by the Sponsor.

Table 14: Summary of Demographic and Baseline Characteristics by Dose Group – Intent-to-Treat Population

Demographic or Baseline Characteristic	Statistic or Characteristic	Low Dose (10 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)	Medium Dose (25 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)	High Dose (50 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)	IIV4 (60 mcg) (N=X)	All Participants (N=X)
Age (years)	Mean (Standard Deviation)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)	x.x (x.x)
	Median	x.x	x.x	x.x	x.x	x.x
	Minimum, Maximum	x, x	x, x	x, x	x, x	x, x
Sex, n (%)	Male	x (x)	x (x)	x (x)	x (x)	x (x)
	Female	x (x)	x (x)	x (x)	x (x)	x (x)
Ethnicity, n (%)	Not Hispanic or Latino	x (x)	x (x)	x (x)	x (x)	x (x)
	Hispanic or Latino	x (x)	x (x)	x (x)	x (x)	x (x)
	Not Reported	x (x)	x (x)	x (x)	x (x)	x (x)
	Unknown	x (x)	x (x)	x (x)	x (x)	x (x)
Race, n (%)	American Indian or Alaska Native	x (x)	x (x)	x (x)	x (x)	x (x)
	Asian	x (x)	x (x)	x (x)	x (x)	x (x)
	Native Hawaiian or Other Pacific Islander	x (x)	x (x)	x (x)	x (x)	x (x)
	Black or African American	x (x)	x (x)	x (x)	x (x)	x (x)
	White	x (x)	x (x)	x (x)	x (x)	x (x)
	Multi-Racial	x (x)	x (x)	x (x)	x (x)	x (x)
	Unknown	x (x)	x (x)	x (x)	x (x)	x (x)
Receipt of prior season's influenza vaccine[a], n (%)	Yes	x (x)	x (x)	x (x)	x (x)	x (x)
	No	x (x)	x (x)	x (x)	x (x)	x (x)

Note: N = Number of participants enrolled.
[a] Captures receipt of influenza vaccine within 12 months of receipt of study vaccination. Participants were allowed to receive the seasonal influenza vaccine more than 90 days before study vaccination.

Table 15: Summary of Participants with Prior and Concurrent Medical Conditions by MedDRA System Organ Class and Dose Group - Safety Population

	Low Dose (10 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)		Medium Dose (25 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)		High Dose (50 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)		IIV4 (60 mcg) (N=X)		All Participants (N=X)	
MedDRA System Organ Class	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Prior Medical Conditions										
Any SOC	x	x	x	x	x	x	x	x	x	x
[SOC 1]	x	x	x	x	x	x	x	x	x	x
[SOC 2]	x	x	x	x	x	x	x	x	x	x
Concurrent Medical Conditions										
Any SOC	x	x	x	x	x	x	x	x	x	x
[SOC 1]	x	x	x	x	x	x	x	x	x	x
[SOC 2]	x	x	x	x	x	x	x	x	x	x

Notes: N = Number of participants in the Safety population and is the denominator for percentages. n = Number of participants in the Safety population reporting medical history within the specified SOC. A participant is only counted once per SOC.

Table 16: Summary of Homologous H1-specific Neutralizing Antibody Median Infectious Dose (ID50) Titers in Serum Measured by a Reporter Microneutralization (RMN) Assay Against A/New Caledonia/20/1999 (H1N1), by Dose Group and Time Point – Intent-to-Treat Population

[Implementation note: replace last footnote with "Confidence intervals based on the bootstrap method (10,000 replicates)" if applicable.]

Study Day	Statistic	Low Dose (10 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)	Medium Dose (25 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)	High Dose (50 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)	IIV4 (60 mcg) (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)
Repeat "Day 8" rows for Day 15, 29, 57, 85, 181 and 366					

Notes: N = Number of participants enrolled. n = Number of participants with available results. CI = Confidence Interval; GMT = Geometric Mean Titer; GMFR = Geometric Mean Fold-Rise from baseline. Confidence intervals calculated based on the Student t-distribution.

[a] Participants were allowed to receive seasonal influenza vaccine >90 days before and >60 days after study vaccination.

Table 17: Summary of Homologous H1-specific Neutralizing Antibody Median Infectious Dose (ID50) Titers in Serum Measured by a Reporter Microneutralization (RMN) Assay Against A/New Caledonia/20/1999 (H1N1), by Receipt of Prior Season's Influenza Vaccine or Subsequent Receipt of Seasonal Influenza Vaccine, Dose Group, and Time Point – Intent-to-Treat Population

[Implementation note: replace last footnote with "Confidence intervals based on the bootstrap method (10,000 replicates)" if applicable.]

Study Day	Statistic	Low Dose (10 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)		Medium Dose (25 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)		High Dose (50 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)		IIV4 (60 mcg) (N=X)	
Stratified by Receipt of Prior Season's Influenza Vaccine[a]									
		Receipt	**No Receipt**	**Receipt**	**No Receipt**	**Receipt**	**No Receipt**	**Receipt**	**No Receipt**
Baseline	n	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)
Day 8	n	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)
	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)
Repeat "Day 8" rows for Day 15, 29, 57, 85, 181 and 366									
Stratified by Subsequent Receipt of Seasonal Influenza Vaccine[a]									
		Receipt	**No Receipt**	**Receipt**	**No Receipt**	**Receipt**	**No Receipt**	**Receipt**	**No Receipt**
Baseline	n	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)
Day 85	n	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)
	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)
Repeat "Day 85" rows for Day 181 and 366									

Notes: N = Number of participants enrolled. n = Number of participants with available results. CI = Confidence Interval; GMT = Geometric Mean Titer; GMFR = Geometric Mean Fold-Rise from baseline. Confidence intervals calculated based on the Student t-distribution.

[a] Participants were allowed to receive seasonal influenza vaccine >90 days before and >60 days after study vaccination.

Table 18: Estimates of Ratios of Geometric Mean Fold-Rise from Baseline for Homologous H1-specific Neutralizing Antibody Median Infectious Dose (ID50) Titers in Serum Measured by a Reporter Microneutralization (RMN) Assay Against A/New Caledonia/20/1999 (H1N1) as Estimated by a Generalized Estimating Equation– Intent-to-Treat Population

GMFR Ratio	Estimate (95% CI)	p-value
High Dose (50 mcg VRC H1ssF_3928 mRNA-LNP) vs. Medium Dose (25 mcg VRC H1ssF_3928 mRNA-LNP)		
Day 8	x.xxx (x.xxx, x.xxx)	0.xxx
Day 15	x.xxx (x.xxx, x.xxx)	0.xxx
Day 29	x.xxx (x.xxx, x.xxx)	0.xxx
Day 57	x.xxx (x.xxx, x.xxx)	0.xxx
Day 85	x.xxx (x.xxx, x.xxx)	0.xxx
Day 181	x.xxx (x.xxx, x.xxx)	0.xxx
Day 366	x.xxx (x.xxx, x.xxx)	0.xxx
Repeat the above for: *High Dose (50 mcg VRC H1ssF_3928 mRNA-LNP) vs. Low Dose (10 mcg VRC H1ssF_3928 mRNA-LNP)* *High Dose (50 mcg VRC H1ssF_3928 mRNA-LNP) vs. IIV4 (60 mcg)* *Medium Dose (25 mcg VRC H1ssF_3928 mRNA-LNP) vs. Low Dose (10 mcg VRC H1ssF_3928 mRNA-LNP)* *Medium Dose (25 mcg VRC H1ssF_3928 mRNA-LNP) vs. IIV4 (60mcg)* *Low Dose (10 mcg VRC H1ssF_3928 mRNA-LNP) vs. IIV4 (60 mcg)*		
From a 2-Fold Increase in Baseline Titer	x.xxx (x.xxx, x.xxx)	0.xxx
Male vs. Female	x.xxx (x.xxx, x.xxx)	0.xxx
From an Increase in 5 Years of Age at Enrollment	x.xxx (x.xxx, x.xxx)	0.xxx
Prior Season's Influenza Vaccine Receipt vs. No Prior Season's Influenza Vaccine Receipt	x.xxx (x.xxx, x.xxx)	0.xxx

Notes: Estimates are from a generalized estimating equations analysis and are adjusted for all other covariates included in the model. CI = Confidence Interval. GMFR = Geometric Mean Fold-Rise. Confidence intervals are Wald Confidence Intervals. Participants were allowed to receive seasonal influenza vaccine >90 days before study vaccination.

Table 19: Summary of Heterologous H1-specific Neutralizing Antibody Median Infectious Dose (ID50) Titers in Serum Measured by a Reporter Microneutralization (RMN) Assay Against [Insert Strain], by Receipt of Prior Season's Influenza Vaccine, Dose Group, and Time Point – Intent-to-Treat Population

[Implementation note: replace last footnote with "Confidence intervals based on the bootstrap method (10,000 replicates)" if applicable.]

Study Day	Statistic	Low Dose (10 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)			Medium Dose (25 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)			High Dose (50 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)			IIV4 (60 mcg) (N=X)		
		Receipt[a]	No Receipt	All Participants	Receipt[a]	No Receipt	All Participants	Receipt[a]	No Receipt	All Participants	Receipt[a]	No Receipt	All Participants
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 29	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)

Notes: N = Number of participants enrolled. n = Number of participants with available results. CI = Confidence Interval; GMT = Geometric Mean Titer; GMFR = Geometric Mean Fold-Rise from baseline. Confidence intervals calculated based on the Student t-distribution.

[a] Participants were allowed to receive seasonal influenza vaccine >90 days study vaccination.

Table 20: Summary of Homologous H1-specific Neutralizing Antibody Endpoint Titers in Serum Measured by a Viral Microneutralization (MN) Assay Against A/New Caledonia/20/1999 (H1N1), by Dose Group and Time Point – Intent-to-Treat Population

[Implementation Note: This will be similar to Table 16.]

Table 21: Summary of Homologous H1-specific Neutralizing Antibody Endpoint Titers in Serum Measured by a Viral Microneutralization (MN) Assay Against A/New Caledonia/20/1999 (H1N1), by Receipt of Prior Season's Influenza Vaccine or Subsequent Receipt of Seasonal Influenza Vaccine, Dose Group and Time Point – Intent-to-Treat Population

[Implementation Note: This will be similar to Table 17.]

Table 22: Estimates of Ratios of Geometric Mean Fold-Rise from Baseline for Homologous H1-specific Neutralizing Antibody Endpoint Titers in Serum Measured by a Viral Microneutralization (MN) Assay Against A/New Caledonia/20/1999 (H1N1) as Estimated by a Generalized Estimating Equation – Intent-to-Treat Population

[Implementation Note: This will be similar to Table 18.]

Table 23: Summary of Heterologous H1-specific Neutralizing Antibody Median Infectious Dose (ID50) Titers in Serum Measured by a Viral Microneutralization (MN) Assay Against [Insert Strain], by Receipt of Prior Season's Influenza Vaccine, Dose Group, and Time Point – Intent-to-Treat Population

[Implementation Note: This will be similar to Table 19.]

Table 24: Summary of Homologous Anti-HA Stalk Serum Antibody Titers ((EU)/mL), Measured by Enzyme Linked Immunosorbent Assay (ELISA) Against A/New Caledonia/20/1999 (H1N1), by Dose Group and Point – Intent-to-Treat Population

[Implementation Note: This will be similar to Table 16.]

Table 25: Summary of Homologous Anti-HA Stalk Serum Antibody Titers ((EU)/mL), Measured by Enzyme Linked Immunosorbent Assay (ELISA) Against A/New Caledonia/20/1999 (H1N1), by Receipt of Prior Season's Influenza Vaccine or Subsequent Receipt of Seasonal Influenza Vaccine, Dose Group and Point – Intent-to-Treat Population

[Implementation Note: This will be similar to Table 17.]

Table 26: Estimates of Ratios of Geometric Mean Fold-Rise from Baseline for Homologous Anti-HA Stalk Serum Antibody Titers ((EU)/mL), Measured by Enzyme Linked Immunosorbent Assay (ELISA) Against A/New Caledonia/20/1999 (H1N1) as Estimated by a Generalized Estimating Equation – Intent-to-Treat Population

[Implementation Note: This will be similar to Table 18.]

Table 27: Summary of Heterologous Anti-HA Stalk Serum Antibody Titers ((EU)/mL), Measured by Enzyme Linked Immunosorbent Assay (ELISA) Against [Insert Strain], by Receipt of Prior Season's Influenza Vaccine, Dose Group, and Time Point – Intent-to-Treat Population

[Implementation Note: This will be similar to Table 19.]

Table 28: Summary of Area Under the Curve of H. Pylori Ferritin Binding as Measured by the Anti-Ferritin Assay by Dose Group and Time Point – Intent-to-Treat Population

[Implementation note: This will be repeated for each parent population and stimulation combination. Replace the last footnote with "Confidence intervals based on the bootstrap method (10,000 replicates)" if applicable.]

Ferritin Subunit	Study Day	Statistic	Low Dose (10 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)	Medium Dose (25 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)	High Dose (50 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)	IIV4 (60 mcg) (N=X)
H. Pylori Ferritin Binding	Baseline	n	x	x	x	x
		Mean (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
		Mean (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)
		Mean Difference from Baseline (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)
Repeat "Day 8" rows for Day 15, 29, 57, 85, 181 and 366						

Table 29: Summary of Area Under the Curve of H. Pylori Ferritin Binding as Measured by the Anti-Ferritin Assay by Receipt of Prior Season's Influenza Vaccine or Subsequent Receipt of Seasonal Influenza Vaccine, Dose Group, and Time Point – Intent-to-Treat Population

[Implementation note: This will be repeated for each parent population and stimulation combination. Replace the last footnote with "Confidence intervals based on the bootstrap method (10,000 replicates)" if applicable.]

Ferritin Subunit	Study Day	Statistic	Low Dose (10 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)		Medium Dose (25 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)		High Dose (50 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)		IIV4 (60 mcg) (N=X)	
	Stratified by Receipt of Prior Season's Influenza Vaccine[a]									
			Receipt	**No Receipt**	**Receipt**	**No Receipt**	**Receipt**	**No Receipt**	**Receipt**	**No Receipt**
H. Pylori Ferritin Binding	Baseline	n	x	x	x	x	x	x	x	x
		Mean (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)
	Day 8	n	x	x	x	x	x	x	x	x
		Mean (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)
		Mean Difference from Baseline (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)
Repeat "Day 8" rows for Day 15, 29, 57, 85, 181 and 366										
	Stratified by Subsequent Receipt of Seasonal Influenza Vaccine[a]									
			Receipt	**No Receipt**	**Receipt**	**No Receipt**	**Receipt**	**No Receipt**	**Receipt**	**No Receipt**
H. Pylori Ferritin Binding	Baseline	n	x	x	x	x	x	x	x	x
		Mean (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)
	Day 85	n	x	x	x	x	x	x	x	x
		Mean (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)

Table 29: Summary of Area Under the Curve of H. Pylori Ferritin Binding as Measured by the Anti-Ferritin Assay by Receipt of Prior Season's Influenza Vaccine or Subsequent Receipt of Seasonal Influenza Vaccine, Dose Group, and Time Point – Intent-to-Treat Population *(continued)*

		Mean Difference from Baseline (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)
Repeat "Day 85" rows for Day 181 and 366										

Notes: N = Number of participants enrolled. n = Number of participants with available results. CI = Confidence Interval; Confidence intervals calculated based on the Student t-distribution.
[a] Participants were allowed to receive seasonal influenza vaccine >90 days before and >60 days after study vaccination.

Table 30: Summary of Area Under the Curve of Human Ferritin Light Chain Binding as Measured by the Anti-Ferritin Assay by Dose Group and Time Point – Intent-to-Treat Population

[Implementation Note: This will be similar to Table 28.]

Table 31: Summary of Area Under the Curve of Human Ferritin Light Chain Binding as Measured by the Anti-Ferritin Assay by Receipt of Prior Season's Influenza Vaccine or Subsequent Receipt of Seasonal Influenza Vaccine, Dose Group, and Time Point – Intent-to-Treat Population

[Implementation Note: This will be similar to Table 29.]

Table 32: Summary of Area Under the Curve of Human Ferritin Heavy Chain Binding as Measured by the Anti-Ferritin Assay by Dose Group and Time Point – Intent-to-Treat Population

[Implementation Note: This will be similar to Table 28.]

Table 33: Summary of Area Under the Curve of Human Ferritin Heavy Chain Binding as Measured by the Anti-Ferritin Assay by Receipt of Prior Season's Influenza Vaccine or Subsequent Receipt of Seasonal Influenza Vaccine, Dose Group, and Time Point – Intent-to-Treat Population

[Implementation Note: This will be similar to Table 29.]

Table 34: Summary of Expression of B-Cells in the [Insert Parent Population] Following [Insert Stimulation] Stimulation by Dose Group and Time Point – Intent-to-Treat Population

[Implementation note: This will be repeated for each parent population and stimulation combination. Replace the last footnote with "Confidence intervals based on the bootstrap method (10,000 replicates)" if applicable. Include a footnote for each cell marker to indicate whether the percentage of cells expressed of median fluorescence intensity is summarized, and for the parent population to indicate the number of total cells is summarized.]

Cell Marker	Study Day	Statistic	Low Dose (10 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)	Medium Dose (25 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)	High Dose (50 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)	IIV4 (60 mcg) (N=X)
[Cell Marker 1]	Baseline	n	**x**	**x**	**x**	**x**
		Mean (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**
		Mean (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)**
		Mean Difference from Baseline (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)**

Repeat "Day 8" rows for Day 15, 29, 57, 85, 181 and 366

Then repeat for each cell marker, and for the parent population

Table 35: Summary of Expression of B-Cells in the [Insert Parent Population] Following [Insert Stimulation] Stimulation by Receipt of Prior Season's Influenza Vaccine or Subsequent Receipt of Seasonal Influenza Vaccine, Dose Group, and Time Point – Intent-to-Treat Population

[Implementation note: This will be repeated for each parent population and stimulation combination. Replace the last footnote with "Confidence intervals based on the bootstrap method (10,000 replicates)" if applicable. Include a footnote for each cell marker to indicate whether the percentage of cells expressed of median fluorescence intensity is summarized, and for the parent population to indicate the number of total cells is summarized.]

Cell Marker	Study Day	Statistic	Low Dose (10 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)		Medium Dose (25 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)		High Dose (50 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)		IIV4 (60 mcg) (N=X)	
	Stratified by Receipt of Prior Season's Influenza Vaccine[a]									
			Receipt	**No Receipt**	**Receipt**	**No Receipt**	**Receipt**	**No Receipt**	**Receipt**	**No Receipt**
[Cell Marker 1]	Baseline	n	x	x	x	x	x	x	x	x
		Mean (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)
	Day 8	n	x	x	x	x	x	x	x	x
		Mean (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)
		Mean Difference from Baseline (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)
Repeat "Day 8" rows for Day 15, 29, 57, 85, 181 and 366 *Then repeat for each cell marker, and for the parent population*										
	Stratified by Subsequent Receipt of Seasonal Influenza Vaccine[a]									
			Receipt	**No Receipt**	**Receipt**	**No Receipt**	**Receipt**	**No Receipt**	**Receipt**	**No Receipt**
[Cell Marker 1]	Baseline	n	x	x	x	x	x	x	x	x
		Mean (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)
	Day 85	n	x	x	x	x	x	x	x	x
		Mean (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)

Table 35: Summary of Expression of B-Cells in the [Insert Parent Population] Following [Insert Stimulation] Stimulation by Receipt of Prior Season's Influenza Vaccine or Subsequent Receipt of Seasonal Influenza Vaccine, Dose Group, and Time Point – Intent-to-Treat Population *(continued)*

		Mean Difference from Baseline (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)
Repeat "Day 85" rows for Day 181 and 366 *Then repeat for each cell marker, and for the parent population*										

Notes: N = Number of participants enrolled. n = Number of participants with available results. CI = Confidence Interval; Confidence intervals calculated based on the Student t-distribution.
[a] Participants were allowed to receive seasonal influenza vaccine >90 days before and >60 days after study vaccination.

Table 36: Summary of Expression of T-Cells in the [Insert Parent Population] Following [Insert Stimulation] Stimulation by Dose Group and Time Point – Intent-to-Treat Population

[Implementation Note: This will be similar to Table 34.]

Table 37: Summary of Expression of T-Cells in the [Insert Parent Population] Following [Insert Stimulation] Stimulation by Receipt of Prior Season's Influenza Vaccine or Subsequent Receipt of Seasonal Influenza Vaccine, Dose Group, and Time Point – Intent-to-Treat Population

[Implementation Note: This will be similar to Table 35.]

Table 38: Summary of Expression of Tfh Cells in the [Insert Parent Population] Following [Insert Stimulation] Stimulation by Dose Group and Time Point – Intent-to-Treat Population

[Implementation Note: This will be similar to Table 34.]

Table 39: Summary of Expression of Tfh Cells in the [Insert Parent Population] Following [Insert Stimulation] Stimulation by Receipt of Prior Season's Influenza Vaccine or Subsequent Receipt of Seasonal Influenza Vaccine, Dose Group, and Time Point – Intent-to-Treat Population

[Implementation Note: This will be similar to Table 35.]

Table 40: Overall Summary of Adverse Events by Group - Safety Population

	Low Dose (10 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)		Medium Dose (25 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)		High Dose (50 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)		Any Non-IIV4 Dose (N=X)		IIV4 (60 mcg) (N=X)	
Participants with at least one:	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Solicited adverse event	x	x	x	x	x	x	x	x	x	x
Solicited local adverse event	x	x	x	x	x	x	x	x	x	x
Solicited systemic adverse event	x	x	x	x	x	x	x	x	x	x
Unsolicited AE	x	x	x	x	x	x	x	x	x	x
Related unsolicited AE[a]	x	x	x	x	x	x	x	x	x	x
Mild	x	x	x	x	x	x	x	x	x	x
Moderate	x	x	x	x	x	x	x	x	x	x
Severe										
Severe unsolicited AE[b]	x	x	x	x	x	x	x	x	x	x
Related	x	x	x	x	x	x	x	x	x	x
Unrelated	x	x	x	x	x	x	x	x	x	x
Unsolicited AE through Day 29	x	x	x	x	x	x	x	x	x	x
Serious adverse event	x	x	x	x	x	x	x	x	x	x
Related, serious adverse event	x	x	x	x	x	x	x	x	x	x
Medically attended adverse event (MAAE)	x	x	x	x	x	x	x	x	x	x
New-onset chronic medical condition (NOCMC)	x	x	x	x	x	x	x	x	x	x
Laboratory adverse event of special interest (AESI)	x	x	x	x	x	x	x	x	x	x
≥ Grade 2 decrease in lymphocyte count	x	x	x	x	x	x	x	x	x	x

Table 40: Overall Summary of Adverse Events by Group - Safety Population *(continued)*

	Low Dose (10 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)		Medium Dose (25 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)		High Dose (50 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)		Any Non-IIV4 Dose (N=X)		IIV4 (60 mcg) (N=X)	
Participants with at least one:	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
≥ Grade 2 decrease in neutrophil count	x	x	x	x	x	x	x	x	x	x
Non-laboratory adverse event of special interest (AESI)	x	x	x	x	x	x	x	x	x	x
Myocarditis	x	x	x	x	x	x	x	x	x	x
Pericarditis	x	x	x	x	x	x	x	x	x	x
Myopericarditis	x	x	x	x	x	x	x	x	x	x
Influenza-like illness (ILI)	x	x	x	x	x	x	x	x	x	x
Clinical laboratory adverse event[c]	x	x	x	x	x	x	x	x	x	x
Chemistry clinical laboratory adverse event	x	x	x	x	x	x	x	x	x	x
Hematology clinical laboratory adverse event	x	x	x	x	x	x	x	x	x	x
Clinical laboratory adverse event through Day 57	x	x	x	x	x	x	x	x	x	x
Chemistry clinical laboratory adverse event	x	x	x	x	x	x	x	x	x	x
Hematology clinical laboratory adverse event	x	x	x	x	x	x	x	x	x	x
Adverse event leading to early termination[d]	x	x	x	x	x	x	x	x	x	x
Adverse event classified as an unanticipated problem[d]	x	x	x	x	x	x	x	x	x	x

Notes: N = Number of participants in the Safety population. n = Number of participants reporting the specified event type. Participants are counted once for each category regardless of the number of events. AESIs corresponding to myocarditis, pericarditis, myopericarditis and clinical laboratory AEs as a primary endpoint are reported through Day 57. AESIs corresponding to a Grade 2 or greater decrease in lymphocyte or neutrophil count, MAAEs, NOCMCs, ILIs and SAEs are reported through the end of the study period.
[a]Participants are counted once at the maximum severity.
[b]Participants are counted once at the maximum relatedness.
[c]Laboratory abnormalities with a grade level increase from baseline in clinical laboratory values.
[d]As reported on the Adverse Event eCRF.

Table 41: Adverse Events Occurring in 5% of Participants in Any Dose Group by MedDRA System Organ Class and Preferred Term - Safety Population

[Implementation Note: This table should include a row for All PT/SOC and for any PT/SOC reported by ≥5% participants in any group. Note, this table summarizes SAEs and non-serious events separately. This includes all adverse events collected (e.g., solicited, unsolicited, AESI, laboratory adverse events, etc.), regardless of relationship to study product. Symptoms reported during the solicited events period as solicited events should be indicated as such (e.g., "Headache (Systematic)" and should be summarized separately from unsolicited AEs for the same event (e.g., label the unsolicited event as "Headache").]

Preferred Term	**MedDRA System Organ Class**	**Low Dose (10 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)**		**Medium Dose (25 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)**		**High Dose (50 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)**		**Any Non-IIV4 Dose (N=X)**		**IIV4 (60 mcg) (N=X)**	
		n (%)	Events	n (%)	Events	n (%)	Events	n (%)	Events	n (%)	Events
Serious Adverse Events											
All	All	x (x)	x	x (x)	x	x (x)	x	x (x)	x	x (x)	x
PT1	SOC1	x (x)	x	x (x)	x	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	x (x)	x	x (x)	x
PT1	SOC1	x (x)	x	x (x)	x	x (x)	x	x (x)	x	x (x)	x
Etc	Etc										

Notes: N = Number of participants in the Safety population. n (%) = number and percentage (out of N) of participants with at least one event. Events = total frequency of events reported.

Table 42: Number and Percentage of Participants Experiencing Solicited Events with 95% Confidence Intervals by Symptom, Maximum Severity, and Dose Group - Safety Population

Symptom	Severity	Low Dose (10 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)		Medium Dose (25 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)		High Dose (50 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)		Any Non-IIV4 Dose (N=X)		IIV4 (60 mcg) (N=X)	
		n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI
Any Solicited Event											
Any Solicited Event	None	x (x)	x.x, x.x	x (x)	x.x, x.x	x (x)	x.x, x.x	x (x)	x.x, x.x	x (x)	x.x, x.x
	Mild	x (x)	x.x, x.x	x (x)	x.x, x.x	x (x)	x.x, x.x	x (x)	x.x, x.x	x (x)	x.x, x.x
	Moderate	x (x)	x.x, x.x	x (x)	x.x, x.x	x (x)	x.x, x.x	x (x)	x.x, x.x	x (x)	x.x, x.x
	Severe	x (x)	x.x, x.x	x (x)	x.x, x.x	x (x)	x.x, x.x	x (x)	x.x, x.x	x (x)	x.x, x.x
Local Solicited Events											
Any Local Solicited Event	None	x (x)	x.x, x.x	x (x)	x.x, x.x	x (x)	x.x, x.x	x (x)	x.x, x.x	x (x)	x.x, x.x
	Mild	x (x)	x.x, x.x	x (x)	x.x, x.x	x (x)	x.x, x.x	x (x)	x.x, x.x	x (x)	x.x, x.x
	Moderate	x (x)	x.x, x.x	x (x)	x.x, x.x	x (x)	x.x, x.x	x (x)	x.x, x.x	x (x)	x.x, x.x
	Severe	x (x)	x.x, x.x	x (x)	x.x, x.x	x (x)	x.x, x.x	x (x)	x.x, x.x	x (x)	x.x, x.x
Repeat for:											
Axillary lymph node swelling (same arm as injection)											
Erythema/Redness Diameter											
Erythema/Redness Functional											
Induration/Hardness Diameter											
Induration/Hardness Functional											
Pain											
Tenderness											
Systemic Solicited Events											
Any Systemic Solicited Event	None	x (x)	(x.x, x.x)	x (x)	(x.x, x.x)	x (x)	(x.x, x.x)	x (x)	(x.x, x.x)	x (x)	(x.x, x.x)
	Mild	x (x)	(x.x, x.x)	x (x)	(x.x, x.x)	x (x)	(x.x, x.x)	x (x)	(x.x, x.x)	x (x)	(x.x, x.x)

Table 42: Number and Percentage of Participants Experiencing Solicited Events with 95% Confidence Intervals by Symptom, Maximum Severity, and Dose Group - Safety Population *(continued)*

	Moderate	x (x)	(x.x, x.x)	x (x)	(x.x, x.x)	x (x)	(x.x, x.x)	x (x)	(x.x, x.x)	x (x)	(x.x, x.x)
	Severe	x (x)	(x.x, x.x)	x (x)	(x.x, x.x)	x (x)	(x.x, x.x)	x (x)	(x.x, x.x)	x (x)	(x.x, x.x)
Repeat for:											
Arthralgia (joint ache)											
Chills											
Diarrhea											
Fatigue											
Headache											
Myalgia (muscle pain other than injection site)											
Nausea											
Temperature (fever)											
Vomiting											

Notes: N = Number of participants in the Safety population. n (%) = number and percentage (out of N) of participants with at least one event. Confidence intervals are calculated via the exact Clopper-Pearson method. Severity is the maximum severity reported post-dosing.

Table 43: Summary of Unsolicited Adverse Events Through Day 29 by MedDRA System Organ Class and Preferred Term, Time Post-Dosing, and Dose Group – Safety Population

[Implementation Note: This table should include all unsolicited AEs, including SAE, AESI, etc., through Day 29. If only one PT is reported for a given SOC, the "Any PT" row should be removed. Any SOC/PT reported should appear for each time period.]

MedDRA System Organ Class	MedDRA Preferred Term	Low Dose (10 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)		Medium Dose (25 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)		High Dose (50 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)		Any Non-IIV4 Dose (N=X)		IIV4 (60 mcg) (N=X)	
		n (%) [95% CI]	Events	n (%) [95% CI]	Events	n (%) [95% CI]	Events	n (%) [95% CI]	Events	n (%) [95% CI]	Events
Day 1-14 Post-Dosing											
Any SOC	Any PT	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x
SOC 1	Any PT	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x
	PT1	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x
	PT2	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x
	…										
SOC 2	Any PT	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x
	PT1	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x
	PT2	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x
Repeat for: Day 15-28 Post-Dosing Day 1-28 Post-Dosing											

Notes: N = Number of participants in the Safety Population; n = Number of participants reporting each SOC/PT. A participant is only counted once per PT/time point. Confidence intervals are calculated via the exact Clopper-Pearson method.

Table 44: Number and Percentage of Participants Experiencing Unsolicited Adverse Events Through Day 29 by MedDRA System Organ Class and Preferred Term, Maximum Severity, and Dose Group – Safety Population

MedDRA System Organ Class	Preferred Term	Severity	Low Dose (10 mcg VRC H1ssF_3928 mRNA-LNP) (N=X) n (%)	Medium Dose (25 mcg VRC H1ssF_3928 mRNA-LNP) (N=X) n (%)	High Dose (50 mcg VRC H1ssF_3928 mRNA-LNP) (N=X) n (%)	Any Non-IIV4 Dose (N=X) n (%)	IIV4 (60 mcg) (N=X) n (%)
Any SOC	Any PT	Any Severity	x (x)	x (x)	x (x)	x (x)	x (x)
		Mild	x (x)	x (x)	x (x)	x (x)	x (x)
		Moderate	x (x)	x (x)	x (x)	x (x)	x (x)
		Severe	x (x)	x (x)	x (x)	x (x)	x (x)
SOC 1	PT 1	Any Severity	x (x)	x (x)	x (x)	x (x)	x (x)
		Mild	x (x)	x (x)	x (x)	x (x)	x (x)
		Moderate	x (x)	x (x)	x (x)	x (x)	x (x)
		Severe	x (x)	x (x)	x (x)	x (x)	x (x)
	PT 2	Any Severity	x (x)	x (x)	x (x)	x (x)	x (x)
		Mild	x (x)	x (x)	x (x)	x (x)	x (x)
		Moderate	x (x)	x (x)	x (x)	x (x)	x (x)
		Severe	x (x)	x (x)	x (x)	x (x)	x (x)
…	…						

Notes: N = Number of participants in the Safety Population; n = Number of participants reporting each SOC/PT.

Similar to Table 44:

Table 45: Number and Percentage of Participants Experiencing Related Unsolicited Adverse Events Through Day 29 by MedDRA System Organ Class and Preferred Term, Maximum Severity, and Dose Group – Safety Population

Table 46: Summary of Laboratory Adverse Events Through Day 57 by Laboratory Parameter, Maximum Severity, and Dose Group – Safety Population

Laboratory Parameter	Severity	Low Dose (10 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)		Medium Dose (25 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)		High Dose (50 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)		Any Non-IIV4 Dose (N=X)		IIV4 (60 mcg) (N=X)	
		n (%) [95% CI]	Events	n (%) [95% CI]	Events	n (%) [95% CI]	Events	n (%) [95% CI]	Events	n (%) [95% CI]	Events
Chemistry Laboratory Parameters											
Any Chemistry Laboratory Parameter	Any Severity	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x
	Mild	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x
	Moderate	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x
	Severe	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x
Alanine Aminotransferase (ALT) increased	Any Severity	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x
	Mild	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x
	Moderate	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x
	Severe	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x
Alkaline Phosphatase (ALP) increased	Any Severity	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x
	Mild	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x
	Moderate	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x

Table 46: Summary of Laboratory Adverse Events Through Day 57 by Laboratory Parameter, Maximum Severity, and Dose Group – Safety Population *(continued)*

	Severe	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x
Aspartate Aminotransferase (AST) increased	Any Severity	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x
	Mild	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x
	Moderate	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x
	Severe	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x
Repeat for: Bilirubin increased, Creatinine increased, Lipase increased											
Hematology Laboratory Parameters											
Any Hematology Laboratory Parameter	Any Severity	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x
	Mild	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x
	Moderate	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x
	Severe	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x
Fibrinogen decreased	Any Severity	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x
	Mild	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x
	Moderate	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x
	Severe	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x
Fibrinogen increased	Any Severity	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x

RESTRICTED

Table 46: Summary of Laboratory Adverse Events Through Day 57 by Laboratory Parameter, Maximum Severity, and Dose Group – Safety Population *(continued)*

	Mild	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x
	Moderate	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x
	Severe	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x
Hemoglobin decreased	Any Severity	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x
	Mild	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x
	Moderate	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x
	Severe	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x	x (x) [x.x, x.x]	x
Repeat for: Lymphocytes decreased, Neutrophils decreased, Partial Thromboplastin Time (PTT) increased, Platelets decreased, Prothrombin Time (PT) increased, White Blood Cells decreased, White Blood Cells increased											

Notes: N = Number of participants in the Safety Population; n = Number of participants reporting the specified laboratory adverse event. Confidence intervals are calculated via the exact Clopper-Pearson method. Severity is the maximum severity reported post-dosing.

Similar to Table 43:

Table 47: Summary of Medically Attended Adverse Events by MedDRA System Organ Class and Preferred Term, Time Post-Dosing, and Dose Group – Safety Population

Similar to Table 44:

Table 48: Number and Percentage of Participants Experiencing Medically Attended Adverse Events by MedDRA System Organ Class and Preferred Term, Maximum Severity, and Dose Group – Safety Population

Table 49: Number and Percentage of Participants Experiencing Related Medically Attended Adverse Events by MedDRA System Organ Class and Preferred Term, Maximum Severity, and Dose Group – Safety Population

Similar to Table 43:

Table 50: Summary of New-Onset Chronic Medical Conditions by MedDRA System Organ Class and Preferred Term, Maximum Severity, and Dose Group – Safety Population

Similar to Table 44:

Table 51: Number and Percentage of Participants Experiencing New-Onset Chronic Medical Conditions by MedDRA System Organ Class and Preferred Term, Maximum Severity, and Dose Group – Safety Population

Table 52: Number and Percentage of Participants Experiencing Related New-Onset Chronic Medical Conditions by MedDRA System Organ Class and Preferred Term, Maximum Severity, and Dose Group – Safety Population

Similar to Table 43:

Table 53: Summary of Influenza-Like Illnesses by MedDRA System Organ Class and Preferred Term, Maximum Severity, and Dose Group – Safety Population

Similar to Table 44:

Table 54: Number and Percentage of Participants Experiencing Influenza-Like Illnesses by MedDRA System Organ Class and Preferred Term, Maximum Severity, and Dose Group – Safety Population

Table 55: Number and Percentage of Participants Experiencing Related Influenza-Like Illnesses by MedDRA System Organ Class and Preferred Term, Maximum Severity, and Dose Group – Safety Population

Table 56. Listing of Serious Adverse Events

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

- *If the event is ongoing (no stop date), indicate "Ongoing" in the "Duration" column.*
- *In "If Not Related, Alternate Etiology", merge the 2 data fields for collecting alternate etiology, separated by a colon.*
- *The MAAE/NOCMC/AESI[a]/ILI column should be populated with the respective classifications only. For example, if an event was classified as an MAAE and NOCMC, but not an AESI or ILI should be reported as "MAAE/NOCMC"*
- *If there are no comments for an event, populate "Comments" column with "None"*
- *Sort order: Dose Group, then Participant ID, then AE Number]*

Adverse Event	Study Day (Duration)	Study Day the Event Became Serious	Reason Reported as an SAE	Severity	Relationship to Study Product	If Not Related, Alternative Etiology	Participant Discontinued Due to AE	Classified as Unanticipated Problem	MAAE/ NOCMC/ AESI[a]/ ILI	Outcome	MedDRA System Organ Class	MedDRA Preferred Term
Participant ID: , Dose Group: , AE Number:												
Comments:												
Notes: AESI = Adverse event of special interest. ILI = Influenza-like illness. MAAE = Medically attended adverse event. NOCMC = New-onset medical condition. [a] Corresponding to myocarditis, pericarditis, or myopericarditis reported through Day 57												
Participant ID: , Dose Group: , AE Number:												
Comments:												
Notes: AESI = Adverse event of special interest. ILI = Influenza-like illness. MAAE = Medically attended adverse event. NOCMC = New-onset medical condition. [a] Corresponding to myocarditis, pericarditis, or myopericarditis reported through Day 57												

Table 57. Listing of Non-Serious, Unsolicited, Moderate or Severe Adverse Events

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

- *If the event is ongoing (no stop date), indicate "Ongoing" in the "Duration" column.*
- *In "If Not Related, Alternate Etiology", merge the 2 data fields for collecting alternate etiology, separated by a colon.*
- *The MAAE/NOCMC/AESI[a]/ILI column should be populated with the respective classifications only. For example, if an event was classified as an MAAE and NOCMC, but not an AESI or ILI should be reported as "MAAE/NOCMC"*
- *If there are no comments for an event, populate "Comments" column with "None"*
- *Sort order: Dose Group, then Participant ID, then AE Number]*

Adverse Event	Study Day (Duration)	Severity	Relationship to Study Product	If Not Related, Alternative Etiology	Participant Discontinued Due to AE	Classified as Unanticipated Problem	MAAE/ NOCMC/ AESI[a]/ ILI	Outcome	MedDRA System Organ Class	MedDRA Preferred Term
Participant ID: , Dose Group: , AE Number:										
Comments:										
Notes: AESI = Adverse event of special interest. ILI = Influenza-like illness. MAAE = Medically attended adverse event. NOCMC = New-onset medical condition. [a] Corresponding to myocarditis, pericarditis, or myopericarditis reported through Day 57										
Participant ID: , Dose Group: , AE Number:										
Comments:										
Notes: AESI = Adverse event of special interest. ILI = Influenza-like illness. MAAE = Medically attended adverse event. NOCMC = New-onset medical condition. [a] Corresponding to myocarditis, pericarditis, or myopericarditis reported through Day 57										

Table 58. Listing of Other Significant Adverse Events

[Implementation Notes:

- *Only AEs classified as a MAAE, NOCMC, AESI (Corresponding to myocarditis, pericarditis, or myopericarditis reported through Day 57), or ILI will be included.*
- *Duration should be calculated as follows: End date – start date + 1*
- *If the event is ongoing (no stop date), indicate "Ongoing" in the "Duration" column.*
- *In "If Not Related, Alternate Etiology", merge the 2 data fields for collecting alternate etiology, separated by a colon.*
- *The SAE/MAAE/NOCMC/AESI[a]/ILI column should be populated with the respective classifications only. For example, if an event was classified as an MAAE and NOCMC, but not an SAE, AESI, or ILI should be reported as "MAAE/NOCMC"*
- *If there are no comments for an event, populate "Comments" column with "None"*
- *Sort order: Dose Group, then Participant ID, then AE Number]*

Adverse Event	Study Day (Duration)	Severity	Relationship to Study Product	If Not Related, Alternative Etiology	Participant Discontinued Due to AE	Classified as Unanticipated Problem	SAE/MAAE/ NOCMC/ AESI[a]/ ILI	Outcome	MedDRA System Organ Class	MedDRA Preferred Term
Participant ID: , Dose Group: , AE Number:										
Comments:										
Notes: AESI = Adverse event of special interest. ILI = Influenza-like illness. MAAE = Medically attended adverse event. NOCMC = New-onset medical condition. SAE = Serious Adverse Event. [a] Corresponding to myocarditis, pericarditis, or myopericarditis reported through Day 57										
Participant ID: , Dose Group: , AE Number:										
Comments:										
Notes: AESI = Adverse event of special interest. ILI = Influenza-like illness. MAAE = Medically attended adverse event. NOCMC = New-onset medical condition. SAE = Serious Adverse Event. [a] Corresponding to myocarditis, pericarditis, or myopericarditis reported through Day 57										

Table 59: Listing of Abnormal Laboratory Results - Chemistry

[Implementation Note: A complete listing of all laboratory results is included separately. In the Laboratory Parameter column, indicate the units after the parameter, e.g., Hemoglobin (g/dL). This listing is not color-coded, but the severity should be included in parentheses after the result, e.g., 16.2 (Grade 1). Participant ID should be USUBJID (not PATID) for purposes of de-identification.]

Participant ID	Dose Group	Sex	Age (years)	Planned Study Day	Actual Study Day	Laboratory Parameter (Units)	Result (Severity)	Relationship to Study Product	If Not Related, Alternate Etiology

Table 60: Listing of Abnormal Laboratory Results - Hematology

Participant ID	Dose Group	Sex	Age (years)	Planned Study Day	Actual Study Day	Laboratory Parameter (Units)	Result (Severity)	Relationship to Study Product	If Not Related, Alternate Etiology

Table 61: Vital Signs by Maximum Severity, Time Point and Dose Group – Any Assessment

Time Point	Dose Group	N	None		Grade 1		Grade 2		Grade 3	
			n	%	n	%	n	%	n	%
Baseline	Low Dose (10 mcg VRC H1ssF_3928 mRNA-LNP)	x	x	x	x	x	x	x	x	x
	Medium Dose (25 mcg VRC H1ssF_3928 mRNA-LNP)	x	x	x	x	x	x	x	x	x
	High Dose (50 mcg VRC H1ssF_3928 mRNA-LNP)	x	x	x	x	x	x	x	x	x
	IIV4 (60 mcg)	x	x	x	x	x	x	x	x	x
Repeat for										
Day 3										
Day 8										
Day 15										
Day 29										
Maximum Severity Post-Baseline										

Notes: N = Number of participants in the Safety population. The "Maximum Severity Post-Baseline" rows indicate the maximum severity of vital signs experienced by each participant at any time point post-baseline, including unscheduled assessments.

Similar to Table 61:

Table 62: Vital Signs by Maximum Severity, Time Point and Dose Group – Oral Temperature

Table 63: Vital Signs by Maximum Severity, Time Point and Dose Group – Heart Rate (beats/min)

Time Point	Dose Group	N	None		Grade 1 (Low)[a]		Grade 1 (High)[b]		Grade 2 (Low)[a]		Grade 2 (High)[b]		Grade 3 (Low)[a]		Grade 3 (High)[b]	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%
Baseline	Low Dose (10 mcg VRC H1ssF_3928 mRNA-LNP)	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Medium Dose (25 mcg VRC H1ssF_3928 mRNA-LNP)	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	High Dose (50 mcg VRC H1ssF_3928 mRNA-LNP)	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	IIV4 (60 mcg)	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Repeat for																
Day 3																
Day 8																
Day 15																
Day 29																
Maximum Severity																

Notes: N = Number of participants in the Safety population. The "Maximum Severity" rows indicate the maximum severity of vital signs experienced by each participant at any time point post-baseline, including unscheduled assessments.
[a]Represents bradycardia.
[b]Represents tachycardia.

Similar to Table 63:

Table 64: Vital Signs by Maximum Severity, Time Point, and Dose Group – Systolic Blood Pressure

[Implementation Note: Footnote "a" will read "[a]Represents hypotension" and footnote "b" will read "[b]Represents hypertension."]

Similar to Table 61:

Table 65: Vital Signs by Maximum Severity, Time Point and Dose Group – Diastolic Blood Pressure

Table 66: Number and Percentage of Participants with Prior and Concomitant Medications by WHO Drug Classification and Dose Group - Safety Population

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

WHO Drug Code Level 1, Anatomic Group	WHO Drug Code Level 2, Therapeutic Subgroup	Low Dose (10 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)	Medium Dose (25 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)	High Dose (50 mcg VRC H1ssF_3928 mRNA-LNP) (N=X)	Any Non-IIV4 Dose (N=X)	IIV4 (60 mcg) (N=X)
		n (%)	n (%)	n (%)	n (%)	n (%)
Prior Medications						
Any Level 1 Codes	Any Level 2 Codes	x (x)	x (x)	x (x)	x (x)	x (x)
[ATC Level 1 – 1]	Any [ATC 1 – 1]	x (x)	x (x)	x (x)	x (x)	x (x)
	[ATC 2 – 1]	x (x)	x (x)	x (x)	x (x)	x (x)
	[ATC 2 – 2]	x (x)	x (x)	x (x)	x (x)	x (x)
	[ATC 2 – 3]	x (x)	x (x)	x (x)	x (x)	x (x)
[ATC Level 1 – 2]	Any [ATC 1 – 2]	x (x)	x (x)	x (x)	x (x)	x (x)
	[ATC 2 – 1]	x (x)	x (x)	x (x)	x (x)	x (x)
	[ATC 2 – 2]	x (x)	x (x)	x (x)	x (x)	x (x)
	[ATC 2 – 3]	x (x)	x (x)	x (x)	x (x)	x (x)
Concomitant Medications						
Any Level 1 Codes	Any Level 2 Codes	x (x)	x (x)	x (x)	x (x)	x (x)
[ATC Level 1 – 1]	Any [ATC 1 – 1]	x (x)	x (x)	x (x)	x (x)	x (x)
	[ATC 2 – 1]	x (x)	x (x)	x (x)	x (x)	x (x)
	[ATC 2 – 2]	x (x)	x (x)	x (x)	x (x)	x (x)
	[ATC 2 – 3]	x (x)	x (x)	x (x)	x (x)	x (x)
[ATC Level 1 – 2]	Any [ATC 1 – 2]	x (x)	x (x)	x (x)	x (x)	x (x)
	[ATC 2 – 1]	x (x)	x (x)	x (x)	x (x)	x (x)
	[ATC 2 – 2]	x (x)	x (x)	x (x)	x (x)	x (x)
	[ATC 2 – 3]	x (x)	x (x)	x (x)	x (x)	x (x)

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

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Figure 1: CONSORT Flow Diagram

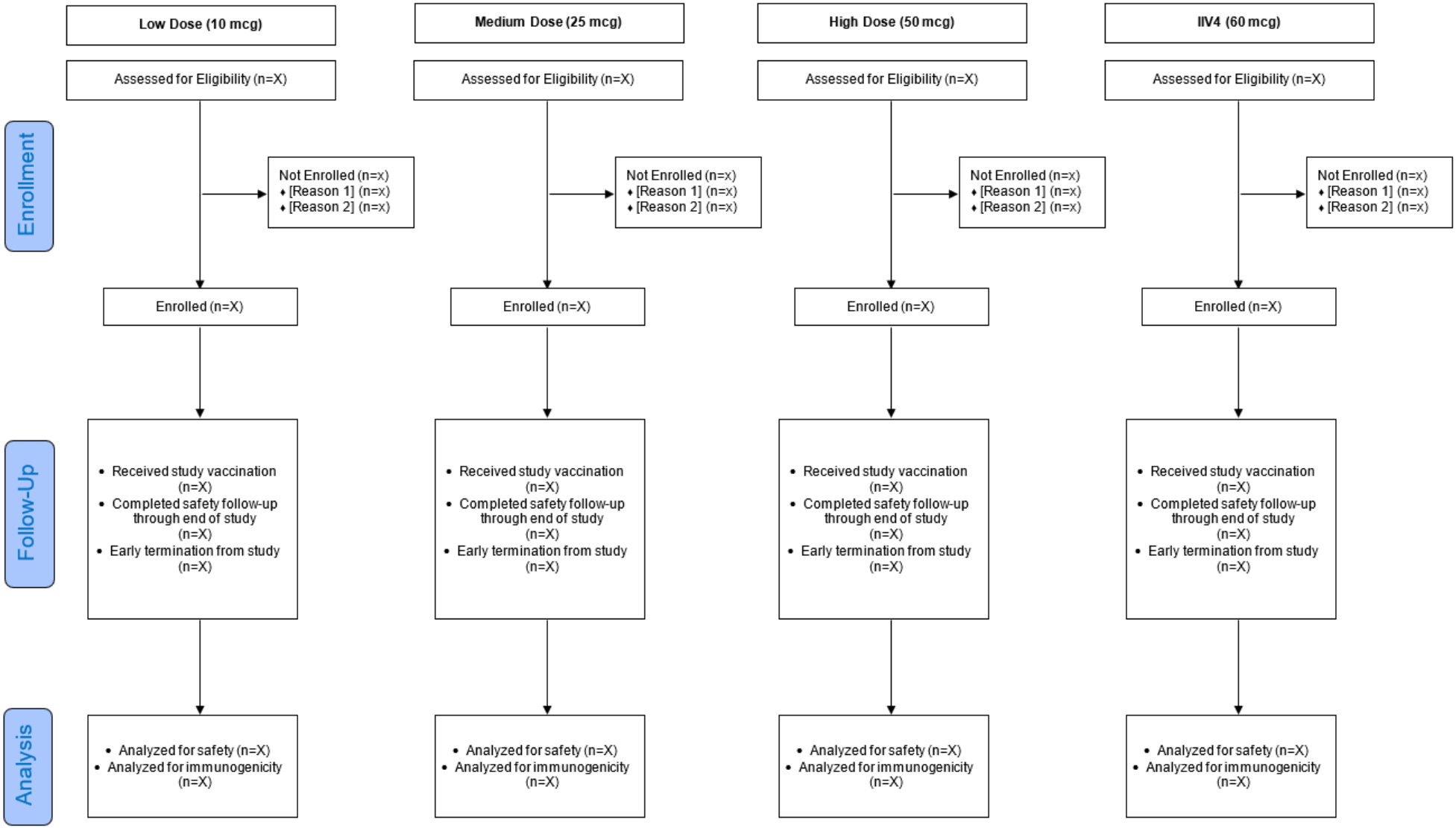


Figure 2: Geometric Mean and Geometric Mean Fold-Rise from Baseline of Homologous H1-specific Neutralizing Antibody Median Infectious Dose (ID50) Titers in Serum Measured by a Reporter Microneutralization (RMN) Assay Against A/New Caledonia/20/1999 (H1N1) by Dose Group and Time Point – Intent-to-Treat Population

[Implementation Note: This is an example figure. 95% CIs calculated using the same method as in the corresponding table, i.e., either using Student's t-distribution or bootstrapping.]

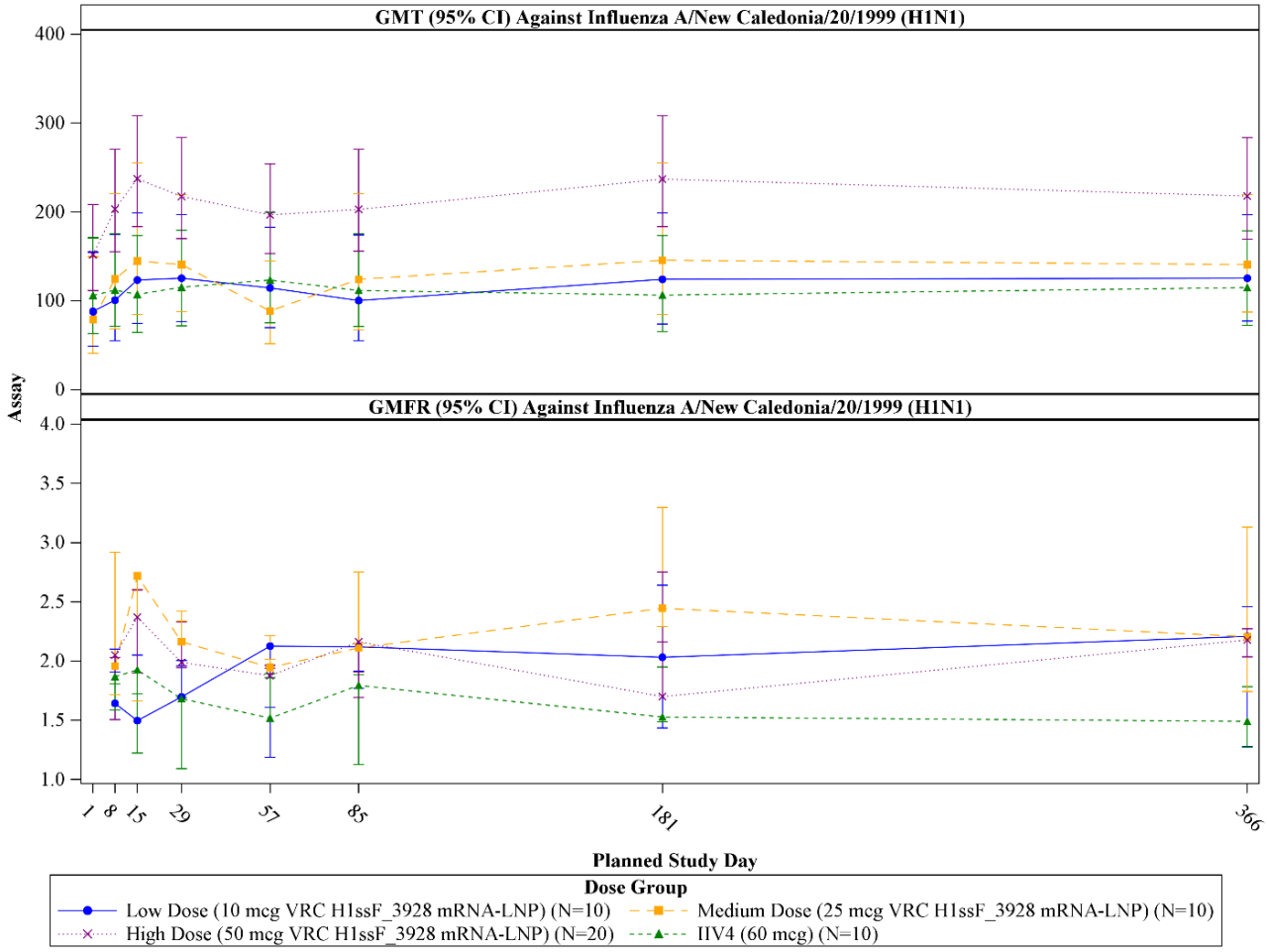


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[Implementation Notes: This is an example figure. 95% CIs calculated using the same method as in the corresponding table, i.e., either using Student's t-distribution or bootstrapping.]

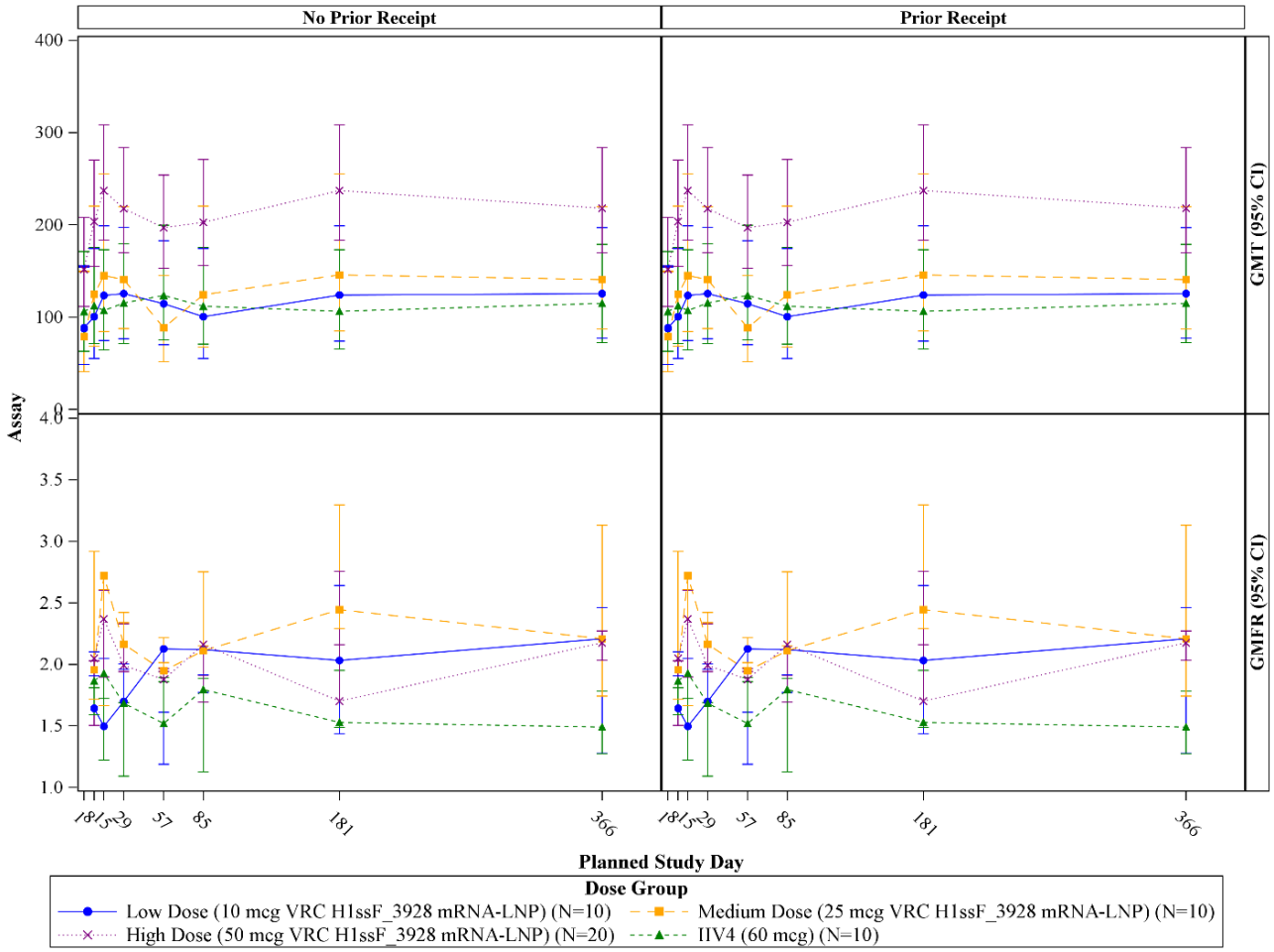


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[Implementation Note: This is an example figure. 95% CIs calculated using the same method as in the corresponding table, i.e., either using Student's t-distribution or bootstrapping.]

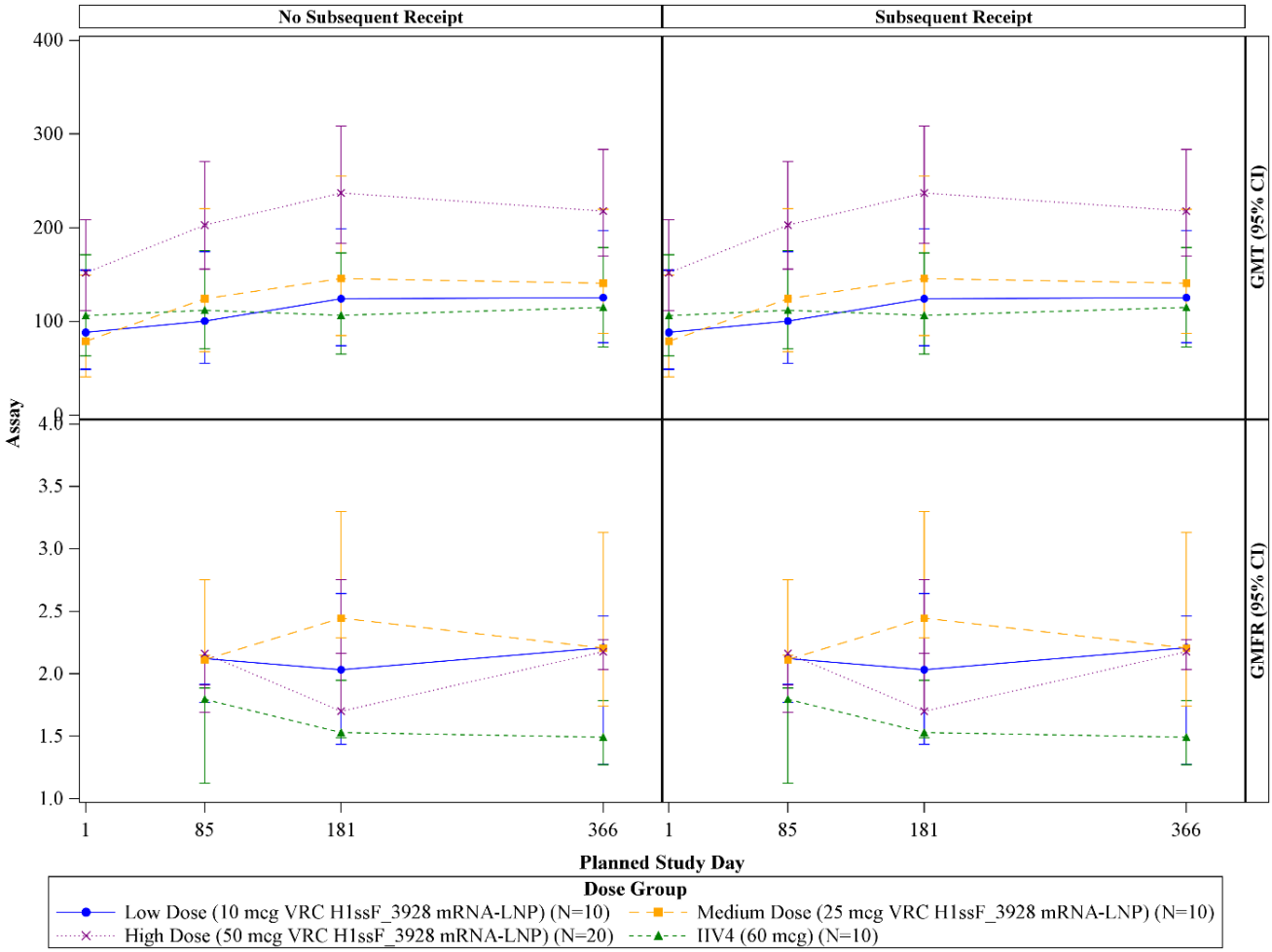
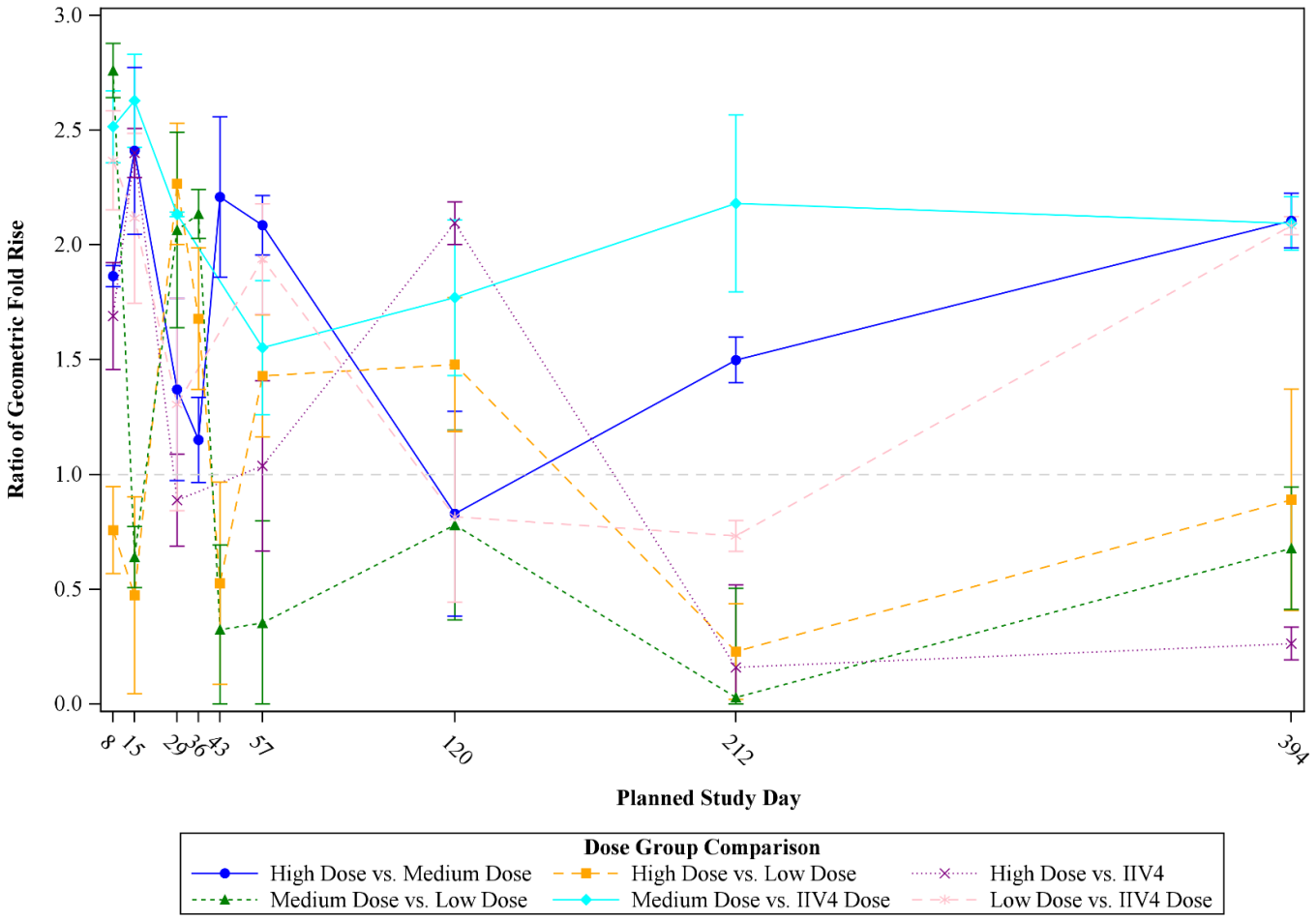


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Note: Estimates are adjusted for participants' (log-2 transformed) baseline titer for <insert assay>, participants' sex, participants' age at enrollment, and prior vaccine receipt.

Figure 6: Geometric Mean and Geometric Mean Fold-Rise from Baseline of Heterologous H1-specific Neutralizing Antibody Median Infectious Dose (ID50) Titers in Serum Measured by a Reporter Microneutralization (RMN) Assay Against [Insert Strain] by Dose Group, and Time Point – Intent-to-Treat Population

[Implementation Notes: This will be similar to Figure 2.]

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[Implementation Notes: This will be similar to Figure 3.]

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[Implementation Notes: This will be similar to Figure 2.]

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[Implementation Notes: This will be similar to Figure 3.]

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[Implementation Notes: This will be similar to Figure 4.]

Figure 11: Estimates of Ratios of Geometric Mean Fold-Rise from Baseline of Homologous H1-specific Neutralizing Antibody Endpoint Titers in Serum Measured by a Viral Microneutralization (MN) Assay Against A/New Caledonia/20/1999 (H1N1) Between Dose Groups by Time Point as Estimated by a Generalized Estimating Equation – Intent- to-Treat Population

[Implementation Notes: This will be similar to Figure 5.]

Figure 12: Geometric Mean and Geometric Mean Fold-Rise from Baseline of Heterologous H1-specific Neutralizing Antibody Endpoint Titers in Serum Measured by a Viral Microneutralization (MN) Assay Against [Insert Strain] by Dose Group, and Time Point – Intent-to- Treat Population

[Implementation Notes: This will be similar to Figure 2.]

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[Implementation Notes: This will be similar to Figure 3.]

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[Implementation Notes: This will be similar to Figure 2.]

Figure 15: Geometric Mean and Geometric Mean Fold-Rise from Baseline of Homologous Anti-HA Stalk Serum Antibody Titers ((EU)/mL), Measured by Enzyme Linked Immunosorbent Assay (ELISA) Against A/New Caledonia/20/1999 (H1N1) by Receipt of Prior Season's Influenza Vaccine, Dose Group, and Time Point – Intent-to-Treat Population

[Implementation Notes: This will be similar to Figure 3.]

Figure 16: Geometric Mean and Geometric Mean Fold-Rise from Baseline of Homologous Anti-HA Stalk Serum Antibody Titers ((EU)/mL), Measured by Enzyme Linked Immunosorbent Assay (ELISA) Against A/New Caledonia/20/1999 (H1N1) by Subsequent Receipt of Seasonal Influenza Vaccine, Dose Group, and Time Point – Intent-to-Treat Population

[Implementation Notes: This will be similar to Figure 4.]

Figure 17: Estimates of Ratios of Geometric Mean Fold-Rise from Baseline of Homologous Anti-HA Stalk Serum Antibody Titers ((EU)/mL), Measured by Enzyme Linked Immunosorbent Assay (ELISA) Against A/New Caledonia/20/1999 (H1N1) Between Dose Groups by Time Point as Estimated by a Generalized Estimating Equation – Intent-to-Treat Population

[Implementation Notes: This will be similar to Figure 5.]

Figure 18: Geometric Mean and Geometric Mean Fold-Rise from Baseline of Heterologous Anti-HA Stalk Serum Antibody Titers ((EU)/mL), Measured by Enzyme Linked Immunosorbent Assay (ELISA) Against [Insert Strain] by Dose Group, and Time Point – Intent-to-Treat Population

[Implementation Notes: This will be similar to Figure 2.]

Figure 19: Geometric Mean and Geometric Mean Fold-Rise from Baseline of Heterologous Anti-HA Stalk Serum Antibody Titers ((EU)/mL), Measured by Enzyme Linked Immunosorbent Assay (ELISA) Against [Insert Strain] by Receipt of Prior Season's Influenza Vaccine, Dose Group, and Time Point – Intent-to-Treat Population

[Implementation Notes: This will be similar to Figure 3.]

Figure 20: Mean Area Under the Curve and Mean Change from Baseline in Area Under the Curve of H. Pylori Ferritin Binding by Dose Group, and Time Point – Intent-to-Treat Population

[Implementation Notes: This will be similar to Figure 2.]

Figure 21: Mean Area Under the Curve and Mean Change from Baseline in Area Under the Curve of H. Pylori Ferritin Binding by Receipt of Prior Season's Influenza Vaccine, Dose Group, and Time Point – Intent-to-Treat Population

[Implementation Notes: This will be similar to Figure 3.]

Figure 22: Mean Area Under the Curve and Mean Change from Baseline in Area Under the Curve of H. Pylori Ferritin Binding by Subsequent Receipt of Seasonal Influenza Vaccine, Dose Group, and Time Point – Intent-to-Treat Population

[Implementation Notes: This will be similar to Figure 4.]

Figure 23: Mean Area Under the Curve and Mean Change from Baseline in Area Under the Curve of Human Ferritin Light Chain Binding by Dose Group, and Time Point – Intent-to-Treat Population

[Implementation Notes: This will be similar to Figure 2.]

Figure 24: Mean Area Under the Curve and Mean Change from Baseline in Area Under the Curve of Human Ferritin Light Chain Binding by Receipt of Prior Season's Influenza Vaccine, Dose Group, and Time Point – Intent-to-Treat Population

[Implementation Notes: This will be similar to Figure 3.]

Figure 25: Mean Area Under the Curve and Mean Change from Baseline in Area Under the Curve of Human Ferritin Light Chain Binding by Subsequent Receipt of Seasonal Influenza Vaccine, Dose Group, and Time Point – Intent-to-Treat Population

[Implementation Notes: This will be similar to Figure 4.]

Figure 26: Mean Area Under the Curve and Mean Change from Baseline in Area Under the Curve of Human Ferritin Heavy Chain Binding by Dose Group, and Time Point – Intent-to-Treat Population

[Implementation Notes: This will be similar to Figure 2.]

Figure 27: Mean Area Under the Curve and Mean Change from Baseline in Area Under the Curve of Human Ferritin Heavy Chain Binding by Receipt of Prior Season's Influenza Vaccine, Dose Group, and Time Point – Intent-to-Treat Population

[Implementation Notes: This will be similar to Figure 3.]

Figure 28: Mean Area Under the Curve and Mean Change from Baseline in Area Under the Curve of Human Ferritin Heavy Chain Binding by Subsequent Receipt of Seasonal Influenza Vaccine, Dose Group, and Time Point – Intent-to-Treat Population

[Implementation Notes: This will be similar to Figure 4.]

Figure 29: Mean Percentage of [Insert Cell Marker] Expressed in the [Insert Parent Population] Following [Insert Stimulation] Stimulation Against [Insert Strain] by Dose Group, and Time Point – Intent-to-Treat Population

[Implementation Notes: This will be similar to Figure 2.]

Figure 30: Mean Percentage of [Insert Cell Marker] Expressed in the [Insert Parent Population] Following [Insert Stimulation] Stimulation Against [Insert Strain] by Receipt of Prior Season's Influenza Vaccine, Dose Group, and Time Point – Intent-to-Treat Population

[Implementation Notes: This will be similar to Figure 3.]

Figure 31: Mean Percentage of [Insert Cell Marker] Expressed in the [Insert Parent Population] Following [Insert Stimulation] Stimulation Against [Insert Strain] by Subsequent of Prior Season's Influenza Vaccine, Dose Group, and Time Point – Intent-to-Treat Population

[Implementation Notes: This will be similar to Figure 4.]

Implementation Note: The above three figures will be repeated for each cell marker summarized by percentage of cells expressed.

Figure 32: Average Median Fluorescence Intensity of [Insert Cell Marker] in the [Insert Parent Population] Following [Insert Stimulation] Stimulation Against [Insert Strain] by Dose Group, and Time Point – Intent-to-Treat Population

[Implementation Notes: This will be similar to Figure 2.]

Figure 33: Average Median Fluorescence Intensity of [Insert Cell Marker] in the [Insert Parent Population] Following [Insert Stimulation] Stimulation Against [Insert Strain] by Receipt of Prior Season's Influenza Vaccine, Dose Group, and Time Point – Intent-to-Treat Population

[Implementation Notes: This will be similar to Figure 3.]

Figure 34: Average Median Fluorescence Intensity of [Insert Cell Marker] in the [Insert Parent Population] Following [Insert Stimulation] Stimulation Against [Insert Strain] by Subsequent of Prior Season's Influenza Vaccine, Dose Group, and Time Point – Intent-to-Treat Population

[Implementation Notes: This will be similar to Figure 4.]

Implementation Note: The above three figures will be repeated for each cell marker summarized by median fluorescence intensity.

Figure 35: Maximum Severity of Solicited Local Adverse Events by Dose Group and Severity – Safety Population

[Implementation Notes: This is an example figure. "Any Local Solicited Event" will be included as the first "Symptom".]

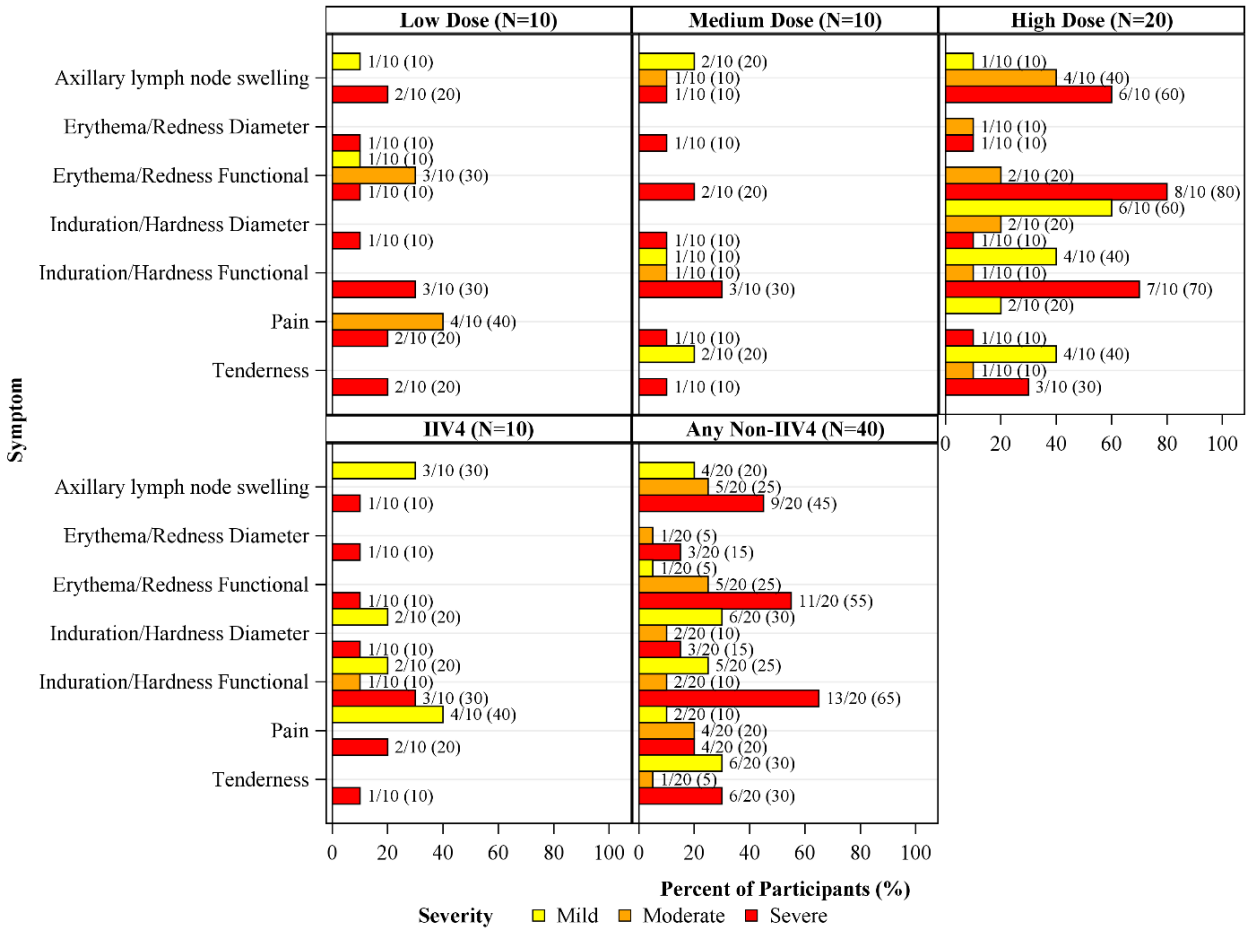


Figure 36: Maximum Severity of Solicited Systemic Adverse Events by Dose Group and Severity – Safety Population

[Implementation Note: This will be similar to Figure 35.]

Figure 37: Maximum Severity of Solicited Local Symptoms by Day Post Dose

[Implementation Notes: This will be similar to Figure 35 with the y-axis labeled as "Study Day" and will present Post-Vac, Days 1-13 individually, and Day 14+.]

Figure 38: Maximum Severity of Solicited Systemic Symptoms by Day Post Dose

[Implementation Note: This will be similar to Figure 35 with the y-axis labeled as "Study Day" and will present Post-Vac, Days 1-13 individually, and Day 14+.]

Figure 39: Frequency of Unsolicited Adverse Events Through Day 29 by Dose Group, MedDRA System Organ Class and Maximum Severity – Safety Population

[Implementation Notes: This is an example figure. The severity color-coding will match Figure 35, with no banding patterns present. "Any SOC" will be presented first, followed by all reported SOCs presented alphabetically. Panels will match Figure 35.]

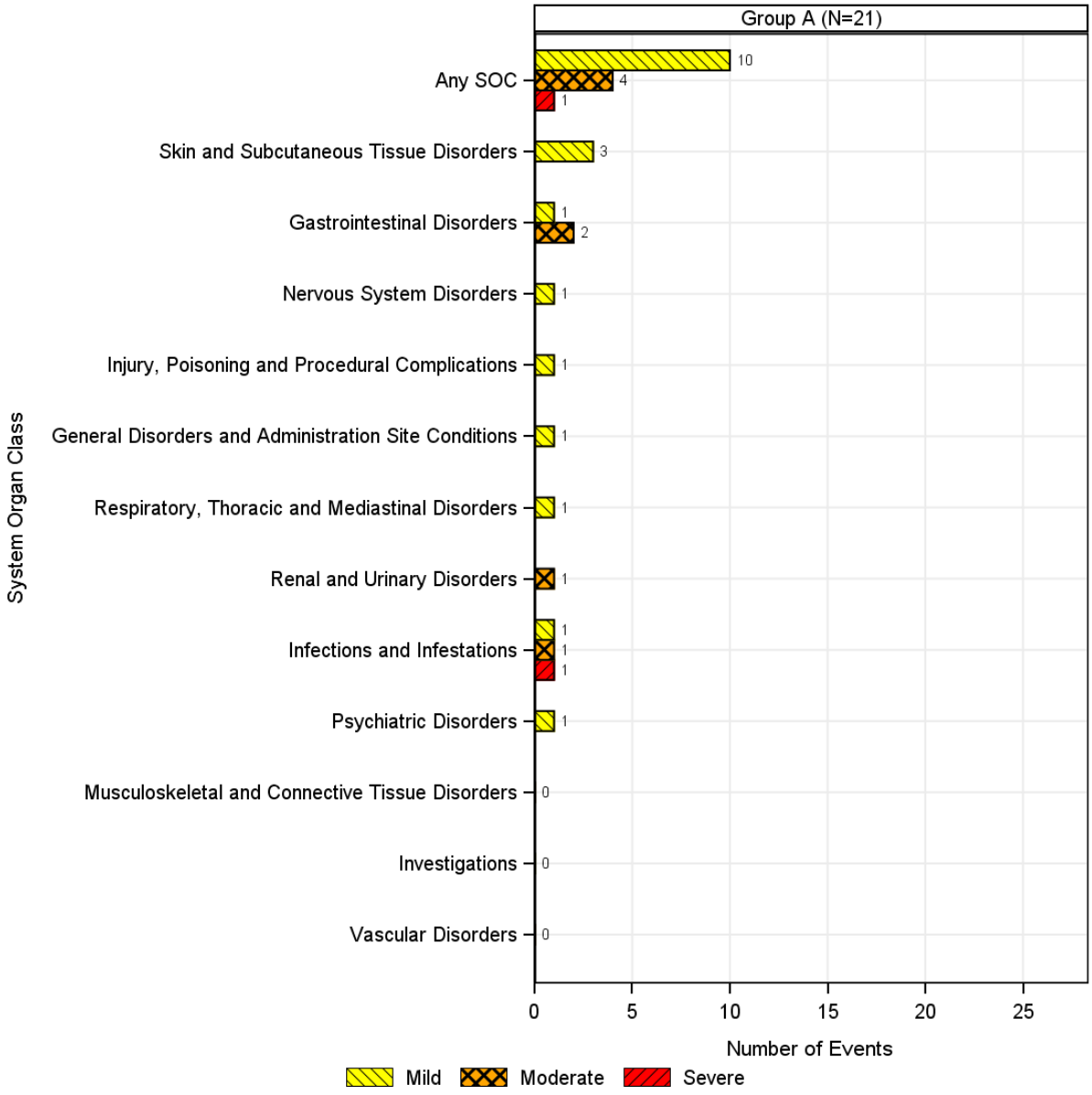


Figure 40: Incidence of Unsolicited Adverse Events Through Day 29 by Dose Group, MedDRA System Organ Class and Maximum Severity – Safety Population

[Implementation Notes: This will be similar to Figure 35 with the y-axis labeled as "System Organ Class". "Any SOC" will be presented first on the y-axis, followed by all reported SOCs presented alphabetically.]

Figure 41: Frequency of Medically Attended Adverse Events by Dose Group, MedDRA System Organ Class and Maximum Severity – Safety Population

[Implementation Note: This will be similar to Figure 39.]

Figure 42: Incidence of Medically Attended Adverse Events by Dose Group, MedDRA System Organ Class and Maximum Severity – Safety Population

[Implementation Note: This will be similar to Figure 35 with the y-axis labeled as "System Organ Class". "Any SOC" will be presented first on the y-axis, followed by all reported SOCs presented alphabetically.]

Figure 43: Frequency of New-Onset Chronic Medical Conditions by Dose Group, MedDRA System Organ Class and Maximum Severity – Safety Population

[Implementation Note: This will be similar to Figure 39.]

Figure 44: Incidence of New-Onset Chronic Medical Conditions by Dose Group, MedDRA System Organ Class and Maximum Severity – Safety Population

[Implementation Note: This will be similar to Figure 35 with the y-axis labeled as "System Organ Class". "Any SOC" will be presented first on the y-axis, followed by all reported SOCs presented alphabetically.]

Figure 45: Frequency of Influenza-Like Illnesses by Dose Group, MedDRA System Organ Class and Maximum Severity – Safety Population

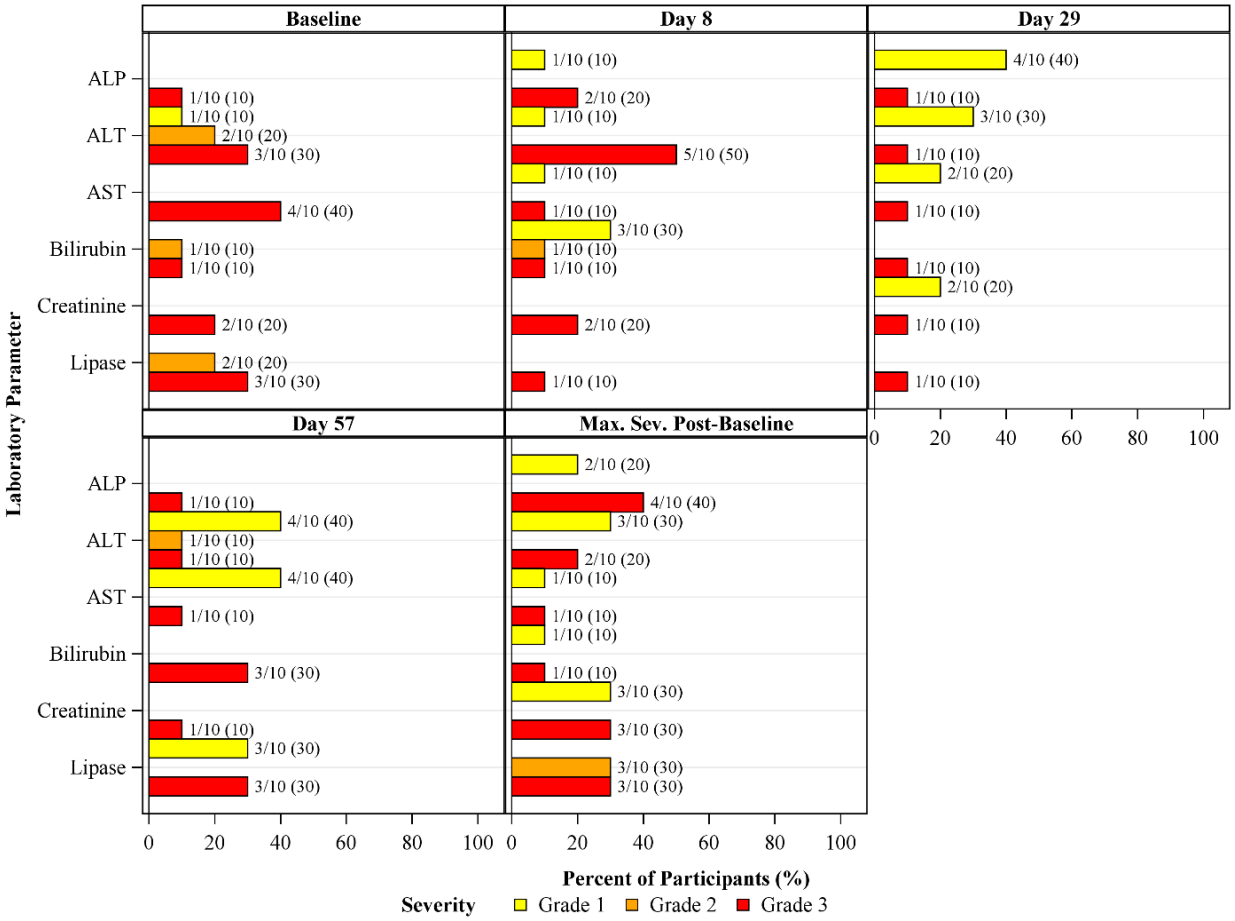
[Implementation Note: This will be similar to Figure 39.]

Figure 46: Incidence of Influenza-Like Illnesses by Dose Group, MedDRA System Organ Class and Maximum Severity – Safety Population

[Implementation Note: This will be similar to Figure 35 with the y-axis labeled as "System Organ Class". "Any SOC" will be presented first on the y-axis, followed by all reported SOCs presented alphabetically.]

Figure 47: Incidence of Graded Chemistry Clinical Laboratory Values by Parameter, and Time Point – Low Dose (10 mcg VRC H1ssF_3928 mRNA-LNP), Safety Population

[Implementation Notes: This is an example figure. "Any Chem. Lab Parameter" will be included as the first "Laboratory Parameter".]



Similar to Figure 47:

Figure 48: Incidence of Graded Chemistry Clinical Laboratory Values by Parameter and Time Point – Medium Dose (25 mcg VRC H1ssF_3928 mRNA-LNP), Safety Population

[Implementation Notes: "Any Chem. Lab Parameter" will be included as the first "Laboratory Parameter".]

Figure 49: Incidence of Graded Chemistry Clinical Laboratory Values by Parameter and Time Point – High Dose (50 mcg VRC H1ssF_3928 mRNA-LNP), Safety Population

[Implementation Notes: "Any Chem. Lab Parameter" will be included as the first "Laboratory Parameter".]

Figure 50: Incidence of Graded Chemistry Clinical Laboratory Values by Parameter and Time Point – IIV4, Safety Population

[Implementation Notes: "Any Chem. Lab Parameter" will be included as the first "Laboratory Parameter".]

Figure 51: Incidence of Graded Hematology Clinical Laboratory Values by Parameter and Time Point – Low Dose (10 mcg VRC H1ssF_3928 mRNA-LNP), Safety Population

[Implementation Notes: "Any Hem. Lab Parameter" will be included as the first "Laboratory Parameter". For applicable parameters, "Increase" and "Decrease" will be presented as separate parameters (e.g., "White Blood Cell Count Increase" and "White Blood Cell Count Decrease" will be presented separately).]

Figure 52: Incidence of Graded Hematology Clinical Laboratory Values by Parameter and Time Point – Medium Dose (25 mcg VRC H1ssF_3928 mRNA-LNP), Safety Population

[Implementation Notes: "Any Hem. Lab Parameter" will be included as the first "Laboratory Parameter". For applicable parameters, "Increase" and "Decrease" will be presented as separate parameters (e.g., "White Blood Cell Count Increase" and "White Blood Cell Count Decrease" will be presented separately).]

Figure 53: Incidence of Graded Hematology Clinical Laboratory Values by Parameter and Time Point – High Dose (50 mcg VRC H1ssF_3928 mRNA-LNP), Safety Population

[Implementation Notes: "Any Hem. Lab Parameter" will be included as the first "Laboratory Parameter". For applicable parameters, "Increase" and "Decrease" will be presented as separate parameters (e.g., "White Blood Cell Count Increase" and "White Blood Cell Count Decrease" will be presented separately).]

Figure 54: Incidence of Graded Hematology Clinical Laboratory Values by Parameter and Time Point – IIV4, Safety Population

[Implementation Notes: "Any Hem. Lab Parameter" will be included as the first "Laboratory Parameter". For applicable parameters, "Increase" and "Decrease" will be presented as separate parameters (e.g., "White Blood Cell Count Increase" and "White Blood Cell Count Decrease" will be presented separately).]

APPENDIX 3. LISTING MOCK-UPS

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

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16.1 Study Information

Listing 1: 16.1.6: Listing of Participants Receiving Study Product

[Implementation Note: Sort order: Dose group, then participant ID, then date of study product administration.]

Dose Group	Study Product Assigned	Participant ID	Date of Study Product Administration	Study Product Administration Deviations
	Presented as "Low Dose (10 mcg VRC H1ssF_3928 mRNA-LNP)" or "Medium Dose (25 mcg VRC H1ssF_3928 mRNA-LNP)" or "High Dose (50 mcg VRC H1ssF_3928 mRNA-LNP)" or "IIV4 - Immunogenicity Comparator (60 mcg [15 mcg / antigen])"			

16.2 Database Listings by Participant

16.2.1 Screen Failed or Discontinued Participants

Listing 2: 16.2.1.1: Reason for Not Enrolling

[Implementation Notes: Sort order: Dose group, then participant ID. If multiple criteria/reasons are not met/met, criteria/reasons should be separated by a semi-colon.]

Dose Group	Participant ID	Inclusion Criteria Not Met	Exclusion Criteria Met	Reason for Not Enrolling if Eligible but not Enrolled

Listing 3: 16.2.1.2: Early Terminations

[Implementation Note: Sort order: Dose group, then participant ID, then study day.]

Dose Group	Participant ID	Study Day	Reason

16.2.2 Protocol Deviations

Listing 4: 16.2.2.1: Participant-Specific Protocol Deviations

[Implementation Note: Sort order: Dose group, then participant ID, then deviation number.
In the "Deviation Description" column, concatenate any and all "specify" fields (including visit number, etc.).
If "Reason for Deviation" is "Other," concatenate "specify" field, separate by a colon, e.g., "Other: Participant refusal."
If IRB reporting was required, display "Yes" with the study day the deviation was reported to the IRB in parentheses, e.g., "Yes (20)".
If "Deviation Resulted in AE" = "Yes" then concatenate with AE number: i.e., "Yes (1)"
If "Deviation Resulted in AE" = "Yes" and Solicited Symptom is specified, then concatenate: "Yes (2)"
In the "Classification" column, "Major" or "Minor" will be indicated as determined by DMID's formal classification.]

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

Listing 5: 16.2.2.2: Non-Participant-Specific Protocol Deviations

[Implementation Notes: Sort order: site, then deviation start date. In the "Deviation Description" column, concatenate any and all "specify" fields (including visit number, etc.). If "Reason for Deviation" is "Other," concatenate "specify" field, separate by a colon, e.g., "Other: Participant refusal." If IRB reporting was required, display "Yes" with the date the deviation was reported to the IRB in parentheses, e.g., "Yes (01JAN2024)". In the "Classification" column, "Major" or "Minor" will be indicated as determined by DMID's formal classifications.]

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

16.2.3 Participants Excluded from Analysis Populations

Listing 6: 16.2.3: Participants Excluded from the Analysis Populations

[Implementation Note: Sort order: Dose group, then participant ID]

Dose Group	Participant ID	Analyses in which Participant is Included	Analyses from which Participant is Excluded	Results Available?	Reason Participant Excluded
		Safety, ITT, PP	Safety, PP		

Note: "Yes" in the "Results Available?" column indicates that available data were removed from the analysis, and "No" indicates that no data were available for inclusion in the analysis.

16.2.4 Demographic Data

Listing 7: 16.2.4.1: Demographic and Baseline Characteristics

[Implementation Note: Sort order: Dose group, then participant ID.]

Dose Group	Participant ID	Age (years)	Sex	Ethnicity	Race	Receipt of Prior Season's Influenza Vaccine[a]

[a] Captures receipt of influenza vaccine within 12 months of receipt of study vaccination. Participants were allowed to receive the seasonal influenza vaccine more than 90 days before study vaccination.

Listing 8: 16.2.4.2: Pre-Existing Medical Conditions

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

Dose Group	Participant ID	Medical History Number	Medical History Term	Condition Start Day	Condition End Day	MedDRA System Organ Class	MedDRA Preferred Term

Listing 9: 16.2.4.2: Prior Vaccinations

[Implementation Notes: Sort order: Dose group, then participant ID, then vaccine type, then date of receipt. Date of receipt should be displayed to the highest level of specificity. For example, when both month and year are known, it should be displayed as "Month YYYY", if just year is known, it should be displayed as "YYYY".]

Dose Group	Participant ID	Vaccine Type	Date of Receipt	Months Relative to Study Vaccination	Product Received	Season at Time of Vaccination[a]

[a] Applicable only for seasonal influenza vaccines

16.2.6 Individual Immunogenicity Response Data

Listing 10: 16.2.6: Individual Immunogenicity Response Data

[Implementation Notes: Sort order: Dose group, then participant ID, then planned study day, then assay, then antigen.
Examples of assays include "Reporter Microneutralization Assay in Serum", "Microneutralization Assay in Serum", "Anti-HA Stalk ELISA", etc.
Examples of units of measurement include "ID50 Titer", "Endpoint Titer", "Titer (EU/mL)", etc.
Examples of antigen include "A/New Caledonia/20/1999 (H1N1)", etc.
If a participant did not receive the prior season's influenza vaccine, the "Study Day of Prior Season's Influenza Vaccine Receipt" column will be denoted with "-"
If a participant did not have subsequent receipt of a seasonal influenza vaccine, the "Study Day of Subsequent Seasonal Influenza Vaccine Receipt" column will be denoted with "-"]

Dose Group	Participant ID	Study Day of Prior Season's Influenza Vaccine Receipt	Study Day of Subsequent Seasonal Influenza Vaccine Receipt	Planned Study Day	Actual Study Day	Assay	Target	Result	Units of Measurement

16.2.7 Adverse Events

16.2.7.1 Solicited Adverse Events

Listing 11: 16.2.7.1.1: Solicited Events -- Local Symptoms

[Implementation Notes: Sort order: Dose group, then participant ID, then post dose day, then symptom.
Study Day will be presented as "Post-Dose", "Day 1", "Day 2", etc.
Symptoms will only be presented on the applicable day if they were reported at a severity level of mild or greater.
Severity to be presented as "Mild", "Moderate", or "Severe"]

Dose Group	Participant ID	Study Day[a]	Assessment[a]	Symptom	Severity

[a]Assessments indicated as "Post-Dose" are collected by clinic staff. All other data are reported by the participant on the Memory Aid and reviewed by clinic staff and reported in the Solicited Events eCRF.

Listing 12: 16.2.7.1.2: Solicited Events – Systemic Symptoms

[Implementation Notes: Sort order: Dose group, then participant ID, then post dose day, then symptom.
Study Day will be presented as "Post-Dose", "Day 1", "Day 2", etc.
Symptoms will only be presented on the applicable day if they were reported at a severity level of mild or greater.
Severity to be presented as "Mild", "Moderate", or "Severe"
Temperature (fever) will be reported as the severity with the temperature in, ºC, in parentheses, e.g., "Mild (38.2)"]

Dose Group	Participant ID	Study Day[a]	Assessment[a]	Symptom	Severity	Attributed to Alternate Etiology?[b]	Alternate Etiology

Note: Graded temperatures are included in parentheses in ºC.
[a]Assessments indicated as "Post-Dose" are collected by clinic staff. All other data are reported by the participant on the Memory Aid and reviewed by clinic staff and reported in the Solicited Events eCRF.
[b]Reported for severe events only.

16.2.7.2 Unsolicited Adverse Events

Listing 13: 16.2.7.2: Unsolicited Adverse Events Through Day 29

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

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

Adverse Event	Study Day (Duration)	Severity	Relationship to Study Product	If Not Related, Alternative Etiology	Action Taken with Study Product	Participant Discontinued Due to AE	Classified as Unanticipated Problem	SAE/ MAAE/ NOCMC/ AESI[a]/ ILI	Outcome	MedDRA System Organ Class	MedDRA Preferred Term
Participant ID: , Dose Group: , AE Number:											
Comments:											
Notes: SAE = Serious AE, MAAE = Medically attended AE, NOCMC = New-onset medical condition, AESI = AE of special interest, ILI = Influenza-like illness. [a] Corresponding to myocarditis, pericarditis, or myopericarditis reported through Day 57											
Participant ID: , Dose Group: , AE Number:											
Comments:											
Notes: SAE = Serious AE, MAAE = Medically attended AE, NOCMC = New-onset medical condition, AESI = AE of special interest, ILI = Influenza-like illness. [a] Corresponding to myocarditis, pericarditis, or myopericarditis reported through Day 57											

16.2.8 Individual Laboratory Measurements and Other Safety Related Assessments

16.2.8.1 Individual Laboratory Measurements

Listing 14: 16.2.8.1.1: Clinical Laboratory Results – Chemistry

[Implementation Notes: This should include all laboratory results, scheduled and unscheduled. The listing is not color-coded, but the severity should be included in parentheses after the result for abnormal results, if applicable, e.g., 16.2 (Grade 1). Sort order: Dose Group, Participant ID, Actual Study Day and Laboratory Parameter. Reference ranges should be applicable to the study day presented.]

Dose Group	Participant ID	Planned Study Day	Actual Study Day	Sex	Age (years)	Laboratory Parameter (Units)	Baseline Result (Severity)	Result (Severity)	Reference Range Low – Reference Range High	Laboratory AE?	Clinical Significance	Relationship to Study Product (Alternate Etiology)	Participant Discontinued from Study Due to Result?
										Yes/No			

Listing 15: 16.2.8.1.2: Clinical Laboratory Results – Hematology

[Implementation Notes: This should include all laboratory results, scheduled and unscheduled. The listing is not color-coded, but the severity should be included in parentheses after the result for abnormal results, if applicable, e.g., 16.2 (Grade 1). Sort order: Dose Group, Participant ID, Actual Study Day and Laboratory Parameter. Reference ranges should be applicable to the study day presented. Include "NA" in the "Laboratory AE?" column for the hematology change from baseline parameter.]

Dose Group	Participant ID	Planned Study Day	Actual Study Day	Sex	Age (years)	Laboratory Parameter (Units)	Baseline Result (Severity)	Result (Severity)	Reference Range Low – Reference Range High	Laboratory AE (AESI)?[a]	Clinical Significance	Relationship to Study Product (Alternate Etiology)	Participant Discontinued from Study Due to Result?
										Yes/No			

Note: AESI = AE of special interest.

[a] For lymphocyte and neutrophil parameters only, the classification as an AESI will be presented in parentheses following the classification as an AE.

16.2.8.2 Vital Signs

Listing 16: 16.2.8.2: Vital Signs

[Implementation Notes: This listing includes all vital sign assessments, scheduled and unscheduled. These listings are not color-coded, but the severity should be included in parentheses after the result for abnormal assessments, e.g., 100.7 (Grade 1). Sort order: Dose Group, Participant ID, Actual Study Day. Multiple assessments from the same day can be entered in one cell with semicolons between values.]

Dose Group	Participant ID	Planned Study Day	Actual Study Day	Oral Temperature (°C)	Systolic Blood Pressure (mmHg)	Diastolic Blood Pressure (mmHg)	Heart Rate (beats/min)

16.2.8.3 Physical Exam Findings

Listing 17: 16.2.8.3: Physical Examination Findings

[Implementation Notes: This listing includes all physical exam findings, scheduled and unscheduled. If a participant 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)". Sort order: Dose Group, Participant ID, Planned Study Day.]

Dose Group	Participant ID	Planned Study Day	Actual Study Day	Body System	Abnormal Finding	Reported as Solicited AE? (Description)	Reported as Unsolicited AE? (AE Number)

16.2.8.4 Concomitant Medications

Listing 18: 16.2.8.4: Prior and Concomitant Medications

[Implementation Notes: sorted by Dose group, participant ID, and CM number.
"Medication Start Day" and "Medication End Day" are relative to enrollment (which is Day 1, day before enrollment is Day -1).
For medications reported > 30 days prior to enrollment, rather than using exact study days, categorize as follows: ">5 years prior to enrollment", "1-5 years prior to enrollment", "1-12 months prior to enrollment".
If ongoing, display "Ongoing" in the "Medication End Day" column.
If taken for an AE (or MH), display "Yes" with the AE (or MH) description and AE (or MH) number in parentheses, e.g., "Yes (COVID-19; 7)".]

Dose Group	Participant ID	CM Number	Medication	Medication Start Day	Medication End Day	Indication	Taken for an AE? (AE Description; Number)	Taken for a MH condition? (MH Description; Number)	ATC Level 1 (ATC Level 2)

16.2.8.5 Pregnancy Reports

Listing 19: 16.2.8.5.1: Pregnancy Reports – Maternal Information

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

Dose Group	Participant ID	Pregnancy Number	Date of Initial Report	Study Day Corresponding to Estimated Date of Conception	Source of Maternal Information	Pregnancy Status	Mother's Pre-Pregnancy BMI	Mother's Weight Gain During Pregnancy	Tobacco, Alcohol, or Drug Use During Pregnancy?	Medications During Pregnancy?	Maternal Complications During Pregnancy?	Maternal Complications During Labor, Delivery, or Post-Partum?

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

Listing 20: 16.2.8.5.2: Pregnancy Reports – Gravida and Para

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

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

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

Listing 21: 16.2.8.5.3: Pregnancy Reports – Live Birth Outcomes

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

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

Listing 22: 16.2.8.5.4: Pregnancy Reports – Still Birth Outcomes

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

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

Listing 23: 16.2.8.6.5: Spontaneous, Elective, or Therapeutic Abortion Outcomes

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

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