16.1.9 Documentation of Statistical Methods

This section contains the following document:

Statistical Analysis Plan version 3.0, dated 25 January 2021

CLINICAL RESEARCH IN INFECTIOUS DISEASES

STATISTICAL ANALYSIS PLAN
FOR
DMID PROTOCOL: 20-0003

STUDY TITLE:
PHASE I, OPEN-LABEL, DOSE-RANGING STUDY OF THE SAFETY AND IMMUNOGENICITY OF 2019-nCoV VACCINE (mRNA-1273) IN HEALTHY ADULTS

NCT04283461

VERSION 3.0

DATE: 25 JANUARY 2021

THIS COMMUNICATION IS PRIVILEGED AND CONFIDENTIAL

STUDY TITLE

Protocol Number Code:	**DMID Protocol:20-0003**
Development Phase:	Phase 1
Products:	
Form/Route:	Injection
Indication Studied:	2019-nCoV
Sponsor:	Division of Microbiology and Infectious Diseases National Institute of Allergy and Infectious Diseases National Institutes of Health
Clinical Trial Initiation Date:	03MAR2020
Clinical Trial Completion Date:	Ongoing
Date of the Analysis Plan:	25 January 2021
Version Number:	3.0

This study was performed in compliance with Good Clinical Practice.

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LIST OF ABBREVIATIONS

AE	Adverse Event
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
AUC	Area Under the Curve
BP	Blood Pressure
C	Celsius
CI	Confidence Interval
CRF	Case Report Form
DMID	Division of Microbiology and Infectious Diseases
EDC	Electronic Data Capture
ELISA	Enzyme-linked Immunosorbent Assay
F	Fahrenheit
FRNT	Focus Reduction Neutralization Test
GMT	Geometric Mean Titer
GMFR	Geometric Mean Fold Rise
ICH	International Council on Harmonisation
IRB	Institutional Review Board
LLN	Lower Limit of Normal
µg	Microgram
MedDRA	Medical Dictionary for Regulatory Activities
N	Number (typically refers to subjects)
NIH	National Institutes of Health
PI	Principal Investigator
PP	Per Protocol
PT	Preferred Term
RBC	Red Blood Cell
S-2P	S Protein in its Prefusion Conformation
SAE	Serious Adverse Event
SD	Standard Deviation
SDCC	Statistical and Data Coordinating Center
SMC	Safety Monitoring Committee

SOC	System Organ Class
SOP	Standard Operating Procedures
ULN	Upper Limit of Normal
WBC	White Blood Cell
WHO	World Health Organization

1. PREFACE

The Statistical Analysis Plan (SAP) for "Phase I, Open-Label, Dose-Ranging Study of the Safety and Immunogenicity of 2019-nCoV Vaccine (mRNA-1273) in Healthy Adults" (DMID Protocol 20-0003) describes and expands upon the statistical information presented in the protocol. This document describes all planned analyses and provides reasons and justifications for these analyses. It also includes sample tables, listings, and figures planned for the final analyses. Regarding the final analyses and Clinical Study Report (CSR), this SAP follows the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Guidelines, as indicated in Topic E3 (Structure and Content of Clinical Study Reports), and more generally is consistent with Topic E8 (General Considerations for Clinical Trials) and Topic E9 (Statistical Principles for Clinical Trials). The structure and content of the SAP provides sufficient detail to meet the requirements identified by the FDA and ICH, while all work planned and reported for this SAP will follow internationally accepted guidelines published by the American Statistical Association and the Royal Statistical Society for statistical practice.

This document contains a review of the study design, general statistical considerations, comprehensive statistical analysis methods for immunogenicity and safety outcomes, and a list of proposed tables and figures. Within the table, figure, and listing mock-ups (Appendix 1, Appendix 2, and Appendix 3), references to CSR sections are included. The reader of this SAP is encouraged to also review the study protocol for details on conduct of the study and the operational aspects of clinical assessments.

2. INTRODUCTION

In December 2019 the Wuhan Municipal Health Committee identified an outbreak of viral pneumonia cases of unknown cause. Coronavirus RNA was quickly identified in some of these patients. This novel Coronavirus (nCoV) was originally referred to as 2019-nCoV but has now been named SARS-CoV-2 (due to its similarity to the Severe Acute Respiratory Syndrome [SARS] Coronavirus [CoV; SARS-CoV]). It has 89% nucleotide identity with bat SARS-like-CoVZXC21 and 82% with that of human SARS-CoV (Chan JF et al., 2020). The disease caused by SARS-CoV-2 is called Coronavirus disease 2019 (COVID-19). On January 5, 2020 there were 59 confirmed cases, 278 cases on January 20, 2118 cases on January 26, rising to more than 110,000 confirmed cases and 3996 deaths as of March 9, 2020 according to various international health reporting agencies. Outbreak forecasting and modeling suggest that these numbers will continue to rise (Wu et al., Lancet, Jan. 31, 2020). On January 30, 2020, the International Health Regulations Emergency Committee of the World Health Organization (WHO) declared the COVID-19 outbreak a Public Health Emergency of International Concern. On January 31, 2020, the US Department of Health and Human Services declared a public health emergency in the United States. On March 11, 2020 the WHO declared COVID-19 a pandemic.

Global efforts to evaluate novel antivirals and therapeutic strategies to treat SARS-CoV-2 severe infections have intensified, but no proven therapeutic currently exists. There is currently no approved vaccine against the SARS-CoV-2 virus. Therefore, there is an urgent public health need for rapid development of novel interventions. Based on currently available information and clinical experience suggesting that older adults may be at higher risk for severe illness from COVID-19, it is important to rapidly assess clinical safety of novel vaccines in this vulnerable population as early as possible. This phase 1 clinical trial proposes to evaluate safety and immunogenicity of Moderna's mRNA-1273 in healthy adults across the age spectrum (≥18 years of age).

ModernaTX, Inc. has developed a rapid response, proprietary messenger RNA (mRNA)-based vaccine platform. This is based on the principle and observations that antigens can be produced in vivo by delivery and uptake of the corresponding mRNA by cells. The mRNA then undergoes intracellular ribosomal translation to endogenously express the protein antigen(s) encoded by the vaccine mRNA. This mRNA-based vaccine does not enter the cellular nucleus or interact with the genome, is nonreplicating, and expression is transient. mRNA vaccines thereby offer a mechanism to stimulate endogenous production of structurally intact protein antigens in a way that mimics wild-type viral infection and are able to induce good immune responses against infectious pathogens such as cytomegalovirus (CMV) (NCT03382405), human metapneumovirus (hMPV) and parainfluenza virus type 3 (PIV3) (NCT03392389) and influenza virus (NCT03076385 and NCT03345043). ModernaTX, Inc. is using its mRNA-based technology to develop a novel LNP-encapsulated messenger RNA (mRNA)-based vaccine against SARS-CoV-2. mRNA-1273 is a novel LNP mRNA-based vaccine that encodes for the full-length spike (S) protein of SARS-CoV-2, modified to introduce two proline residues to stabilize the S protein into a pre-fusogenic form.

2.1. Purpose of the Analyses

These analyses will assess the immunogenicity and safety of mRNA-1273 vaccine at 4 different dosages (25µg, 50µg, 100 µg and 250 µg; 10 µg cohort was not enrolled) and in 3 different age cohorts: 18-55 years old, 56-70 years old, and ≥71 years old.

3. STUDY OBJECTIVES AND ENDPOINTS

3.1. Study Objectives and Endpoints

OBJECTIVES	ENDPOINTS (OUTCOME MEASURES)
Primary	
To evaluate the safety and reactogenicity of a 2-dose vaccination schedule of mRNA-1273, given 28 days apart, across 5 dosages in healthy adults.	• Frequency and grade of each solicited local and systemic reactogenicity AE during a 7-day follow-up period post each vaccination. • Frequency and grade of any unsolicited AEs during the 28-day follow-up period post each vaccination. • Frequency of any SAEs, NOCMCs and MAAEs from Day 1 to Day 394.
Secondary	
To evaluate the immunogenicity as measured by IgG ELISA to the SARS-CoV-2 S (spike) protein following a 2-dose vaccination schedule of mRNA-1273 at Day 57.	• GMT of antibody at Day 57. • Percentage of subjects who seroconverted, defined as a 4-fold change in antibody titer from baseline. • The GMFR in IgG titer from baseline.
Exploratory	
To evaluate the immunogenicity as measured by IgG ELISA to the SARS-CoV-2 S (spike) protein following a 2-dose vaccination schedule of mRNA-1273 at all timepoints, other than Day 57.	• GMT of antibody at each timepoint. • Percentage of subjects who seroconverted at each timepoint. • The GMFR in IgG titer from baseline for each post-vaccination timepoint.
To evaluate the immunogenicity as measured by IgM and IgA ELISA to the SARS-CoV-2 S (spike) protein following a 2-dose vaccination schedule of mRNA-1273 given 28 days apart.	• GMT at each timepoint. • Percentage of subjects who seroconverted at each timepoint. • The GMFR in IgM and IgA titer from baseline at each post-vaccination timepoint.

OBJECTIVES	ENDPOINTS (OUTCOME MEASURES)
To evaluate the immunogenicity as measured by pseudovirus neutralization following a 2-dose vaccination schedule of mRNA-1273 given 28 days apart.	• GMT of Neut antibody at each timepoint. • Percentage of subjects who seroconverted, defined as a 4-fold change in Neut antibody titer from baseline at each timepoint. • The GMFR Neut antibody titer from baseline at each post-vaccination timepoint.
To evaluate the immunogenicity as measured by live wild-type SARS-CoV-2 neutralization following a 2-dose vaccination schedule of mRNA-1273 given 28 days apart.	• GMT of Neut antibody at each timepoint. • Percentage of subjects who seroconverted, defined as a 4-fold change in Neut antibody titer from baseline at each timepoint. • The GMFR in Neut antibody titer from baseline at each post-vaccination timepoint.
To assess, in at least a subset of samples, the SARS-CoV-2 S protein-specific T cell responses.	• Magnitude, phenotype, and percentage of cytokine producing S protein-specific T cells, as measured by flow cytometry at different timepoints post vaccination relative to baseline.

3.2. Study Definitions and Derived Variables

The baseline value will be defined as the last value obtained prior to the first vaccination of study product. Treatment Group and Cohort will be used interchangeably.

The Williams mean is a variation of the geometric mean using log(1+x) transformation of the data, where x is each data point. The Williams mean is used in cases where 0 is a possible and/or reported value of the data.

4. INVESTIGATIONAL PLAN

4.1. Overall Study Design and Plan

This is a phase I, open-label, dose ranging clinical trial in males and non-pregnant females, ≥18 years of age, who are in good health and meet all eligibility criteria. This clinical trial is designed to assess the safety, reactogenicity and immunogenicity of mRNA-1273 manufactured by ModernaTX, Inc. mRNA-1273 is a novel LNP-encapsulated mRNA-based vaccine that encodes for a full-length, prefusion stabilized spike (S) protein of SARS-CoV-2. Enrollment will occur at up to three domestic clinical research sites.

One hundred and fifty-five (155) subjects will be enrolled into one of thirteen cohorts (10 µg, 25 µg, 50 µg, 100 µg, 250 µg). Subjects will receive an IM injection (0.5 mL) of mRNA-1273 on Days 1 and 29 in the deltoid muscle and will be followed through 12 months post second vaccination (Day 394). The second dose of vaccine (0.5 mL) will be administered preferably in the same arm used for the first dose.

Follow-up visits will occur 1, 2 and 4 weeks post each vaccination (Days 8, 15, 29, 36, 43, and 57), as well as 3, 6 and 12 months post second vaccination (Days 119, 209 and 394).

Reactogenicity will be assessed at these visits, as well as blood will be drawn for immunogenicity assays. Additional safety and reactogenicity data will be solicited via telephone calls to subjects 1 and 2 days post each vaccination (Days 2, 3, 30, and 31).

To determine early safety signals for this phase I study, vaccination will proceed in a staged fashion. Sentinel subject dosing will begin with 4 subjects in cohort 1 (25 µg). The 4 sentinel subjects for cohort 2 (100 µg) will be enrolled no earlier than one day after enrollment of the last of the 4 sentinel subjects in cohort 1. If no halting rules have been met after the 8 sentinel subjects have completed Day 5, then full enrollment will proceed first with the remaining subjects in cohort 1, followed by the remaining subjects in cohort 2 without interruption. If no halting rules have been met after all subjects in cohort 2 have completed Day 8, then dosing of 4 sentinel subjects will begin in cohort 3. If no halting rules have been met after the 4 sentinel subjects in cohort 3 have completed Day 5, then full enrollment of cohort 3 will proceed.

If no halting rules have been met after all subjects in cohorts 1 and 2 have completed Day 8, dosing will begin for cohorts 4 (25 µg; 56-70 years of age) and 5 (100 µg; 56-70 years of age). If no halting rules have been met after all subjects in cohorts 4 and 5 have completed Day 8, dosing will begin for cohorts 7 (25 µg; ≥71 years of age) and 8 (100 µg; ≥71 years of age).

Based on the interim immunogenicity data available as of May 15, 2020, enrollment into cohorts 6 and 9 (250 µg; 56-70 years of age and ≥71 years of age) will be deferred in order to explore lower dosages. Therefore, enrollment of cohorts 10-12 (50 µg; 18-55 years of age, 56-70 years of age and ≥71 years of age) will be prioritized. Subjects will be enrolled simultaneously in cohorts 10-12; there will be no staging. To further explore dosage sparing, cohort 13 (10 µg dose; 18-55 years of age) may be enrolled. A decision regarding the enrollment of cohorts 6, 9 and 13 will be made after review of interim immunogenicity data from cohorts 1-5, 7, 8, and 10-12.

If no halting rules have been met after all subjects in cohorts 5 and 8 have completed Day 8, dosing will begin concurrently for cohorts 10-12. If no halting rules have been met after all subjects in cohorts 3, 7 and 8 have completed Day 8, dosing may begin for cohort 6, if enrolled.

If no halting rules have been met after all subjects in cohort 6 have completed Day 8, dosing may begin for cohort 9, if enrolled.

Note: cohorts 6, 9 and 13 were not enrolled.

For public health reasons the following early data reviews by the study team are anticipated:

- Sentinels in cohorts 1 and 2, ELISA IgG data through Day 29;
- All subjects in cohorts 1 and 2, ELISA IgG data through Day 29;
- Sentinels in cohort 3, ELISA IgG data through Day 29;
- All subjects in cohort 3, ELISA IgG data through Day 29;
- All subjects in cohorts 4, 5, 7 and 8, ELISA IgG data through Day 29;
- All subjects in cohorts 10-12, ELISA IgG data through Day 29;Sentinels in cohorts 1 and 2, ELISA IgG data through Day 57;
- All subjects in cohorts 1 and 2, ELISA IgG data through Day 57;
- Sentinels in cohort 3, ELISA IgG data through Day 57;
- All subjects in cohort 3, ELISA IgG data through Day 57;
- All subjects in cohorts 4, 5, 7 and 8, ELISA IgG data through Day 57;
- All subjects in cohorts 10-12, ELISA IgG data through Day 57;
- Additional data review of immunogenicity may be performed to inform public health decisions.
- AEs and SAEs by cohort can be reviewed as necessary.
- After Day 57 of the last subject in cohort 3, all data can be reviewed when applicable.
- After Day 57 of the last subject in cohorts 5 and 8, all available data can be reviewed when applicable.

Data may be disseminated to public health officials and partners as needed and included in scientific publications and presentations to inform the global scientific community.

Reactogenicity will be measured by the occurrence of solicited injection site and systemic reactions from the time of each vaccination through 7 days post each vaccination. Unsolicited non-serious AEs will be collected from the time of each vaccination through 28 days post each vaccination. SAEs, NOCMCs and MAAEs, will be collected through 12 months after the last vaccination (Day 394).

Clinical safety laboratory evaluations will be performed at screening, as well as immediately prior to and 7 days post each vaccination (Days 1, 8, 29, and 36).

Evaluation of immunogenicity will include quantitation of antibodies to the SARS-CoV-2 S protein at multiple timepoints post vaccination as measured by ELISA, pseudovirus and live wild-type virus neutralization assays. In addition, exploratory studies to characterize T cell responses are planned. Venous blood will also be collected at multiple timepoints post vaccination for the secondary research use of serum, plasma and PBMCs.

To support development of diagnostics, therapeutics and vaccines, a subset of subjects enrolled in cohorts 2, 3, 5, 10, and 11 have undergone leukapheresis to collect additional samples for secondary research. If enrollment in cohort 6 proceeds, a subset of subjects in this cohort may also undergo leukapheresis.

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

This study is designed as an open-label study, without a placebo arm. Given the small sample size, the use of a placebo group is unlikely to improve understanding of AEs. Additionally, having the study unblinded will facilitate the need for rapid review and dissemination of study data for public health reasons.

No human trials of mRNA-1273 have been conducted to date. Preclinical evaluations will occur in parallel with this phase I study. In several ongoing phase 1 dose-ranging studies (mRNA-1653, a combination vaccine against human metapneumovirus, hMPV and human parainfluenza type 3; mRNA-1647 and mRNA-1443, both CMV vaccines; mRNA-1893 against Zika virus) dosage levels of mRNA between 10 and 300 µg were administered IM as one-, two- or three-dose vaccination schedules. Immunogenicity and reactogenicity increased in a dose-dependent manner. The dosage levels proposed for this trial (10 µg, 25 µg, 50 µg, 100 µg, 250 µg) are within the range of previous trials. However, in support of development of mRNA-1273 for prophylaxis against SARS-CoV-2 infection, nonclinical immunogenicity, biodistribution, and safety studies have been completed with similar mRNA-based vaccines formulated in SM-102-containing LNPs.

4.3. Selection of Study Population

Up to one hundred and fifty-five (155) males and non-pregnant females, ≥18 years of age, who are in good health and meet all eligibility criteria will be enrolled, depending on enrollment of cohorts 6, 9, and 13. The target population should reflect the community at large. The estimated time from initiation of enrollment to complete enrollment in this trial is approximately 12 weeks. Information regarding this trial may be provided to potential subjects who have previously participated in other vaccine trials conducted at the site. Other forms and/or mechanisms of recruitment may also be used. The IRB will approve the recruitment process and all materials prior to use. Screening can occur up to 42 days prior to the first dose.

Subject Inclusion and Exclusion Criteria must be confirmed by a study clinician, licensed to make medical diagnoses and listed on the Form FDA 1572 as the participating site PI or appropriate sub-investigator. No exemptions are granted on Subject Inclusion or Exclusion Criteria in DMID-sponsored studies.

Inclusion Criteria

A subject must meet all of the following criteria to be eligible to participate in this study:

1. Provides written informed consent prior to initiation of any study procedures.
2. Be able to understand and agrees to comply with planned study procedures and be available for all study visits.
3. Agrees to the collection of venous blood per protocol.

4. Male or non-pregnant female, ≥18 years of age, at time of enrollment.
5. Body Mass Index 18-35 kg/m^2, inclusive, at screening.
6. Women of childbearing potential[1] must agree to use or have practiced true abstinence[2] or use at least one acceptable primary form of contraception.[3,4]

   Note: These criteria are applicable to females in a heterosexual relationship and child-bearing potential (i.e., the criteria do not apply to subjects in a same sex relationship).

   [1]Not of childbearing potential – post-menopausal females (defined as having a history of amenorrhea for at least one year) or a documented status as being surgically sterile (hysterectomy, bilateral oophorectomy, tubal ligation/salpingectomy, or Essure® placement).

   [2]True abstinence is 100% of time no sexual intercourse (male's penis enters the female's vagina). (Periodic abstinence [e.g., calendar, ovulation, symptothermal, post-ovulation methods] and withdrawal are not acceptable methods of contraception).

   [3]Acceptable forms of primary contraception include monogamous relationship with a vasectomized partner who has been vasectomized for 180 days or more prior to the subject's first vaccination, intrauterine devices, birth control pills, and injectable/implantable/insertable hormonal birth control products.

   [4]Must use at least one acceptable primary form of contraception for at least 30 days prior to the first vaccination and at least one acceptable primary form of contraception for 60 days after the last vaccination.
7. Women of childbearing potential must have a negative urine or serum pregnancy test within 24 hours prior to each vaccination.
8. Male subjects of childbearing potential[5]: use of condoms to ensure effective contraception with a female partner of childbearing potential from first vaccination until 60 days after the last vaccination.

   [5]*Biological males who are post-pubertal and considered fertile until permanently sterile by bilateral orchiectomy or vasectomy.*
9. Male subjects agree to refrain from sperm donation from the time of first vaccination until 60 days after the last vaccination.
10. In good health.[6]

    [6]*As determined by medical history and physical examination to evaluate acute or ongoing chronic medical diagnoses/conditions that have been present for at least 90 days, which would affect the assessment of safety of subjects. Chronic medical diagnoses/conditions should be stable for the last 60 days (no hospitalizations, ER, or urgent care for condition or need for supplemental oxygen). This includes no change in chronic prescription medication, dose, or frequency as a result of deterioration of the chronic medical diagnosis/condition in the 60 days before enrollment. Any prescription change that is due to change of health care provider, insurance company, etc., or done for financial reasons, and in the same class of medication, will not be considered a deviation of this inclusion criterion. Any change in prescription medication due to* ***improvement*** *of*

a disease outcome, as determined by the site principal investigator or appropriate sub-investigator, will not be considered a deviation of this inclusion criterion. Subjects may be on chronic or as needed (prn) medications if, in the opinion of the site principal investigator or appropriate sub-investigator, they pose no additional risk to subject safety or assessment of reactogenicity and immunogenicity, and do not indicate a worsening of medical diagnosis/condition. Similarly, medication changes subsequent to enrollment and study vaccination are acceptable provided the change was not precipitated by deterioration in the chronic medical condition, and there is no anticipated additional risk to the subject or interference with the evaluation of responses to study vaccination.

11. Oral temperature is less than 100.0°F (37.8°C).
12. Pulse no greater than 100 beats per minute.
13. Systolic BP is 85 to 150 mmHg, inclusive (<65 years of age); Systolic BP is 85 to 160 mm Hg, inclusive (subjects ≥65 years of age).
14. Clinical screening laboratory evaluations (WBC, Hgb, PLTs, ALT, AST, Cr, ALP, T. Bili, Lipase, PT, and PTT) are within acceptable normal reference ranges at the clinical laboratory being used.
15. Must agree to have samples stored for secondary research.
16. Agrees to adhere to Lifestyle Considerations (defined in Section 5.4 of the protocol) throughout study duration.
17. The subject must agree to refrain from donating blood or plasma during the study (outside of this study).

Leukapheresis Inclusion Criteria

A subject must meet all of the following criteria to be eligible for leukapheresis:

1. Written informed consent for leukapheresis is provided.
2. Weight ≥110 pounds.
3. Screening laboratory evaluations are within acceptable ranges at the site where the leukapheresis procedure will be performed.
4. Negative urine or serum pregnancy test within 48 hours of the leukapheresis procedure for women of childbearing potential.
5. Adequate bilateral antecubital venous access.
6. No use of blood thinners, aspirin or NSAIDs at least 5 days before the leukapheresis procedure.
7. Enrolled in cohorts 2, 3, 5, 10, or 11, and completed the two-dose vaccination series.

Exclusion Criteria

A subject who meets any of the following criteria will be excluded from participation in this study:

1. Positive pregnancy test either at screening or just prior to each vaccine administration.

2. Female subject who is breastfeeding or plans to breastfeed from the time of the first vaccination through 60 days after the last vaccination.
3. Has any medical disease or condition that, in the opinion of the site PI or appropriate sub-investigator, precludes study participation.[7]

   [7]*Including acute, subacute, intermittent or chronic medical disease or condition that would place the subject at an unacceptable risk of injury, render the subject unable to meet the requirements of the protocol, or may interfere with the evaluation of responses or the subject's successful completion of this trial.*
4. Presence of self-reported or medically documented significant medical or psychiatric condition(s).[8]

   [8]*Significant medical or psychiatric conditions include but are not limited to:*

   Respiratory disease (e.g., chronic obstructive pulmonary disease [COPD], asthma) requiring daily medications currently or any treatment of respiratory disease exacerbations (e.g., asthma exacerbation) in the last 5 years. Asthma medications: inhaled, oral, or intravenous (IV) corticosteroids, leukotriene modifiers, long and short acting beta agonists, theophylline, ipratropium, biologics.

   Significant cardiovascular disease (e.g., congestive heart failure, cardiomyopathy, ischemic heart disease) or history of myocarditis or pericarditis as an adult, myocardial infarction (MI) within past 6 months, coronary artery bypass surgery or stent placement, or uncontrolled cardiac arrhythmia.

   Neurological or neurodevelopmental conditions (e.g., history of migraines in the past 5 years, epilepsy, stroke, seizures in the last 3 years, encephalopathy, focal neurologic deficits, Guillain-Barré syndrome, encephalomyelitis or transverse myelitis, stroke or transient ischemic attack, multiple sclerosis, Parkinson's disease, amyotrophic lateral sclerosis, Creutzfeldt-Jakob disease, or Alzheimer's disease).

   Ongoing malignancy or recent diagnosis of malignancy in the last five years excluding basal cell and squamous cell carcinoma of the skin, which are allowed.

   An autoimmune disease, including hypothyroidism without a defined non-autoimmune cause, localized or history of psoriasis.

   An immunodeficiency of any cause.

   Chronic kidney disease, estimated glomerular filtration rate (eGFR) <60 mL/min/1.73m^2.
5. Has an acute illness[9], as determined by the site PI or appropriate sub-investigator, with or without fever [oral temperature ≥38.0°C (100.4°F)] within 72 hours prior to each vaccination.

   [9]*An acute illness which is nearly resolved with only minor residual symptoms remaining is allowable if, in the opinion of the site PI or appropriate sub-investigator, the residual symptoms will not interfere with the ability to assess safety parameters as required by the protocol.*
6. Has a positive test result for hepatitis B surface antigen, hepatitis C virus antibody, or HIV types 1 or 2 antibodies at screening.

7. Has participated in another investigational study involving any investigational product[10] within 60 days, or 5 half-lives, whichever is longer, before the first vaccine administration.

   [10]*study drug, biologic or device*

8. Currently enrolled in or plans to participate in another clinical trial with an investigational agent[11] that will be received during the study-reporting period.[12]

   [11]*Including licensed or unlicensed vaccine, drug, biologic, device, blood product, or medication.*

   [12]*13 months after the first vaccination.*

9. Has previously participated in an investigational study involving LNPs (a component of the investigational vaccine assessed in this trial).
10. Has a history of hypersensitivity or severe allergic reaction (e.g., anaphylaxis, generalized urticaria, angioedema, other significant reaction) to any previous licensed or unlicensed vaccines.
11. Chronic use (more than 14 continuous days) of any medications that may be associated with impaired immune responsiveness.[13]

    [13]*Including, but not limited to, systemic corticosteroids exceeding 10 mg/day of prednisone equivalent, allergy injections, immunoglobulin, interferon, immunomodulators, cytotoxic drugs, or other similar or toxic drugs during the preceding 6-month period prior to vaccine administration (Day 1). The use of low dose topical, ophthalmic, inhaled and intranasal steroid preparations will be permitted.*

12. Anticipating the need for immunosuppressive treatment within the next 6 months.
13. Received immunoglobulins and/or any blood or blood products within the 4 months before the first vaccine administration or at any time during the study.
14. Has any blood dyscrasias or significant disorder of coagulation.
15. Has any chronic liver disease, including fatty liver.
16. Has a history of alcohol abuse or other recreational drug (excluding cannabis) use within 6 months before the first vaccine administration.
17. Has a positive test result for drugs of abuse at screening or before the first vaccine administration. If cannabis is the only detected drug, inclusion is permitted.
18. Has any abnormality or permanent body art (e.g., tattoo) that would interfere with the ability to observe local reactions at the injection site (deltoid region).
19. Received or plans to receive a licensed, live vaccine within 4 weeks before or after each vaccination.
20. Received or plans to receive a licensed, inactivated vaccine within 2 weeks before or after each vaccination.
21. Receipt of any other SARS-CoV-2 or other experimental coronavirus vaccine at any time prior to or during the study.

22. Close contact of anyone known to have SARS-CoV-2 infection within 30 days prior to vaccine administration.
23. History of COVID-19 diagnosis.
24. On current treatment with investigational agents for prophylaxis of COVID-19.
25. Current use of any prescription or over-the-counter medications within 7 days prior to vaccination, unless approved by the investigator or necessary to manage a chronic condition.
26. Plan to travel outside the US (continental US, Hawaii, and Alaska) from enrollment through 28 days after the second vaccination.
27. Reside in a nursing home or other skilled nursing facility or have a requirement for skilled nursing care.
28. Non-ambulatory.
29. For subjects ≥56 years of age, history of chronic smoking within the prior year.
30. For subjects ≥56 years of age, current smoking or vaping.
31. For subjects ≥56 years of age, individuals currently working with high risk of exposure to SARS-CoV-2 (e.g., active health care workers with direct patient contact, emergency response personnel).

Exclusion of Specific Populations

This is a first-in-human trial in healthy subjects, ≥18 years of age. Because the effects on the fetus are not known, pregnant women will not be eligible for the trial. Women of childbearing potential must utilize a highly effective method of contraception and will be required to have a negative urine or serum pregnancy test within 24 hours prior to each vaccination. Children will not be included in this trial as presently there are no safety or efficacy data in adults. Should the outcome of this trial be deemed acceptable, additional trials may be initiated, including those in other populations.

4.4. Treatments

4.4.1. Treatments Administered

Two doses of mRNA-1273 will be administered at 3 dose levels on Days 1 and 29.

4.4.2. Identity of Investigational Product(s)

Product: mRNA-1273

mRNA-1273 is an LNP dispersion containing an mRNA that encodes for the pre fusion stabilized spike protein SARS-CoV-2. mRNA-1273 consists of an mRNA Drug Substance that is manufactured into LNPs composed of a proprietary ionizable lipid and 3 commercially available lipids, cholesterol, DSPC, and PEG2000 DMG. mRNA-1273 has a total lipid content of 9.7 mg/mL and is formulated at a concentration of 0.5 mg/mL in 20 mM trometamol (Tris) buffer containing 87 mg/mL sucrose and 10.7 mM sodium acetate, at pH 7.5.

Diluent: 0.9% NaCl for injection, USP

The USP grade 0.9% NaCl or normal saline for injection is a sterile, nonpyrogenic, isotonic solution; each mL contains NaCl 9 mg. It contains no bacteriostatic agent, antimicrobial agent, preservatives, or added buffer and is supplied only in single-dose containers. The solution may contain hydrochloric acid and/or sodium hydroxide for pH adjustment (pH 5.3, range 4.5-7.0). This product should be used to dilute the vaccine to the desired concentration.

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

This is an open-label trial with sequential group enrollment so randomization and blinding will not be utilized.

4.4.4. Selection of Doses in the Study

No human trials of mRNA-1273 have been conducted to date. Preclinical evaluations will occur in parallel with this phase I study. In several ongoing phase 1 dose-ranging studies (mRNA-1653, a combination vaccine against human metapneumovirus, hMPV and human parainfluenza type 3; mRNA-1647 and mRNA-1443, both CMV vaccines; mRNA-1893 against Zika virus) dosage levels of mRNA between 10 and 300 µg were administered IM as one-, two- or three-dose vaccination schedules. Immunogenicity and reactogenicity increased in a dose-dependent manner. The dosage levels proposed for this trial (25 µg, 100 µg, 250 µg) are within the range of previous trials. However, in support of development of mRNA-1273 for prophylaxis against SARS-CoV-2 infection, nonclinical immunogenicity, biodistribution, and safety studies have been completed with similar mRNA-based vaccines formulated in SM-102-containing LNPs.

4.4.5. Prior and Concomitant Therapy

Information about prior medications, including hormonal contraceptives, taken by the subject in the 30 days prior to providing informed consent will be recorded on the appropriate DCF.

Concomitant medications include all medications (prescription, over the counter, supplements, and vaccines received outside of the study) taken by the subject from the time the informed consent is signed through Day 394. At each study visit following dosing, including telephone calls, subjects will be queried about new concomitant medications and changes to existing medications.

Medications that might interfere with the evaluation of the investigational product should not be used by the subject during the study-reporting period (12 months after the last vaccination) unless clinically indicated as part of the subject's health care.

In the event medical conditions dictate the use of medications, subjects are encouraged to obtain adequate care, comply with the course of therapy as prescribed by their physician, and inform the study Investigator as soon as practical. Any drug or vaccine used or received by the subject during the trial should be recorded on the appropriate DCF.

4.4.6. Treatment Compliance

All subjects are to receive 2 doses of study product administered in the clinic.

5. SAMPLE SIZE CONSIDERATIONS

Rare AEs are not demonstrable in a clinical study of this size; however, the probabilities of observing one or more AEs given various true event rates are presented in Table 3. With the assumption that all enrolled subjects will likely complete immunizations and safety visits in this relatively short duration study, the following statistical considerations apply. With 15 subjects in each dose group (cohorts 1-3,10,13), the chance of observing at least one AE of probability 20% or more is approximately 97%. Therefore, if no AEs of a given type occur in a dose group (cohorts 1-3,10,13), we can be relatively confident that they will occur in fewer than 20% of people once the vaccine is implemented. With 60 subjects across these four dosing cohorts (1-3,10), the chance of observing at least one AE of probability 5% or more is at least 95%. Therefore, if no AEs of a given type occur across the combined doses, we can be very confident that any dosage-independent event will occur in fewer than 5% of people once the vaccine is implemented. If Cohort 13 is enrolled and there are 75 subjects across five dosing cohorts (1-3,10,13), the chance of observing at least one AE of probability 5% or more is at least 97.9%. Therefore, if no AEs of a given type occur across the combined doses, we can be very confident that any dosage-independent event will occur in fewer than 5% of people once the vaccine is implemented. With 10 subjects in each dose group (cohorts 4-9,11-12), the chance of observing at least one AE of probability 20% or more is approximately 89.3%. Therefore, if no AEs of a given type occur in a dose group (cohorts 4-9,11-12), we can be relatively confident that they will occur in fewer than 20% of people once the vaccine is implemented in the older population. With 30 subjects across each of the two older subject dosing cohorts (i.e., cohorts 4,5,11 and 7,8,12), the chance of observing at least one AE of probability 5% or more is at least 78.5%. Therefore, if no AEs of a given type occur across the combined doses, we can be very confident that any dosage-independent event will occur in fewer than 5% of older people once the vaccine is implemented. If Cohorts 6 and 9 are enrolled and there are 40 subjects across each of the two older subject dosing cohorts (i.e., cohorts 4,5,6,11 and 7,8,9,12), the chance of observing at least one AE of probability 5% or more is at least 87.1%. Therefore, if no AEs of a given type occur across the combined doses, we can be very confident that any dosage-independent event will occur in fewer than 5% of older people once the vaccine is implemented.

6. GENERAL STATISTICAL CONSIDERATIONS

6.1. General Principles

All continuous variables will be summarized using the following descriptive statistics: n (non-missing sample size), mean, standard deviation, median, maximum and minimum. The frequency and percentages (based on the non-missing sample size) of observed levels will be reported for all categorical measures. In general, all data will be listed, sorted by site, treatment and subject, and when appropriate by visit number within subject. All summary tables will be structured with a column for each treatment and will be annotated with the total population size relevant to that table/cohort, including any missing observations.

6.2. Analysis Populations

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

The modified intent-to-treat (mITT) population includes all subjects who received one dose of vaccine and contributed both pre- and at least one post-vaccination venous blood samples for immunogenicity testing for which valid results were reported.

6.2.2. Per Protocol Population

In the final analysis, protocol deviations will be reviewed to determine which protocol deviations may affect the analysis. The per protocol (PP) population will then be defined – and this includes all subjects in the mITT subset with the following exclusions:

- Data from all available visits for subjects found to be ineligible at baseline.
- Data from all visits subsequent for the protocol deviations that are considered to affect the science.
- Data from any visit that occurs substantially out of window.

6.2.3. Safety Population

The Safety Analysis population includes all subjects who received one dose of vaccine.

6.3. Covariates and Subgroups

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

6.4. Missing Data

There are no imputations planned for missing data.

For neutralization assays, any percent neutralization below zero will be imputed as zero for modeling purposes.

6.5. Interim Analyses and Data Monitoring

Cumulative safety information, study status, and primary endpoint results may be published, presented at a public forum, or presented as summaries aggregated by study arm at the discretion of the sponsor while the primary study is ongoing. Any ad-hoc analyses, jointly developed by the SDCC and/or the VRC and ModernaTX, Inc., will be executed by the SDCC as needed. None of the interim analyses will include any formal statistical hypothesis testing; therefore, p value adjustment will not be made to any analyses.

The SMC will not need to meet (unless halting rules are met) and materials will be provided electronically. Documentation of review and any concerns will be solicited electronically.

The SMC will review cumulative AE data after all subjects in cohorts 1 and 2 have completed Day 8. In addition, cumulative AE data will be provided to the SMC after all subjects in cohorts 3, 4, 5, 7, and 8 have completed Day 8. Cumulative AE data will also be provided to the SMC after all subjects in all cohorts have completed Day 57. Documentation of review and any concerns noted will be solicited electronically.

For public health reasons there will be several immunogenicity reviews. The following reviews are anticipated once data are available:

- For sentinel subjects in cohorts 1 and 2, the ELISA IgG data through Day 29;
- For all subjects in cohorts 1 and 2, the ELISA IgG data through Day 29;
- For sentinel subjects in cohort 3, the ELISA IgG data through Day 29;
- For all subjects in cohort 3, the ELISA IgG data through Day 29;
- All subjects in cohorts 4, 5, 7 and 8, ELISA IgG data through Day 29;
- All subjects in cohorts 10-12, ELISA IgG data through Day 29;
- Sentinels in cohorts 1 and 2, ELISA IgG data through Day 57;
- All subjects in cohorts 1 and 2, ELISA IgG data through Day 57;
- Sentinels in cohort 3, ELISA IgG data through Day 57;
- All subjects in cohort 3, ELISA IgG data through Day 57;
- All subjects in cohorts 4, 5, 7 and 8, ELISA IgG data through Day 57;
- All subjects in cohorts 10-12, ELISA IgG data through Day 57;
- Additional data review of immunogenicity may be performed to inform public health decisions.

Data may be disseminated to public health officials and partners as needed and included in scientific publications and presentations to inform the global scientific community.

An interim clinical study report (CSR) will be completed for cohorts 1-5 and 7-8 through Day 119 and cohorts 10-12 through Day 57. Analysis will include safety, reactogenicity and immunogenicity and will be done once data are entered in the database, validate and monitored

according to the clinical monitoring plan (CMP). Immunogenicity data for the interim CSR will be based on the per protocol population. .

6.6. Multicenter Studies

Data will be pooled across all clinical sites. Center effects are not anticipated because the sites are using standardized procedures for vaccination and assessment of solicited and unsolicited adverse events, and the study relies on central laboratories for the assessment of immunogenicity endpoints.

6.7. Multiple Comparisons/Multiplicity

There are no adjustments planned for multiple comparisons.

7. STUDY SUBJECTS

7.1. Disposition of Subjects

Table 14 will present a summary of the reasons that subjects were screened but not enrolled.

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

The disposition of subjects in the study will be tabulated by treatment group (Table 10, Table 11 and Table 12). The table shows the total number of subjects screened, enrolled, receiving first vaccination, discontinuing treatment, receiving second vaccination, study ongoing or terminated from study follow-up and the number completing the study.

A flowchart showing the disposition of study subjects, adapted from the Consort Statement [1] will be included (Figure 1, Figure 2 and Figure 3). This figure will present the number of subjects screened, enrolled, lost to follow-up, and analyzed, by treatment group.

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

7.2. Protocol Deviations

A summary of subject-specific protocol deviations will be presented by the reason for the deviation, the deviation category, and treatment group for all subjects (Table 4, Table 5, Table 6) as well as similar summaries for major subject-specific protocol deviations (Table 7, Table 8 and Table 9). All subject-specific protocol deviations and non-subject specific protocol deviations will be included in Appendix 3 as data listings (Listing 3 and Listing 4, respectively).

8. IMMUNOGENICITY EVALUATION

8.1. Primary Immunogenicity Analysis

See Section 9 for safety analyses which are the primary endpoints of this study.

8.2. Secondary Immunogenicity Analyses

Summaries and analysis of immunogenicity data will be presented for the mITT population. If there are protocol deviations which may affect the analysis, a per-protocol (PP) analysis may also be performed. If PP population is different than mITT then the PP population will be used in the interim CSR (iCSR).

Seroconversion is defined as a 4-fold increase in antibody titer over baseline. AUC is calculated using the trapezoidal method applied to a serial dilution curve. For samples with an AUC of zero at baseline, fold-rise will be calculated by dividing post-vaccination result by the lowest reported value.

Seroconversion rates, GMFR, GMT or Williams mean of the AUC for SARS-CoV-2 (S-2P and RBD) as measured by IgG ELISA will be calculated at Days 1 (GMT only) and 57 by cohort and will be summarized graphically (log_{10} scale). Seroconversion rates, GMFR, GMT or Williams mean of the AUC will be presented with their corresponding 95% confidence interval (CI) estimates (using Student's t-distribution) at each timepoint and overall peak GMT/AUC (starting at Table 24 and ending at Table 47 for GMT/Williams mean and starting at Table 114 and ending at Table 137 for GMFR and seroconversion summaries). Graphical displays will include reverse cumulative distribution plots (Figure 4, Figure 5, Figure 6, Figure 7, Figure 8, Figure 9, Figure 10 and Figure 11), individual titer values over time (starting at Figure 12 and ending at Figure 19), geometric mean over time (Figure 24, Figure 25, Figure 26, Figure 27, Figure 28, Figure 29, Figure 30 and Figure 31) and distributions of responses over time (starting at Figure 48 and ending at Figure 71). Note only endpoint titer values will be reported in the iCSR.

Individual immunogenicity responses are shown in Listing 8.

8.3. Exploratory Immunogenicity Analyses

Summaries and analysis of immunogenicity data will be presented for the mITT population. If there are protocol deviations which may affect the analysis, a PP analysis may also be performed. If PP population is different than mITT then the PP population will be used in the interim CSR.

Seroconversion is defined as a 4-fold increase in antibody titer over baseline.

Seroconversion rates, GMFR, GMT or Williams mean of AUC for SARS-CoV-2 (S-2P and RBD) as measured by IgG, IgA and IgM ELISA, calculated for specified timepoints by cohort and will be summarized graphically (log_{10} scale). Seroconversion rates, GMFR, GMT, and Williams mean of AUC will be presented with their corresponding 95% CI estimates (using Student's t-distribution) at each timepoint and overall peak GMT/AUC (starting at Table 24 and ending at Table 47 for GMT/Williams mean and starting at Table 114 and ending at Table 137 for GMFR and seroconversion summaries). AUC is calculated using the trapezoidal method applied to a serial dilution curve. For samples with an AUC of zero at baseline, fold-rise will be

calculated by dividing post-vaccination result by the lowest reported value. Graphical displays will include reverse cumulative distribution plots (Figure 4, Figure 5, Figure 6, Figure 7, Figure 8, Figure 9, Figure 10 and Figure 11), individual titer values over time (starting at Figure 12 and ending at Figure 23), geometric mean over time (Figure 24, Figure 25, Figure 26, Figure 27, Figure 28, Figure 29, Figure 30 and Figure 31) and distributions of responses over time (starting at Figure 48 and ending at Figure 71). Note only endpoint titer values will be reported in the iCSR.

Neutralization assays using SARS-CoV-2 pseudovirus neutralization assay (PsVNA) or a wild-type SARS-CoV-2 plaque reduction neutralization test (PRNT) will be run using serial dilutions. ID_{50} and ID_{80} will be calculated for PsVNA data using a 5-parameter logistic regression model. ID_{50} and ID_{80} will be summarized by group using the geometric mean and 95% CI (using Student's t-distribution) (starting at Table 48 and ending at Table 59). Table 60, Table 61, Table 62 and Table 63 show the day 43 GM summaries of the PsVNA assay at day 43 of the 614D variant. Similarly, for PRNT data, $PRNT_{80}$ will be calculated using a 5-parameter logistic model. $PRNT_{80}$ will be summarized using a geometric mean and 95% CI (Table 64, Table 65, Table 66, Table 67, Table 68 and Table 69). Neutralization endpoints will also be displayed graphically on a $\log_2$ or a $\log_{10}$ scale. Similar methods will be used to summarize all additional neutralization assays performed (nanoluciferase-based live virus high throughput neutralization assay, nLuc HTNA, and 2 versions of a live virus focus-reduction neutralization test, FRNT and FRNT-mNG) (starting at Table 70 and ending at Table 95). Graphical displays for PsVNA will include individual titer values over time (Figure 20, Figure 21, Figure 22, and Figure 23), geometric mean over time (Figure 32, Figure 33, Figure 34, and Figure 35) and distributions of responses over time (starting at Figure 72 and ending at Figure 83). Graphical displays for PRNT, nLuc-HTNA, FRNT and FRNT-mNG will include geometric mean over time (starting and Figure 36 and ending at Figure 47) and distributions of responses over time (starting at Figure 84 and ending at Figure 103).

Individual immunogenicity responses are shown in Listing 8.

Spearman correlation between various binding and neutralization assays will be assessed starting at Figure 104 and ending at Figure 115.

Summaries and analysis of cellular assay data will be presented for the mITT population. If there are protocol deviations which may affect the analysis, a PP analysis may also be performed. If PP population is different than mITT, then the PP population will be used in the interim CSR.

The magnitude, phenotype and percentage of cytokine producing S protein-specific T cells will be summarized at each timepoint by Treatment Group. Mean percentages of CD4 T-cells and 95% confidence will be presented for Th1 and Th2 responses using S1 and S2 peptide pool stimulations starting at Table 96 and ending at Table 107. The Th1 cell types tested will be interferon gamma (IFN-γ), interleukin-2 (IL-2) and tumor necrosis factor alpha (TNF-α). The Th2 cell types tested will be interleukin-13 (IL-13) and interleukin-4 (IL-4). Mean percentages of CD8 T-cells and 95% confidence will be presented using S1 and S2 peptide pool stimulations starting at Table 108 and ending at Table 113. The CD8 cell types tested will be IFN-γ, IL-2 and TNF-α. Distributions of T-cell percentages will be graphically displayed in Figure 116, Figure 117, Figure 118, Figure 119, Figure 120, and Figure 121.

Individual T-cell responses are shown in Listing 9.

9. SAFETY EVALUATION

Summaries and analysis of safety data will be presented for the Safety Analysis Population.

Solicited AEs will be summarized by severity for each day post vaccination (Days 1-8) and as the maximum severity over all 8 days. Additionally, solicited AEs will be analyzed by taking the most severe response over the follow-up period, dichotomizing into a binary variable (none versus mild, moderate, or severe) and using standard techniques, such as exact confidence intervals (CI), to summarize the proportion of subjects reporting each symptom, any application site symptom, and any systemic symptom.

Unsolicited non-serious AEs will be collected from the time of first vaccination through 28 days after the last vaccination. Unsolicited AEs will be coded by MedDRA® for preferred term and system organ class (SOC). All SAEs, MAAEs and NOCMCs will be collected from the time of first vaccination through the end of the study (Day 394). The numbers of SAEs and MAAEs will be reported by detailed listings showing the event description, MedDRA® preferred term and SOC, relevant dates (vaccinations and AEs), severity, relatedness, and outcome for each event. Non-serious unsolicited AEs will be summarized as number and percentage of subjects reporting at least one event in each MedDRA® preferred term and SOC, cross-tabulated by severity and relationship to study product. Additionally, the proportion of subjects and exact 95% CIs of AEs in aggregate and by MedDRA® categories will be computed.

Clinical laboratory data will be summarized by severity and relationship for each visit, and as the maximum over all post-vaccination visits. Graphical presentations will include bar plots.

9.1. Demographic and Other Baseline Characteristics

Summaries of age, sex, ethnicity, and race will be presented by Treatment Group (Table 15, Table 16, Table 17, Table 18, Table 19, and Table 20). Ethnicity is categorized as Hispanic or Latino, or not Hispanic and not Latino. In accordance with NIH reporting policy, subjects may self-designate as belonging to more than one race or may refuse to identify a race, the latter reflected in the CRF as "No" to each racial option.

Individual subject listings will be presented for all demographics (Listing 6).

9.1.1. Prior and Concurrent Medical Conditions

All current illnesses and past pre-existing medical conditions will be MedDRA® coded using MedDRA dictionary version 23.0r higher.

Summaries of subjects' pre-existing medical conditions will be presented by Treatment Group (Table 21, Table 22, and Table 23).

Individual subject listings will be presented for all medical conditions (Listing 7).

9.1.2. Prior and Concomitant Medications

Summaries of medications that were started prior to dosing and continuing at the time of dosing will be presented by WHO Drug Terms 2 and 3 and Treatment Group (Table 314, Table 315, and Table 316).

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

9.2. Measurements of Treatment Compliance

The number of doses of study product administered to subjects will be presented by Treatment Group as part of the subject disposition table (Table 10, Table 11, and Table 12).

9.3. Adverse Events

When calculating the incidence of adverse events (i.e., on a per subject basis), each subject will only be counted once and any repetitions of adverse events within a subject will be ignored; the denominator will be the total population size. All adverse events reported will be included in the summaries and analyses.

9.3.1. Solicited Events and Symptoms

Systemic solicited adverse events were collected pre-vaccination, and systemic and local solicited adverse events were collected 30 minutes post-vaccination and then daily for 7 days after each vaccination and graded on a scale of 0 (absent), 1 (mild), 2 (moderate) and 3 (severe). Systemic events include: fatigue, headache, myalgia, arthralgia, nausea, chills and fever. Local events include: pain at injection site, erythema, and induration.

The proportion of subjects reporting at least one solicited adverse event will be summarized for each solicited adverse event, any systemic symptom, any local symptom, and any symptoms. The 95% CI calculated using Clopper-Pearson methodology from a binomial distribution (SAS Proc Freq with a binomial option) will be presented (Table 144, Table 145, and Table 146).

For each systemic and local event, any systemic event, any local event, and any solicited event, the maximum severity over 7 days after each vaccination will be summarized for the Safety population. The number and percentage of subjects reporting each event will be summarized by the maximum severity and treatment group, separately for each vaccination and over all vaccinations (Table 147, Table 148, Table 149, Table 150, Table 151, and Table 152). For each event the denominator is the number of subjects with non-missing data for the specific event.

The number of subjects reporting a solicited adverse event will be summarized for each day post vaccination for each vaccination and for all vaccinations combined both in a summary table starting at Table 153 and ending at Table 212 and graphically in a bar chart (Figure 122, Figure 123, Figure 124, Figure 125, Figure 126, and Figure 127).

The mean, standard deviation, median, minimum and maximum duration of solicited events will be summarized (Table 213, Table 214, Table 215).

Day of solicited symptom onset will be summarized graphically (starting at Figure 128 and ending at Figure 139).

Solicited adverse events by subject will be presented in listings (Listing 10 and Listing 11) and graphically (starting at Figure 140 and ending at Figure 175).

9.3.2. Unsolicited Adverse Events

The proportion of subjects reporting at least one unsolicited adverse event will be summarized by MedDRA system organ class and preferred term for each vaccination and over all vaccinations.

Denominators for percentages are the number of subjects who received the vaccination being summarized.

Adverse events by subject will be presented in Listing 12.

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

- Subject incidence and total frequency of adverse events (starting at Table 216 and ending at Table 228);
- Summary of severity and relationship to study product (starting at Table 229 and ending at Table 241);
- Subject incidence and total frequency of adverse events over time (starting at Table 242 and ending at Table 254);
- Subject listing of non-serious adverse events of moderate or greater severity (Table 256);
- Listing of MAAEs and NOCMCs (Table 257);
- Bar chart of non-serious adverse events by severity and MedDRA system organ class (Figure 176, Figure 177, and Figure 178);
- Bar chart of non-serious adverse events by severity (Figure 179, Figure 180, and Figure 181).

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

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

- Deaths and Serious Adverse Events (Table 255);
- New Onset Chronic Medical Conditions and Medically Attended Adverse Events (Table 257).

9.5. Pregnancies

For any subjects in the Safety population who became pregnant during the study, every attempt will be made to follow these subjects to completion of pregnancy to document the outcome, including information regarding any complications with pregnancy and/or delivery. A table summarizing the total pregnancies, number of live births, and number of spontaneous abortions, elective abortions or still births by treatment will be presented. In addition, a listing of pregnancies and outcomes will be presented (Listing 18, Listing 19, Listing 20, Listing 21, and Listing 22).

9.6. Clinical Laboratory Evaluations

The safety laboratories presented will be white blood cells, hemoglobin, platelets, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, total bilirubin, creatinine and serum lipase. The distribution of laboratory results by severity, time point, and Treatment Group will be presented starting at Table 259 and ending at Table 280 and graphically in Figure 182, Figure 183, and Figure 184. Shift tables will be presented starting at Table 281 and ending at Table 289. Descriptive statistics including mean, standard deviation, median, minimum and maximum values by time point, for each laboratory parameter, will be summarized starting at Table 290 and ending at Table 298). Subject visits with abnormal laboratory results, Grade 1 severity or higher, will be presented (Table 258). A complete listing of individual clinical laboratory results with applicable reference ranges will be presented (Listing 13 and Listing 14).

9.7. Vital Signs and Physical Evaluations

Vital sign measurements included systolic blood pressure, diastolic blood pressure, pulse and oral temperature. Vital signs were assessed at Day 1, Day 8, Day 15, Day 29, Day 36, Day 43, Day 57, Day 119, Day 209 and Day 394. Vital signs will be tabulated by visit and Treatment Group starting at Table 299 and ending at Table 313 (Listing 15).

Physical Examinations performed at Day 1, Day 8, Day 15, Day 29, Day 36, Day 43, Day 57, Day 119, Day 209 and Day 394. The change in physical examination data from Day 1 will be summarized for each visit by Treatment Group for subjects in the Safety population. The following body systems will be assessed: Abdomen, Cardiovascular/heart, Extremities, General Appearance, Hepatobiliary/spleen, HEENT, Lymph nodes, Musculoskeletal, Neck, Neurological, Pulmonary/Chest, and Skin (Listing 16).

9.8. Concomitant Medications

Concomitant medications will be coded to the Anatomical Therapeutic Classification using the WHO Drug Dictionary. The use of prior and concomitant medications taken during the study will be recorded on the CRFs. A by-subject listing of concomitant medication use will be presented (Listing 17). The use of concomitant medications during the study will be summarized by ATC1, ATC2 code and Treatment Group for the Safety population (Table 314, Table 315, and Table 316).

9.9. Other Safety Measures

Not applicable.

10. PHARMACOKINETICS

Not applicable.

11. IMMUNOGENICITY

See Section 8.

12. OTHER ANALYSES

Not Applicable.

13. REPORTING CONVENTIONS

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

14. TECHNICAL DETAILS

SAS version 9.4, R 3.6.2 and PRISM v8.2.0 or above will be used to generate all tables, figures and listings.

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

Not Applicable.

16. REFERENCES

1. Drummond R. CONSORT Revised: Improving the Reporting of Randomized Clinical Trials. JAMA. 2001; 285(15): 2006-2007.

APPENDIX 1. TABLE MOCK-UPS

Tables with an * will be included in the interim CSR.

LIST OF TABLES

9.1 Overall Study Design and Plan Description

Table 1: Study Design*

Cohort	Sample Size	Stratum (Years of Age)	First and Second Dose
1	15	18-55	25 µg mRNA-1273
2	15	18-55	100 µg mRNA-1273
3	15	18-55	250 µg mRNA-1273
4	10	56-70	25 µg mRNA-1273
5	10	56-70	100 µg mRNA-1273
6*	10	56-70	250 µg mRNA-1273
7	10	≥71	25 µg mRNA-1273
8	10	≥71	100 µg mRNA-1273
9*	10	≥71	250 µg mRNA-1273
10	15	18-55	50 µg mRNA-1273
11	10	56-70	50 µg mRNA-1273
12	10	≥71	50 µg mRNA-1273
13*	15	18-55	10 µg mRNA-1273

*Sponsor decision to not enroll these cohorts.

9.5.1 Efficacy/Immunogenicity and Safety Measurements Assessed and Flow Chart

Table 2: Schedule of Study Procedures*

Procedures	Screening Visit 00, Day -42 to -1	Enrollment/Baseline Visit 01, Day 1	Visit 02, Day 2 1 day post Dose 1	Visit 03, Day 3 2 days post Dose 1	Visit 04 Day 8 +/- 1 day	Visit 05 Day 15 +/- 2 days	Visit 06 Day 29 +/- 2 days	Visit 07, Day 30 1 day post Dose 2	Visit 08, Day 31 2 days post Dose 2	Visit 09[f] Day 36 +/- 1 day	Visit 10[f] Day 43 +/- 2 days	Visit 11[f] Day 57 +/- 2 days	Visit 11A[f] Day 71 -7/+ 21 days	Visit 12[f] Day 119 +/- 7 days	Visit 13[f] Day 209 +/-7 days	Final Study Visit 14[f] Day 394 +/- 14 days	Unscheduled Visit	Early Termination Visit
Informed Consent	X																	
Review Eligibility Criteria	X	X					X											
Medical History	X																	
Concomitant Medications	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X
Vaccination		X					X											
Telephone Contact			X	X				X	X									
Interim History		X			X	X	X			X	X	X		X	X	X	X	X
Physical Examination[a]	X	X			X	X	X			X	X	X		X	X	X	X	X
Vital Signs	X	X			X	X	X			X	X	X		X	X	X	X	X
Height and Weight (for BMI)	X																	
Hematology[b]	X	X			X		X			X								
Chemistry[b]	X	X			X		X			X								
Serology[b]	X																	
Pregnancy Test[c]	X	X					X											
Urine Drug Screen	X																	
Memory Aid: Solicited AEs		Days 1-8					Days 29-36											
Unsolicited AEs		Days 1-57																
SAEs, MAAEs and NOCMCs			Days 1-394															
Serum for Serological Immunogenicity Assays		X				X	X			X	X	X		X	X	X		X
Peripheral Blood Mononuclear Cells (PBMCs) for Cellular Immunology Assays		X				X	X			X	X	X		X	X			X
Serum for Secondary Research[d]		X				X	X			X	X	X		X	X	X		X
Serum for Product Assay Development		X				X	X			X	X	X		X	X	X		X
Leukocytes for Secondary Research (subset of subjects)													X[e]					

a) Full physical examination will be performed at screening and symptom-directed (targeted) physical examination at all other timepoints if indicated.

b) Clinical screening laboratory evaluations will include WBCs, Hgb, PLTs, Cr, ALT, AST, ALP, T. Bili, Lipase, PT, PTT, hepatitis B surface antigen, hepatitis C virus antibody, and HIV types 1 and 2 antigen/antibody. Clinical safety laboratory evaluations obtained on Days 1, 8, 29, and 36 will include WBCs, Hgb, PLTs, Cr, ALT, AST, ALP, T. Bili, and Lipase.

c) For women of childbearing potential serum pregnancy test at screening, and urine or serum pregnancy test on Days 1 and 29 with results confirmed as negative prior to enrollment on Day 1 and administration of each vaccination.

d) Depending on the timepoint approximately 8 or 16 mL of each venous blood sample is designated for secondary research.

e) For those subjects consented for leukapheresis, screening procedures, including screening laboratory evaluations, will be performed locally prior to the leukapheresis procedure. Refer to the protocol-specific MOP for details on the leukapheresis procedure.

f) Visits 09-14 windows should be based off the actual Visit 06 date.

9.7.1 Sample Size

Table 3: Sample Size/Probability Estimates*

N	"True" Event Rate	Probability of Observation (%)	N	"True" Event Rate	Probability of Observation (%)	N	"True" Event Rate	Probability of Observation (%)
15	0.1%	1.5	60	0.1%	5.8	75	0.1%	7.2
	0.5%	7.2		0.5%	26.0		0.5%	31.3
	1.0%	14.0		1.0%	45.3		1.0%	52.9
	2.0%	26.1		2.0%	70.2		2.0%	78.0
	3.0%	36.7		3.0%	83.9		3.0%	89.8
	4.0%	45.8		4.0%	91.4		4.0%	95.3
	5.0%	53.7		5.0%	95.4		5.0%	97.9
	10.0%	79.4		10.0%	99.8		10.0%	>99.9
	15.0%	91.3		15.0%	>99.9		15.0%	>99.9
	20.0%	96.5		20.0%	>99.9		20.0%	>99.9
N	**"True" Event Rate**	**Probability of Observation (%)**	**N**	**"True" Event Rate**	**Probability of Observation (%)**	**N**	**"True" Event Rate**	**Probability of Observation (%)**
10	0.1%	1.0	30	0.1%	3.0	40	0.1%	3.9
	0.5%	4.9		0.5%	14.0		0.5%	18.2
	1.0%	9.6		1.0%	26.0		1.0%	33.1
	2.0%	18.3		2.0%	45.5		2.0%	55.4
	3.0%	26.3		3.0%	59.9		3.0%	70.4
	4.0%	33.5		4.0%	70.6		4.0%	80.5
	5.0%	40.1		5.0%	78.5		5.0%	87.1
	10.0%	65.1		10.0%	95.8		10.0%	98.5
	15.0%	80.3		15.0%	99.2		15.0%	99.8
	20.0%	89.3		20.0%	99.9		20.0%	>99.9

10.2 Protocol Deviations

Table 4: Distribution of Protocol Deviations by Category, Type, and Treatment Group 18-55 Years of Age*

		25 µg mRNA-1273 (N=X)		50 µg mRNA -1273 (N=X)		100 µg mRNA -1273 (N=X)		250 µg mRNA -1273 (N=X)		All Subjects (N=X)	
Category	**Deviation Type**	**# of Subj.**	**# of Dev.**	**# of Subj.**	**# of Dev.**	**# of Subj.**	**# of Dev.**	**# of Subj.**	**# of Dev.**	**# of Subj.**	**# of Dev.**
Follow-up visit schedule	**Missed visit/visit not conducted**										
	Out of window visit										
Protocol procedure/assessment	**Other: breach of confidentiality**										
	Other: non-required lab tests performed										
	Other: v4 safety labs collected out of window										
	Required procedure done incorrectly										
	Required procedure not conducted										
	Specimen result not obtained										
	Too few aliquots obtained										
Treatment administration schedule	**Required procedure done incorrectly**										

Tables with Similar Format:

Table 5: Distribution of Protocol Deviations by Category, Type, and Treatment Group 56-70 Years of Age*

Table 6: Distribution of Protocol Deviations by Category, Type, and Treatment Group ≥ 71 Years of Age*

Table 7: Distribution of Major Protocol Deviations by Category, Type, and Treatment Group 18-55 Years of Age*

Table 8: Distribution of Major Protocol Deviations by Category, Type, and Treatment Group 56-70 Years of Age*

Table 9: Distribution of Major Protocol Deviations by Category, Type, and Treatment Group ≥ 71 Years of Age*

12.2.2 Displays of Adverse Events

All AEs or SAEs will be assessed for severity, according to the toxicity grading scales in the FDA "Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials".

14.1 Description of Study Subjects

14.1.1 Disposition of Subjects

Table 10: Subject Disposition by Treatment Group - All Subjects 18-55 Years of Age*

	25 µg mRNA-1273 (N=X)		50 µg mRNA -1273 (N=X)		100 µg mRNA -1273 (N=X)		250 µg mRNA -1273 (N=X)		All Subjects (N=X)	
Subject Disposition	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Screened										
Enrolled										
Received the first vaccination										
Discontinued treatment[a]										
Received the second vaccination										
Study ongoing										
Early termination[a]										
Completed study										
[a]Refer to Listing 2 for reasons subjects discontinued or terminated early.										

Implementation Note: Omit the row "Study Ongoing" for final CSR, as all subjects will have completed study or terminated early at that time.

Tables with Similar Format:

Table 11: Subject Disposition by Treatment Group - All Subjects 56-70 Years of Age*

Table 12: Subject Disposition by Treatment Group - All Subjects ≥ 71 Years of Age*

Table 13: Analysis Populations by Treatment Group

Analysis Populations	Reason Subjects Excluded	All Subjects (N=120)	
		%	n
Safety	Any Reason	x	xx
Modified Intent-To-Treat	Any Reason		
Per Protocol	Any Reason		
	[Reason 1]		
Note: The subjects removed from the Per Protocol Population were in Cohorts X and on visits post Day 29 were removed.			

Table 14: Ineligibility Summary of Screen Failures*

Inclusion/Exclusion Category	Inclusion/Exclusion Criterion	n[a]	%[b]
Inclusion and Exclusion	Number of subjects failing any eligibility criterion	x	100
Inclusion	Any inclusion criterion	x	xx
	[inclusion criterion 1]	x	xx
	[inclusion criterion 2]	x	xx
	[inclusion criterion 3]	x	xx
Exclusion	Any exclusion criterion	x	xx
	[exclusion criterion 1]	x	xx
	[exclusion criterion 2]	x	xx
	[exclusion criterion 3]	x	xx

[a] More than one criterion may be marked per subject.

[b] Denominator for percentages is the total number of screen failures.

14.1.2 Demographic Data by Treatment Group

Table 15: Summary of Categorical Demographic and Baseline Characteristics by Treatment Group - All Subjects 18-55 Years of Age*

		25 µg mRNA-1273 (N=X)		50 µg mRNA -1273 (N=X)		100 µg mRNA -1273 (N=X)		250 µg mRNA -1273 (N=X)		All Subjects (N=X)	
Demographic Category	**Characteristic**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Sex	Male										
	Female										
Ethnicity	Not Hispanic or Latino										
	Hispanic or Latino										
	Not Reported										
	Unknown										
Race	American Indian or Alaska Native										
	Asian										
	Native Hawaiian or other Pacific Islander										
	Black										
	White										
	Multi Racial										
	Unknown										

Tables with Similar Format:

Table 16: Summary of Categorical Demographic and Baseline Characteristics by Treatment Group - All Subjects 56-70 Years of Age*

Table 17: Summary of Categorical Demographic and Baseline Characteristics by Treatment Group - All Subjects ≥71 Years of Age*

Table 18: Summary of Continuous Demographic and Baseline Characteristics by Treatment Group - All Subjects 18-55 Years of Age*

		25 µg mRNA-1273 (N=X)	50 µg mRNA -1273 (N=X)	100 µg mRNA -1273 (N=X)	250 µg mRNA -1273 (N=X)	All Subjects (N=X)
Variable	**Statistic**	**n**	**n**	**n**	**n**	**n**
Age (Years)	Mean					
	Standard Deviation					
	Median					
	Minimum					
	Maximum					
Height (cm)	Mean					
	Standard Deviation					
	Median					
	Minimum					
	Maximum					
Weight (kg)	Mean					
	Standard Deviation					
	Median					
	Minimum					
	Maximum					
BMI (kg/m^2)	Mean					
	Standard Deviation					
	Median					
	Minimum					
	Maximum					

Tables with Similar Format:

Table 19: Summary of Continuous Demographic and Baseline Characteristics by Treatment Group - All Subjects 56-70 Years of Age*

Table 20: Summary of Continuous Demographic and Baseline Characteristics by Treatment Group - All Subjects ≥71 Years of Age*

14.1.3 Prior and Concurrent Medical Conditions

Table 21: Summary of Subjects with Pre-Existing Medical Conditions by MedDRA System Organ Class and Treatment Group - All Subjects 18-55 Years of Age*

MedDRA System Organ Class	25 µg mRNA-1273 (N=X)		50 µg mRNA -1273 (N=X)		100 µg mRNA -1273 (N=X)		250 µg mRNA -1273 (N=X)		All Subjects (N=X)	
	n	%	n	%	n	%	n	%	n	%
Any SOC	x	xx	x	xx	x	xx	x	xx	x	xx
[SOC 1]										
[SOC 2]										
Note: N= Number of subjects in the Safety Population; n = Number of subjects reporting medical history within the specified SOC. A subject is only counted once per SOC.										

Tables with Similar Format:

Table 22: Summary of Subjects with Pre-Existing Medical Conditions by MedDRA System Organ Class and Treatment Group - All Subjects 56-70 Years of Age*

Table 23: Summary of Subjects with Pre-Existing Medical Conditions by MedDRA System Organ Class and Treatment Group - All Subjects ≥71 Years of Age*

14.2 Immunogenicity Data

Table 24: Serum IgG ELISA Endpoint Titer Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group - S-2P – Age 18 -55, mITT Population

Time Point	Statistic	25 µg mRNA-1273 18-55 years (N=X)	50 µg mRNA-1273 18-55 years (N=X)	100 µg mRNA-1273 18-55 years (N=X)	250 µg mRNA-1273 18-55 years (N=X)	18-55 years (N=X)	Convalescent Sera
Day 1 (Pre-Vaccination 1)	n						
	GMT						
	95% CI						
Day 15 (14 Days Post Vaccination 1)	n						
	GMT						
	95% CI						
Day 29 Post Vaccination 1 (Pre-Vaccination 2)	n						
	GMT						
	95% CI						
Day 36 Post Vaccination 1 (7 Days Post Vaccination 2)	n						
	GMT						
	95% CI						
Day 43 Post Vaccination 1 (14 Days Post Vaccination 2)	n						
	GMT						
	95% CI						
Day 57 Post Vaccination 1 (28 Days Post Vaccination 2)	n						
	GMT						
	95% CI						
Day 119 Post Vaccination 1 (90 Days Post Vaccination 2)	n						
	GMT						

Time Point	Statistic	25 µg mRNA-1273 18-55 years (N=X)	50 µg mRNA-1273 18-55 years (N=X)	100 µg mRNA-1273 18-55 years (N=X)	250 µg mRNA-1273 18-55 years (N=X)	18-55 years (N=X)	Convalescent Sera
	95% CI						

Note: N=Number of Subjects.
n=Number of subjects with results available at time point.
NE=Not Estimable

Tables with Similar Format:

Table 25: Serum IgG ELISA Endpoint Titer Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group - S-2P – Age 18 -55, Per Protocol Population*

Table 26: Serum IgG ELISA Endpoint Titer Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group - S-2P – Age 56 -70, mITT Population

Table 27: Serum IgG ELISA Endpoint Titer Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group - S-2P – Age 56 -70, Per Protocol Population*

Table 28: Serum IgG ELISA Endpoint Titer Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group - S-2P – Age ≥71, mITT Population

Table 29: Serum IgG ELISA Endpoint Titer Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group - S-2P – Age ≥71, Per Protocol Population*

Table 30: Serum IgG ELISA Endpoint Titer Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group - RBD – Age 18 -55, mITT Population

Table 31: Serum IgG ELISA Endpoint Titer Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group - RBD – Age 18 -55, Per Protocol Population*

Table 32: Serum IgG ELISA Endpoint Titer Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group - RBD – Age 56 -70, mITT Population

Table 33: Serum IgG ELISA Endpoint Titer Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group - RBD – Age 56 -70, Per Protocol Population*

Table 34: Serum IgG ELISA Endpoint Titer Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group - RBD – Age ≥71, mITT Population

Table 35: Serum IgG ELISA Endpoint Titer Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group - RBD – Age ≥71, Per Protocol Population*

Table 36: Serum IgG ELISA Area Under the Curve (AUC) Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group - S-2P – Age 18 -55, mITT Population

Implementation Note: For all AUC table, add footnote for GMT row "Geometric Mean Titer is calculated as the Williams mean using log(1+x).

Table 37: Serum IgG ELISA Area Under the Curve (AUC) Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group - S-2P – Age 18 -55, Per Protocol Population

Table 38: Serum IgG ELISA Area Under the Curve (AUC) Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group - S-2P – Age 56 -70, mITT Population

Table 39: Serum IgG ELISA Area Under the Curve (AUC) Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group - S-2P – Age 56 -70, Per Protocol Population

Table 40: Serum IgG ELISA Area Under the Curve (AUC) Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group - S-2P – Age ≥71, mITT Population

Table 41: Serum IgG ELISA Area Under the Curve (AUC) Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group - S-2P – Age ≥71, Per Protocol Population

Table 42: Serum IgG ELISA Area Under the Curve (AUC) Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group - RBD – Age 18 -55, mITT Population

Table 43: Serum IgG ELISA Area Under the Curve (AUC) Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group - RBD – Age 18 -55, Per Protocol Population

Table 44: Serum IgG ELISA Area Under the Curve (AUC) Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group - RBD – Age 56 -70, mITT Population

Table 45: Serum IgG ELISA Area Under the Curve (AUC) Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group - RBD – Age 56 -70, Per Protocol Population

Table 46: Serum IgG ELISA Area Under the Curve (AUC) Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group - RBD – Age ≥71, mITT Population

Table 60. Pseudovirus Neutralization Assay Geometric Mean Results with 95% Confidence Intervals by Variant - ID_{50}, mITT Population

Variant	Time Point	Statistic	100 µg mRNA-1273 18-55 years (N=X)	100 µg mRNA-1273 56-70 years (N=X)	100 µg mRNA-1273 ≥71 years (N=X)
614D	**Day 43 Post Vaccination 1 (14 Days Post Vaccination 2)**	n			
		GM			
		95% CI			
614G	**Day 43 Post Vaccination 1 (14 Days Post Vaccination 2)**	n			
		GM			
		95% CI			

Note: N=Number of Subjects.
n=Number of subjects with results available at time point.

Tables with Similar Format:

Table 61. Pseudovirus Neutralization Assay Geometric Mean Results with 95% Confidence Intervals by Variant - ID_{50}, Per Protocol Population*

Table 62. Pseudovirus Neutralization Assay Geometric Mean Results with 95% Confidence Intervals by Variant – ID_{80}, mITT Population

Table 63. Pseudovirus Neutralization Assay Geometric Mean Results with 95% Confidence Intervals by Variant – ID_{80}, Per Protocol Population*

Table 64. Plaque Reduction Neutralization Test Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group – $PRNT_{80}$ - 18-55 Years, mITT Population

Time Point	Statistic	25 µg mRNA-1273 18-55 years (N=X)	100 µg mRNA-1273 18-55 years (N=X)	18-55 years (N=X)
Day 1 (Pre-Vaccination 1)	n			
	GM			
	95% CI			
Day 43 Post Vaccination 1 (14 Days Post Vaccination 2)	n			
	GM			
	95% CI			
Day 119 Post Vaccination 1 (90 Days Post Vaccination 2)	n			
	GM			
	95% CI			

Note: N=Number of Subjects.
n=Number of subjects with results available at time point.
NE=Not Estimable

Tables with Similar Format:

Table 65. Plaque Reduction Neutralization Test Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group – $PRNT_{80}$ - 18-55 Years, Per Protocol Population*

Table 66. Plaque Reduction Neutralization Test Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group – $PRNT_{80}$ - 56-70 Years, mITT Population

Table 67. Plaque Reduction Neutralization Test Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group – $PRNT_{80}$ - 56-70 Years, Per Protocol Population*

Table 68. Plaque Reduction Neutralization Test Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group – $PRNT_{80}$ - ≥71 Years, mITT Population

Table 69. Plaque Reduction Neutralization Test Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group – $PRNT_{80}$ - ≥71 Years, Per Protocol Population*

Table 70. Focus Reduction Neutralization Test Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group - ID_{50}, mITT Population

Time Point	Statistic	25 µg mRNA-1273 18-55 years (N=X)	100 µg mRNA -1273 18-55 years (N=X)	18-55 years (N=X)
Day 1 (Pre-Vaccination 1)	n			
	GM			
	95% CI			
Day 29 Post Vaccination 1 (Pre-Vaccination 2)	n			
	GM			
	95% CI			
Day 43 Post Vaccination 1 (14 Days Post Vaccination 2)	n			
	GM			
	95% CI			

Note: N=Number of Subjects.
n=Number of subjects with results available at time point.
NE=Not Estimable

Table with Similar Format:

Table 71. Focus Reduction Neutralization Test Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group - ID_{50}, Per Protocol Population

Table 72. FRNT-mNG Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group - ID_{50} - 18-55 Years, mITT Population

Time Point	Statistic	25 µg mRNA-1273 18-55 years (N=X)	100 µg mRNA-1273 18-55 years (N=X)	250 µg mRNA-1273 18-55 years (N=X)	18-55 years (N=X)	Convalescent Sera
Day 1 (Pre-Vaccination 1)	n					
	GM					
	95% CI					
Day 29 Post Vaccination 1 (Pre-Vaccination 2)	n					
	GM					
	95% CI					
Day 43 Post Vaccination 1 (14 Days Post Vaccination 2)	n					
	GM					
	95% CI					
Day 119 Post Vaccination 1 (90 Days Post Vaccination 2)	n					
	GM					
	95% CI					

Note: N=Number of Subjects.
n=Number of subjects with results available at time point.
NE=Not Estimable

Tables with Similar Format:

Table 73. FRNT-mNG Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group - ID_{50} - 18-55 Years, Per Protocol Population*

Table 74. FRNT-mNG Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group - ID_{50} - 56-70 Years, mITT Population

Table 75. FRNT-mNG Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group - ID_{50} - 56-70 Years, Per Protocol Population*

Table 84. nLuciferase Neutralization Assay Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group - ID_{50} – Age 18-55, mITT Population

Time Point	Statistic	25 µg mRNA-1273 18-55 years (N=X)	100 µg mRNA-1273 18-55 years (N=X)	18-55 years (N=X)	Convalescent Sera
Day 1 (Pre-Vaccination 1)	n				
	GM				
	95% CI				
Day 29 Post Vaccination 1 (Pre-Vaccination 2)	n				
	GM				
	95% CI				
Day 43 Post Vaccination 1 (14 Days Post Vaccination 2)	n				
	GM				
	95% CI				

Note: N=Number of Subjects.
n=Number of subjects with results available at time point.
NE=Not Estimable

Tables with Similar Format:

Table 85. nLuciferase Neutralization Assay Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group - ID_{50} – Age 18-55, Per Protocol Population

Table 86. nLuciferase Neutralization Assay Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group - ID_{50} – Age 56-70, mITT Population

Table 87. nLuciferase Neutralization Assay Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group - ID_{50} – Age 56-70, Per Protocol Population

Table 88. nLuciferase Neutralization Assay Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group - ID_{50} – Age ≥71, mITT Population

Table 96. Mean Percentages of CD4 T Cells Expressing Cytokines with 95% CI - Th1 Response – Age 18-55, mITT Population

Time Point	Simulation	Cell Type	Statistic	25 µg mRNA-1273 18-55 years (N=X)	100 µg mRNA-1273 18-55 years (N=X)	18-55 years (N=X)
Day 1 (Pre-Vaccination 1)	**SARS-CoV-2 S1**	**Any Th1**	n			
			Mean			
			95% CI			
		IFNγ	n			
			Mean			
			95% CI			
		IL-2	n			
			Mean			
			95% CI			
		TNF	n			
			Mean			
			95% CI			
	SARS-CoV-2 S2	**Any Th1**	n			
			Mean			
			95% CI			
		IFNγ	n			
			Mean			
			95% CI			
		IL-2	n			
			Mean			
			95% CI			
		TNF	n			

Time Point	Simulation	Cell Type	Statistic	25 µg mRNA-1273 18-55 years (N=X)	100 µg mRNA-1273 18-55 years (N=X)	18-55 years (N=X)
			Mean			
			95% CI			
Day 29 Post Vaccination 1 (Pre-Vaccination 2)	**SARS-CoV-2 S1**	**Any Th1**	n			
			Mean			
			95% CI			
		IFNγ	n			
			Mean			
			95% CI			
		IL-2	n			
			Mean			
			95% CI			
		TNF	n			
			Mean			
			95% CI			
	SARS-CoV-2 S2	**Any Th1**	n			
			Mean			
			95% CI			
		IFNγ	n			
			Mean			
			95% CI			
		IL-2	n			
			Mean			
			95% CI			

Time Point	Simulation	Cell Type	Statistic	25 µg mRNA-1273 18-55 years (N=X)	100 µg mRNA-1273 18-55 years (N=X)	18-55 years (N=X)
		TNF	n			
			Mean			
			95% CI			
Day 43 Post Vaccination 1 (14 Days Post Vaccination 2)	**SARS-CoV-2 S1**	**Any Th1**	n			
			Mean			
			95% CI			
		IFNγ	n			
			Mean			
			95% CI			
		IL-2	n			
			Mean			
			95% CI			
		TNF	n			
			Mean			
			95% CI			
	SARS-CoV-2 S2	**Any Th1**	n			
			Mean			
			95% CI			
		IFNγ	n			
			Mean			
			95% CI			
		IL-2	n			
			Mean			

Time Point	Simulation	Cell Type	Statistic	25 µg mRNA-1273 18-55 years (N=X)	100 µg mRNA-1273 18-55 years (N=X)	18-55 years (N=X)
			95% CI			
		TNF	n			
			Mean			
			95% CI			

Note: N=Number of Subjects.
n=Number of subjects with results available at time point.
NE=Not Estimable

Tables with Similar Format:

Table 97. Mean Percentages of CD4 T Cells Expressing Cytokines with 95% CI - Th1 Response – Age 18-55, Per Protocol Population*

Table 98. Mean Percentages of CD4 T Cells Expressing Cytokines with 95% CI - Th1 Response – Age 56-70, mITT Population

Table 99. Mean Percentages of CD4 T Cells Expressing Cytokines with 95% CI - Th1 Response – Age 56-70, Per Protocol Population*

Table 100. Mean Percentages of CD4 T Cells Expressing Cytokines with 95% CI - Th1 Response – Age ≥71, mITT Population

Table 101. Mean Percentages of CD4 T Cells Expressing Cytokines with 95% CI - Th1 Response – Age ≥71, Per Protocol Population*

Table 102. Mean Percentages of CD4 T Cells Expressing Cytokines with 95% CI – Th2 Response – Age 18-55, mITT Population

Time Point	Simulation	Cell Type	Statistic	25 µg mRNA-1273 18-55 years (N=X)	100 µg mRNA-1273 18-55 years (N=X)	18-55 years (N=X)
Day 1 (Pre-Vaccination 1)	**SARS-CoV-2 S1**	**Any Th2**	n			
			Mean			
			95% CI			
		IL-13	n			
			Mean			
			95% CI			
		IL-4	n			
			Mean			
			95% CI			
	SARS-CoV-2 S2	**Any Th2**	n			
			Mean			
			95% CI			
		IL-13	n			
			Mean			
			95% CI			
		IL-4	n			
			Mean			
			95% CI			
Day 29 Post Vaccination 1 (Pre-Vaccination 2)	**SARS-CoV-2 S1**	**Any Th2**	n			
			Mean			
			95% CI			
		IL-13	n			

Time Point	Simulation	Cell Type	Statistic	25 µg mRNA-1273 18-55 years (N=X)	100 µg mRNA-1273 18-55 years (N=X)	18-55 years (N=X)
			Mean			
			95% CI			
		IL-4	n			
			Mean			
			95% CI			
	SARS-CoV-2 S2	**Any Th2**	n			
			Mean			
			95% CI			
		IL-13	n			
			Mean			
			95% CI			
		IL-4	n			
			Mean			
			95% CI			
Day 43 Post Vaccination 1 (14 Days Post Vaccination 2)	**SARS-CoV-2 S1**	**Any Th2**	n			
			Mean			
			95% CI			
		IL-13	n			
			Mean			
			95% CI			
		IL-4	n			
			Mean			
			95% CI			

Time Point	Simulation	Cell Type	Statistic	25 µg mRNA-1273 18-55 years (N=X)	100 µg mRNA-1273 18-55 years (N=X)	18-55 years (N=X)
	SARS-CoV-2 S2	Any Th2	n			
			Mean			
			95% CI			
		IL-13	n			
			Mean			
			95% CI			
		IL-4	n			
			Mean			
			95% CI			

Note: N=Number of Subjects.
n=Number of subjects with results available at time point.
NE=Not Estimable

Tables with Similar Format:

Table 103. Mean Percentages of CD4 T Cells Expressing Cytokines with 95% CI – Th2 Response – Age 18-55, Per Protocol Population*

Table 104. Mean Percentages of CD4 T Cells Expressing Cytokines with 95% CI – Th2 Response – Age 56-70, mITT Population

Table 105. Mean Percentages of CD4 T Cells Expressing Cytokines with 95% CI – Th2 Response – Age 56-70, Per Protocol Population*

Table 106. Mean Percentages of CD4 T Cells Expressing Cytokines with 95% CI – Th2 Response – Age ≥71, mITT Population

Table 107. Mean Percentages of CD4 T Cells Expressing Cytokines with 95% CI – Th2 Response – Age ≥71, Per Protocol Population*

Table 108. Mean Percentages of CD8 T Cells Expressing Cytokines with 95% CI – Age 18-55, mITT Population

Time Point	Simulation	Cell Type	Statistic	25 µg mRNA-1273 18-55 years (N=X)	100 µg mRNA-1273 18-55 years (N=X)	18-55 years (N=X)
Day 1 (Pre-Vaccination 1)	**SARS-CoV-2 S1**	**Any CD8**	n			
			Mean			
			95% CI			
		IFNγ	n			
			Mean			
			95% CI			
		IL-2	n			
			Mean			
			95% CI			
		TNF	n			
			Mean			
			95% CI			
	SARS-CoV-2 S2	**Any CD8**	n			
			Mean			
			95% CI			
		IFNγ	n			
			Mean			
			95% CI			
		IL-2	n			
			Mean			
			95% CI			
		TNF	n			

Time Point	Simulation	Cell Type	Statistic	25 µg mRNA-1273 18-55 years (N=X)	100 µg mRNA-1273 18-55 years (N=X)	18-55 years (N=X)
			Mean			
			95% CI			
Day 29 Post Vaccination 1 (Pre-Vaccination 2)	**SARS-CoV-2 S1**	**Any CD8**	n			
			Mean			
			95% CI			
		IFNγ	n			
			Mean			
			95% CI			
		IL-2	n			
			Mean			
			95% CI			
		TNF	n			
			Mean			
			95% CI			
	SARS-CoV-2 S2	**Any CD8**	n			
			Mean			
			95% CI			
		IFNγ	n			
			Mean			
			95% CI			
		IL-2	n			
			Mean			
			95% CI			

Time Point	Simulation	Cell Type	Statistic	25 µg mRNA-1273 18-55 years (N=X)	100 µg mRNA-1273 18-55 years (N=X)	18-55 years (N=X)
		TNF	n			
			Mean			
			95% CI			
Day 43 Post Vaccination 1 (14 Days Post Vaccination 2)	**SARS-CoV-2 S1**	**Any CD8**	n			
			Mean			
			95% CI			
		IFNγ	n			
			Mean			
			95% CI			
		IL-2	n			
			Mean			
			95% CI			
		TNF	n			
			Mean			
			95% CI			
	SARS-CoV-2 S2	**Any CD8**	n			
			Mean			
			95% CI			
		IFNγ	n			
			Mean			
			95% CI			
		IL-2	n			
			Mean			

Time Point	Simulation	Cell Type	Statistic	25 µg mRNA-1273 18-55 years (N=X)	100 µg mRNA-1273 18-55 years (N=X)	18-55 years (N=X)
			95% CI			
		TNF	n			
			Mean			
			95% CI			

Note: N=Number of Subjects.
n=Number of subjects with results available at time point.
NE=Not Estimable

Tables with Similar Format:

Table 109. Mean Percentages of CD8 T Cells Expressing Cytokines with 95% CI – Age 18-55, Per Protocol Population*

Table 110. Mean Percentages of CD8 T Cells Expressing Cytokines with 95% CI – Age 56-70, mITT Population

Table 111. Mean Percentages of CD8 T Cells Expressing Cytokines with 95% CI – Age 56-70, Per Protocol Population*

Table 112. Mean Percentages of CD8 T Cells Expressing Cytokines with 95% CI – Age ≥71, mITT Population

Table 113. Mean Percentages of CD8 T Cells Expressing Cytokines with 95% CI – Age ≥71, Per Protocol Population*

Table 114. Serum IgG ELISA Geometric Mean Fold Rise (GMFR) and 4-Fold Rise Results by Time Point and Treatment Group - S-2P – Age 18-55, mITT Population

Time Point	Statistic	25 µg mRNA-1273 18-55 years (N=X)	50 µg mRNA-1273 18-55 years (N=X)	100 µg mRNA-1273 18-55 years (N=X)	250 µg mRNA-1273 18-55 years (N=X)	18-55 years (N=X)
Day 15 (14 Days Post Vaccination 1)	n					
	GMFR[a]					
	95% CI					
	4-Fold Rise[b]					
	95% CI					
Day 29 Post Vaccination 1 (Pre-Vaccination 2)	n					
	GMFR[a]					
	95% CI					
	4-Fold Rise[b]					
	95% CI					
Day 36 Post Vaccination 1 (7 Days Post Vaccination 2)	n					
	GMFR[a]					
	95% CI					
	4-Fold Rise[b]					
	95% CI					
Day 43 Post Vaccination 1 (14 Days Post Vaccination 2)	n					
	GMFR[a]					
	95% CI					
	4-Fold Rise[b]					
	95% CI					
	n					

Time Point	Statistic	25 µg mRNA-1273 18-55 years (N=X)	50 µg mRNA-1273 18-55 years (N=X)	100 µg mRNA-1273 18-55 years (N=X)	250 µg mRNA-1273 18-55 years (N=X)	18-55 years (N=X)
Day 57 Post Vaccination 1 (28 Days Post Vaccination 2)	GMFR[a]					
	95% CI					
	4-Fold Rise[b]					
	95% CI					
Day 119 Post Vaccination 1 (90 Days Post Vaccination 2)	n					
	GMFR[a]					
	95% CI					
	4-Fold Rise[b]					
	95% CI					

Note: N=Number of Subjects.
Note: n=number of subjects with baseline and data at corresponding visit.
[a]GMFR represents the geometric mean fold rise in Endpoint Titer compared to pre-dose 1
[b]4-Fold Rise represents the percentage of subjects with at least a 4-Fold Rise in Endpoint Titer compared to pre-dose 1

Tables with Similar Format:

Table 115. Serum IgG ELISA Geometric Mean Fold Rise (GMFR) and 4-Fold Rise Results by Time Point and Treatment Group - S-2P – Age 18-55, Per Protocol Population*

Table 116. Serum IgG ELISA Geometric Mean Fold Rise (GMFR) and 4-Fold Rise Results by Time Point and Treatment Group - S-2P – Age 56-70, mITT Population

Table 117. Serum IgG ELISA Geometric Mean Fold Rise (GMFR) and 4-Fold Rise Results by Time Point and Treatment Group - S-2P – Age 56-70, Per Protocol Population*

Table 118. Serum IgG ELISA Geometric Mean Fold Rise (GMFR) and 4-Fold Rise Results by Time Point and Treatment Group - S-2P – Age ≥71, mITT Population

Table 119. Serum IgG ELISA Geometric Mean Fold Rise (GMFR) and 4-Fold Rise Results by Time Point and Treatment Group - S-2P – Age ≥71, Per Protocol Population*

Table 126. Serum IgG ELISA Area Under the Curve (AUC) Geometric Mean Fold Rise (GMFR) and 4-Fold Rise Results by Time Point and Treatment Group - S-2P – Age 18-55, mITT Population

Time Point	Statistic	25 µg mRNA-1273 18-55 years (N=X)	50 µg mRNA-1273 18-55 years (N=X)	100 µg mRNA-1273 18-55 years (N=X)	250 µg mRNA-1273 18-55 years (N=X)	18-55 years (N=X)
Day 15 (14 Days Post Vaccination 1)	n					
	GMFR[a]					
	95% CI					
	4-Fold Rise[b]					
	95% CI					
Day 29 Post Vaccination 1 (Pre-Vaccination 2)	n					
	GMFR[a]					
	95% CI					
	4-Fold Rise[b]					
	95% CI					
Day 36 Post Vaccination 1 (7 Days Post Vaccination 2)	n					
	GMFR[a]					
	95% CI					
	4-Fold Rise[b]					
	95% CI					
Day 43 Post Vaccination 1 (14 Days Post Vaccination 2)	n					
	GMFR[a]					
	95% CI					
	4-Fold Rise[b]					
	95% CI					
	n					

Time Point	Statistic	25 µg mRNA-1273 18-55 years (N=X)	50 µg mRNA-1273 18-55 years (N=X)	100 µg mRNA-1273 18-55 years (N=X)	250 µg mRNA-1273 18-55 years (N=X)	18-55 years (N=X)
Day 57 Post Vaccination 1 (28 Days Post Vaccination 2)	GMFR[a]					
	95% CI					
	4-Fold Rise[b]					
	95% CI					
Day 119 Post Vaccination 1 (90 Days Post Vaccination 2)	n					
	GMFR[a]					
	95% CI					
	4-Fold Rise[b]					
	95% CI					

Note: N=Number of Subjects.
Note: n=number of subjects with baseline and data at corresponding visit.
[a]GMFR represents the geometric mean fold rise in AUC compared to pre-dose 1
[b]4-Fold Rise represents the percentage of subjects with at least a 4-Fold Rise in AUC compared to pre-dose 1
AUC results reported as 0 were imputed to the lowest non-zero reported value for the purposes of fold-rise calculations.

Tables with Similar Format:

Table 127. Serum IgG ELISA Area Under the Curve (AUC) Geometric Mean Fold Rise (GMFR) and 4-Fold Rise Results by Time Point and Treatment Group - S-2P – Age 18-55, Per Protocol Population

Table 128. Serum IgG ELISA Area Under the Curve (AUC) Geometric Mean Fold Rise (GMFR) and 4-Fold Rise Results by Time Point and Treatment Group - S-2P – Age 56-70, mITT Population

Table 129. Serum IgG ELISA Area Under the Curve (AUC) Geometric Mean Fold Rise (GMFR) and 4-Fold Rise Results by Time Point and Treatment Group - S-2P – Age 56-70, Per Protocol Population

Table 130. Serum IgG ELISA Area Under the Curve (AUC) Geometric Mean Fold Rise (GMFR) and 4-Fold Rise Results by Time Point and Treatment Group - S-2P – Age ≥71, mITT Population

Table 131. Serum IgG ELISA Area Under the Curve (AUC) Geometric Mean Fold Rise (GMFR) and 4-Fold Rise Results by Time Point and Treatment Group - S-2P – Age ≥71, Per Protocol Population

14.3 Safety Data

14.3.1 Displays of Adverse Events

Table 138: Overall Summary of Adverse Events by Treatment Group - All Subjects 18-55 Years of Age*

Subjects[a] with		25 µg mRNA-1273 (N=X)		50 µg mRNA -1273 (N=X)		100 µg mRNA -1273 (N=X)		250 µg mRNA -1273 (N=X)		All Subjects (N=X)	
Category 1	**Category 2**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
At least one local solicited adverse event	NA										
At least one systemic solicited adverse event	NA										
At least one unsolicited adverse event	NA										
At least one related unsolicited adverse event	Any Grade										
	Mild (Grade 1)										
	Moderate (Grade 2)										
	Severe (Grade 3)										
At least one severe (Grade 3) unsolicited adverse event	Any relationship										
Related	Related										
Unrelated	Unrelated										
At least one serious adverse event[b]	Any relationship										
	Related										

Subjects[a] with		25 µg mRNA-1273 (N=X)		50 µg mRNA -1273 (N=X)		100 µg mRNA -1273 (N=X)		250 µg mRNA -1273 (N=X)		All Subjects (N=X)	
Category 1	**Category 2**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
At least one adverse event leading to early termination[c]	NA										
Any laboratory Adverse Event											
Any Vitals Signs Adverse Event											
At least one medically attended adverse event	NA										
At least one new onset chronic medical condition	NA										

N = Number of subjects in the Safety Population
[a]Subjects are counted once for each category regardless of the number of events.
[b]A listing of Serious Adverse Events is included in Table 255.
[c]As reported on the Adverse Event eCRF.

Tables with Similar Format:

Table 139: Overall Summary of Adverse Events by Treatment Group - All Subjects 56-70 Years of Age*

Table 140: Overall Summary of Adverse Events by Treatment Group - All Subjects ≥71 Years of Age*

Table 141: Serious Adverse Events and Non-Serious Adverse Events Occurring in 5% of Subjects in Any Treatment Group by MedDRA System Organ Class and Preferred Term, and Treatment Group - All Subjects 18-55 Years of Age

Preferred Term	MedDRA System Organ Class	25 µg mRNA-1273 (N=X)			50 µg mRNA -1273 (N=X)			100 µg mRNA -1273 (N=X)			250 µg mRNA -1273 (N=X)			All Subjects (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
PT1	SOC1	x	x	x	x	x	x							x	x	x
Etc.	Etc.															
Other (Non-serious) Adverse Events																
All	All	x	x	x	x	x	x							x	x	x
PT1	SOC1	x	x	x	x	x	x							x	x	x
Etc	Etc															

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

Tables with Similar Format:

Table 142: Serious Adverse Events and Non-Serious Adverse Events Occurring in 5% of Subjects in Any Treatment Group by MedDRA System Organ Class and Preferred Term, and Treatment Group - All Subjects 56-70 Years of Age

Table 143: Serious Adverse Events and Non-Serious Adverse Events Occurring in 5% of Subjects in Any Treatment Group by MedDRA System Organ Class and Preferred Term, and Treatment Group - All Subjects ≥71 Years of Age

14.3.1.1 Solicited Adverse Events

Table 144: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity, Dose, and Treatment Group - Any Symptom - 18-55 Years of Age*

			25 µg mRNA-1273 (N=X)		50 µg mRNA -1273 (N=X)		100 µg mRNA -1273 (N=X)		250 µg mRNA -1273 (N=X)		All Subjects (N=X)	
Symptom	**Dose**	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Any Symptom	**Dose 1**	**None**										
		Mild										
		Moderate										
		Severe										
	Dose 2	**None**										
		Mild										
		Moderate										
		Severe										
	Any Dose	**None**										
		Mild										
		Moderate										
		Severe										

Severity is the maximum severity reported over all solicited symptoms post dosing for each subject.
N=All subjects receiving Dose 1 with any solicited event data recorded in the database.

Tables with Similar Format:

Table 145: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity, Dose, and Treatment Group - Any Symptom – 56-70 Years of Age*

Table 146: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity, Dose, and Treatment Group - Any Symptom - ≥71 Years of Age*

Table 147: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity, Dose, and Treatment Group - Systemic Symptoms - 18-55 Years of Age*

			25 µg mRNA-1273 (N=X)		50 µg mRNA -1273 (N=X)		100 µg mRNA -1273 (N=X)		250 µg mRNA -1273 (N=X)		All Subjects (N=X)	
Symptom	**Dose**	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Any Systemic Symptom	**Dose 1**	**None**										
		Mild										
		Moderate										
		Severe										
	Dose 2	**None**										
		Mild										
		Moderate										
		Severe										
	Any Dose	**None**										
		Mild										
		Moderate										
		Severe										
Arthralgia	**Dose 1**	**None**										
		Mild										
		Moderate										
		Severe										
	Dose 2	**None**										
		Mild										
		Moderate										
		Severe										

			25 µg mRNA-1273 (N=X)		50 µg mRNA -1273 (N=X)		100 µg mRNA -1273 (N=X)		250 µg mRNA -1273 (N=X)		All Subjects (N=X)	
Symptom	**Dose**	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
	Any Dose	**None**										
		Mild										
		Moderate										
		Severe										
Fatigue	**Dose 1**	**None**										
		Mild										
		Moderate										
		Severe										
	Dose 2	**None**										
		Mild										
		Moderate										
		Severe										
	Any Dose	**None**										
		Mild										
		Moderate										
		Severe										
Fever[a]	**Dose 1**	**None**										
		Mild										
		Moderate										
		Severe										
	Dose 2	**None**										
		Mild										

			25 µg mRNA-1273 (N=X)		50 µg mRNA -1273 (N=X)		100 µg mRNA -1273 (N=X)		250 µg mRNA -1273 (N=X)		All Subjects (N=X)	
Symptom	**Dose**	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
		Moderate										
		Severe										
	Any Dose	**None**										
		Mild										
		Moderate										
		Severe										
Feverishness	**Dose 1**	**None**										
		Mild										
		Moderate										
		Severe										
	Dose 2	**None**										
		Mild										
		Moderate										
		Severe										
	Any Dose	**None**										
		Mild										
		Moderate										
		Severe										
Headache	**Dose 1**	**None**										
		Mild										
		Moderate										
		Severe										

			25 µg mRNA-1273 (N=X)		50 µg mRNA -1273 (N=X)		100 µg mRNA -1273 (N=X)		250 µg mRNA -1273 (N=X)		All Subjects (N=X)	
Symptom	**Dose**	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
	Dose 2	**None**										
		Mild										
		Moderate										
		Severe										
	Any Dose	**None**										
		Mild										
		Moderate										
		Severe										
Myalgia	**Dose 1**	**None**										
		Mild										
		Moderate										
		Severe										
	Dose 2	**None**										
		Mild										
		Moderate										
		Severe										
	Any Dose	**None**										
		Mild										
		Moderate										
		Severe										
Nausea	**Dose 1**	**None**										
		Mild										

			25 µg mRNA-1273 (N=X)		50 µg mRNA -1273 (N=X)		100 µg mRNA -1273 (N=X)		250 µg mRNA -1273 (N=X)		All Subjects (N=X)	
Symptom	**Dose**	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
		Moderate										
		Severe										
	Dose 2	**None**										
		Mild										
		Moderate										
		Severe										
	Any Dose	**None**										
		Mild										
		Moderate										
		Severe										

Severity is the maximum severity reported over all solicited symptoms post dosing for each subject.
N=All subjects receiving Dose 1 with any solicited event data recorded in the database.
[a]Fever percentages reflect the number of subjects with at least one measurement available in the data system as the denominator. This denominator may differ from other systemic symptoms, which are solicited in-clinic at the post-dose assessment.

Tables with Similar Format:

Table 148: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity, Dose, and Treatment Group - Systemic Symptoms - 56-70 Years of Age*

Table 149: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity, Dose, and Treatment Group - Systemic Symptoms - ≥71 Years of Age*

Table 150: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity, Dose, and Treatment Group - Local Symptoms - 18-55 Years of Age*

			25 µg mRNA-1273 (N=X)		50 µg mRNA -1273 (N=X)		100 µg mRNA -1273 (N=X)		250 µg mRNA -1273 (N=X)		All Subjects (N=X)	
Symptom	**Dose**	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Any Local Symptom	**Dose 1**	**None**										
		Mild										
		Moderate										
		Severe										
	Dose 2	**None**										
		Mild										
		Moderate										
		Severe										
	Any Dose	**None**										
		Mild										
		Moderate										
		Severe										
Erythema/Redness	**Dose 1**	**None**										
		Mild										
		Moderate										
		Severe										
	Dose 2	**None**										
		Mild										
		Moderate										
		Severe										

			25 µg mRNA-1273 (N=X)		50 µg mRNA -1273 (N=X)		100 µg mRNA -1273 (N=X)		250 µg mRNA -1273 (N=X)		All Subjects (N=X)	
Symptom	**Dose**	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
	Any Dose	**None**										
		Mild										
		Moderate										
		Severe										
Erythema/Redness Measurement (mm)	**Dose 1**	**None**										
		Mild										
		Moderate										
		Severe										
	Dose 2	**None**										
		Mild										
		Moderate										
		Severe										
	Any Dose	**None**										
		Mild										
		Moderate										
		Severe										
Induration/Swelling	**Dose 1**	**None**										
		Mild										
		Moderate										
		Severe										
	Dose 2	**None**										
		Mild										

			25 µg mRNA-1273 (N=X)		50 µg mRNA -1273 (N=X)		100 µg mRNA -1273 (N=X)		250 µg mRNA -1273 (N=X)		All Subjects (N=X)	
Symptom	**Dose**	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
		Moderate										
		Severe										
	Any Dose	**None**										
		Mild										
		Moderate										
		Severe										
Induration/Swelling (mm)	**Dose 1**	**None**										
		Mild										
		Moderate										
		Severe										
	Dose 2	**None**										
		Mild										
		Moderate										
		Severe										
	Any Dose	**None**										
		Mild										
		Moderate										
		Severe										
Pain	**Dose 1**	**None**										
		Mild										
		Moderate										
		Severe										

			25 µg mRNA-1273 (N=X)		50 µg mRNA -1273 (N=X)		100 µg mRNA -1273 (N=X)		250 µg mRNA -1273 (N=X)		All Subjects (N=X)	
Symptom	**Dose**	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
	Dose 2	**None**										
		Mild										
		Moderate										
		Severe										
	Any Dose	**None**										
		Mild										
		Moderate										
		Severe										

Severity is the maximum severity reported over all solicited symptoms post dosing for each subject.
N=All subjects receiving Dose 1 with any solicited event data recorded in the database.

Tables with Similar Format:

Table 151: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity, Dose, and Treatment Group - Local Symptoms - 56-70 Years of Age*

Table 152: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity, Dose, and Treatment Group - Local Symptoms - ≥71Years of Age*

Table 153: Summary of Systemic Solicited Events by Days Post Treatment and Treatment Group
Dose Number = Dose 1
Treatment Group – 25 µg mRNA-1273 (18-55 years)

		Pre-Dose (N=X)		Post-Dose (N=X)		Day 1 (N=X)		Day 2 (N=X)		Day 3 (N=X)		Day 4 (N=X)		Day 5 (N=X)		Day 6 (N=X)		Day 7 (N=X)		Day 8+ [1] (N=X)		Any Post-Dose[2]	
Symptom	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Any Systemic Symptom	**None**																						
	Mild																						
	Moderate																						
	Severe																						
	Not Reported																						
Arthralgia	**None**																						
	Mild																						
	Moderate																						
	Severe																						
	Not Reported																						
Fatigue	**None**																						
	Mild																						
	Moderate																						
	Severe																						
	Not Reported																						
Fever	**None**																						
	Mild																						
	Moderate																						

		Pre-Dose (N=X)		Post-Dose (N=X)		Day 1 (N=X)		Day 2 (N=X)		Day 3 (N=X)		Day 4 (N=X)		Day 5 (N=X)		Day 6 (N=X)		Day 7 (N=X)		Day 8+ [1] (N=X)		Any Post-Dose[2]	
Symptom	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
	Severe																						
	Not Reported																						
Feverishness	**None**																						
	Mild																						
	Moderate																						
	Severe																						
	Not Reported																						
Headache	**None**																						
	Mild																						
	Moderate																						
	Severe																						
	Not Reported																						
Myalgia	**None**																						
	Mild																						
	Moderate																						
	Severe																						
	Not Reported																						
Nausea	**None**																						
	Mild																						
	Moderate																						
	Severe																						

		Pre-Dose (N=X)		Post-Dose (N=X)		Day 1 (N=X)		Day 2 (N=X)		Day 3 (N=X)		Day 4 (N=X)		Day 5 (N=X)		Day 6 (N=X)		Day 7 (N=X)		Day 8+ [1] (N=X)		Any Post-Dose[2]	
Symptom	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
	Not Reported																						

Severity is the maximum severity reported post dosing for each subject for each day.
[1] Day 8+ includes the maximum severity of each symptom reported on or after Day 8 (includes ongoing symptoms)
[2]Indicateshow many subjects had “None”, “Mild”, “Moderate”, “Severe”, or “Not Reported” as their maximum severity for any day. A subject may be counted in more than one of these categories.

Tables with Similar Format:

Table 154: Summary of Systemic Solicited Events by Days Post Treatment and Treatment Group
Dose Number = Dose 2
Treatment Group – 25 µg mRNA-1273 (18-55 years)

Table 155: Summary of Systemic Solicited Events by Days Post Treatment and Treatment Group
Dose Number = Any Dose
Treatment Group – 25 µg mRNA-1273 (18-55 years)

Table 156: Summary of Systemic Solicited Events by Days Post Treatment and Treatment Group
Dose Number = Dose 1
Treatment Group – 50 µg mRNA-1273 (18-55 years)

Table 157: Summary of Systemic Solicited Events by Days Post Treatment and Treatment Group
Dose Number = Dose 2
Treatment Group – 50 µg mRNA-1273 (18-55 years)

Table 158: Summary of Systemic Solicited Events by Days Post Treatment and Treatment Group
Dose Number = Any Dose
Treatment Group – 50 µg mRNA-1273 (18-55 years)

Table 159: Summary of Systemic Solicited Events by Days Post Treatment and Treatment Group
Dose Number = Dose 1
Treatment Group – 100 µg mRNA-1273 (18-55 years)

Table 160: Summary of Systemic Solicited Events by Days Post Treatment and Treatment Group
Dose Number = Dose 2
Treatment Group – 100 µg mRNA-1273 (18-55 years)

Table 161: Summary of Systemic Solicited Events by Days Post Treatment and Treatment Group
Dose Number = Any Dose
Treatment Group – 100 µg mRNA-1273 (18-55 years)

Table 162: Summary of Systemic Solicited Events by Days Post Treatment and Treatment Group
Dose Number = Dose 1
Treatment Group – 250 µg mRNA-1273 (18-55 years)

Table 163: Summary of Systemic Solicited Events by Days Post Treatment and Treatment Group
Dose Number = Dose 2
Treatment Group – 250 µg mRNA-1273 (18-55 years)

Table 164: Summary of Systemic Solicited Events by Days Post Treatment and Treatment Group
Dose Number = Any Dose
Treatment Group – 250 µg mRNA-1273 (18-55 years)

Table 165: Summary of Systemic Solicited Events by Days Post Treatment and Treatment Group
Dose Number = Dose 1
Treatment Group – 25 µg mRNA-1273 (56-70 years)

Table 166: Summary of Systemic Solicited Events by Days Post Treatment and Treatment Group
Dose Number = Dose 2
Treatment Group – 25 µg mRNA-1273 (56-70 years)

Table 167: Summary of Systemic Solicited Events by Days Post Treatment and Treatment Group
Dose Number = Any Dose
Treatment Group – 25 µg mRNA-1273 (56-70 years)

Table 168: Summary of Systemic Solicited Events by Days Post Treatment and Treatment Group
Dose Number = Dose 1
Treatment Group – 50 µg mRNA-1273 (56-70 years)

Table 169: Summary of Systemic Solicited Events by Days Post Treatment and Treatment Group
Dose Number = Dose 2
Treatment Group – 50 µg mRNA-1273 (56-70 years)

Table 170: Summary of Systemic Solicited Events by Days Post Treatment and Treatment Group
Dose Number = Any Dose
Treatment Group – 50 µg mRNA-1273 (56-70 years)

Table 171: Summary of Systemic Solicited Events by Days Post Treatment and Treatment Group
Dose Number = Dose 1
Treatment Group – 100 µg mRNA-1273 (56-70 years)

Table 181: Summary of Systemic Solicited Events by Days Post Treatment and Treatment Group
Dose Number = Dose 2
Treatment Group – 100 µg mRNA-1273 (≥71 years)

Table 182: Summary of Systemic Solicited Events by Days Post Treatment and Treatment Group
Dose Number = Any Dose
Treatment Group – 100 µg mRNA-1273 (≥71 years)

Table 183: Summary of Local Solicited Events by Days Post Treatment and Treatment Group
Dose Number = Dose 1
Treatment Group – 25 µg mRNA-1273 (18-55 years)

		Post-Dose (N=X)		Day 1 (N=X)		Day 2 (N=X)		Day 3 (N=X)		Day 4 (N=X)		Day 5 (N=X)		Day 6 (N=X)		Day 7 (N=X)		Day 8+ [1] (N=X)		Any Post-Dose[2]	
Symptom	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**N**	**%**	**n**	**%**
Any Local Symptom	**None**																				
	Mild																				
	Moderate																				
	Severe																				
	Not Reported																				
Erythema /Redness	**None**																				
	Mild																				
	Moderate																				
	Severe																				
	Not Reported																				
Erythema /Redness Measurement (mm)	**None**																				
	Mild																				
	Moderate																				
	Severe																				
	Not Reported																				
Induration /Swelling	**None**																				
	Mild																				
	Moderate																				

		Post-Dose (N=X)		Day 1 (N=X)		Day 2 (N=X)		Day 3 (N=X)		Day 4 (N=X)		Day 5 (N=X)		Day 6 (N=X)		Day 7 (N=X)		Day 8+ [1] (N=X)		Any Post-Dose[2]	
Symptom	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**N**	**%**	**n**	**%**
	Severe																				
	Not Reported																				
Induration /Swelling (mm)	**None**																				
	Mild																				
	Moderate																				
	Severe																				
	Not Reported																				
Pain	**None**																				
	Mild																				
	Moderate																				
	Severe																				
	Not Reported																				

Severity is the maximum severity reported post dosing for each subject for each day.

[1] Day 8+ includes the maximum severity of each symptom reported on or after Day 8 (includes ongoing symptoms)

[2]Indicates how many subjects had "None", "Mild", "Moderate", "Severe", or "Not Reported" as their maximum severity for any day. A subject may be counted in more than one of these categories.

Tables with Similar Format:

Table 184: Summary of Local Solicited Events by Days Post Treatment and Treatment Group
Dose Number = Dose 2
Treatment Group – 25 µg mRNA-1273 (18-55 years)

Table 185: Summary of Local Solicited Events by Days Post Treatment and Treatment Group
Dose Number = Any Dose
Treatment Group – 25 µg mRNA-1273 (18-55 years)

Table 213: Summary of Duration of Solicited Symptoms by Treatment Group - All Subjects 18-55 Years of Age*

		25 µg mRNA-1273 (N=X)			50 µg mRNA -1273 (N=X)			100 µg mRNA -1273 (N=X)			250 µg mRNA -1273 (N=X)			All Subjects (N=X)		
Variable	**Statistic**	**Dose 1**	**Dose 2**	**All**	**Dose 1**	**Dose 2**	**All**	**Dose 1**	**Dose 2**	**All**	**Dose 1**	**Dose 2**	**All**	**Dose 1**	**Dose 2**	**All**
Any Symptom	n															
	Mean															
	Standard Deviation															
	Median															
	Minimum															
	Maximum															
Any Local Symptom	n															
	Mean															
	Standard Deviation															
	Median															
	Minimum															
	Maximum															
Erythema/redness	n															
	Mean															
	Standard Deviation															
	Median															
	Minimum															
	Maximum															
Induration/swelling	n															

		25 µg mRNA-1273 (N=X)			50 µg mRNA -1273 (N=X)			100 µg mRNA -1273 (N=X)			250 µg mRNA -1273 (N=X)			All Subjects (N=X)		
Variable	**Statistic**	**Dose 1**	**Dose 2**	**All**	**Dose 1**	**Dose 2**	**All**	**Dose 1**	**Dose 2**	**All**	**Dose 1**	**Dose 2**	**All**	**Dose 1**	**Dose 2**	**All**
	Mean															
	Standard Deviation															
	Median															
	Minimum															
	Maximum															
Pain	n															
	Mean															
	Standard Deviation															
	Median															
	Minimum															
	Maximum															
Any Systemic Symptom	n															
	Mean															
	Standard Deviation															
	Median															
	Minimum															
	Maximum															
Arthralgia	n															
	Mean															
	Standard Deviation															

		25 µg mRNA-1273 (N=X)			50 µg mRNA -1273 (N=X)			100 µg mRNA -1273 (N=X)			250 µg mRNA -1273 (N=X)			All Subjects (N=X)		
Variable	**Statistic**	**Dose 1**	**Dose 2**	**All**	**Dose 1**	**Dose 2**	**All**	**Dose 1**	**Dose 2**	**All**	**Dose 1**	**Dose 2**	**All**	**Dose 1**	**Dose 2**	**All**
	Median															
	Minimum															
	Maximum															
Fatigue	n															
	Mean															
	Standard Deviation															
	Median															
	Minimum															
	Maximum															
Fever	n															
	Mean															
	Standard Deviation															
	Median															
	Minimum															
	Maximum															
Feverishness	n															
	Mean															
	Standard Deviation															
	Median															
	Minimum															
	Maximum															

		25 µg mRNA-1273 (N=X)			50 µg mRNA -1273 (N=X)			100 µg mRNA -1273 (N=X)			250 µg mRNA -1273 (N=X)			All Subjects (N=X)		
Variable	**Statistic**	**Dose 1**	**Dose 2**	**All**	**Dose 1**	**Dose 2**	**All**	**Dose 1**	**Dose 2**	**All**	**Dose 1**	**Dose 2**	**All**	**Dose 1**	**Dose 2**	**All**
Headache	n															
	Mean															
	Standard Deviation															
	Median															
	Minimum															
	Maximum															
Myalgia	n															
	Mean															
	Standard Deviation															
	Median															
	Minimum															
	Maximum															
Nausea	n															
	Mean															
	Standard Deviation															
	Median															
	Minimum															
	Maximum															
n=number of solicited adverse events																

Tables with Similar Format:

Table 214: Summary of Duration of Solicited Symptoms by Treatment Group - All Subjects 56-70 Years of Age*

Table 215: Summary of Duration of Solicited Symptoms by Treatment Group - All Subjects ≥71 Years of Age*

14.3.1.2 Unsolicited Adverse Events

Table 216: All Adverse Events Cross-Classified byMedDRA® System Organ Class, Severity, and Relationship to Study Treatment, and Treatment Group – 25 µg mRNA-1273 18-55 years (N=X)*

		Relationship to Vaccination		
MedDRA System Organ Class	**Severity**	**Not Related (n)**	**Related (n)**	**Not Yet Determined (n)**
Any SOC	**Mild**			
	Moderate			
	Severe			
Blood And Lymphatic System Disorders	**Mild**			
	Moderate			
	Severe			
Cardiac Disorders	**Mild**			
	Moderate			
	Severe			
Ear And Labyrinth Disorders	**Mild**			
	Moderate			
	Severe			
Eye Disorders	**Mild**			
	Moderate			
	Severe			
Gastrointestinal Disorders	**Mild**			
	Moderate			
	Severe			
	Mild			

		Relationship to Vaccination		
MedDRA System Organ Class	**Severity**	**Not Related (n)**	**Related (n)**	**Not Yet Determined (n)**
General Disorders And Administration Site Conditions	**Moderate**			
	Severe			
Immune System Disorders	**Mild**			
	Moderate			
	Severe			
Infections And Infestations	**Mild**			
	Moderate			
	Severe			
Injury, Poisoning And Procedural Complications	**Mild**			
	Moderate			
	Severe			
Investigations	**Mild**			
	Moderate			
	Severe			
Metabolism And Nutrition Disorders	**Mild**			
	Moderate			
	Severe			
Musculoskeletal And Connective Tissue Disorders	**Mild**			
	Moderate			
	Severe			
Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps)	**Mild**			
	Moderate			

		Relationship to Vaccination		
MedDRA System Organ Class	**Severity**	**Not Related (n)**	**Related (n)**	**Not Yet Determined (n)**
	Severe			
Nervous System Disorders	**Mild**			
	Moderate			
	Severe			
Psychiatric Disorders	**Mild**			
	Moderate			
	Severe			
Reproductive System And Breast Disorders	**Mild**			
	Moderate			
	Severe			
Respiratory, Thoracic And Mediastinal Disorders	**Mild**			
	Moderate			
	Severe			
Skin And Subcutaneous Tissue Disorders	**Mild**			
	Moderate			
	Severe			
Vascular Disorders	**Mild**			
	Moderate			
	Severe			
[Repeat for all reported SOC]				

Tables with Similar Format:

Table 217: All Adverse Events Cross-Classified byMedDRA® System Organ Class, Severity, and Relationship to Study Treatment, and Treatment Group – 50 µg mRNA-1273 18-55 years (N=X)*

Table 218: All Adverse Events Cross-Classified byMedDRA® System Organ Class, Severity, and Relationship to Study Treatment, and Treatment Group – 100 µg mRNA-1273 18-55 years (N=X)*

Table 219: All Adverse Events Cross-Classified byMedDRA® System Organ Class, Severity, and Relationship to Study Treatment, and Treatment Group – 250 µg mRNA-1273 18-55 years (N=X)*

Table 220: All Adverse Events Cross-Classified byMedDRA® System Organ Class, Severity, and Relationship to Study Treatment, and Treatment Group – All Subjects 18-55 years (N=X)*

Table 221: All Adverse Events Cross-Classified byMedDRA® System Organ Class, Severity, and Relationship to Study Treatment, and Treatment Group – 25 µg mRNA-1273 56-70 years (N=X)*

Table 222: All Adverse Events Cross-Classified byMedDRA® System Organ Class, Severity, and Relationship to Study Treatment, and Treatment Group – 50 µg mRNA-1273 56-70 years (N=X)*

Table 223: All Adverse Events Cross-Classified byMedDRA® System Organ Class, Severity, and Relationship to Study Treatment, and Treatment Group – 100 µg mRNA-1273 56-70 years (N=X)*

Table 224: All Adverse Events Cross-Classified byMedDRA® System Organ Class, Severity, and Relationship to Study Treatment, and Treatment Group – All Subjects 56-70 years (N=X)*

Table 225: All Adverse Events Cross-Classified byMedDRA® System Organ Class, Severity, and Relationship to Study Treatment, and Treatment Group – 25 µg mRNA-1273 ≥71 years (N=X)*

Table 226: All Adverse Events Cross-Classified byMedDRA® System Organ Class, Severity, and Relationship to Study Treatment, and Treatment Group – 50 µg mRNA-1273 ≥71 years (N=X)*

Table 227: All Adverse Events Cross-Classified byMedDRA® System Organ Class, Severity, and Relationship to Study Treatment, and Treatment Group – 100 µg mRNA-1273 ≥71 years (N=X)*

Table 228: All Adverse Events Cross-Classified byMedDRA® System Organ Class, Severity, and Relationship to Study Treatment, and Treatment Group – All Subjects ≥71 years (N=X)*

Table 229: Summary of All Unsolicited Adverse Events by MedDRA® System Organ Class and Preferred Term, Severity, Relationship, and Treatment Group – 25 µg mRNA-1273 18-55 years (N=X)*

			Severity			Relationship to Study Vccination		
System Organ Class (SOC)	Preferred Term (PT)	Total Events (n)	Mild (n)	Moderate (n)	Severe (n)	Not Related (n)	Related (n)	Not Yet Determined (n)
Any SOC	Any PT							
Gastrointestinal disorders	Any PT							
	Flatulence							
	Vomiting							
General disorders and administration site conditions	Any PT							
	Fatigue							
	Injection site irritation							
	Vessel puncture site bruise							
Infections and infestations	Any PT							
	Hordeolum							
	Pustule							
Injury, poisoning and procedural complications	Any PT							
	Contusion							
	Muscle strain							
	Skin abrasion							
	Skin laceration							
	Wound							
Musculoskeletal and connective tissue disorders	Any PT							
	Muscular weakness							
	Pain in jaw							

			Severity			Relationship to Study Vccination		
System Organ Class (SOC)	**Preferred Term (PT)**	**Total Events (n)**	**Mild (n)**	**Moderate (n)**	**Severe (n)**	**Not Related (n)**	**Related (n)**	**Not Yet Determined (n)**
Nervous system disorders	**Presyncope**							
Respiratory, thoracic and mediastinal disorders	**Any PT**							
	Dyspnoea exertional							
	Oropharyngeal pain							
Skin and subcutaneous tissue disorders	**Any PT**							
	Dermatitis contact							
	Erythema							
	Petechiae							
	Urticaria							
Vascular disorders	**Systolic hypertension**							
[Repeat for all reported SOC]	**[Repeat for all reported PT]**							

Tables with Similar Format:

Table 230: Summary of All Unsolicited Adverse Events by MedDRA® System Organ Class and Preferred Term, Severity, Relationship, and Treatment Group – 50 µg mRNA-1273 18-55 years (N=X)*

Table 231: Summary of All Unsolicited Adverse Events by MedDRA® System Organ Class and Preferred Term, Severity, Relationship, and Treatment Group – 100 µg mRNA-1273 18-55 years (N=X)*

Table 232: Summary of All Unsolicited Adverse Events by MedDRA® System Organ Class and Preferred Term, Severity, Relationship, and Treatment Group – 250 µg mRNA-1273 18-55 years (N=X)*

Table 233: Summary of All Unsolicited Adverse Events by MedDRA® System Organ Class and Preferred Term, Severity, Relationship, and Treatment Group – All Subjects 18-55 years (N=X)*

Table 234: Summary of All Unsolicited Adverse Events by MedDRA® System Organ Class and Preferred Term, Severity, Relationship, and Treatment Group – 25 µg mRNA-1273 56-70 years (N=X)*

Table 242: Number and Percentage of Subjects Experiencing Unsolicited Adverse Events by MedDRA® System Organ Class and Preferred Term, Severity, Relationship, and Treatment Group – 25 µg mRNA-1273 18-55 Years of Age (N=X)*

				Severity						Relationship to Study Vaccination			
		Any Incidence		Mild		Moderate		Severe		Not Related		Related	
MedDRA System Organ Class	MedDRA Preferred Term	n	%	n	%	n	%	n	%	n	%	n	%
Any SOC	Any PT												
Gastrointestinal disorders	Any PT												
	Flatulence												
	Vomiting												
General disorders and administration site conditions	Any PT												
	Fatigue												
	Injection site irritation												
	Vessel puncture site bruise												
Infections and infestations	Any PT												
	Hordeolum												
	Pustule												
Injury, poisoning and procedural complications	Any PT												
	Contusion												
	Muscle strain												
	Skin abrasion												
	Skin laceration												
	Wound												
	Any PT												

				Severity						Relationship to Study Vaccination			
		Any Incidence		Mild		Moderate		Severe		Not Related		Related	
MedDRA System Organ Class	MedDRA Preferred Term	n	%	n	%	n	%	n	%	n	%	n	%
Musculoskeletal and connective tissue disorders	Muscular weakness												
	Pain in jaw												
Nervous system disorders	Presyncope												
Respiratory, thoracic and mediastinal disorders	Any PT												
	Dyspnoea exertional												
	Oropharyngeal pain												
Skin and subcutaneous tissue disorders	Any PT												
	Dermatitis contact												
	Erythema												
	Petechiae												
	Urticaria												
Vascular disorders	Systolic hypertension												
[Repeat for all reported SOC]	[Repeate for all reported PT]												
Note: This table presents number and percentage of subjects. A subject is only counted once per PT and is summarized according to their highest severity and closest relationship.													

Tables with Similar Format:

Table 243: Number and Percentage of Subjects Experiencing Unsolicited Adverse Events by MedDRA® System Organ Class and Preferred Term, Severity, Relationship, and Treatment Group – 50 µg mRNA-1273 18-55 Years of Age (N=X)*

Table 244: Number and Percentage of Subjects Experiencing Unsolicited Adverse Events by MedDRA® System Organ Class and Preferred Term, Severity, Relationship, and Treatment Group – 100 µg mRNA-1273 18-55 Years of Age (N=X)*

Table 245: Number and Percentage of Subjects Experiencing Unsolicited Adverse Events by MedDRA® System Organ Class and Preferred Term, Severity, Relationship, and Treatment Group – 250 µg mRNA-1273 18-55 Years of Age (N=X)*

Table 246: Number and Percentage of Subjects Experiencing Unsolicited Adverse Events by MedDRA® System Organ Class and Preferred Term, Severity, Relationship, and Treatment Group – All Subjects 1273 18-55 Years of Age (N=X)*

Table 247: Number and Percentage of Subjects Experiencing Unsolicited Adverse Events by MedDRA® System Organ Class and Preferred Term, Severity, Relationship, and Treatment Group – 25 µg mRNA-1273 56-70 Years of Age (N=X)*

Table 248: Number and Percentage of Subjects Experiencing Unsolicited Adverse Events by MedDRA® System Organ Class and Preferred Term, Severity, Relationship, and Treatment Group – 50 µg mRNA-1273 56-70 Years of Age (N=X)*

Table 249: Number and Percentage of Subjects Experiencing Unsolicited Adverse Events by MedDRA® System Organ Class and Preferred Term, Severity, Relationship, and Treatment Group – 100 µg mRNA-1273 56-70 Years of Age (N=X)*

Table 250: Number and Percentage of Subjects Experiencing Unsolicited Adverse Events by MedDRA® System Organ Class and Preferred Term, Severity, Relationship, and Treatment Group – All Subjects 1273 56-70 Years of Age (N=X)*

Table 251: Number and Percentage of Subjects Experiencing Unsolicited Adverse Events by MedDRA® System Organ Class and Preferred Term, Severity, Relationship, and Treatment Group – 25 µg mRNA-1273 ≥71 Years of Age (N=X)*

Table 252: Number and Percentage of Subjects Experiencing Unsolicited Adverse Events by MedDRA® System Organ Class and Preferred Term, Severity, Relationship, and Treatment Group – 50 µg mRNA-1273 ≥71 Years of Age (N=X)*

Table 253: Number and Percentage of Subjects Experiencing Unsolicited Adverse Events by MedDRA® System Organ Class and Preferred Term, Severity, Relationship, and Treatment Group – 100 µg mRNA-1273 ≥71 Years of Age (N=X)*

Table 254: Number and Percentage of Subjects Experiencing Unsolicited Adverse Events by MedDRA® System Organ Class and Preferred Term, Severity, Relationship, and Treatment Group – All Subjects 1273 ≥71 Years of Age (N=X)*

14.3.2 Listing of Deaths, Other Serious and Significant Adverse Events

Table 255: Listing of Serious Adverse Events*

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

Table 256: Listing of Non-Serious, Unsolicited, Moderate or Severe Adverse Events*

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

Table 257: Listing of MAAEs and NOCMCs*

Subject ID	Treatment Group	Event Description	Number of Doses Received at Time of Event	Date of Product Administration[a]	Duration of Event	Date of Onset	MedDRA® Sytem Organ Class	MAAEs	NOCMCs	Relationship[b]	Outcome

14.3.3 Narratives of Deaths, Other Serious and Significant Adverse Events

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

14.3.4 Abnormal Laboratory Value Listings (by Subject)

Table 258: Listing of Abnormal Laboratory Results*

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

14.3.5 Displays of Laboratory Results

14.3.5.1 Chemistry Results

Table 259: Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Any Chemistry Parameter*

				None		Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
Timepoint	**Treatment Group**	**N**	**N***	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Screening (Day -42 to -1)	**25 µg (18-55 years)**										
	50 µg (18-55 years)										
	100 µg (18-55 years)										
	250 µg (18-55 years)										
	25 µg (56-70 years)										
	50 µg (56-70 years)										
	100 µg (56-70 years)										
	25 µg (≥71 years)										
	50 µg (≥71 years)										
	100 µg (≥71 years)										
	All Subjects										
Day 1, Baseline	**25 µg (18-55 years)**										
	50 µg (18-55 years)										
	100 µg (18-55 years)										
	250 µg (18-55 years)										
	25 µg (56-70 years)										
	50 µg (56-70 years)										
	100 µg (56-70 years)										
	25 µg (≥71 years)										

				None		Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
Timepoint	**Treatment Group**	**N**	**N***	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
	50 µg (≥71 years)										
	100 µg (≥71 years)										
	All Subjects										
Day 8 (Days 7 to 9)	**25 µg (18-55 years)**										
	50 µg (18-55 years)										
	100 µg (18-55 years)										
	250 µg (18-55 years)										
	25 µg (56-70 years)										
	50 µg (56-70 years)										
	100 µg (56-70 years)										
	25 µg (≥71 years)										
	50 µg (≥71 years)										
	100 µg (≥71 years)										
	All Subjects										
Day 29 (Days 27 to 31)	**25 µg (18-55 years)**										
	50 µg (18-55 years)										
	100 µg (18-55 years)										
	250 µg (18-55 years)										
	25 µg (56-70 years)										
	50 µg (56-70 years)										
	100 µg (56-70 years)										
	25 µg (≥71 years)										
	50 µg (≥71 years)										

				None		Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
Timepoint	**Treatment Group**	**N**	**N***	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
	100 µg (≥71 years)										
	All Subjects										
Day 36 (Days 35 to 37)	**25 µg (18-55 years)**										
	50 µg (18-55 years)										
	100 µg (18-55 years)										
	250 µg (18-55 years)										
	25 µg (56-70 years)										
	50 µg (56-70 years)										
	100 µg (56-70 years)										
	25 µg (≥71 years)										
	50 µg (≥71 years)										
	100 µg (≥71 years)										
	All Subjects										
Max Severity Post Baseline	**25 µg (18-55 years)**										
	50 µg (18-55 years)										
	100 µg (18-55 years)										
	250 µg (18-55 years)										
	25 µg (56-70 years)										
	50 µg (56-70 years)										
	100 µg (56-70 years)										
	25 µg (≥71 years)										
	50 µg (≥71 years)										
	100 µg (≥71 years)										

				None		Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
Timepoint	**Treatment Group**	**N**	**N***	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
	All Subjects										

Note: The "Max Severity Post Baseline" rows indicate the maximum severity experienced by each subject at any time point post baseline, including unscheduled assessments.
N = Number of subjects enrolled and vaccinated; N* = Number of subjects that completed the visit.

Tables with Similar Format:

Table 260: Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Alanine Aminotransferase*

Table 261: Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Aspartate Aminotransferase*

Table 262: Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Alkaline Phosphatase*

Table 263: Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Total Bilirubin*

Table 264: Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Serum Creatinine*

Table 265: Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Serum Lipase*

Table 266: Abnormal Laboratory Results Related to Study Treatment by Parameter, Maximum Severity, Time Point, and Treatment Group – Any Chemistry Parameter*

Table 267: Abnormal Laboratory Results Related to Study Treatment by Parameter, Maximum Severity, Time Point, and Treatment Group – Alanine Aminotransferase*

Table 268: Abnormal Laboratory Results Related to Study Treatment by Parameter, Maximum Severity, Time Point, and Treatment Group – Aspartate Aminotransferase*

Table 269: Abnormal Laboratory Results Related to Study Treatment by Parameter, Maximum Severity, Time Point, and Treatment Group – Alkaline Phosphatase*

Table 270: Abnormal Laboratory Results Related to Study Treatment by Parameter, Maximum Severity, Time Point, and Treatment Group – Total Bilirubin*

Table 271: Abnormal Laboratory Results Related to Study Treatment by Parameter, Maximum Severity, Time Point, and Treatment Group – Serum Creatinine*

Table 272: Abnormal Laboratory Results Related to Study Treatment by Parameter, Maximum Severity, Time Point, and Treatment Group – Serum Lipase*

14.3.5.2 Hematology Results

Table 273: Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Any Hematology Parameter*

				None		Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
Timepoint	**Treatment Group**	**N**	**N***	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Screening (Day -42 to -1)	**25 µg (18-55 years)**										
	50 µg (18-55 years)										
	100 µg (18-55 years)										
	250 µg (18-55 years)										
	25 µg (56-70 years)										
	50 µg (56-70 years)										
	100 µg (56-70 years)										
	25 µg (≥71 years)										
	50 µg (≥71 years)										
	100 µg (≥71 years)										
	All Subjects										
Day 1, Baseline	**25 µg (18-55 years)**										
	50 µg (18-55 years)										
	100 µg (18-55 years)										
	250 µg (18-55 years)										
	25 µg (56-70 years)										
	50 µg (56-70 years)										
	100 µg (56-70 years)										
	25 µg (≥71 years)										
	50 µg (≥71 years)										

				None		Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
Timepoint	**Treatment Group**	**N**	**N***	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
	100 µg (≥71 years)										
	All Subjects										
Day 8 (Days 7 to 9)	**25 µg (18-55 years)**										
	50 µg (18-55 years)										
	100 µg (18-55 years)										
	250 µg (18-55 years)										
	25 µg (56-70 years)										
	50 µg (56-70 years)										
	100 µg (56-70 years)										
	25 µg (≥71 years)										
	50 µg (≥71 years)										
	100 µg (≥71 years)										
	All Subjects										
Day 29 (Days 27 to 31)	**25 µg (18-55 years)**										
	50 µg (18-55 years)										
	100 µg (18-55 years)										
	250 µg (18-55 years)										
	25 µg (56-70 years)										
	50 µg (56-70 years)										
	100 µg (56-70 years)										
	25 µg (≥71 years)										
	50 µg (≥71 years)										
	100 µg (≥71 years)										

				None		Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
Timepoint	**Treatment Group**	**N**	**N***	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
	All Subjects										
Day 36 (Days 35 to 37)	**25 µg (18-55 years)**										
	50 µg (18-55 years)										
	100 µg (18-55 years)										
	250 µg (18-55 years)										
	25 µg (56-70 years)										
	50 µg (56-70 years)										
	100 µg (56-70 years)										
	25 µg (≥71 years)										
	50 µg (≥71 years)										
	100 µg (≥71 years)										
	All Subjects										
Max Severity Post Baseline	**25 µg (18-55 years)**										
	50 µg (18-55 years)										
	100 µg (18-55 years)										
	250 µg (18-55 years)										
	25 µg (56-70 years)										
	50 µg (56-70 years)										
	100 µg (56-70 years)										
	25 µg (≥71 years)										
	50 µg (≥71 years)										
	100 µg (≥71 years)										
	All Subjects										

				None		Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
Timepoint	**Treatment Group**	**N**	**N***	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Note: The "Max Severity Post Baseline" rows indicate the maximum severity experienced by each subject at any time point post baseline, including unscheduled assessments. N = Number of subjects enrolled and vaccinated; N* = Number of subjects that completed the visit.											

Tables with Similar Format:

Table 274: Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – White Blood Cells*

Table 275: Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Hemoglobin*

Table 276: Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Platelets*

Table 277: Abnormal Laboratory Results Related to Study Treatment by Parameter, Maximum Severity, Time Point, and Treatment Group – Any Hematology Parameter*

Table 278: Abnormal Laboratory Results Related to Study Treatment by Parameter, Maximum Severity, Time Point, and Treatment Group – White Blood Cells*

Table 279: Abnormal Laboratory Results Related to Study Treatment by Parameter, Maximum Severity, Time Point, and Treatment Group – Hemoglobin*

Table 280: Abnormal Laboratory Results Related to Study Treatment by Parameter, Maximum Severity, Time Point, and Treatment Group – Platelets*

Table 281: Shift Table of Laboratory Parameters – White Blood Cells*

Baseline Severity			Normal		Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
Treatment Group	**Time Point**	**Post-Baseline Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
25 µg (18-55 years)	**Day 8 (N=X)**	**Normal**								
		Mild								
		Moderate								
		Severe								
	Day 29 (N=X)	**Normal**								
		Mild								
		Moderate								
		Severe								
	Day 36 (N=X)	**Normal**								
		Mild								
		Moderate								
		Severe								
50 µg (18-55 years)	**Day 8 (N=X)**	**Normal**								
		Mild								
		Moderate								
		Severe								
	Day 29 (N=X)	**Normal**								
		Mild								
		Moderate								
		Severe								
		Normal								

Baseline Severity			Normal		Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
Treatment Group	**Time Point**	**Post-Baseline Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
	Day 36 (N=X)	**Mild**								
		Moderate								
		Severe								
100 µg (18-55 years)	**Day 8 (N=X)**	**Normal**								
		Mild								
		Moderate								
		Severe								
	Day 29 (N=X)	**Normal**								
		Mild								
		Moderate								
		Severe								
	Day 36 (N=X)	**Normal**								
		Mild								
		Moderate								
		Severe								
250 µg (18-55 years)	**Day 8 (N=X)**	**Normal**								
		Mild								
		Moderate								
		Severe								
	Day 29 (N=14)	**Normal**								
		Mild								
		Moderate								
		Severe								

Baseline Severity			Normal		Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
Treatment Group	**Time Point**	**Post-Baseline Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
	Day 36 (N=X)	**Normal**								
		Mild								
		Moderate								
		Severe								
25 µg (56-70 years)	**Day 8 (N=X)**	**Normal**								
		Mild								
		Moderate								
		Severe								
	Day 29 (N=X)	**Normal**								
		Mild								
		Moderate								
		Severe								
	Day 36 (N=X)	**Normal**								
		Mild								
		Moderate								
		Severe								
50 µg (56-70 years)	**Day 8 (N=X)**	**Normal**								
		Mild								
		Moderate								
		Severe								
	Day 29 (N=X)	**Normal**								
		Mild								
		Moderate								

Baseline Severity			Normal		Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
Treatment Group	**Time Point**	**Post-Baseline Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
		Severe								
	Day 36 (N=X)	**Normal**								
		Mild								
		Moderate								
		Severe								
100 µg (56-70 years)	**Day 8 (N=X)**	**Normal**								
		Mild								
		Moderate								
		Severe								
	Day 29 (N=X)	**Normal**								
		Mild								
		Moderate								
		Severe								
	Day 36 (N=X)	**Normal**								
		Mild								
		Moderate								
		Severe								
25 µg (≥71 years)	**Day 8 (N=X)**	**Normal**								
		Mild								
		Moderate								
		Severe								
	Day 29 (N=X)	**Normal**								
		Mild								

Baseline Severity			Normal		Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
Treatment Group	**Time Point**	**Post-Baseline Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
		Moderate								
		Severe								
	Day 36 (N=X)	**Normal**								
		Mild								
		Moderate								
		Severe								
50 µg (≥71 years)	**Day 8 (N=X)**	**Normal**								
		Mild								
		Moderate								
		Severe								
	Day 29 (N=X)	**Normal**								
		Mild								
		Moderate								
		Severe								
	Day 36 (N=X)	**Normal**								
		Mild								
		Moderate								
		Severe								
100 µg (≥71 years)	**Day 8 (N=X)**	**Normal**								
		Mild								
		Moderate								
		Severe								
		Normal								

Baseline Severity			Normal		Mild/ Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
Treatment Group	**Time Point**	**Post-Baseline Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
	Day 29 (N=X)	**Mild**								
		Moderate								
		Severe								
	Day 36 (N=X)	**Normal**								
		Mild								
		Moderate								
		Severe								
N = Number of subjects that completed the visit and data available at both baseline and corresponding timepoint.										

Tables with Similar Format:

Table 282: Shift Table of Laboratory Parameters – Hemoglobin*

Table 283: Shift Table of Laboratory Parameters – Platelets*

Table 284: Shift Table of Laboratory Parameters – Alanine Aminotransferase*

Table 285: Shift Table of Laboratory Parameters – Aspartate Aminotransferase*

Table 286: Shift Table of Laboratory Parameters – Alkaline Phosphatase*

Table 287: Shift Table of Laboratory Parameters – Total Bilirubin*

Table 288: Shift Table of Laboratory Parameters – Serum Creatinine*

Table 289: Shift Table of Laboratory Parameters – Serum Lipase*

Table 290: Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – White Blood Cells*

Time Point	Treatment Group	N	Mean	Standard Deviation	Median	Min, Max
Baseline	25 µg (18-55 years)					
	50 µg (18-55 years)					
	100 µg (18-55 years)					
	250 µg (18-55 years)					
	All Subjects (18-55 years)					
	25 µg (56-70 years)					
	50 µg (56-70 years)					
	100 µg (56-70 years)					
	All Subjects (56-70 years)					
	25 µg (≥71 years)					
	50 µg (≥71 years)					
	100 µg (≥71 years)					
	All Subjects (≥71 years)					
	All Subjects					
Day 8	25 µg (18-55 years)					
	50 µg (18-55 years)					
	100 µg (18-55 years)					
	250 µg (18-55 years)					
	All Subjects (18-55 years)					
	25 µg (56-70 years)					
	50 µg (56-70 years)					
	100 µg (56-70 years)					

Time Point	Treatment Group	N	Mean	Standard Deviation	Median	Min, Max
	All Subjects (56-70 years)					
	25 µg (≥71 years)					
	50 µg (≥71 years)					
	100 µg (≥71 years)					
	All Subjects (≥71 years)					
	All Subjects					
Day 8, Change from Baseline	25 µg (18-55 years)					
	50 µg (18-55 years)					
	100 µg (18-55 years)					
	250 µg (18-55 years)					
	All Subjects (18-55 years)					
	25 µg (56-70 years)					
	50 µg (56-70 years)					
	100 µg (56-70 years)					
	All Subjects (56-70 years)					
	25 µg (≥71 years)					
	50 µg (≥71 years)					
	100 µg (≥71 years)					
	All Subjects (≥71 years)					
	All Subjects					
Day 29	25 µg (18-55 years)					
	50 µg (18-55 years)					
	100 µg (18-55 years)					

Time Point	Treatment Group	N	Mean	Standard Deviation	Median	Min, Max
	250 µg (18-55 years)					
	All Subjects (18-55 years)					
	25 µg (56-70 years)					
	50 µg (56-70 years)					
	100 µg (56-70 years)					
	All Subjects (56-70 years)					
	25 µg (≥71 years)					
	50 µg (≥71 years)					
	100 µg (≥71 years)					
	All Subjects (≥71 years)					
	All Subjects					
Day 29, Change from Baseline	25 µg (18-55 years)					
	50 µg (18-55 years)					
	100 µg (18-55 years)					
	250 µg (18-55 years)					
	All Subjects (18-55 years)					
	25 µg (56-70 years)					
	50 µg (56-70 years)					
	100 µg (56-70 years)					
	All Subjects (56-70 years)					
	25 µg (≥71 years)					
	50 µg (≥71 years)					
	100 µg (≥71 years)					

Time Point	Treatment Group	N	Mean	Standard Deviation	Median	Min, Max
	All Subjects (≥71 years)					
	All Subjects					
Day 36	25 µg (18-55 years)					
	50 µg (18-55 years)					
	100 µg (18-55 years)					
	250 µg (18-55 years)					
	All Subjects (18-55 years)					
	25 µg (56-70 years)					
	50 µg (56-70 years)					
	100 µg (56-70 years)					
	All Subjects (56-70 years)					
	25 µg (≥71 years)					
	50 µg (≥71 years)					
	100 µg (≥71 years)					
	All Subjects (≥71 years)					
	All Subjects					
Day 36, Change from Baseline	25 µg (18-55 years)					
	50 µg (18-55 years)					
	100 µg (18-55 years)					
	250 µg (18-55 years)					
	All Subjects (18-55 years)					
	25 µg (56-70 years)					
	50 µg (56-70 years)					

Time Point	Treatment Group	N	Mean	Standard Deviation	Median	Min, Max
	100 µg (56-70 years)					
	All Subjects (56-70 years)					
	25 µg (≥71 years)					
	50 µg (≥71 years)					
	100 µg (≥71 years)					
	All Subjects (≥71 years)					
	All Subjects					
N=Number of subjects in the Safety Population						

Tables with Similar Format:

Table 291: Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Hemoglobin*

Table 292: Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Platelets*

Table 293: Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Alanine Aminotransferase*

Table 294: Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Aspartate Aminotransferase*

Table 295: Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Alkaline Phosphatase*

Table 296: Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Total Bilirubin*

Table 297: Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Serum Creatinine*

Table 298: Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Serum Lipase*

14.3.5.3 Urinalysis Results

Not Applicable.

14.3.6 Displays of Vital Signs

Table 299: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group – All Subjects 18-55 Years of Age –Any Assessment*

		25 µg mRNA-1273 (N=X)		50 µg mRNA -1273 (N=X)		100 µg mRNA -1273 (N=X)		250 µg mRNA -1273 (N=X)		All Subjects (N=X)	
Time Point	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Baseline	**None**										
	Mild										
	Moderate										
	Severe										
Day 8	**None**										
	Mild										
	Moderate										
	Severe										
Day 15	**None**										
	Mild										
	Moderate										
	Severe										
Day 29	**None**										
	Mild										
	Moderate										
	Severe										
Day 36	**None**										
	Mild										
	Moderate										

		25 µg mRNA-1273 (N=X)		50 µg mRNA -1273 (N=X)		100 µg mRNA -1273 (N=X)		250 µg mRNA -1273 (N=X)		All Subjects (N=X)	
Time Point	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
	Severe										
Day 43	**None**										
	Mild										
	Moderate										
	Severe										
Day 57	**None**										
	Mild										
	Moderate										
	Severe										
Day 119	**None**										
	Mild										
	Moderate										
	Severe										
Max Severity Post Baseline	**None**										
	Mild										
	Moderate										
	Severe										

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

Tables with Similar Format:

Table 300: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group – All Subjects 18-55 Years of Age –Systolic Blood Pressure*

Table 301: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group – All Subjects 18-55 Years of Age –Diastolic Blood Pressure*

Table 302: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group – All Subjects 18-55 Years of Age –Pulse Rate*

Table 303: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group – All Subjects 18-55 Years of Age – Temperature*

Table 304: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group – All Subjects 56-70 Years of Age –Any Assessment*

Table 305: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group – All Subjects 56-70 Years of Age –Systolic Blood Pressure*

Table 306: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group – All Subjects 56-70 Years of Age –Diastolic Blood Pressure*

Table 307: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group – All Subjects 56-70 Years of Age –Pulse Rate*

Table 308: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group – All Subjects 56-70 Years of Age – Temperature*

Table 309: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group – All Subjects ≥71 Years of Age –Any Assessment*

Table 310: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group – All Subjects ≥71 Years of Age –Systolic Blood Pressure*

Table 311: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group – All Subjects ≥71 Years of Age –Diastolic Blood Pressure*

Table 312: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group – All Subjects ≥71 Years of Age –Pulse Rate*

Table 313: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group – All Subjects ≥71 Years of Age – Temperature*

14.4 Summary of Concomitant Medications

Table 314: Number and Percentage of Subjects with Prior and Concurrent Medications by WHO Drug Classification and Treatment Group – All Subjects 18-55 Years Old*

		25 µg mRNA-1273 (N=X)		50 µg mRNA -1273 (N=X)		100 µg mRNA -1273 (N=X)		250 µg mRNA -1273 (N=X)		All Subjects (N=X)	
WHO Drug Code Level 1, Anatomic Group	WHO Drug Code Level 2, Therapeutic Group	n	%	n	%	n	%	n	%	n	%
Any Level 1 Codes	Any Level 2 Codes										
Alimentary Tract And Metabolism	Any Level 2 Codes										
	Antidiarrheals, Intestinal Antiinflammatory /Antiinfective Agents										
	Antiemetics And Antinauseants										
	Digestives, Incl. Enzymes										
	Drugs For Acid Related Disorders										
	Drugs For Constipation										
	Drugs Used In Diabetes										
	Mineral Supplements										
	Other Alimentary Tract And Metabolism Products										
	Stomatological Preparations										
	Vitamins										
	Any Level 2 Codes										

		25 µg mRNA-1273 (N=X)		50 µg mRNA -1273 (N=X)		100 µg mRNA -1273 (N=X)		250 µg mRNA -1273 (N=X)		All Subjects (N=X)	
WHO Drug Code Level 1, Anatomic Group	**WHO Drug Code Level 2, Therapeutic Group**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Antiinfectives For Systemic Use	**Antibacterials For Systemic Use**										
	Antimycotics For Systemic Use										
	Antivirals For Systemic Use										
	Vaccines										
Antineoplastic And Immunomodulating Agents	**Any Level 2 Codes**										
	Antineoplastic Agents										
	Endocrine Therapy										
Blood And Blood Forming Organs	**Any Level 2 Codes**										
	Antianemic Preparations										
	Antithrombotic Agents										
Cardiovascular System	**Any Level 2 Codes**										
	Agents Acting On The Renin-Angiotensin System										
	Beta Blocking Agents										
	Calcium Channel Blockers										
	Cardiac Therapy										
	Diuretics										
	Lipid Modifying Agents										
	Vasoprotectives										

		25 µg mRNA-1273 (N=X)		50 µg mRNA -1273 (N=X)		100 µg mRNA -1273 (N=X)		250 µg mRNA -1273 (N=X)		All Subjects (N=X)	
WHO Drug Code Level 1, Anatomic Group	**WHO Drug Code Level 2, Therapeutic Group**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Dermatologicals	**Any Level 2 Codes**										
	Anti-Acne Preparations										
	Antibiotics And Chemotherapeutics For Dermatological Use										
	Antifungals For Dermatological Use										
	Antipruritics, Incl. Antihistamines, Anesthetics, Etc.										
	Antiseptics And Disinfectants										
	Corticosteroids, Dermatological Preparations										
	Emollients And Protectives										
	Other Dermatological Preparations										
	Preparations For Treatment Of Wounds And Ulcers										
Genito Urinary System And Sex Hormones	**Any Level 2 Codes**										
	Gynecological Antiinfectives And Antiseptics										
	Other Gynecologicals										

		25 µg mRNA-1273 (N=X)		50 µg mRNA -1273 (N=X)		100 µg mRNA -1273 (N=X)		250 µg mRNA -1273 (N=X)		All Subjects (N=X)	
WHO Drug Code Level 1, Anatomic Group	**WHO Drug Code Level 2, Therapeutic Group**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
	Sex Hormones And Modulators Of The Genital System										
	Urologicals										
Musculo-Skeletal System	**Any Level 2 Codes**										
	Antiinflammatory And Antirheumatic Products										
	Drugs For Treatment Of Bone Diseases										
	Muscle Relaxants										
	Other Drugs For Disorders Of The Musculo-Skeletal System										
Nervous System	**Any Level 2 Codes**										
	Analgesics										
	Anesthetics										
	Other Nervous System Drugs										
	Psychoanaleptics										
	Psycholeptics										
Respiratory System	**Any Level 2 Codes**										
	Antihistamines For Systemic Use										
	Cough And Cold Preparations										

		25 µg mRNA-1273 (N=X)		50 µg mRNA -1273 (N=X)		100 µg mRNA -1273 (N=X)		250 µg mRNA -1273 (N=X)		All Subjects (N=X)	
WHO Drug Code Level 1, Anatomic Group	**WHO Drug Code Level 2, Therapeutic Group**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
	Drugs For Obstructive Airway Diseases										
	Nasal Preparations										
Sensory Organs	**Any Level 2 Codes**										
	Ophthalmologicals										
Systemic Hormonal Preparations, Excl. Sex Hormones And Insulins	**Any Level 2 Codes**										
	Corticosteroids For Systemic Use										
	Thyroid Therapy										
Various	**Any Level 2 Codes**										
	General Nutrients										
	Unspecified Herbal And Traditional Medicine										
N=Number of subjects in the Safety Population].n=Number of subjects reporting taking at least one medication in the specific WHO Drug Class.											

Tables with Similar Format:

Table 315: Number and Percentage of Subjects with Prior and Concurrent Medications by WHO Drug Classification and Treatment Group – All Subjects 56-70 Years Old*

Table 316: Number and Percentage of Subjects with Prior and Concurrent Medications by WHO Drug Classification and Treatment Group – All Subjects ≥71 Years Old*

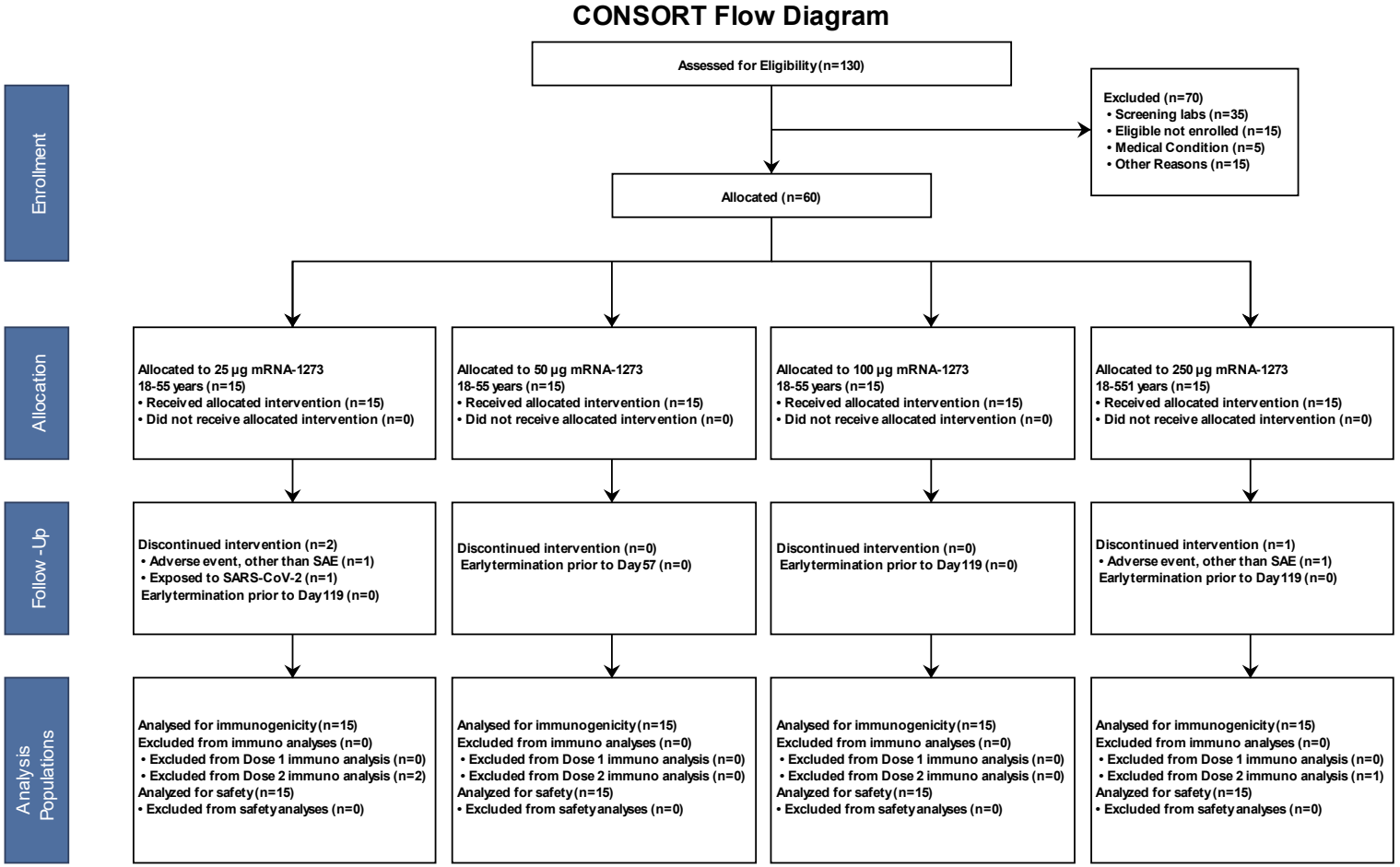
APPENDIX 2. FIGURE MOCK-UPS

Figures marked with an * will be included in the iCSR.

LIST OF FIGURES

10.1 Disposition of Subjects

Figure 1: CONSORT Flow Diagram – 18-55 Years Old*



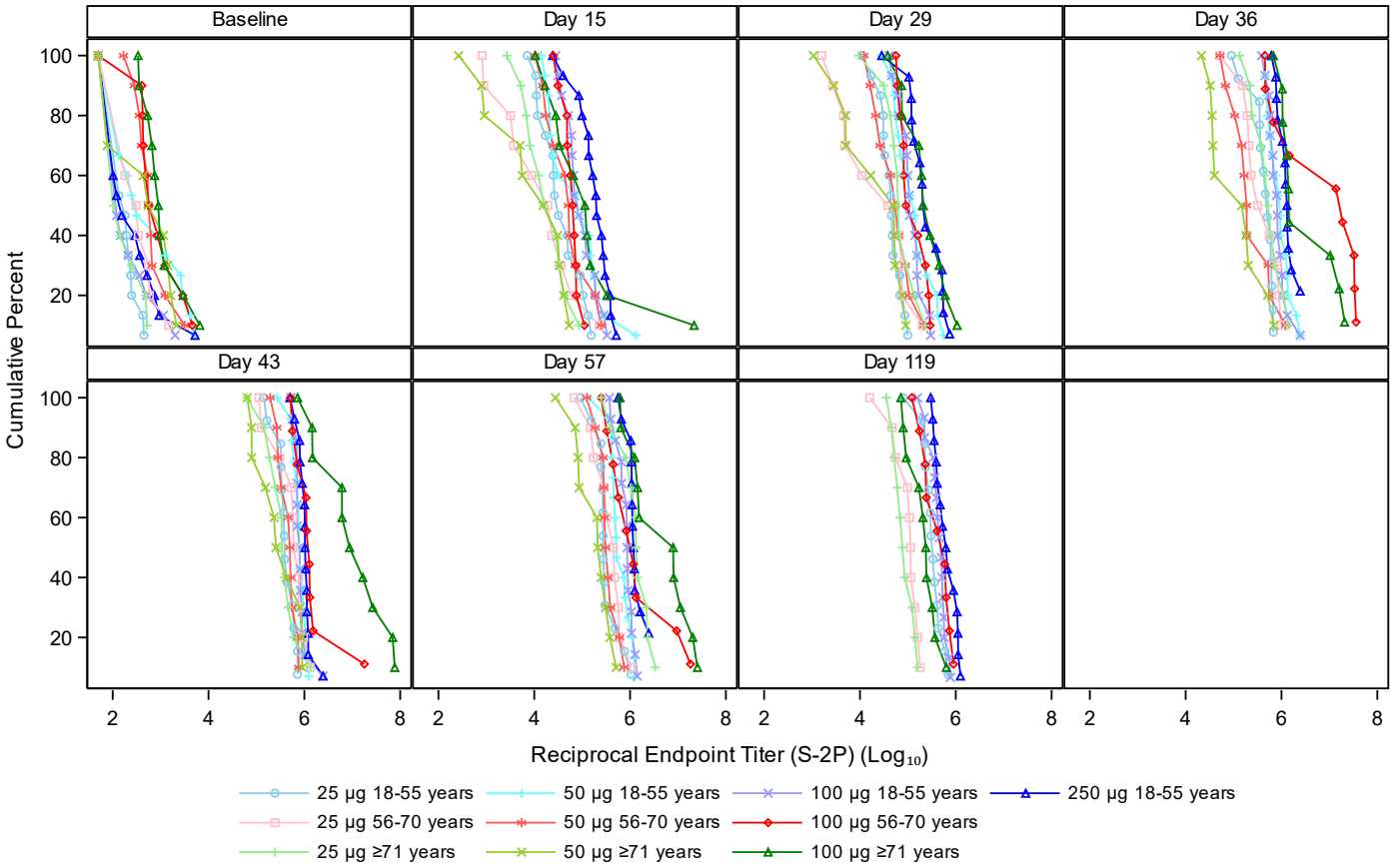
Figures with Similar Format:

Figure 2: CONSORT Flow Diagram – 56-70 Years Old*

Figure 3: CONSORT Flow Diagram – ≥71 Years Old*

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

Figure 4: Reverse Cumulative Distribution of Serum IgG ELISA Endpoint Titer Values by Time Point and Treatment Group - S-2P, mITT Population



Figures with Similar Format:

Figure 5: Reverse Cumulative Distribution of Serum IgG ELISA Endpoint Titer Values by Time Point and Treatment Group - S-2P, Per Protocol Population*

Figure 6: Reverse Cumulative Distribution of Serum IgG ELISA Endpoint Titer Values by Time Point and Treatment Group – RBD, mITT Population

Figure 7: Reverse Cumulative Distribution of Serum IgG ELISA Endpoint Titer Values by Time Point and Treatment Group – RBD, Per Protocol Population*

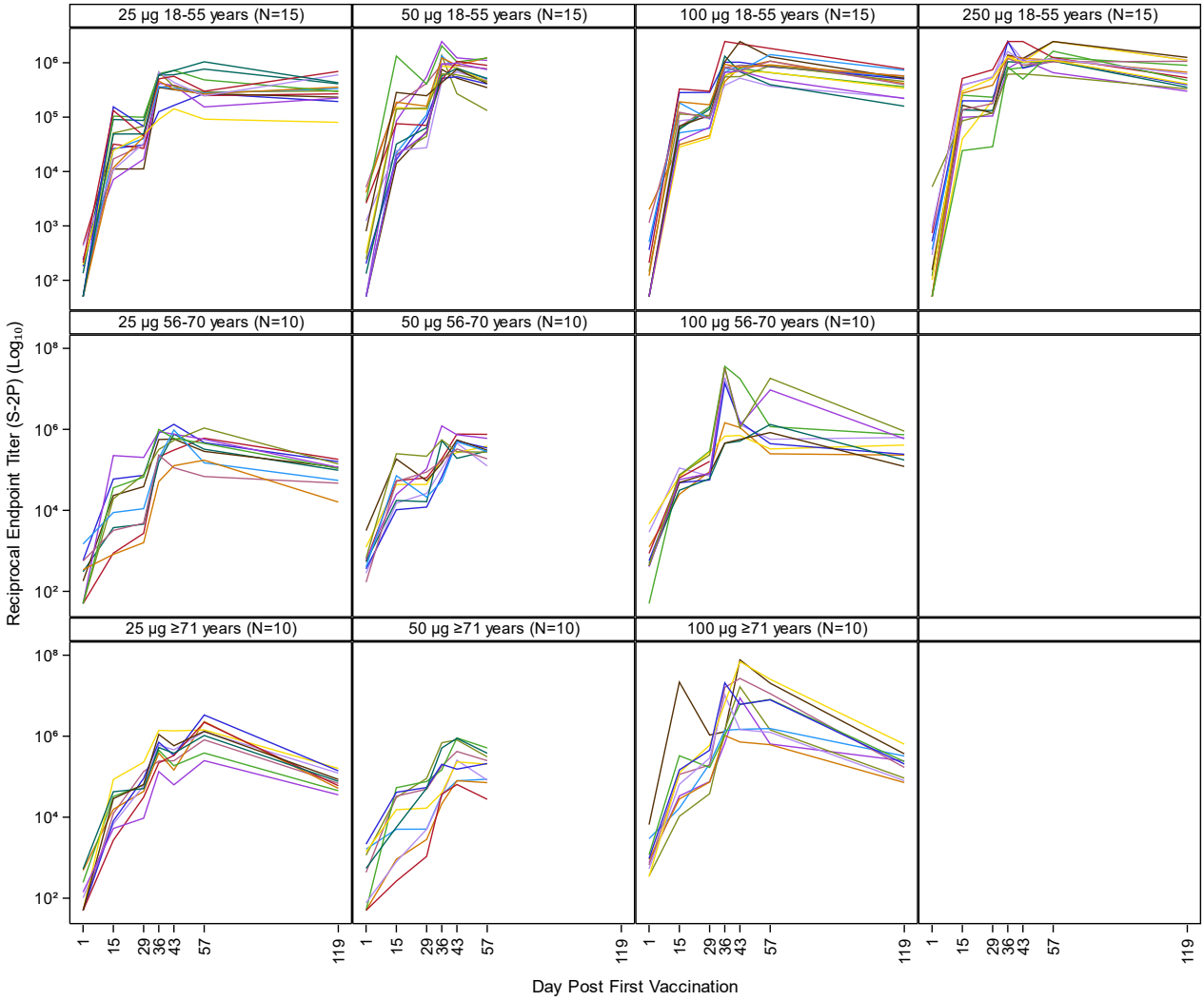
Figure 8: Reverse Cumulative Distribution of Serum IgG ELISA Area Under the Curve (AUC) Values by Time Point and Treatment Group - S-2P, mITT Population

Figure 9: Reverse Cumulative Distribution of Serum IgG ELISA Area Under the Curve (AUC) Values by Time Point and Treatment Group - S-2P, Per Protocol Population

Figure 10: Reverse Cumulative Distribution of Serum IgG ELISA Area Under the Curve (AUC) Values by Time Point and Treatment Group – RBD, mITT Population

Figure 11: Reverse Cumulative Distribution of Serum IgG ELISA Area Under the Curve (AUC) Values by Time Point and Treatment Group – RBD, Per Protocol Population

Figure 12: Serum IgG ELISA Endpoint Titer Values by Time Point and Treatment Group - S-2P, mITT Population



Figures with Similar Format:

Figure 13: Serum IgG ELISA Endpoint Titer Values by Time Point and Treatment Group - S-2P, Per Protocol Population*

Figure 14: Serum IgG ELISA Endpoint Titer Values by Time Point and Treatment Group – RBD, mITT Population

Figure 15: Serum IgG ELISA Endpoint Titer Values by Time Point and Treatment Group – RBD, Per Protocol Population*

Figure 16: Serum IgG ELISA Area Under the Curve (AUC) Values by Time Point and Treatment Group - S-2P, mITT Population

Figure 17: Serum IgG ELISA Area Under the Curve (AUC) Values by Time Point and Treatment Group - S-2P, Per Protocol Population

Figure 18: Serum IgG ELISA Area Under the Curve (AUC) Values by Time Point and Treatment Group – RBD, mITT Population

Figure 19: Serum IgG ELISA Area Under the Curve (AUC) Values by Time Point and Treatment Group – RBD, Per Protocol Population

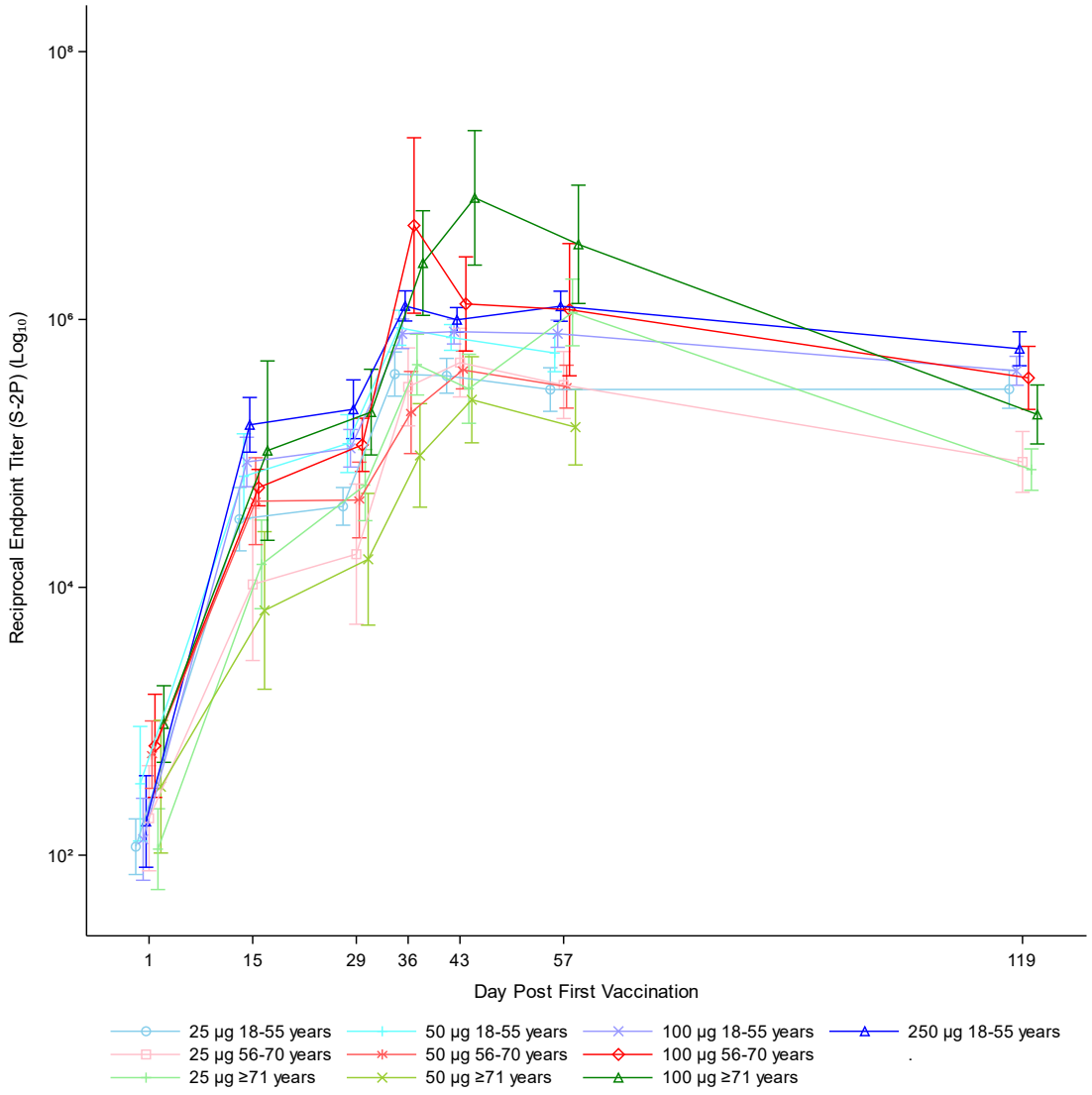
Figure 20: Pseudovirus Neutralization Assay Titers by Time Point and Treatment Group - ID_{50}, mITT Population

Figure 21: Pseudovirus Neutralization Assay Titers by Time Point and Treatment Group - ID_{50}, Per Protocol Population*

Figure 22: Pseudovirus Neutralization Assay Titers by Time Point and Treatment Group – ID_{80}, mITT Population

Figure 23: Pseudovirus Neutralization Assay Titers by Time Point and Treatment Group – ID_{80}, Per Protocol Population*

Figure 24: Geometric Mean Endpoint Titer Values by Time Point and Treatment Group - S-2P, mITT Population



Figures with Similar Format:

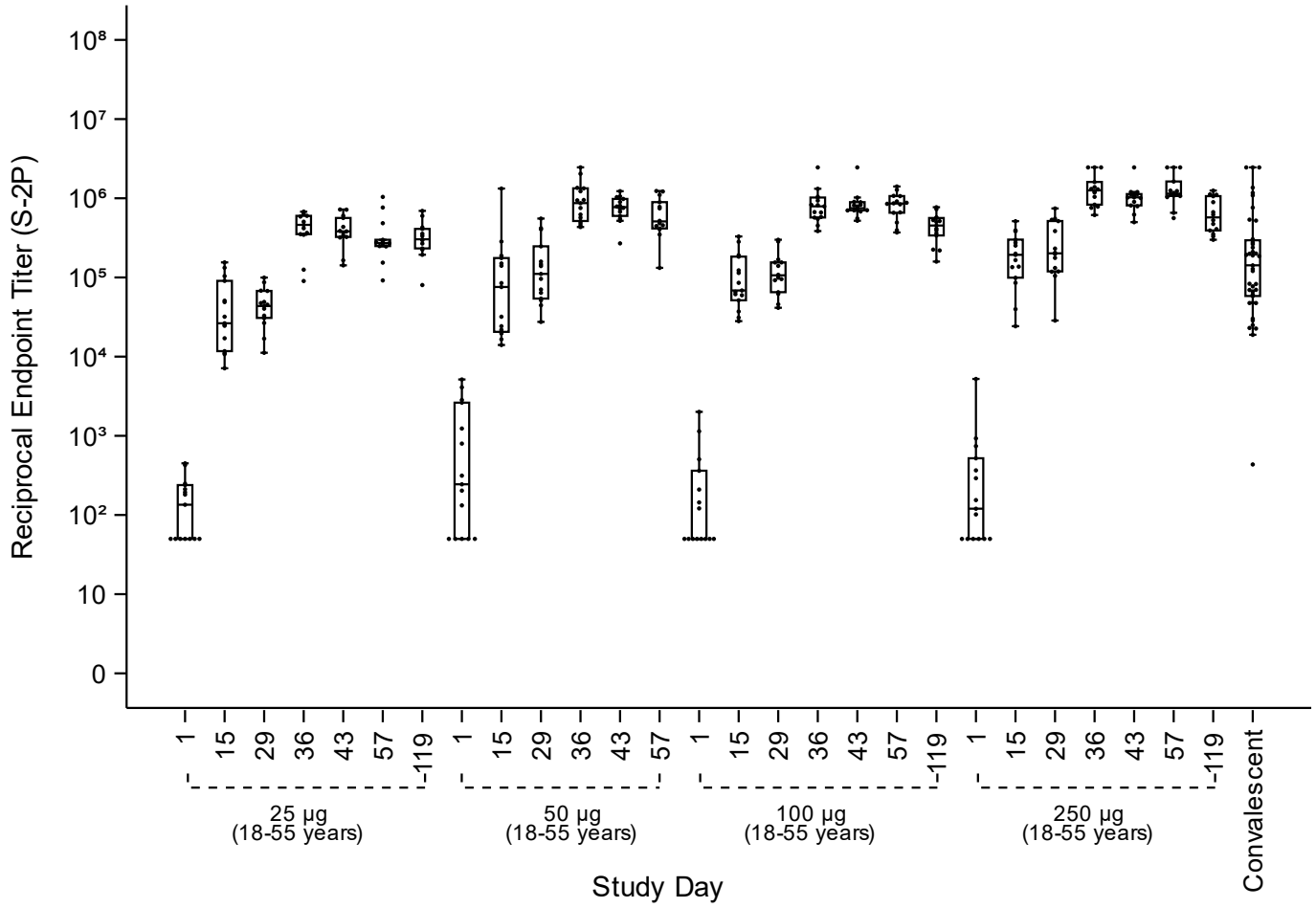
Figure 25: Geometric Mean Endpoint Titer Values by Time Point and Treatment Group - S-2P, Per Protocol Population*

Figure 26: Geometric Mean Endpoint Titer Values by Time Point and Treatment Group – RBD, mITT Population

Figure 27: Geometric Mean Endpoint Titer Values by Time Point and Treatment Group – RBD, Per Protocol Population*

Figure 28: Geometric Mean Area Under the Curve (AUC) Values by Time Point and Treatment Group - S-2P, mITT Population

Figure 48: Serum IgG ELISA Endpoint Titer Distribution by Time Point and Treatment Group - S-2P – Age 18-55, mITT Population



Figures with Similar Format:

Figure 49: Serum IgG ELISA Endpoint Titer Distribution by Time Point and Treatment Group - S-2P – Age 18-55, Per Protocol Population*

Figure 50: Serum IgG ELISA Endpoint Titer Distribution by Time Point and Treatment Group - S-2P – Age 56-70, mITT Population

Figure 51: Serum IgG ELISA Endpoint Titer Distribution by Time Point and Treatment Group - S-2P – Age 56-70, Per Protocol Population*

Figure 52: Serum IgG ELISA Endpoint Titer Distribution by Time Point and Treatment Group - S-2P – Age ≥71, mITT Population

Figure 53: Serum IgG ELISA Endpoint Titer Distribution by Time Point and Treatment Group - S-2P – Age ≥71, Per Protocol Population*

Figure 54: Serum IgG ELISA Endpoint Titer Distribution by Time Point and Treatment Group - RBD – Age 18-55, mITT Population

Figure 104: Binding to SARS-CoV-2 Spike Proteins in ELISA Expressed as Area-Under-the-Curve (AUC) is Highly Correlated with Binding Expressed as Endpoint Dilution Titer, mITT Population

A, vaccinee sera binding to S-2P expressed as endpoint vs AUC. **B**, vaccinee sera binding to RBD expressed as endpoint vs AUC. **C**, convalescent sera binding to S-2P expressed as endpoint vs AUC. **D**, convalescent sera binding to RBD expressed as endpoint vs AUC.

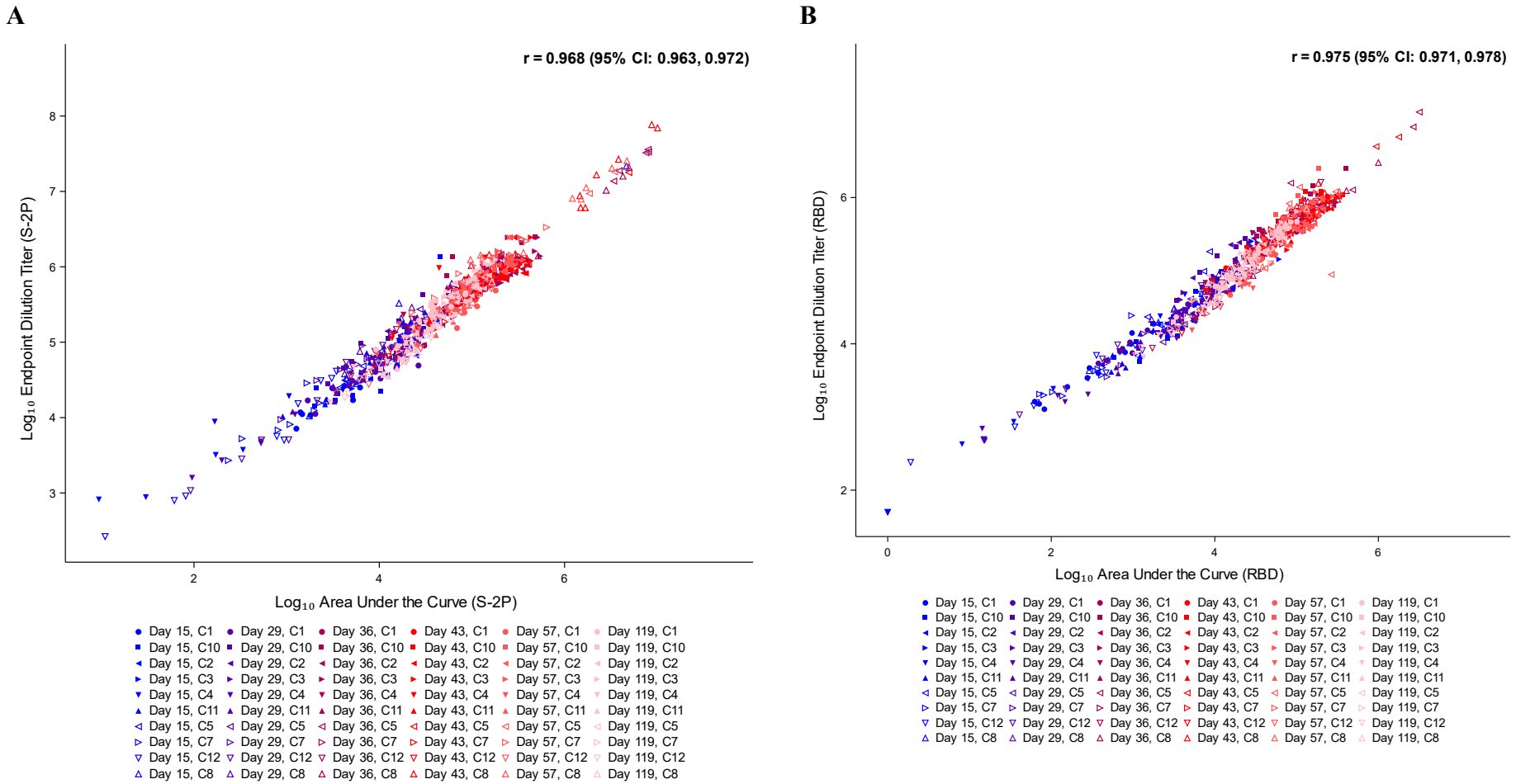
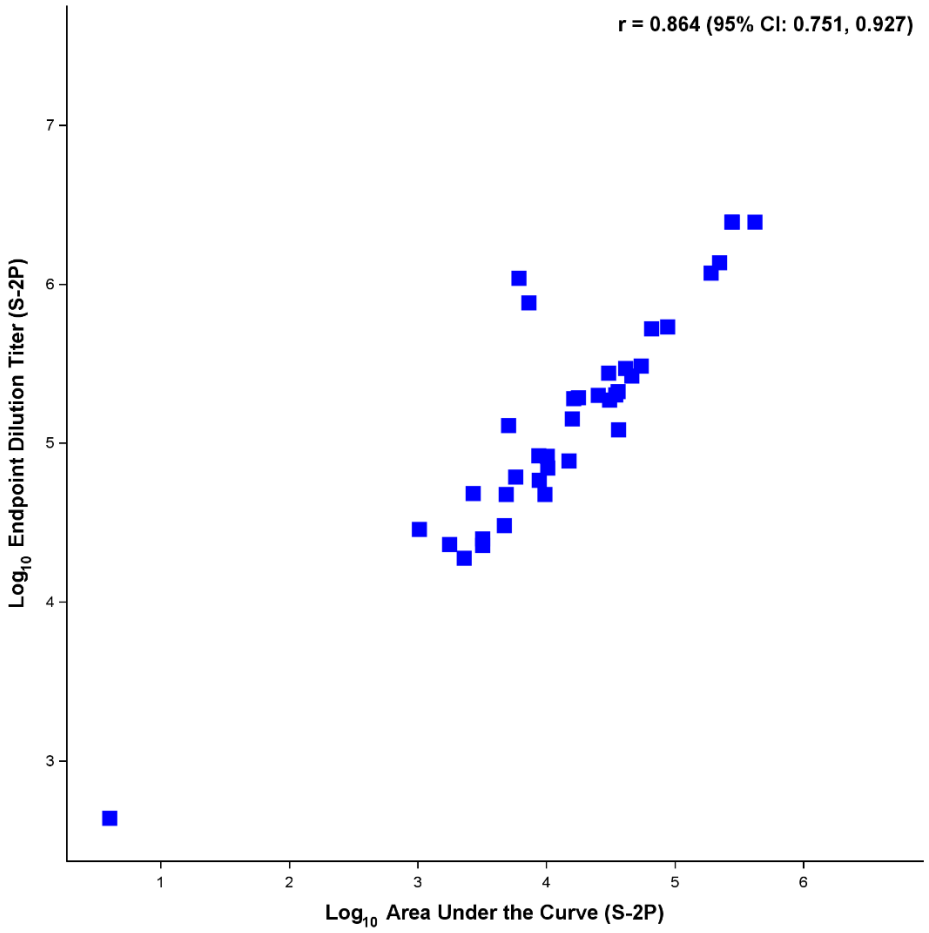
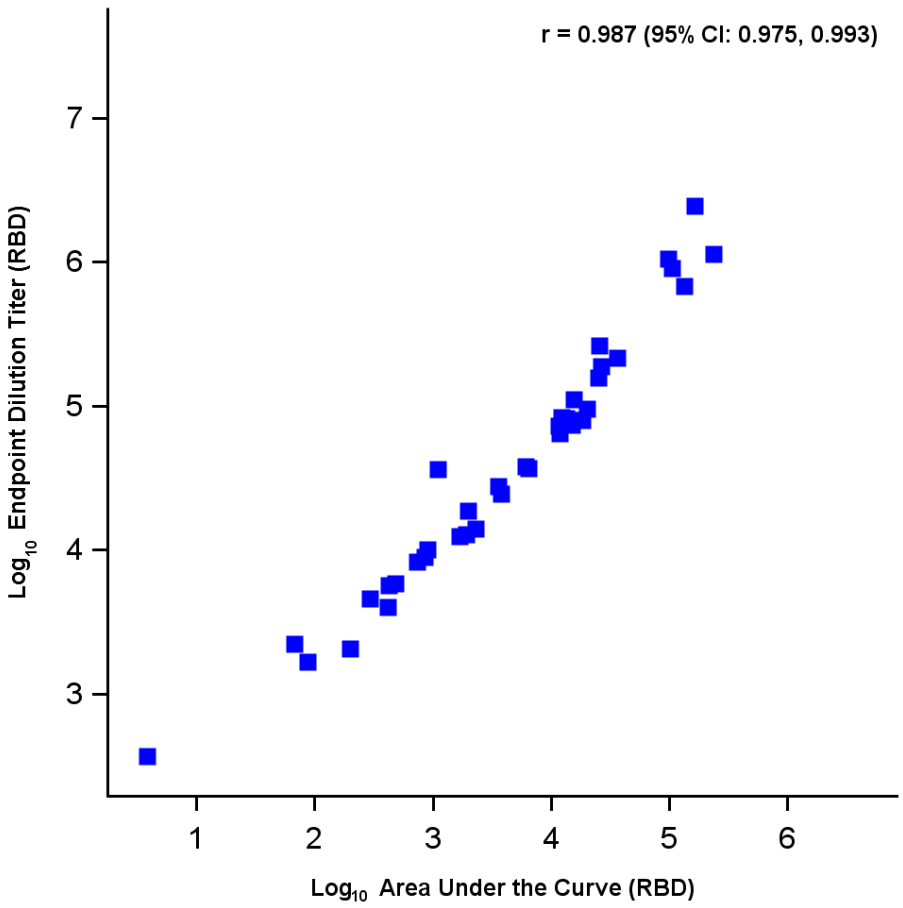


Figure 104 (continued)

C



D



Figures with Similar Format:

Figure 105: Binding to SARS-CoV-2 Spike Proteins in ELISA Expressed as Area-Under-the-Curve (AUC) is Highly Correlated with Binding Expressed as Endpoint Dilution Titer, Per Protocol Population*

A, vaccinee sera binding to S-2P expressed as endpoint vs AUC. **B**, vaccinee sera binding to RBD expressed as endpoint vs AUC.
C, convalescent sera binding to S-2P expressed as endpoint vs AUC. **D**, convalescent sera binding to RBD expressed as endpoint vs AUC.

Figure 106: Binding to S-2P or RBD Proteins are Highly Correlated, mITT Population

A, vaccinee sera binding to S-2P vs. RBD, expressed as area under the curve (AUC). **B**, vaccinee sera binding to S-2P vs. RBD, expressed as endpoint dilution titer.
C, convalescent sera binding to S-2P vs. RBD, expressed as AUC. **D**, convalescent sera binding to S-2P vs. RBD, expressed as endpoint dilution titer.

Figure 107: Binding to S-2P or RBD Proteins are Highly Correlated, Per Protocol Population*

A, vaccinee sera binding to S-2P vs. RBD, expressed as area under the curve (AUC). **B**, vaccinee sera binding to S-2P vs. RBD, expressed as endpoint dilution titer.
C, convalescent sera binding to S-2P vs. RBD, expressed as AUC. **D**, convalescent sera binding to S-2P vs. RBD, expressed as endpoint dilution titer.

Figure 108: Pseudovirus Neutralization Correlates with Binding in ELISA, mITT Population

A, PsVNA vaccinee sera ID_{50} vs. AUC S2P. **B**, PsVNA vaccinee sera ID_{80} vs. AUC S2P. **C**, PsVNA convalescent sera ID_{50} vs. AUC S2P. **D**, PsVNAconvalescent sera ID_{80} vs. AUC S2P

Figure 109: Pseudovirus Neutralization Correlates with Binding in ELISA, Per Protocol Population*

A, PsVNA vaccinee sera ID_{50} vs. AUC S2P. **B**, PsVNA vaccinee sera ID_{80} vs. AUC S2P. **C**, PsVNA convalescent sera ID_{50} vs. AUC S2P. **D**, PsVNAconvalescent sera ID_{80} vs. AUC S2P

Figure 110: Live-Virus Neutralization ($PRNT_{80}$) Correlates with Binding in ELISA, mITT Population

A, $PRNT_{80}$ vs. S-2P binding (AUC) . **B**, $PRNT_{80}$ vs. RBD binding (AUC).

Figure 111: Live-Virus Neutralization ($PRNT_{80}$) Correlates with Binding in ELISA, Per Protocol Population*

A, $PRNT_{80}$ vs. S-2P binding (AUC) . **B**, $PRNT_{80}$ vs. RBD binding (AUC).

Figure 112: FRNT-mNG Correlates with Binding in ELISA, mITT Population

A,.FRNT50 vs. S-2P binding (AUC) ; **B**, FRNT50 vs. RBD binding (AUC).

Figure 113: FRNT-mNG Correlates with Binding in ELISA, Per Protocol Population*

A,.FRNT50 vs. S-2P binding (AUC) ; **B**, FRNT50 vs. RBD binding (AUC).

Figure 114: Correlation Heatmap, mITT Population

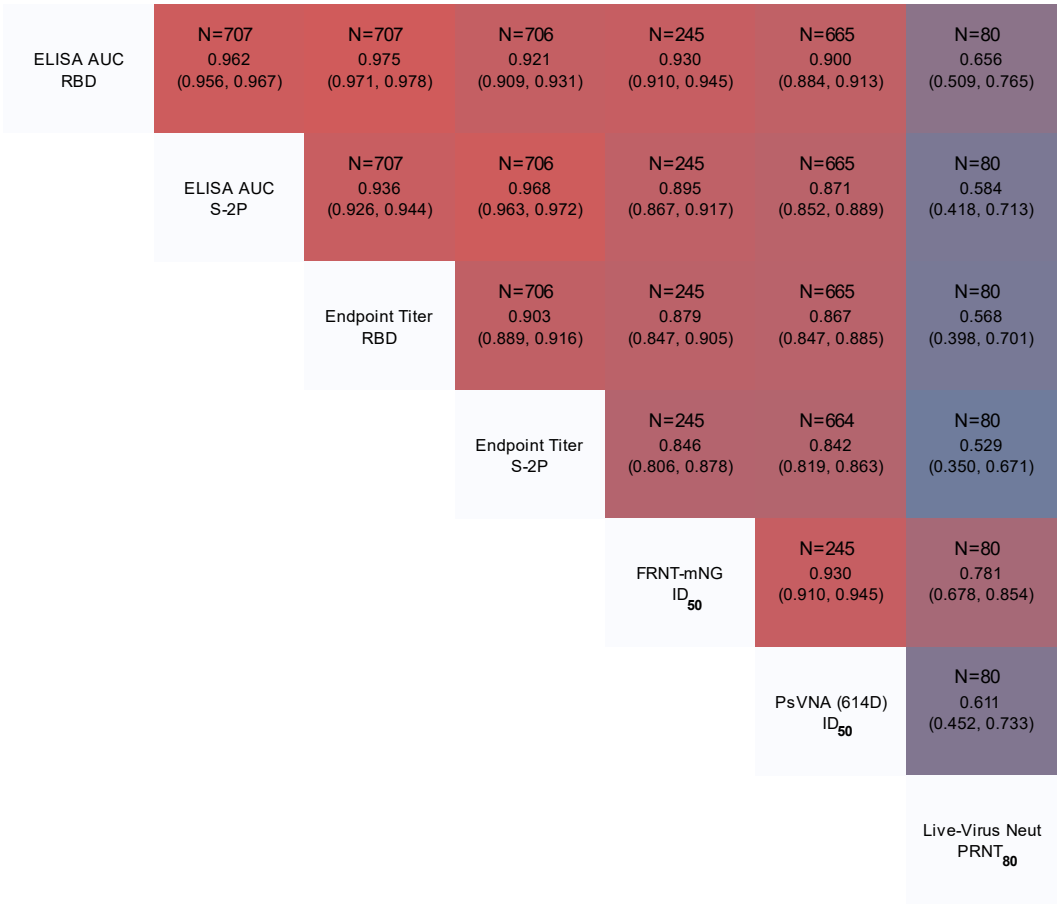
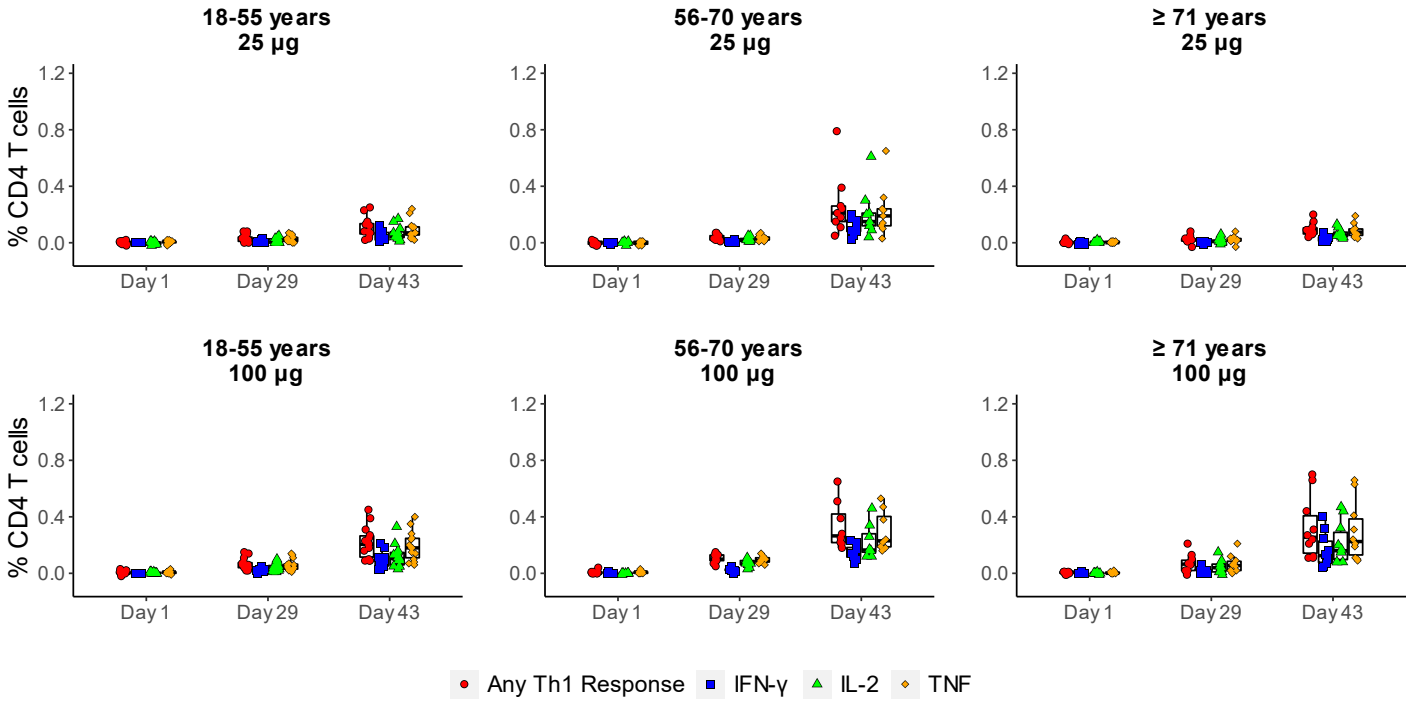


Figure with Similar Format:

Figure 115: Correlation Heatmap, Per Protocol Population*

Figure 116: Percentages of CD4 T Cells Expressing Th1 Cytokines S1 Peptide Pool*



Figures with Similar Format:

Figure 117: Percentages of CD4 T Cells Expressing Th2 Cytokines S1 Peptide Pool*

Figure 118: Percentages of CD4 T Cells Expressing Th1 Cytokines S2 Peptide Pool*

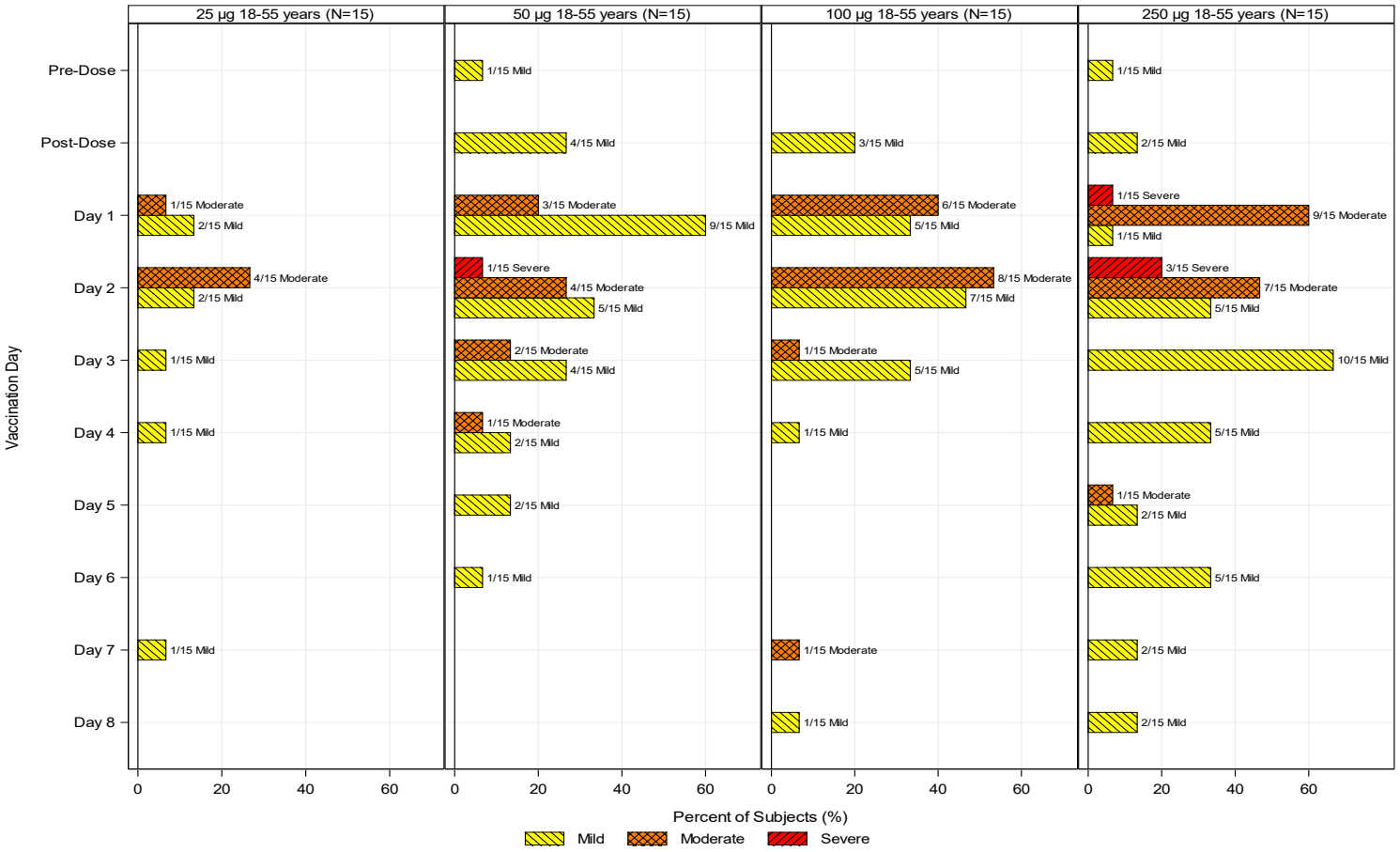
Figure 119: Percentages of CD4 T Cells Expressing Th2 Cytokines S2 Peptide Pool*

Figure 120: Percentages of CD8 T Cells Expressing Cytokines S1 Peptide Pool*

Figure 121: Percentages of CD8 T Cells Expressing Cytokines S2 Peptide Pool*

14.3.1.1 Solicited Adverse Events

Figure 122: Maximum Severity of Solicited Systemic Symptoms by Days Post Vaccination and Treatment Group - 18-55 Years of Age*

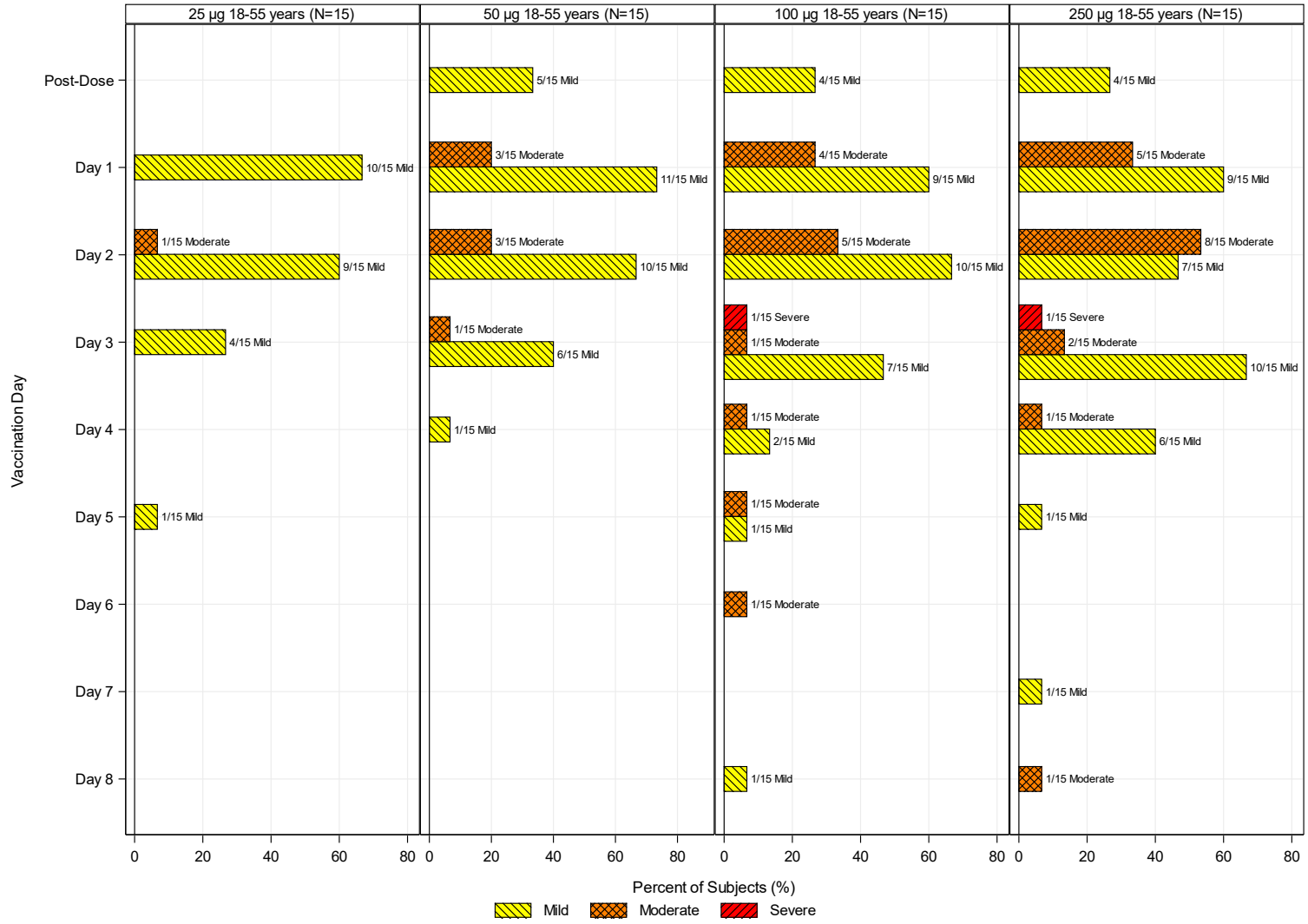


Figures with Similar Format:

Figure 123: Maximum Severity of Solicited Systemic Symptoms by Days Post Vaccination and Treatment Group – 56-70 Years of Age*

Figure 124: Maximum Severity of Solicited Systemic Symptoms by Days Post Vaccination and Treatment Group - ≥71 Years of Age*

Figure 125: Maximum Severity of Solicited Local Symptoms by Days Post Vaccination and Treatment Group 18-55 Years of Age*

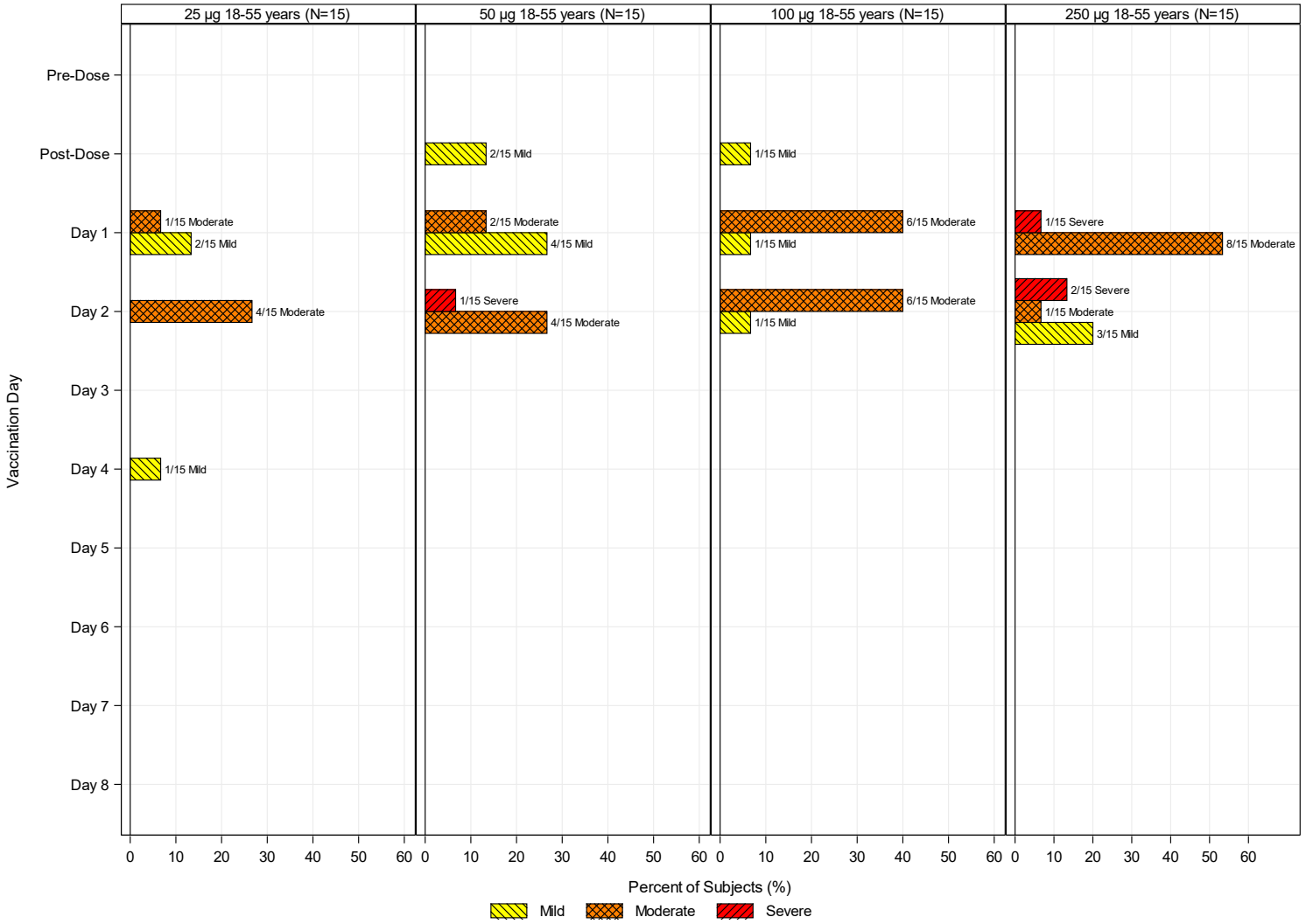


Figures with Similar Format:

Figure 126: Maximum Severity of Solicited Local Symptoms by Days Post Vaccination and Treatment Group 56-70 Years of Age*

Figure 127: Maximum Severity of Solicited Local Symptoms by Days Post Vaccination and Treatment Group ≥71 Years of Age*

Figure 128: Onset of Solicited Systemic Symptoms by Days Post Vaccination and Treatment Group 18-55 Years of Age Dose 1*



Figures with Similar Format:

Figure 129: Onset of Solicited Systemic Symptoms by Days Post Vaccination and Treatment Group 56-70 Years of Age – Dose 1*

Figure 130: Onset of Solicited Systemic Symptoms by Days Post Vaccination and Treatment Group ≥71 Years of Age – Dose 1*

Figure 131: Onset of Solicited Local Symptoms by Days Post Vaccination and Treatment Group 18-55 Years of Age -Dose 1*

Figure 132: Onset of Solicited Local Symptoms by Days Post Vaccination and Treatment Group 56-70 Years of Age – Dose 1*

Figure 133: Onset of Solicited Local Symptoms by Days Post Vaccination and Treatment Group ≥71 Years of Age – Dose 1*

Figure 134: Onset of Solicited Systemic Symptoms by Days Post Vaccination and Treatment Group 18-55 Years of Age Dose 2*

Figure 135: Onset of Solicited Systemic Symptoms by Days Post Vaccination and Treatment Group 56-70 Years of Age – Dose 2*

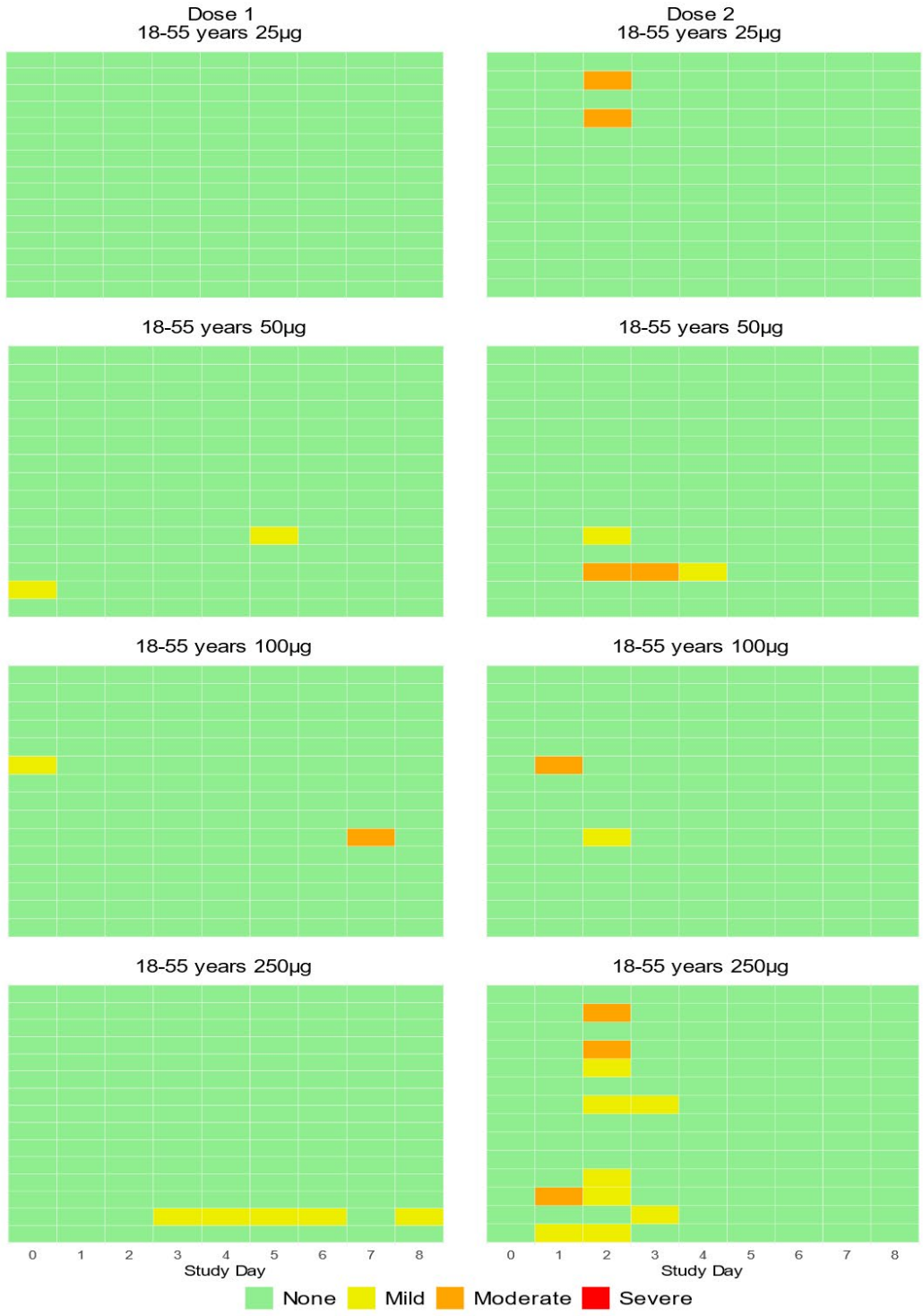
Figure 136: Onset of Solicited Systemic Symptoms by Days Post Vaccination and Treatment Group ≥71 Years of Age – Dose 2*

Figure 137: Onset of Solicited Local Symptoms by Days Post Vaccination and Treatment Group 18-55 Years of Age -Dose 2*

Figure 138: Onset of Solicited Local Symptoms by Days Post Vaccination and Treatment Group 56-70 Years of Age – Dose 2*

Figure 139: Onset of Solicited Local Symptoms by Days Post Vaccination and Treatment Group ≥71 Years of Age – Dose 2*

Figure 140: Solicited Symptoms by Days Post Vaccination and Treatment Group 18-55 Years of Age – Arthralgia*



Figures with Similar Format:

Figure 141: Solicited Symptoms by Days Post Vaccination and Treatment Group 56-70 Years of Age – Arthralgia*

Figure 142: Solicited Symptoms by Days Post Vaccination and Treatment Group ≥71 Years of Age – Arthralgia*

Figure 143: Solicited Symptoms by Days Post Vaccination and Treatment Group 18-55 Years of Age – Chills*

Figure 144: Solicited Symptoms by Days Post Vaccination and Treatment Group 56-70 Years of Age – Chills*

Figure 145: Solicited Symptoms by Days Post Vaccination and Treatment Group ≥71 Years of Age – Chills*

Figure 146: Solicited Symptoms by Days Post Vaccination and Treatment Group 18-55 Years of Age – Erythema*

Figure 147: Solicited Symptoms by Days Post Vaccination and Treatment Group 56-70 Years of Age – Erythema*

Figure 148: Solicited Symptoms by Days Post Vaccination and Treatment Group ≥71 Years of Age – Erythema*

Figure 149: Solicited Symptoms by Days Post Vaccination and Treatment Group 18-55 Years of Age – Erythema (mm)*

Figure 150: Solicited Symptoms by Days Post Vaccination and Treatment Group 56-70 Years of Age – Erythema (mm)*

Figure 151: Solicited Symptoms by Days Post Vaccination and Treatment Group ≥71 Years of Age – Erythema (mm)*

Figure 152: Solicited Symptoms by Days Post Vaccination and Treatment Group 18-55 Years of Age – Fatigue*

Figure 153: Solicited Symptoms by Days Post Vaccination and Treatment Group 56-70 Years of Age – Fatigue*

Figure 154: Solicited Symptoms by Days Post Vaccination and Treatment Group ≥71 Years of Age – Fatigue*

Figure 155: Solicited Symptoms by Days Post Vaccination and Treatment Group 18-55 Years of Age – Fever*

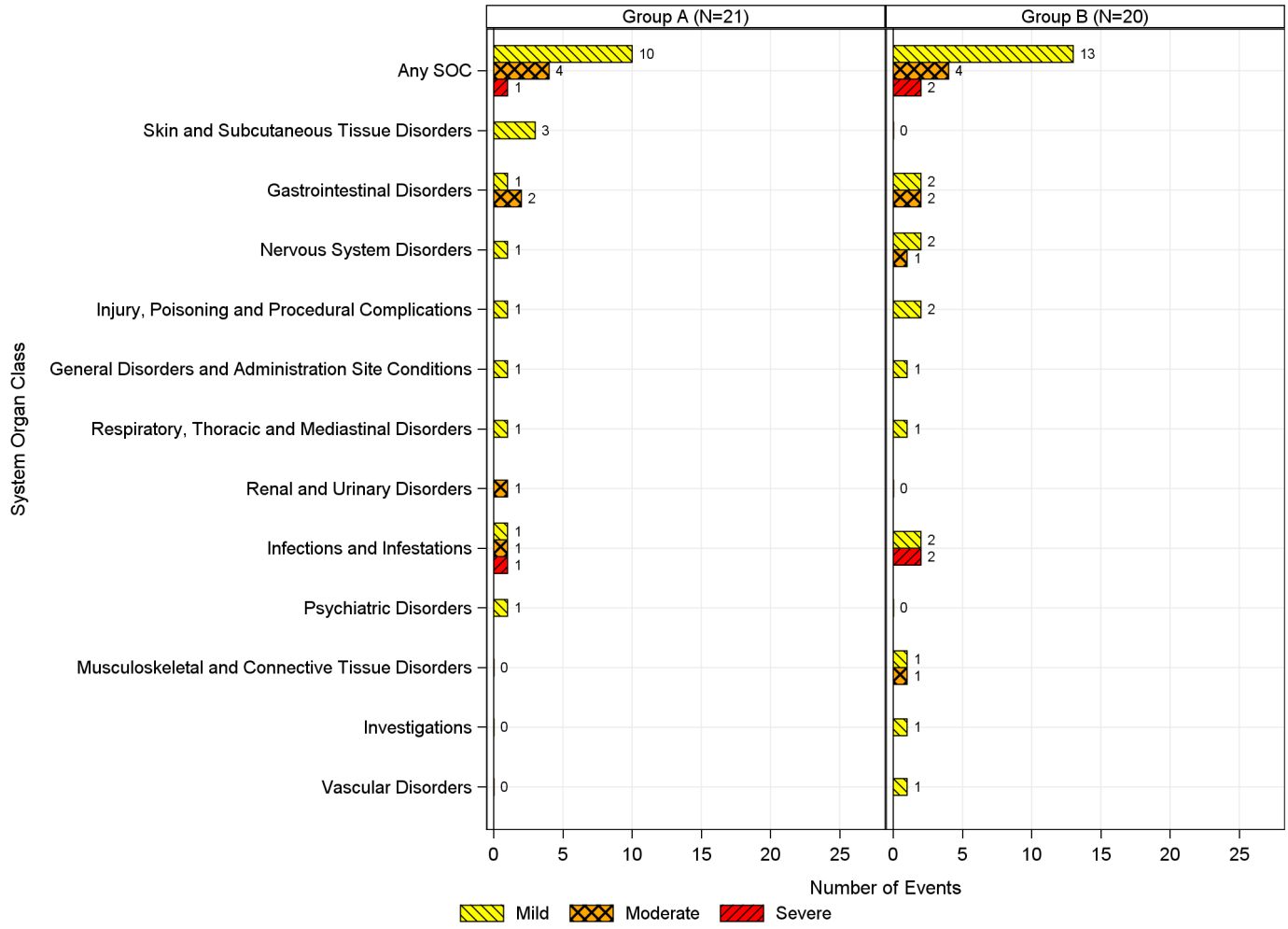
Figure 156: Solicited Symptoms by Days Post Vaccination and Treatment Group 56-70 Years of Age – Fever*

Figure 157: Solicited Symptoms by Days Post Vaccination and Treatment Group ≥71 Years of Age – Fever*

Figure 158: Solicited Symptoms by Days Post Vaccination and Treatment Group 18-55 Years of Age – Headache*

14.3.1.2 Unsolicited Adverse Events

Figure 176: Frequency of Adverse Events by MedDRA System Organ Class and Severity 18-55 Years of Age*

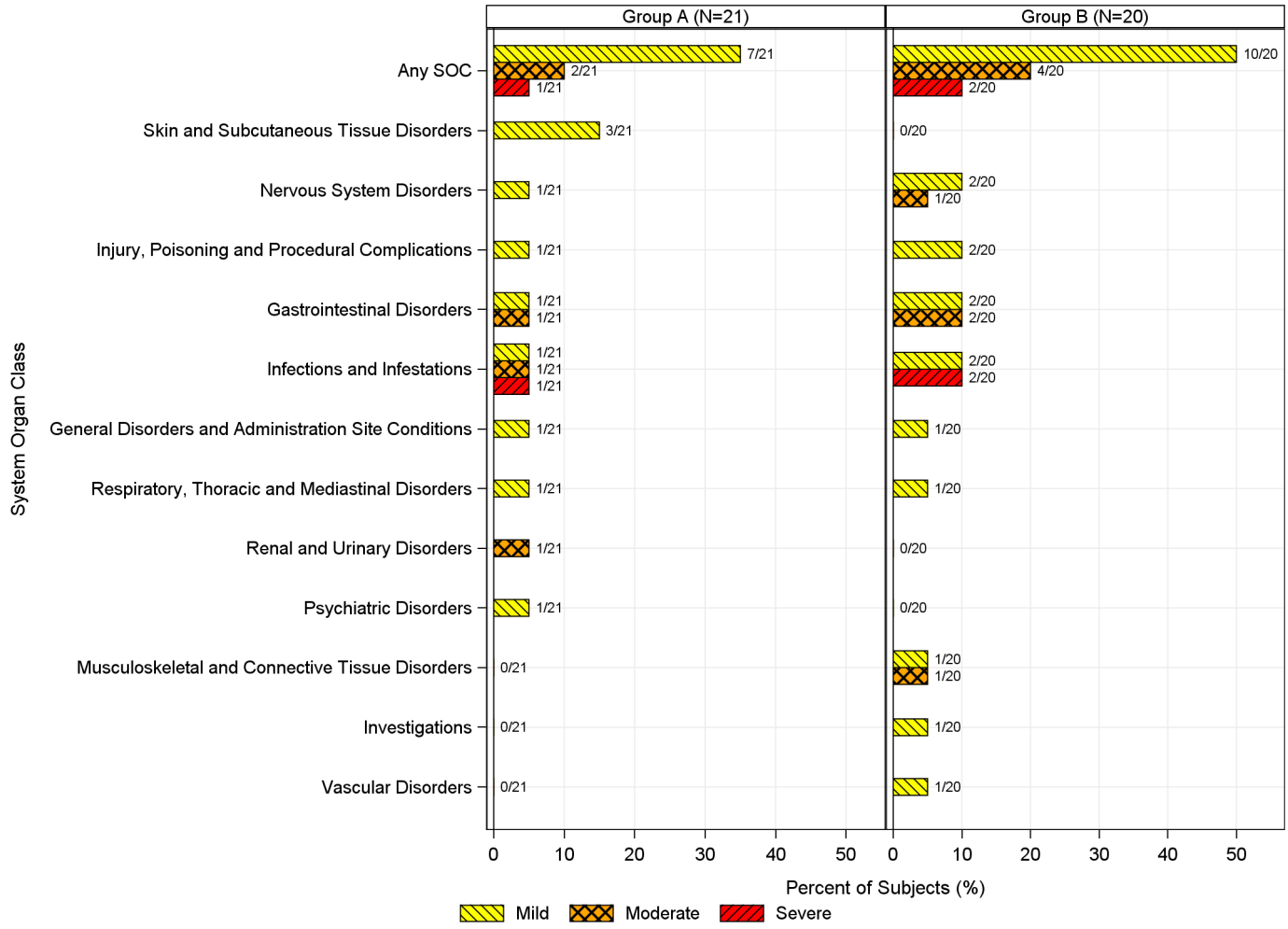


Figures with Similar Format:

Figure 177: Frequency of Adverse Events by MedDRA System Organ Class and Severity 56-70 Years of Age*

Figure 178: Frequency of Adverse Events by MedDRA System Organ Class and Severity ≥71 Years of Age*

Figure 179: Incidence of Adverse Events by MedDRA® System Organ Class and Maximum Severity 18-55 Years of Age*



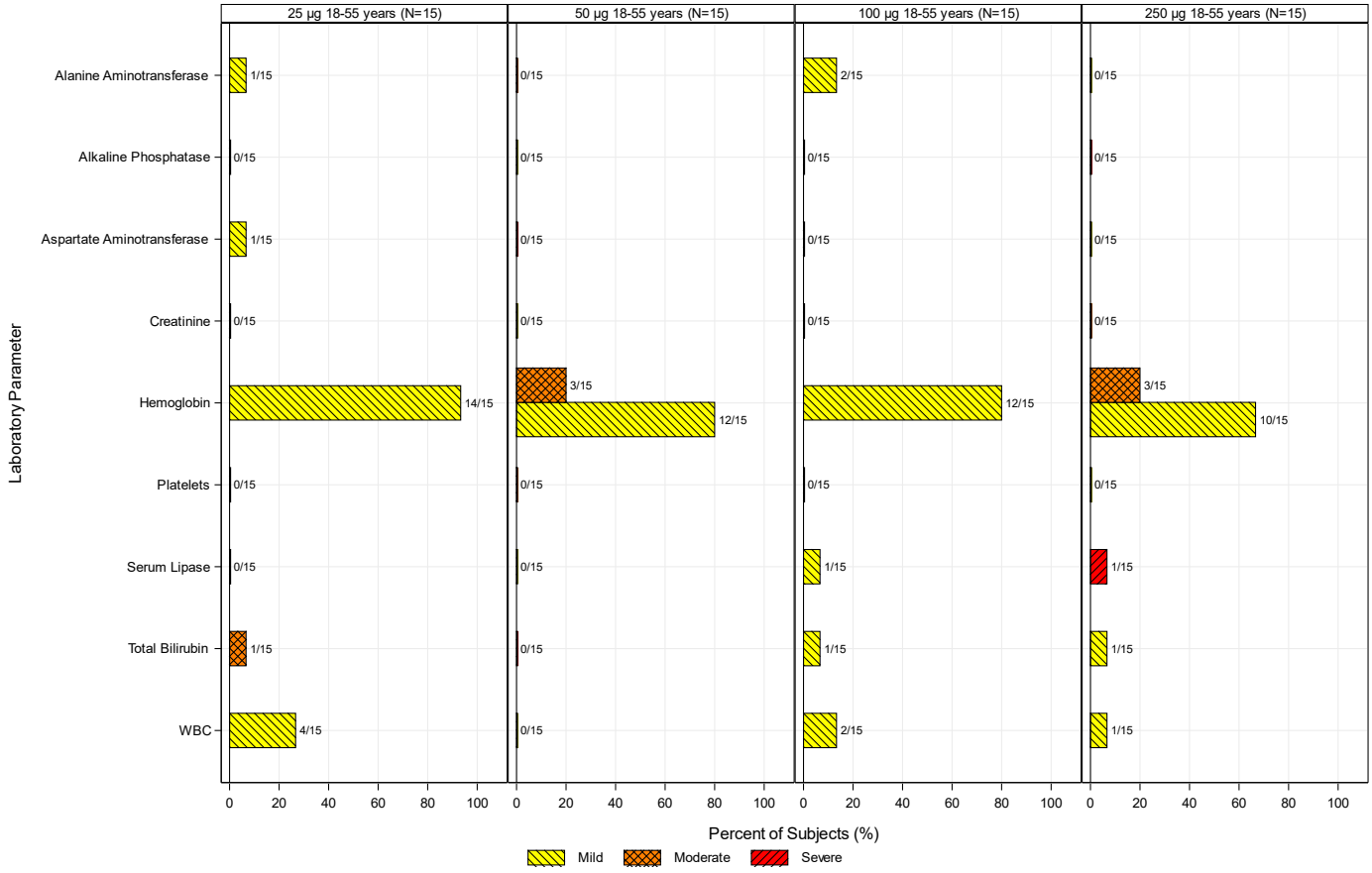
Figures with Similar Format:

Figure 180: Incidence of Adverse Events by MedDRA® System Organ Class and Maximum Severity 56-70 Years of Age*

Figure 181: Incidence of Adverse Events by MedDRA® System Organ Class and Maximum Severity ≥71 Years of Age*

14.3.5 Displays of Laboratory Results

Figure 182: Clinical Laboratory Results by Severity and Treatment Group 18-55 Years of Age*



Figures with Similar Format:

Figure 183: Clinical Laboratory Results by Severity and Treatment Group 56-70 Years of Age*

Figure 184: Clinical Laboratory Results by Severity and Treatment Group ≥71 Years of Age*

APPENDIX 3. LISTINGS MOCK-UPS

LISTINGS

Listing 1: **16.1.6: Listing of Subjects Receiving Investigational Product***

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

16.2 Database Listings by Subject

16.2.1 Discontinued Subjects

Listing 2: 16.2.1: Early Terminations or Discontinued Subjects*

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

16.2.2 Protocol Deviations

Listing 3: 16.2.2.1: Subject-Specific Protocol Deviations*

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

Listing 4: 16.2.2.2: Non-Subject-Specific Protocol Deviations*

Site	Deviation Number	Deviation	Deviation Severity	Reason for Deviation	Deviation Resulted in Subject Termination?	Deviation Affected Product Stability?	Deviation Category	Deviation Resolution	Comments

16.2.3 Subjects Excluded from the Efficacy Analysis

Listing 5: 16.2.3: Subjects Excluded from Analysis Populations*

Treatment Group	Subject ID	Analyses in which Subject is Included	Analyses from which Subject is Excluded	Results Available?	Reason Subject Excluded
		[e.g., Safety, ITT, PP]	[e.g., Safety, ITT, PP, Day x]		
Note: "Yes" in the "Results available" column indicates that available data were removed from the analysis. "No" indicates that no data were available for inclusion in the analysis.					

16.2.4 Demographic Data

Listing 6: 16.2.4.1: Demographic Data*

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

Listing 7: 16.2.4.2: Pre-Existing and Concurrent Medical Conditions*

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

16.2.5 Compliance and/or Drug Concentration Data (if available)

Not Applicable.

16.2.6 Individual Immunogenicity Response Data

Listing 8: 16.2.6: Individual Immunogenicity Response Data*

Treatment Group	Subject ID	Planned Time Point	Actual Study Day	Assay	Titer

Listing 9: 16.2.6: Individual T-cell Response Data*

Treatment Group	Subject ID	Planned Time Point	Actual Study Day	T-Cell	Stimulation	Cell Type	Percent

16.2.7 Adverse Events

Listing 10: 16.2.7.1: Solicited Events – Systemic Symptoms*

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

[a] MA = Data reported by subject on the Memory Aid and reviewed by clinic staff and reported in Solicited Events eCRF.

[b] Grade 3 events only.

Note: Clinic = Data collected by clinic staff during physical exam or symptom assessment (treatment administration record, in-clinic assessment, etc.)

Listing 11: 16.2.7.2: Solicited Events – Local Symptoms*

Treatment Group	Subject ID	Dose Number	Post Dose Day	Assessment[a]	Symptom	Severity
				MA		
				Clinic		

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

Listing 12: 16.2.7.3: Unsolicited Adverse Events*

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

16.2.8 Individual Laboratory Measurements

Listing 13: 16.2.8.1: Clinical Laboratory Results – Chemistry*

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

Listing 14: 16.2.8.2: Clinical Laboratory Results – Hematology*

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

16.2.9 Vital Signs and Physical Exam Findings

Listing 15: 16.2.9.1: Vital Signs*

Treatment Group	Subject ID	Planned Time Point	Actual Study Day	Temperature (°C)	Systolic Blood Pressure (mmHg)	Diastolic Blood Pressure (mmHg)	Heart Rate (beats/min)	Weight (kg)	Height (cm)

Listing 16: 16.2.9.2: Physical Exam Findings*

Treatment Group	Subject ID	Visit Number	Body System	Interpretation	If Abnormal, Findings	If Abnormal, Reported as an AE?

16.2.10 Concomitant Medications

Listing 17: 16.2.10: Concomitant Medications*

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

16.2.11 Pregnancy Reports

Listing 18: 16.2.11.1: Pregnancy Reports – Maternal Information*

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

Listing 19: 16.2.11.2: Pregnancy Reports – Gravida and Para*

			Live Births												
Subject ID	Pregnancy Number	Gravida	Extremely PB[a]	Very Early PB[a]	Early PB[a]	Late PB[a]	Early TB[b]	Full TB[b]	Late TB[b]	Post TB[b]	Still Births	Spontaneous Abortion/ Miscarriage	Elective Abortions	Therapeutic Abortions	Major Congenital Anomaly with Previous Pregnancy?
Note: Gravida includes the current pregnancy, para events do not.															

[a] Preterm Birth
[b] Term Birth

Listing 20: 16.2.11.3: Pregnancy Reports – Live Birth Outcomes*

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

Listing 21: 16.2.11.4: Pregnancy Reports – Still Birth Outcomes*

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

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

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

SIGNATURE PAGE

SPONSOR:	Division of Microbiology and Infectious Diseases National Institute of Allergy and Infectious Diseases National Institutes of Health
STUDY TITLE:	Phase I, Open-Label, Dose-Ranging Study of the Safety and Immunogenicity of 2019-nCoV Vaccine (mRNA-1273) in Healthy Adults
PROTOCOL NUMBER:	DMID 20-0003

Principal Investigator: (Lisa Jackson, MD, MPH)

Lisa Jackson I am approving this document. 01/25/2021 05:14 PM EST

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DMID Scientific Lead: (Chris Roberts, PhD)

Chris Roberts I am approving this document. 01/25/2021 07:12 PM EST

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