CLINICAL RESEARCH IN INFECTIOUS DISEASES

STATISTICAL ANALYSIS PLAN
FOR
DMID PROTOCOL: 21-0002 (COHORT 1)

STUDY TITLE:

PHASE I, OPEN-LABEL, RANDOMIZED STUDY OF THE SAFETY AND IMMUNOGENICITY OF A SARS-CoV-2 VARIANT VACCINE (mRNA-1273.351) IN NAÏVE AND PREVIOUSLY VACCINATED ADULTS

NCT04785144

VERSION 2.0

DATE: 23 MAY 2023

THIS COMMUNICATION IS PRIVILEGED AND CONFIDENTIAL

STUDY TITLE

Protocol Number Code:	**DMID Protocol: 21-0002 Cohort 1**
Development Phase:	Phase 1
Products:	mRNA-1273/mRNA-1273.351
Form/Route:	Injection
Indication Studied:	COVID-19
Sponsor:	Division of Microbiology and Infectious Diseases National Institute of Allergy and Infectious Diseases National Institutes of Health
Clinical Trial Initiation Date:	30MAR2021
Clinical Trial Completion Date:	Ongoing
Date of the Analysis Plan:	23 May 2023
Version Number:	2.0

This study was performed in compliance with Good Clinical Practice.

TABLE OF CONTENTS

TABLE OF CONTENTS

Table of Contents *(continued)*

Table of Contents *(continued)*

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
ECLIA	Electro-chemiluminescence
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 1, Open-Label, Randomized Study of the Safety and Immunogenicity of a SARS-CoV-2 Variant Vaccine (mRNA-1273.351) in Naïve and Previously Vaccinated Adults" (DMID Protocol 21-0002) describes and expands upon the statistical information presented in the protocol for cohort 1 only. A separate SAP will be written for cohort 2. 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, figures and listings. 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

An outbreak of COVID-19 caused by a novel SARS-CoV-2 began in Wuhan, Hubei Province, China in December 2019, and the disease has since spread globally [10]. The World Health Organization (WHO) declared COVID-19 a pandemic on 11 Mar 2020; however, widespread community transmission was already occurring in many locations. As of 14 Jan 2021, more than 92 million cases and 1.9 million deaths worldwide have been attributed to the COVID-19 pandemic [2,10].

ModernaTX, Inc has developed a vaccine platform based on the principle and observations that cells *in vivo* can take up mRNA, translate it, and then express protein viral antigen(s) on the cell surface. mRNA is highly precise in its translation into proteins that match viral antigens. The delivered mRNA does not enter the cell nucleus or interact with the genome, is nonreplicating, and is expressed transiently. The estimated half-life for mRNA after injection is approximately 8 to 10 hours, before degradation by native RNases in the body, but the duration of effect also depends on the half-life of the expressed protein, which persists in the body for several days. mRNA vaccines have been used to induce immune responses against infectious viral pathogens such as cytomegalovirus, human metapneumovirus, parainfluenza virus type 3, Zika, and influenza.

The mRNA-1273 encodes for the full-length spike (S) protein of SARS-CoV-2, modified to introduce 2 proline residues to stabilize the S protein (S-2P) in a prefusion conformation, derived from the Wuhan-Hu-1 strain [5]. The mRNA-1273 vaccine is currently being evaluated for safety and immunogenicity in a dose-ranging Phase 1 study sponsored by DMID (NCT04283461), for safety and immunogenicity in a Moderna-sponsored Phase 2a study (NCT04405076), and for safety, efficacy, and immunogenicity in a Moderna-sponsored Phase 3 study (NCT04470427). All three of these studies are ongoing and conducted in the US.

The primary efficacy objective of the Phase 3 study was met, with the vaccine efficacy of mRNA-1273 to prevent symptomatic COVID-19 disease observed to be 94.1%. The vaccine was also observed to be efficacious in preventing severe COVID-19. In December 2020 the FDA issued Emergency Use Authorization of mRNA-1273 (Moderna COVID-19 Vaccine) for active immunization to prevent COVID-19 in individuals 18 years of age and older.

Recently, SARS-CoV-2 variants with mutations in the S protein have emerged. A variant first identified in South Africa (B.1.351) is associated with increased transmission, higher viral burden, and possibly increased mortality in infected persons [8]. To date, four vaccines, all based on the Wuhan-sequence of the S protein, have shown reduced activity against the B.1.351 variant. Sera from individuals vaccinated with mRNA-based vaccines had a 6-to-9-fold reduction in neutralizing activity against a B.1.351-matched pseudovirion relative to a Wuhan-matched pseudovirion [9,11]. More recently, pivotal studies testing both viral vector and adjuvanted protein technologies had lower efficacy in regions where B.1.351 was known to be circulating [2]. Hence, the development and testing of vaccines targeting this SARS-CoV-2 variant is urgently needed.

mRNA-1273.351, like mRNA-1273, encodes the prefusion stabilized S protein of SARS-CoV-2. However, the mRNA of mRNA-1273.351 incorporates the key mutations present in the B.1.351 strain of the virus. This phase 1 clinical trial will evaluate the immunological benefit of boosting subjects previously vaccinated with mRNA-1273 (DMID 20-0003) with the B.1.351

strain-specific S protein, as well as the breadth of response induced by vaccinating with mRNA-1273 and mRNA-1273.351 in naïve persons, who have not previously received a SARS-CoV-2 vaccine and are not known to have been previously infected with SARS-CoV-2.

2.1. Purpose of the Analyses

These analyses will assess the immunogenicity and safety of monovalent mRNA-1273.351 vaccine at a dose 50 µg and bivalent mRNA-1273/mRNA-1273.351 at a dose of 25 µg each (50 µg total) in subjects opting to terminate DMID 20-0003 early and enrolling in 21-0002 Cohort 1.

3. STUDY OBJECTIVES AND ENDPOINTS

3.1. Study Objectives and Endpoints

OBJECTIVES	ENDPOINTS (OUTCOME MEASURES)
Primary	
• To evaluate the safety and reactogenicity of mRNA-1273 and mRNA-1273.351 vaccines, in previously vaccinated individuals.	• 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, Protocol Specified AESIs, NOCMCs, and MAAEs from the first vaccination through 12 months after the last vaccination.
Secondary	
• To assess humoral immunogenicity of mRNA-1273 and mRNA-1273.351 vaccines, in previously vaccinated individuals.	• Response rate, and magnitude of SARS-CoV-2-specific antibody binding and neutralization titers in serum samples as assessed via a range of assays at all timepoints.
Exploratory	
• To assess, in at least a subset of samples the innate immune response and B cell response following vaccination.	• Magnitude, phenotype, and percentage of innate immune cells and SARS-CoV-2 specific B cells, as measured by flow cytometry, and targeted B cell repertoire analysis at different timepoints post vaccination relative to baseline.
• 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

For calculations using the baseline value, the value obtained pre-third vaccination (Day 1) will be used. For samples with an AUC of zero at baseline, fold-rise will be calculated by dividing post-vaccination result by the lowest reported value. AUC is calculated using the trapezoidal method applied to a serial dilution curve. 20-0003 Cohort will be used to refer to the 20-0003 cohort that the subjects were originally assigned.

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 1, open-label, randomized clinical trial in males and non-pregnant females, 18 years of age and older, who are in good health, have no known history of COVID-19 or SARS-CoV-2 infection, and meet all other eligibility criteria. This clinical trial is designed to assess the safety, reactogenicity and immunogenicity of mRNA-1273.351 manufactured by ModernaTX, Inc, given in vaccination schedules alone, sequentially, or coadministered with mRNA-1273. mRNA-1273.351 is a novel LNP-encapsulated mRNA-based vaccine that encodes for a full-length, prefusion stabilized S protein of the SARS-CoV-2 B.1.351 variant. Enrollment will occur at approximately five domestic clinical research sites.

This study includes two cohorts. Cohort 1 will provide rapid information about the immunogenicity of mRNA-1273.351 in a previously vaccinated group. This cohort can inform near term public health decisions if the variant virus becomes more widespread. Cohort 2 will evaluate different strategies for generation of cross protective immune responses in a naïve population. This cohort will take longer to provide information on the immunogenicity of mRNA-1273.351, but is important to inform future public health strategies. As Cohorts 1 and 2 are in different populations, they can be enrolled in parallel as determined by each site.

Cohort 1 will include subjects 18 years of age and older who received two vaccinations of mRNA-1273 at dosages of 50 mcg, 100 mcg, or 250 mcg in the Phase 1 clinical trial (DMID 20-0003). Those subjects will be offered enrollment into this study approximately 9 to 12 months after they received the second vaccination in DMID 20-0003. At enrollment in this study, their long-term follow-up in DMID 20-0003 will be terminated. Subjects will be randomized, within each of the DMID 20-0003 cohorts (age and dosage groups – 50 mcg, 100 mcg, and 250 mcg), 1:1 (as outlined in Table 7) to either:

- Arm 1A, vaccination with a 50-mcg dose of the mRNA-1273.351 variant, or
- Arm 1B, vaccination with a combination vaccination that includes 25 mcg of mRNA-1273 and 25 mcg of mRNA-1273.351.

The anticipated sample size to be drawn from the DMID 20-0003 study population is approximately 45 subjects 18 through 55 years of age and approximately 20 subjects 56 years of age and older.

Subjects in Cohort 1 will receive a single intramuscular (IM) injection of the designated vaccine and will be followed through 12 months after vaccination. Follow-up visits will occur on Days 8, 15, and 29, as well as 3, 6, and 12 months after the vaccination.

Cohort 2 will include approximately 150 participants 18 through 55 years of age who have not received a COVID-19 vaccine, have no known history of COVID-19 or SARS-CoV-2 infection, and do not have underlying conditions that are associated with an increased risk of severe illness from SARS-CoV-2 infection. Enrollment may close before the full 150 participants based on estimates on the timing of immunogenicity results and the need to inform public health decisions. They will be randomly assigned to one of 8 treatment arms and will receive 2 or 3 IM injections of the vaccine and followed through 12 months after the last vaccination. Follow-up

visits will occur 7, 14, and 28 days after each vaccination, as well as 3, 6, and 12 months post the last vaccination.

For both Cohorts 1 and 2, reactogenicity will be assessed and blood will be drawn for immunogenicity assays.

After the IND is in effect, IRB review and approval, and site activation, the participating sites will begin recruitment outreach efforts, which can include fliers, letters, telephone calls, etc. Information regarding this trial may be provided to potential subjects who have previously participated in other vaccine trials conducted at the participating 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.

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

This phase 1 clinical trial is designed as an open-label study, without administration of a placebo formulation. An open-label study will facilitate the need for rapid review and dissemination of study data for public health reasons.

In the Phase 1 clinical trial, DMID 20-0003, mRNA-1273, administered as two injections 28 days apart, was investigated at dosages of 25, 50, 100 and 250 mcg in subjects 18 through 55 years of age, and at dosages of 25, 50, and 100 mcg in older cohorts (56-70 years of age and >71 years of age) [1,7]. The 100-mcg dose induced higher antibody titers than the 25-mcg dose, whereas the 250-mcg dose did not lead to significant increases, which supported evaluation of the 100-mcg dose in Phase 2 and Phase 3 trials. Subsequent to the start of the Phase 3 trial, an interim analysis of immunogenicity data from the Phase 2 demonstrated that the 50 and 100-mcg doses in a two-dose series are similarly immunogenic [4] and warrants further evaluation. The primary efficacy analysis from the Phase 3 trial evaluating a two-dose schedule of a 100-mcg mRNA-1273 vaccine led to the issuance of the EUA and initiation of a vaccination campaign in the United States.

The Phase 2 trial of mRNA-1273 evaluated doses of 50 mcg and 100 mcg, administered as a two-vaccination series, in 600 adults ≥18 years of age. The safety profile of both formulations was acceptable [4]. Anti-SARS-CoV-2 S binding and neutralizing antibodies were induced by both dose levels of mRNA-1273 within 28 days after the first vaccination, and rose substantially to peak titers by 14 days after the second vaccination, exceeding levels of convalescent sera from COVID-19 patients. The antibodies remained elevated through the last timepoint assessed at 57 days. Neutralizing responses met criteria for seroconversion within 28 days after the first vaccination in the majority of participants, with rates of 100% observed at 14 and 28 days after the second vaccination. Binding and neutralizing antibody responses were generally comparable in participants who received the 100 mcg mRNA-1273 and the 50 mcg dose at all time points and across the age groups of ≥18 to <55 years and ≥55 years. These findings support the evaluation of mRNA-1273 and mRNA-1273.351 at total dosages of 50 or 100 mcg per vaccination.

4.3. Selection of Study Population

Two cohorts will be enrolled. For Cohort 1, approximately 60 males and non-pregnant female subjects 18 years of age and older, who are in good health and received two vaccinations of mRNA-1273 at dosages of 50 mcg, 100 mcg or 250 mcg in DMID 20-0003 will be invited to participate in this study.

For Cohort 2, approximately 150 males and non-pregnant females, 18 through 55 years of age, who have never been vaccinated against SARS-CoV-2 or are not known to have been infected with SARS-CoV-2, and are at low risk for severe disease, in good health, and meet all eligibility criteria will be enrolled. The target population should reflect the community at large.

The estimated time from initiation of enrollment to complete enrollment in this clinical trial is approximately 4 weeks (though could take up to 8 weeks). Information regarding this trial may be provided to potential subjects who have previously participated in other vaccine trials conducted at the participating 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 vaccination.

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 principal investigator (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 the following criteria to be eligible to participate in this substudy:

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. Cohort 1: previously received 2 doses of mRNA-1273 IM as part of DMID 20-0003.
5. Cohort 1: Male or non-pregnant female, ≥18 years of age at time of enrollment.

   Cohort 2: Male or non-pregnant female, 18 through 55 years of age at time of enrollment.
6. Women of childbearing potential[1] must agree to practice abstinence or use at least one acceptable primary form of contraception.[2,3]

   - *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]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.

[3]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. In good health.[4]

   - *[4]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 or for dose optimization, as determined by the participating site PI 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 participating site PI 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.*

8. Oral temperature is less than 100.0°F (37.8°C).
9. Must agree to have samples stored for secondary research.
10. Agrees to adhere to Lifestyle Considerations (defined in Section 5.4 of the Protocol) throughout study duration.
11. Must agree to refrain from donating blood or plasma during the study (outside of this study).

Exclusion Criteria

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

1. Positive pregnancy test prior to each vaccine administration.
2. BMI >40.0 kg/m^2.

3. Female subject who is breastfeeding.
4. Has any medical disease or condition that, in the opinion of the participating site PI or appropriate sub-investigator, precludes study participation.[5]

   [5]*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.*
5. Presence of self-reported or medically documented significant medical or psychiatric condition(s).[6]

   [6]*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), 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, 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.
   - Type 2 diabetes mellitus, not including prediabetes.
6. Has an acute illness[7], as determined by the participating 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.

   [7]*An acute illness which is nearly resolved with only minor residual symptoms remaining is allowable if, in the opinion of the participating site PI or appropriate sub-investigator, the residual symptoms will not interfere with the ability to assess safety parameters as required by the protocol.*

7. Has participated in another investigational study involving any investigational product[8] within 5 half-lives before the first vaccine administration.

   [8]*study drug, biologic or device*

8. Currently enrolled in or plans to participate in another clinical trial with an investigational agent[9] that will be received during the study-reporting period.[10]

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

   [10]*Up to 15 months after the first vaccination.*

9. Has a history of hypersensitivity or severe allergic reaction (e.g., anaphylaxis, generalized urticaria, angioedema, other significant reaction) to drugs or any previous licensed or unlicensed vaccines or to polyethylene glycol (PEG) or a PEG-containing product.

10. Chronic use (more than 14 continuous days) of any medications that may be associated with impaired immune responsiveness.[11]

    [11]*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.*

11. Anticipating the need for immunosuppressive treatment within the next 6 months.

12. 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.

13. Has any blood dyscrasias or significant disorder of coagulation.

14. Received or plans to receive a licensed, live vaccine within 4 weeks before or after each vaccination.

15. Received or plans to receive a licensed, inactivated vaccine within 2 weeks before or after each vaccination.

16. Receipt of any other SARS-CoV-2 vaccine or any experimental coronavirus vaccine at any time prior to or during the study, except Cohort 1 subjects who received mRNA-1273 in DMID 20-0003.

17. Close contact of anyone known to have SARS-CoV-2 infection within 14 days prior to vaccine administration.

18. History of COVID-19 diagnosis, positive SARS-CoV-2 PCR test, or, for Cohort 2 only, a known positive SARS-CoV-2 serologic test.

19. On current treatment with investigational agents for prophylaxis of COVID-19.

4.4. Treatments

4.4.1. Treatments Administered

A booster dose of monovalent mRNA-1273.351 will be administered at 50mcg or a booster dose of bivalent mRNA-1273.351/ mRNA-1273 will be administered at 50mcg (25mcg of each).

4.4.2. Identity of Investigational Product(s)

Product: There are two clinical presentations of mRNA-1273 — mRNA-1273 and mRNA-1273.351

mRNA-1273 (0.2 mg/mL) is an LNP dispersion containing an mRNA that encodes for the pre fusion stabilized S protein of the Wuhan-Hu-1 strain of SARS-CoV-2. mRNA-1273 consists of an mRNA Drug Substance that is manufactured into LNPs composed of the proprietary ionizable lipid, SM-102, and 3 commercially available lipids, cholesterol, 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), and PEG2000 DMG.

mRNA-1273.351 (0.5 mg/mL) is formulated in the same way but contains mRNA that encodes for the prefusion stabilized S protein of the B.1.351 variant SARS-CoV-2 strain.

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

Subjects in Cohort 1 will be stratified by DMID 20-0003 cohort (age and dosage group) and randomized 1:1 to Arm 1A or 1B. Randomization will be done in the SDCC's Advantage eClinical^{SM} (Electronic Data Capture System).

4.4.4. Selection of Dose in the Study

See Section 4.2 for a discussion of dose selection for this study.

4.4.5. Prior and Concomitant Therapy

Concomitant medications include only prescription medications and vaccines received outside of the study taken by the subject at the time of enrollment through 28 days after the last vaccination. At each study visit, if there are new SAEs, Protocol Specified AESIs, MAAEs, or NOCMCs, concomitant medications should be recorded on the appropriate DCF.

4.4.6. Treatment Compliance

All subjects are to receive 1 additional dose 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 approximately 30 subjects in each arm (Arms 1A and 1B), the chance of observing at least one AE of probability 10% or more is approximately 96%. Therefore, if no AEs of a given type occur in a Cohort 1 Arm, we can be relatively confident that they will occur in fewer than 10% of people once the vaccine is implemented. With approximately 60 subjects across these two Arms (1A and 1B), 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 Cohort 1, we can be very confident that any combination independent event will occur in fewer than 5% of people once the vaccine is implemented as a boost.

6. GENERAL STATISTICAL CONSIDERATIONS

6.1. General Principles

In general 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. Safety Population

The Safety Analysis population includes all subjects who received the third vaccination.

6.2.2. Modified Intent-to Treat Population

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

6.2.3. 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.

6.3. 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 immunogenicity assays, any values below zero may be imputed as zero (or slightly above zero) for analysis purposes. Any such imputations will be noted in the corresponding analysis.

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 study is ongoing. Any ad-hoc analyses, jointly developed by the SDCC and/or the Vaccine Research Center (VRC), other participating laboratories 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 noted will be solicited electronically. The SMC will review cumulative AE data after all subjects in Cohort 1 have been dosed and completed Day 8.

- Interim data review of immunogenicity may be performed to inform public health decisions.

Statistical analyses of secondary immunogenicity endpoints, by vaccine schedule group, may be performed when subjects have completed key immunogenicity visits. Immunogenicity reviews may be shared with the SMC, as determined by DMID.

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

Interim analyses of safety, reactogenicity, and immunologic response data may be done, as needed.

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 8 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 7.

The disposition of subjects in the study will be tabulated by treatment group (Table 6). 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 [5] will be included (Figure 1). 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) as well as similar summaries for major subject-specific protocol deviations (Table 5). 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.

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

Binding will be measured three types of ECLIA assays. The first is a single-plex (ECLIA) that produces arbitrary units/mL that is a validated assay and can be converted to binding antibody units for Wa-1 S-2P binding. The second is a 4-plex (ECLIAv2) assay that is also validated and produces arbitrary units/mL to measure variant specific binding. The final assay is a 10-plex (ECLIAv2) that is a fit for purpose assay that produces area under the curve and is used to assess binding for variants of concern.

Seroconversion rates, geometric mean fold rise (GMFR) and geometric mean (GM) or Williams mean of arbitrary units per mL (AU/mL), binding antibody unit/mL (BAU, only for Wa-1 [S2-P] variant), and AUC for SARS-CoV-2 will be calculated at Study Days 1 (GM only), 15, 29, 91, 181 and 366 post third vaccination by treatment group and will include both tabular and graphical summaries. Seroconversion rates, GMFR and GM will be presented with their corresponding 95% confidence interval (CI) estimates (using Student's t-distribution for GM and GMFR and the Clopper-Pearson binomial method for seroconversion) at each post vaccination timepoint and overall peak GM. Summaries of GM are included starting with Table 12 and ending with Table 33 and summaries of GMFR and seroconversion are included starting with Table 78 and ending with Table 99. Graphical displays will include reverse cumulative distribution plots (starting with Figure 2 and ending with Figure 23), individual values over time (starting with Figure 24 and ending with Figure 45), geometric mean over time (starting with Figure 46 and ending with Figure 67), and distribution of responses over time (starting with Figure 108 and ending with Figure 129).

Neutralization assays using SARS-CoV-2 pseudovirus neutralization assay (PsVNA) and focus reduction neutralization test (FRNT) will be run using serial dilutions against available variants (e.g., Beta, Delta). ID_{50} and ID_{80} will be calculated 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) at each post vaccination timepoint and overall peak GM (starting with Table 34 and ending with Table 73). Summaries of GMFR and seroconversion are included starting with Table 100 and ending with Table 139. The ratio of the result for each variant divided by the result of the D614G variant will be calculated and summarized as the geometric mean ratio (GMR) (Table 140, Table 141, Table 142, Table 143, Table 144, Table 145, Table 146, Table 147). Graphical displays for PsVNA and FRNT will include geometric mean over time (starting with Figure 68 and ending with Figure 107) and distributions of responses over time (starting with Figure 130 and ending with Figure 169).

Correlations between all assays will be displayed in a heatmap (Figure 170, Figure 171, Figure 172, Figure 173, Figure 174, Figure 175, Figure 176, Figure 177, Figure 178, Figure 179).

Individual immunogenicity responses are shown in Listing 8.

Any additional variants of concern not listed in the appendices that are of scientific interest may be analyzed in an analogous manner in the final report.

8.3. Exploratory Immunogenicity Analyses

The magnitude, phenotype and percentage of cytokine expressing S protein specific T cells will be summarized at each timepoint by Treatment Group. Mean percentages of CD4 and CD8 T cells expressing cytokines and proportions of responders with 95% CI along with median, minimum, and maximum will be presented by peptide pool stimulation (Table 74, Table 75, Table 76, Table 77). Distributions of T cell percentages will be graphically displayed (starting with Figure 180 and ending with Figure 299).

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 third vaccination (Study 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 and using standard techniques, such as exact confidence intervals (CI), to summarize the proportion of subjects reporting each symptom, any local symptom, and any systemic symptom.

Unsolicited non-serious AEs will be collected from the time of the third vaccination through 28 days after the third vaccination. Unsolicited AEs will be coded by MedDRA for preferred term and system organ class (SOC). SAEs, Protocol Specified AESIs, MAAEs, and NOCMCs will be collected from the time of third vaccination through 12 months after the third vaccination. 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.

9.1. Demographic and Other Baseline Characteristics

Summaries of age, sex, ethnicity, time since second dose, and race will be presented by Treatment Group (Table 9 and Table 10). 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 11).

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 165).

Individual subject listings will be presented for all concomitant medications (Listing 15).

9.2. Measurements of Treatment Compliance

All subjects are to receive 1 additional dose of study product administered in the clinic. The number of subjects receiving experimental (third) dose will be summarized as part of the subject disposition table (Table 6).

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-third vaccination, and systemic and local solicited adverse events were collected 30 minutes post-third vaccination and then daily for 7 days after the third 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 149).

For each systemic and local event, any systemic event, any local event, and any solicited event, the maximum severity over 7 days after the third 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 (Table 150). 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-third vaccination both in a summary table (Table 151 and Table 152) and graphically in a bar chart (Figure 300 and Figure 301).

The mean, standard deviation, median, minimum and maximum duration of solicited events will be summarized (Table 153).

Day of solicited symptom onset will be summarized graphically (Figure 302 and Figure 303).

Solicited adverse events by subject will be presented in listings (Listing 10 and Listing 11) and graphically (starting with Figure 304 and ending with Figure 315).

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

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, and Treatment Group:

- Subject incidence and total frequency of adverse events (Table 156);
- Summary of severity and relationship to study product (Table 154 and Table 155);
- Listing of Non-Serious, Unsolicited, Moderate or Severe Adverse Events (Table 158);
- Bar chart of frequency of adverse events by severity and MedDRA system organ class (Figure 316);
- Bar chart of incidence of adverse events by severity and MedDRA system organ class (Figure 317).

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 157);
- New Onset Chronic Medical Conditions and Medically Attended Adverse Events (Table 159).

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 listing of pregnancies and outcomes will be presented (Listing 16, Listing 17, Listing 18, Listing 19, and Listing 20).

9.6. Clinical Laboratory Evaluations

Not applicable.

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 Study Day 1, Study Day 15, Study Day 29, Study Day 91, Study Day 118, and Study Day 366. Vital signs will be tabulated by visit and Treatment Group in Table 160, Table 161, Table 162, Table 163, Table 164 (Listing 13).

Physical Examinations were only to be performed if clinically indicated at Study Day 1, Study Day 15, Study Day 29, Study Day 91, Study Day 118, and Study Day 366. 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 14).

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 15). The use of concomitant medications during the study will be summarized by ATC1, ATC2 code and Treatment Group for the Safety population (Table 165).

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 and R 3.6.2 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. Anderson, E. J., Rouphael, N. G., Widge, A. T., Jackson, L. A., Roberts, P. C., Makhene, M., Chappell, J. D., Denison, M. R., Stevens, L. J., Pruijssers, A. J., McDermott, A. B., Flach, B., Lin, B. C., Doria-Rose, N. A., O'Dell, S., Schmidt, S. D., Corbett, K. S., Swanson, P. A., 2nd, Padilla, M., Neuzil, K. M., … mRNA-1273 Study Group (2020). Safety and Immunogenicity of SARS-CoV-2 mRNA-1273 Vaccine in Older Adults. The New England Journal of Medicine, 383(25), 2427–2438. https://doi.org/10.1056/NEJMoa2028436.
2. Callaway, E. & Mallapaty, S. (2021). Novavax offers first evidence that COVID vaccines protect people against variants. Nature, 10.1038/d41586-021-00268-9. Advance online publication. https://doi.org/10.1038/d41586-021-00268-9.
3. Center for Systems Science and Engineering (CCSE) at Johns Hopkins University (JHU). COVID-19 Dashboard. 2020. https://coronavirus.jhu.edu/map.html. Accessed 04 Feb 2021.
4. Chu L., McPhee R., Huang W., Bennett H., Pajon R., Nestorova B., Leav B., … mRNA-1273 Study Group (2021). A Preliminary Report of a Randomized Controlled Phase 2 Trial of the Safety and Immunogenicity of mRNA-1273 SARS-CoV-2 Vaccine. Vaccine. Advance online publication. https://doi.org/10.1016/j.vaccine.2021.02.007.
5. Corbett, K. S., Edwards, D. K., Leist, S. R., Abiona, O. M., Boyoglu-Barnum, S., Gillespie, R. A., Himansu, S., Schäfer, A., Ziwawo, C. T., DiPiazza, A. T., Dinnon, K. H., Elbashir, S. M., Shaw, C. A., Woods, A., Fritch, E. J., Martinez, D. R., Bock, K. W., Minai, M., Nagata, B. M., Hutchinson, G. B., … Graham, B. S. (2020). SARS-CoV-2 mRNA vaccine design enabled by prototype pathogen preparedness. Nature, 586(7830), 567–571. https://doi.org/10.1038/s41586-020-2622-0
6. Drummond R. CONSORT Revised: Improving the Reporting of Randomized Clinical Trials. JAMA. 2001; 285(15): 2006-2007.
7. Jackson, L. A., Anderson, E. J., Rouphael, N. G., Roberts, P. C., Makhene, M., Coler, R. N., McCullough, M. P., Chappell, J. D., Denison, M. R., Stevens, L. J., Pruijssers, A. J., McDermott, A., Flach, B., Doria-Rose, N. A., Corbett, K. S., Morabito, K. M., O'Dell, S., Schmidt, S. D., Swanson, P. A., 2nd, Padilla, M., … mRNA-1273 Study Group (2020). An mRNA Vaccine against SARS-CoV-2 - Preliminary Report. The New England Journal of Medicine, 383(20), 1920–1931. https://doi.org/10.1056/NEJMoa2022483.
8. Tegally H, Wilkinson E, Giovanetti M, Iranzadeh A, Fonseca V, Giandhari J, Doolabh D, Pillay S, San EJ, Msomi N, et al. Emergence and rapid spread of a new severe acute respiratory syndrome-related coronavus 2 (SARS-CoV-2) lineage with multiple spike mutations in South Africa. MedRxiv 2020.12.21.20248640.
9. Wang P, Liu L, Iketani S, et al. Increased resistance of SARS-CoV-2 variants B.1.351 and B.1.1.7 to antibody neutralization. bioRxiv : the preprint server for biology, 2021.01.428137. https://doi.org/10.1101/2021.01.25.428137.
10. World Health Organization (WHO). (Data reported as of 13 Nov 2020). Weekly Operational Update on COVID-19. 2020a.

https://www.who.int/publications/m/item/weekly-operational-update-on-covid-19---13-november-2020. Accessed 04 Feb 2021.

11. Wu, K., Werner, A. P., Moliva, J. I., Koch, M., Choi, A., Stewart-Jones, G., Bennett, H., Boyoglu-Barnum, S., Shi, W., Graham, B. S., Carfi, A., Corbett, K. S., Seder, R. A., & Edwards, D. K. (2021). mRNA-1273 vaccine induces neutralizing antibodies against spike mutants from global SARS-CoV-2 variants. bioRxiv : the preprint server for biology, 2021.01.25.427948. https://doi.org/10.1101/2021.01.25.427948.

APPENDIX 1. TABLE MOCK-UPS

LIST OF TABLES

9.1 Overall Study Design and Plan Description

Table 1: Study Design

Arm	Sample Size	Vaccination Product and Dose
1A	~30	50 mcg mRNA-1273.351
1B	~30	25 mcg mRNA-1273 + 25 mcg mRNA-1273.351

9.5.1 Efficacy/Immunogenicity and Safety Measurements Assessed and Flow Chart

Table 2: Schedule of Study Procedures

Study Day	-42 to -1	1	8*	15	29	91	181	366	Unscheduled Visit	Early Termination Visit
Visit Window (±number of days)		0	1	2	2	7	7	14		
Study Visit	Screening (optional) 00	01	02	03	04	05	06	07		
Informed Consent	X	X[a]								
Review Eligibility Criteria	X	X								
Medical History	X	X[a]								
Vaccination		X								
Concomitant Medications		X	X	X	X					
Interim History		X[b]		X	X	X	X	X	X	X
Symptom-Directed Physical Examination	X	X		X	X	X	X	X	X	X
Vital Signs[c]		X		X	X	X	X	X	X	X
Height and Weight (for BMI)	X	X[a]								
Pregnancy Test[d]		X								
Memory Aid: Solicited AEs		X	X	X[e]						
Unsolicited AEs		X	X	X	X				X	X
SAEs, Protocol Specified AESIs, MAAEs, and NOCMCs		X	X	X	X	X	X	X	X	X
Serum for Serological Immunogenicity Assays		X		X	X	X	X	X		X
Peripheral Blood Mononuclear Cells (PBMCs) for Cellular Immunology Assays (and Plasma)		X		X			X	X		X

* Telephone call.

a) If not performed at Visit 00.
b) If medical history performed at Visit 00, then interim history at Visit 01.
c) Vital signs to be obtained pre and post vaccination. Otherwise, only as clinically indicated.
d) For women of childbearing potential, a negative urine pregnancy test on Day 1 with results confirmed prior to enrollment.
e) Collect Memory Aid and assess for delayed onset local reactions.

9.7.1 Sample Size

Table 3: Sample Size/Probability Estimates

Cohort 1					
N	**"True" Event Rate**	**Probability of Observation (%)**	**N**	**"True" Event Rate**	**Probability of Observation (%)**
30	0.1%	3.0	60	0.1%	5.8
	0.5%	14.0		0.5%	26.0
	1.0%	26.0		1.0%	45.3
	2.0%	45.5		2.0%	70.2
	3.0%	59.9		3.0%	83.9
	4.0%	70.6		4.0%	91.4
	5.0%	78.5		5.0%	95.4
	10.0%	95.8		10.0%	99.8
	15.0%	99.2		15.0%	>99.9
	20.0%	99.9		20.0%	>99.9

10.2 Protocol Deviations

Table 4: Distribution of Protocol Deviations by Category, Type, and Treatment Group

[Implementation Note: Below are example categories and deviation types. All reported categories and deviations types will be presented.]

		50 µg mRNA-1273.351 (N=X)		25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)		All Subjects (N=X)	
Category	**Deviation Type**	**# 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						
	Required procedure done incorrectly						
	Required procedure not conducted						
	Specimen result not obtained						
	Too few aliquots obtained						
Treatment administration schedule	**Required procedure done incorrectly**						

Table with Similar Format:

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

14.1 Description of Study Subjects

14.1.1 Disposition of Subjects

Table 6: Subject Disposition by Treatment Group

	50 µg mRNA-1273.351 (N=X)		25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)		All Subjects (N=X)	
Subject Disposition	**n**	**%**	**n**	**%**	**n**	**%**
Screened						
Enrolled						
Received the third vaccination						
Early termination[a]						
Completed study						
[a]Refer to Listing 2 for reasons subjects discontinued or terminated early.						

Table 7: Analysis Populations by Treatment Group - All Subjects

Analysis Populations	Reason Subjects Excluded	50 µg mRNA-1273.351 (N=X)		25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)		All Subjects (N=X)	
		%	n	%	n	%	n
Safety	Any Reason	x	xx	x	xx	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 8: 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 9: Summary of Categorical Demographic and Baseline Characteristics by Treatment Group

		50 µg mRNA-1273.351 (N=X)		25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)		All Subjects (N=X)	
Demographic Category	**Characteristic**	**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						

Table 10: Summary of Continuous Demographic and Baseline Characteristics by Treatment Group

Variable	Statistic	50 µg mRNA-1273.351 (N=X)	25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)	All Subjects (N=X)
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			
Time Between Dose 2 and Dose 3 (Days)	Mean			
	Standard Deviation			
	Median			
	Minimum			
	Maximum			

14.1.3 Prior and Concurrent Medical Conditions

Table 11: Summary of Subjects with Pre-Existing Medical Conditions by MedDRA System Organ Class and Treatment Group

MedDRA System Organ Class	50 µg mRNA-1273.351 (N=X)		25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)		All Subjects (N=X)	
	n	%	n	%	n	%
Any SOC	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.

14.2 Immunogenicity Data

Table 12: Serum IgG Binding Assay Arbitrary Units/mL Measured by ECLIA Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group, S-2P–Wa-1 – mITT Population

Planned Time Point	Statistic	50 µg mRNA-1273.351 (N=X)	25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)	All Subjects (N=X)
Day 1, Pre-Booster Dose	n			
	GM			
	95% CI			
Day 8	n			
	GM			
	95% CI			
Day 15	n			
	GM			
	95% CI			
Day 29	n			
	GM			
	95% CI			
Day 91	n			
	GM			
	95% CI			
Day 181	n			
	GM			

	95% CI			
Day 366	n			
	GM			
	95% CI			
Peak GM	n			
	GM			
	95% CI			

Notes: N=Number of subjects in the mITT population.
n=Number of subjects with results available at time point.
GM=Geometric Mean, NE=Not Estimable.
Confidence intervals of the geometric means were calculated with the Student's t distribution on log-transformed data.

Tables with Similar Format:

Implementation notes:

For tables using the PP population, update footnote to read: "Notes: N=Number of subjects in the Per Protocol population."

For all AUC tables, add footnote reading: "Geometric Mean is calculated as the Williams mean using log(1+x)."

Table 13: Serum IgG Binding Assay Arbitrary Units/mL Measured by ECLIA Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group, S-2P–Wa-1 – Per Protocol Population

Table 14: Serum IgG Binding Assay Arbitrary Units/mL Measured by ECLIA Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group, RBD–Wa-1 – mITT Population

Table 15: Serum IgG Binding Assay Arbitrary Units/mL Measured by ECLIA Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group, RBD–Wa-1 – Per Protocol Population

Table 16: Serum IgG Binding Assay Arbitrary Units/mL Measured by ECLIAv2 (4-plex) Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group, S-2P–Wa-1 – mITT Population

Table 17: Serum IgG Binding Assay Arbitrary Units/mL Measured by ECLIAv2 (4-plex) Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group, S-2P–Wa-1 – Per Protocol Population

Table 34: Pseudovirus Neutralization Assay ID_{50} Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group, D614G – mITT Population

Planned Time Point	Statistic	50 µg mRNA-1273.351 (N=X)	25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)	All Subjects (N=X)
Day 1, Pre-Booster Dose	n			
	GM			
	95% CI			
Day 8	n			
	GM			
	95% CI			
Day 15	n			
	GM			
	95% CI			
Day 29	n			
	GM			
	95% CI			
Day 91	n			
	GM			
	95% CI			
Day 181	n			
	GM			
	95% CI			
Day 366	n			

Planned Time Point	Statistic	50 µg mRNA-1273.351 (N=X)	25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)	All Subjects (N=X)
	GM			
	95% CI			
Peak GM	n			
	GM			
	95% CI			

Notes: N=Number of subjects in the mITT population.
n=Number of subjects with results available at time point.
GM=Geometric Mean, NE=Not Estimable.
Confidence intervals of the geometric means were calculated with the Student's t distribution on log-transformed data.

Tables with Similar Format:

Implementation note: For tables using the PP population, update footnote to read: "Notes: N=Number of subjects in the Per Protocol population."

Table 35: Pseudovirus Neutralization Assay ID_{50} Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group, D614G – Per Protocol Population

Table 36: Pseudovirus Neutralization Assay ID_{80} Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group, D614G – mITT Population

Table 37: Pseudovirus Neutralization Assay ID_{80} Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group, D614G – Per Protocol Population

Table 38: Pseudovirus Neutralization Assay ID_{50} Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group, B.1.351 – mITT Population

Table 39: Pseudovirus Neutralization Assay ID_{50} Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group, B.1.351 – Per Protocol Population

Table 53: Pseudovirus Neutralization Assay ID_{80} Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group, B.1.1.7 – Per Protocol Population

Table 54: Focus Reduction Neutralization Test ID_{50} Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group, D614G – mITT Population

Planned Time Point	Statistic	50 µg mRNA-1273.351 (N=X)	25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)	All Subjects (N=X)
Day 1, Pre-Booster Dose	n			
	GM			
	95% CI			
Day 8	n			
	GM			
	95% CI			
Day 15	n			
	GM			
	95% CI			
Day 29	n			
	GM			
	95% CI			
Day 91	n			
	GM			
	95% CI			
Day 181	n			
	GM			
	95% CI			
Day 366	n			

Planned Time Point	Statistic	50 µg mRNA-1273.351 (N=X)	25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)	All Subjects (N=X)
	GM			
	95% CI			
Peak GM	n			
	GM			
	95% CI			

Notes: N=Number of subjects in the mITT population.
n=Number of subjects with results available at time point.
GM=Geometric Mean, NE=Not Estimable.
Confidence intervals of the geometric means were calculated with the Student's t distribution on log-transformed data.

Tables with Similar Format:

Implementation note: For tables using the PP population, update footnote to read: "Notes: N=Number of subjects in the Per Protocol population."

Table 55: Focus Reduction Neutralization Test ID_{50} Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group, D614G – Per Protocol Population

Table 56: Focus Reduction Neutralization Test ID_{80} Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group, D614G – mITT Population

Table 57: Focus Reduction Neutralization Test ID_{80} Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group, D614G – Per Protocol Population

Table 58: Focus Reduction Neutralization Test ID_{50} Geometric Mean Results with 95% Confidence Intervals by Time Point and Treatment Group, B.1.351 – mITT Population

Table 74: Mean Percentages of CD4 T Cells Expressing Cytokines with 95% CI – mITT Population

[Implementation Note: Tables should include rows for median, min, max, GMFR and 95% CI of GMFR. Column order should be Peptide Pool, Cytokine and Time Point.]

Time Point	Peptide Pool	Cytokine	Statistic	50 µg mRNA-1273.351 (N=X)	25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)	All Subjects (N=X)
Day 1, Pre-Booster Dose	**Beta Mutations**	**IFNγ**	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2/CM	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2/EM	n			
			Mean			
			95% CI[a]			
			Response Rate			

Time Point	Peptide Pool	Cytokine	Statistic	50 µg mRNA-1273.351 (N=X)	25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)	All Subjects (N=X)
			95% CI[b]			
		IFNγ or IL-2/N	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2/TD	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2 and 154	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2 or 154	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2 or 154/C	n			
			Mean			

Time Point	Peptide Pool	Cytokine	Statistic	50 µg mRNA-1273.351 (N=X)	25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)	All Subjects (N=X)
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2 or 154/E	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2 or 154/N	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2 or 154/T	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IL-17a	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			

Time Point	Peptide Pool	Cytokine	Statistic	50 µg mRNA-1273.351 (N=X)	25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)	All Subjects (N=X)
		IL-2	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IL-4 and 154	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IL-4 IL-5 IL-13 and 154	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		TNFα	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
	Beta S	**IFNγ**	n			
			Mean			
			95% CI[a]			

Time Point	Peptide Pool	Cytokine	Statistic	50 µg mRNA-1273.351 (N=X)	25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)	All Subjects (N=X)
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2/CM	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2/EM	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		Repeat for all cytokines				
	Conserved S1	**IFNγ**	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			

Time Point	Peptide Pool	Cytokine	Statistic	50 µg mRNA-1273.351 (N=X)	25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)	All Subjects (N=X)
		IFNγ or IL-2	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2/CM	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2/EM	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		Repeat for all cytokines				
	Conserved S2	**IFNγ**	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2	n			
			Mean			

Time Point	Peptide Pool	Cytokine	Statistic	50 µg mRNA-1273.351 (N=X)	25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)	All Subjects (N=X)
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2/CM	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2/EM	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		Repeat for all cytokines				
	Original Matched	**IFNγ**	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2	n			
			Mean			
			95% CI[a]			
			Response Rate			

Time Point	Peptide Pool	Cytokine	Statistic	50 µg mRNA-1273.351 (N=X)	25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)	All Subjects (N=X)
			95% CI[b]			
		IFNγ or IL-2/CM	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2/EM	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		Repeat for all cytokines				
	Original S	**IFNγ**	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2/CM	n			

Time Point	Peptide Pool	Cytokine	Statistic	50 µg mRNA-1273.351 (N=X)	25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)	All Subjects (N=X)
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2/EM	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		Repeat for all cytokines				
Repeat for all study days						

Note: N=Number of Subjects.
n=Number of subjects with results available at time point.
NE=Not Estimable
[a] Confidence interval calculated based on the Student's t-distribution
[b] Exact binomial confidence interval calculated using the Clopper-Pearson methodology.

Table with Similar Format:

Table 75: Mean Percentages of CD4 T Cells Expressing Cytokines with 95% CI – Per Protocol Population

Table 76: Mean Percentages of CD8 T Cells Expressing Cytokines with 95% CI – mITT Population

[Implementation Note: Tables should include rows for median, min, max, GMFR and 95% CI of GMFR. Column order should be Peptide Pool, Cytokine and Time Point.]

Time Point	Peptide Pool	Cytokine	Statistic	50 µg mRNA-1273.351 (N=X)	25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)	All Subjects (N=X)
Day 1, Pre-Booster Dose	**Beta Mutations**	**IFNγ or IL-2**	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2/CM	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2/EM	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2/N	n			
			Mean			
			95% CI[a]			
			Response Rate			

Time Point	Peptide Pool	Cytokine	Statistic	50 µg mRNA-1273.351 (N=X)	25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)	All Subjects (N=X)
			95% CI[b]			
		IFNγ or IL-2/TD	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
	Beta S	**IFNγ or IL-2**	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2/CM	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2/EM	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2/N	n			
			Mean			

Time Point	Peptide Pool	Cytokine	Statistic	50 µg mRNA-1273.351 (N=X)	25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)	All Subjects (N=X)
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2/TD	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
	Conserved S1	**IFNγ or IL-2**	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2/CM	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2/EM	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			

Time Point	Peptide Pool	Cytokine	Statistic	50 µg mRNA-1273.351 (N=X)	25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)	All Subjects (N=X)
		IFNγ or IL-2/N	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2/TD	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
	Conserved S2	**IFNγ or IL-2**	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2/CM	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2/EM	n			
			Mean			
			95% CI[a]			

Time Point	Peptide Pool	Cytokine	Statistic	50 µg mRNA-1273.351 (N=X)	25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)	All Subjects (N=X)
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2/N	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2/TD	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
	Original Matched	**IFNγ or IL-2**	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2/CM	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2/EM	n			

Time Point	Peptide Pool	Cytokine	Statistic	50 µg mRNA-1273.351 (N=X)	25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)	All Subjects (N=X)
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2/N	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2/TD	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
	Original S	**IFNγ or IL-2**	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2/CM	n			
			Mean			
			95% CI[a]			
			Response Rate			

Time Point	Peptide Pool	Cytokine	Statistic	50 µg mRNA-1273.351 (N=X)	25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)	All Subjects (N=X)
			95% CI[b]			
		IFNγ or IL-2/EM	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2/N	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
		IFNγ or IL-2/TD	n			
			Mean			
			95% CI[a]			
			Response Rate			
			95% CI[b]			
Repeat for all study days						

Note: N=Number of Subjects.
n=Number of subjects with results available at time point.
NE=Not Estimable
[a] Confidence interval calculated based on the Student's t-distribution
[b] Exact binomial confidence interval calculated using the Clopper-Pearson methodology.

Table with Similar Format:

Table 77: Mean Percentages of CD8 T Cells Expressing Cytokines with 95% CI – Per Protocol Population

Table 78: Serum IgG Binding Assay Arbitrary Units/mL Measured by ECLIA Geometric Mean Fold Rise and 4-Fold Rise Results by Time Point and Treatment Group, S-2P–Wa-1 – mITT Population

Planned Time Point	Statistic	50 µg mRNA-1273.351 (N=X)	25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)	All Subjects (N=X)
Day 15	n			
	GMFR (95% CI)[a]			
	4-Fold Rise - % (95% CI)[b]			
Day 29	n			
	GMFR (95% CI)[a]			
	4-Fold Rise - % (95% CI)[b]			
Day 91	n			
	GMFR (95% CI)[a]			
	4-Fold Rise - % (95% CI)[b]			
Day 181	n			
	GMFR (95% CI)[a]			
	4-Fold Rise - % (95% CI)[b]			
Day 366	n			
	GMFR (95% CI)[a]			
	4-Fold Rise - % (95% CI)[b]			

Notes: N=Number of subjects in the mITT population.
n=Number of subjects with results available at time point.
GMFR=Geometric Mean Fold Rise, NE=Not Estimable.
[a] Confidence interval calculated based on the Student's t-distribution
[b] Exact binomial confidence interval calculated using the Clopper-Pearson methodology.

Tables with Similar Format:

Implementation notes:

- For tables using the PP population, update footnote to read: "Notes: N=Number of subjects in the Per Protocol population."
- For all AUC tables, add footnote reading: "AUC results reported as 0 were imputed to the lowest non-zero reported value for the purposes of fold-rise calculations."

Table 79: Serum IgG Binding Assay Arbitrary Units/mL Measured by ECLIA Geometric Mean Fold Rise and 4-Fold Rise Results with 95% Confidence Intervals by Time Point and Treatment Group, S-2P–Wa-1 – Per Protocol Population

Table 80: Serum IgG Binding Assay Arbitrary Units/mL Measured by ECLIA Geometric Mean Fold Rise and 4-Fold Rise Results with 95% Confidence Intervals by Time Point and Treatment Group, RBD–Wa-1 – mITT Population

Table 81: Serum IgG Binding Assay Arbitrary Units/mL Measured by ECLIA Geometric Mean Fold Rise and 4-Fold Rise Results with 95% Confidence Intervals by Time Point and Treatment Group, RBD–Wa-1 – Per Protocol Population

Table 82: Serum IgG Binding Assay Arbitrary Units/mL Measured by ECLIAv2 (4-plex) Geometric Mean Fold Rise and 4-Fold Rise Results with 95% Confidence Intervals by Time Point and Treatment Group, S-2P–Wa-1 – mITT Population

Table 83: Serum IgG Binding Assay Arbitrary Units/mL Measured by ECLIAv2 (4-plex) Geometric Mean Fold Rise and 4-Fold Rise Results with 95% Confidence Intervals by Time Point and Treatment Group, S-2P–Wa-1 – Per Protocol Population

Table 84: Serum IgG Binding Assay Arbitrary Units/mL Measured by ECLIAv2 (4-plex) Geometric Mean Fold Rise and 4-Fold Rise Results with 95% Confidence Intervals by Time Point and Treatment Group, S-2P–B.1.351 – mITT Population

Table 85: Serum IgG Binding Assay Arbitrary Units/mL Measured by ECLIAv2 (4-plex) Geometric Mean Fold Rise and 4-Fold Rise Results with 95% Confidence Intervals by Time Point and Treatment Group, S-2P– B.1.351 – Per Protocol Population

Table 86: Serum IgG Binding Assay Arbitrary Units/mL Measured by ECLIAv2 (4-plex) Geometric Mean Fold Rise and 4-Fold Rise Results with 95% Confidence Intervals by Time Point and Treatment Group, RBD–B.1.351 – mITT Population

Table 87: Serum IgG Binding Assay Arbitrary Units/mL Measured by ECLIAv2 (4-plex) Geometric Mean Fold Rise and 4-Fold Rise Results with 95% Confidence Intervals by Time Point and Treatment Group, RBD– B.1.351 – Per Protocol Population

Table 88: Serum IgG Binding Assay Binding Antibody Units/mL Measured by ECLIAv2 (4-plex) Geometric Mean Fold Rise and 4-Fold Rise Results with 95% Confidence Intervals by Time Point and Treatment Group, S-2P–Wa-1 – mITT Population

Table 100: Pseudovirus Neutralization Assay ID_{50} Geometric Mean Fold Rise and 4-Fold Rise Results by Time Point and Treatment Group, S-2P–Wa-1, mITT Population

Planned Time Point	Statistic	50 µg mRNA-1273.351 (N=X)	25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)	All Subjects (N=X)
Day 15	n			
	GMFR (95% CI)[a]			
	4-Fold Rise - % (95% CI)[b]			
Day 29	n			
	GMFR (95% CI)[a]			
	4-Fold Rise - % (95% CI)[b]			
Day 91	n			
	GMFR (95% CI)[a]			
	4-Fold Rise - % (95% CI)[b]			
Day 181	n			
	GMFR (95% CI)[a]			
	4-Fold Rise - % (95% CI)[b]			
Day 366	n			
	GMFR (95% CI)[a]			
	4-Fold Rise - % (95% CI)[b]			

Notes: N=Number of subjects in the mITT population.
n=Number of subjects with results available at time point.
GMFR=Geometric Mean Fold Rise, NE=Not Estimable.
[a] Confidence interval calculated based on the Student's t-distribution
[b] Exact binomial confidence interval calculated using the Clopper-Pearson methodology.

Tables with Similar Format:

Implementation notes:

For tables using the PP population, update footnote to read: "Notes: N=Number of subjects in the Per Protocol population."

Table 101: Pseudovirus Neutralization Assay ID_{50} Geometric Mean Fold Rise and 4-Fold Rise Results by Time Point and Treatment Group, D614G – Per Protocol Population

Table 102: Pseudovirus Neutralization Assay ID_{80} Geometric Mean Fold Rise and 4-Fold Rise Results by Time Point and Treatment Group,1 D614G – mITT Population

Table 103: Pseudovirus Neutralization Assay ID_{80} Geometric Mean Fold Rise and 4-Fold Rise Results by Time Point and Treatment Group, D614G – Per Protocol Population

Table 104: Pseudovirus Neutralization Assay ID_{50} Geometric Mean Fold Rise and 4-Fold Rise Results by Time Point and Treatment Group, B.1.351 – mITT Population

Table 105: Pseudovirus Neutralization Assay ID_{50} Geometric Mean Fold Rise and 4-Fold Rise Results by Time Point and Treatment Group, B.1.351 – Per Protocol Population

Table 106: Pseudovirus Neutralization Assay ID_{80} Geometric Mean Fold Rise and 4-Fold Rise Results by Time Point and Treatment Group, B.1.351 – mITT Population

Table 107: Pseudovirus Neutralization Assay ID_{80} Geometric Mean Fold Rise and 4-Fold Rise Results by Time Point and Treatment Group, B.1.351 – Per Protocol Population

Table 108: Pseudovirus Neutralization Assay ID_{50} Geometric Mean Fold Rise and 4-Fold Rise Results by Time Point and Treatment Group, B.1.617.2 – mITT Population

Table 109: Pseudovirus Neutralization Assay ID_{50} Geometric Mean Fold Rise and 4-Fold Rise Results by Time Point and Treatment Group, B.1.617.2 – Per Protocol Population

Table 110: Pseudovirus Neutralization Assay ID_{80} Geometric Mean Fold Rise and 4-Fold Rise Results by Time Point and Treatment Group, B.1.617.2 – mITT Population

Table 111: Pseudovirus Neutralization Assay ID_{80} Geometric Mean Fold Rise and 4-Fold Rise Results by Time Point and Treatment Group, B.1.617.2 – Per Protocol Population

Table 112: Pseudovirus Neutralization Assay ID_{50} Geometric Mean Fold Rise and 4-Fold Rise Results by Time Point and Treatment Group, P.1 – mITT Population

Table 120: Focus Reduction Neutralization Test ID_{50} Geometric Mean Fold Rise and 4-Fold Rise Results by Time Point and Treatment Group, S-2P–Wa-1 – mITT Population

Planned Time Point	Statistic	50 µg mRNA-1273.351 (N=X)	25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)	All Subjects (N=X)
Day 15	n			
	GMFR (95% CI)[a]			
	4-Fold Rise - % (95% CI)[b]			
Day 29	n			
	GMFR (95% CI)[a]			
	4-Fold Rise - % (95% CI)[b]			
Day 91	n			
	GMFR (95% CI)[a]			
	4-Fold Rise - % (95% CI)[b]			
Day 181	n			
	GMFR (95% CI)[a]			
	4-Fold Rise - % (95% CI)[b]			
Day 366	n			
	GMFR (95% CI)[a]			
	4-Fold Rise - % (95% CI)[b]			

Notes: N=Number of subjects in the mITT population.
n=Number of subjects with results available at time point.
GMFR=Geometric Mean Fold Rise, NE=Not Estimable.
[a] Confidence interval calculated based on the Student's t-distribution
[b] Exact binomial confidence interval calculated using the Clopper-Pearson methodology.

Tables with Similar Format:

Implementation notes:

For tables using the PP population, update footnote to read: "Notes: N=Number of subjects in the Per Protocol population."

Table 121: Focus Reduction Neutralization Test ID_{50} Geometric Mean Fold Rise and 4-Fold Rise Results by Time Point and Treatment Group, D614G – Per Protocol Population

Table 122: Focus Reduction Neutralization Test ID_{80} Geometric Mean Fold Rise and 4-Fold Rise Results by Time Point and Treatment Group, D614G – mITT Population

Table 123: Focus Reduction Neutralization Test ID_{80} Geometric Mean Fold Rise and 4-Fold Rise Results by Time Point and Treatment Group, D614G – Per Protocol Population

Table 124: Focus Reduction Neutralization Test ID_{50} Geometric Mean Fold Rise and 4-Fold Rise Results by Time Point and Treatment Group, B.1.351 – mITT Population

Table 125: Focus Reduction Neutralization Test ID_{50} Geometric Mean Fold Rise and 4-Fold Rise Results by Time Point and Treatment Group, B.1.351 – Per Protocol Population

Table 126: Focus Reduction Neutralization Test ID_{80} Geometric Mean Fold Rise and 4-Fold Rise Results by Time Point and Treatment Group, B.1.351 – mITT Population

Table 127: Focus Reduction Neutralization Test ID_{80} Geometric Mean Fold Rise and 4-Fold Rise Results by Time Point and Treatment Group, B.1.351 – Per Protocol Population

Table 128: Focus Reduction Neutralization Test ID_{50} Geometric Mean Fold Rise and 4-Fold Rise Results by Time Point and Treatment Group, B.1.617.2 – mITT Population

Table 129: Focus Reduction Neutralization Test ID_{50} Geometric Mean Fold Rise and 4-Fold Rise Results by Time Point and Treatment Group, B.1.617.2 – Per Protocol Population

Table 130: Focus Reduction Neutralization Test ID_{80} Geometric Mean Fold Rise and 4-Fold Rise Results by Time Point and Treatment Group, B.1.617.2 – mITT Population

Table 131: Focus Reduction Neutralization Test ID_{80} Geometric Mean Fold Rise and 4-Fold Rise Results by Time Point and Treatment Group, B.1.617.2 – Per Protocol Population

Table 132: Focus Reduction Neutralization Test ID_{50} Geometric Mean Fold Rise and 4-Fold Rise Results by Time Point and Treatment Group, P.1 – mITT Population

Table 140: Pseudovirus Neutralization Assay ID_{50} Geometric Mean Ratio to D614G Variant with 95% Confidence Intervals by Variant, Time Point, and Treatment Group – mITT Population

Variant	Planned Time Point	Statistic	50 µg mRNA-1273.351 (N=X)	25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)	All Subjects (N=X)
B.1.351	**Day 1, Pre-Booster Dose**	n			
		GMR			
		95% CI			
	Day 8	n			
		GMR			
		95% CI			
	Day 15	n			
		GMR			
		95% CI			
	Day 29	n			
		GMR			
		95% CI			
	Day 91	n			
		GMR			
		95% CI			
	Day 181	n			
		GMR			
		95% CI			
	Day 366	n			

Variant	Planned Time Point	Statistic	50 µg mRNA-1273.351 (N=X)	25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)	All Subjects (N=X)
		GMR			
		95% CI			
B.1.617.2	**Day 1, Pre-Booster Dose**	n			
		GMR			
		95% CI			
	Day 15	n			
		GMR			
		95% CI			
	Day 29	n			
		GMR			
		95% CI			
	Day 91	n			
		GMR			
		95% CI			
	Day 181	n			
		GMR			
		95% CI			
	Day 366	n			
		GMR			
		95% CI			
P.1		n			

Variant	Planned Time Point	Statistic	50 µg mRNA-1273.351 (N=X)	25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)	All Subjects (N=X)
	Day 1, Pre-Booster Dose	GMR			
		95% CI			
	Day 15	n			
		GMR			
		95% CI			
	Day 29	n			
		GMR			
		95% CI			
	Day 91	n			
		GMR			
		95% CI			
	Day 181	n			
		GMR			
		95% CI			
	Day 366	n			
		GMR			
		95% CI			
B.1.1.7	**Day 1, Pre-Booster Dose**	n			
		GMR			
		95% CI			
	Day 15	n			

Variant	Planned Time Point	Statistic	50 µg mRNA-1273.351 (N=X)	25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)	All Subjects (N=X)
		GMR			
		95% CI			
	Day 29	n			
		GMR			
		95% CI			
	Day 91	n			
		GMR			
		95% CI			
	Day 181	n			
		GMR			
		95% CI			
	Day 366	n			
		GMR			
		95% CI			

Notes: N=Number of subjects in the mITT population.
n=Number of subjects with results available at time point.
GMR=Geometric Mean Ratio, NE=Not Estimable.
Geometric Mean Ratio was calculated by taking the ratio of the result for each variant divided by the result of the D614G variant for each subject and calculating the geometric mean.
Confidence interval calculated based on the Student's t-distribution

Tables with Similar Format:

Table 141: Pseudovirus Neutralization Assay ID_{50} Geometric Mean Ratio to D614G Variant with 95% Confidence Intervals by Variant, Time Point, and Treatment Group – Per Protocol Population

Table 142: Pseudovirus Neutralization Assay ID_{80} Geometric Mean Ratio to D614G Variant with 95% Confidence Intervals by Variant, Time Point, and Treatment Group – mITT Population

Table 143: Pseudovirus Neutralization Assay ID_{80} Geometric Mean Ratio to D614G Variant with 95% Confidence Intervals by Variant, Time Point, and Treatment Group – Per Protocol Population

Table 144: Focus Reduction Neutralization Test ID_{50} Geometric Mean Ratio to D614G Variant with 95% Confidence Intervals by Variant, Time Point, and Treatment Group – mITT Population

Variant	Planned Time Point	Statistic	50 µg mRNA-1273.351 (N=X)	25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)	All Subjects (N=X)
B.1.351	**Day 1, Pre-Booster Dose**	n			
		GMR			
		95% CI			
	Day 8	n			
		GMR			
		95% CI			
	Day 15	n			
		GMR			
		95% CI			
	Day 29	n			
		GMR			
		95% CI			
	Day 91	n			
		GMR			
		95% CI			
	Day 181	n			
		GMR			
		95% CI			
	Day 366	n			

Variant	Planned Time Point	Statistic	50 µg mRNA-1273.351 (N=X)	25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)	All Subjects (N=X)
		GMR			
		95% CI			
B.1.617.2	**Day 1, Pre-Booster Dose**	n			
		GMR			
		95% CI			
	Day 15	n			
		GMR			
		95% CI			
	Day 29	n			
		GMR			
		95% CI			
	Day 91	n			
		GMR			
		95% CI			
	Day 181	n			
		GMR			
		95% CI			
	Day 366	n			
		GMR			
		95% CI			
P.1		n			

Variant	Planned Time Point	Statistic	50 µg mRNA-1273.351 (N=X)	25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)	All Subjects (N=X)
	Day 1, Pre-Booster Dose	GMR			
		95% CI			
	Day 15	n			
		GMR			
		95% CI			
	Day 29	n			
		GMR			
		95% CI			
	Day 91	n			
		GMR			
		95% CI			
	Day 181	n			
		GMR			
		95% CI			
	Day 366	n			
		GMR			
		95% CI			
B.1.1.7	**Day 1, Pre-Booster Dose**	n			
		GMR			
		95% CI			
	Day 15	n			

Variant	Planned Time Point	Statistic	50 µg mRNA-1273.351 (N=X)	25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)	All Subjects (N=X)
		GMR			
		95% CI			
	Day 29	n			
		GMR			
		95% CI			
	Day 91	n			
		GMR			
		95% CI			
	Day 181	n			
		GMR			
		95% CI			
	Day 366	n			
		GMR			
		95% CI			

Notes: N=Number of subjects in the mITT population.
n=Number of subjects with results available at time point.
GMR=Geometric Mean Ratio, NE=Not Estimable.
Geometric Mean Ratio was calculated by taking the ratio of the result for each variant divided by the result of the D614G variant for each subject and calculating the geometric mean.
Confidence interval calculated based on the Student's t-distribution

Tables with Similar Format:

Table 145: Focus Reduction Neutralization Test ID_{50} Geometric Mean Ratio to D614G Variant with 95% Confidence Intervals by Variant, Time Point, and Treatment Group – Per Protocol Population

Table 146: Focus Reduction Neutralization Test ID_{80} Geometric Mean Ratio to D614G Variant with 95% Confidence Intervals by Variant, Time Point, and Treatment Group – mITT Population

Table 147: Focus Reduction Neutralization Test ID_{80} Geometric Mean Ratio to D614G Variant with 95% Confidence Intervals by Variant, Time Point, and Treatment Group – Per Protocol Population

14.3 Safety Data

14.3.1 Displays of Adverse Events

Table 148: Overall Summary of Adverse Events by Treatment Group - All Subjects

Subjects[a] with		50 µg mRNA-1273.351 (N=X)		25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)		All Subjects (N=X)	
Category 1	**Category 2**	**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						
	Unrelated						
At least one serious adverse event[b]	Any relationship						
	Related						
	Unrelated						
At least one adverse event leading to early termination[c]	NA						

Subjects[a] with		**50 µg mRNA-1273.351 (N=X)**		**25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)**		**All Subjects (N=X)**	
Category 1	**Category 2**	**n**	**%**	**n**	**%**	**n**	**%**
Any Vitals Signs Adverse Event	NA						
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 157.
[c]As reported on the Adverse Event eCRF.

Table 149: 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

Preferred Term	MedDRA System Organ Class	50 µg mRNA-1273.351 (N=X)			25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)			All Subjects (N=X)		
		n	%	Events	n	%	Events	n	%	Events
Serious Adverse Events										
All	All	x	x	x	x	x	x	x	x	x
PT1	SOC1	x	x	x	x	x	x	x	x	x
Etc.	Etc.									
Other (Non-serious) Adverse Events										
All	All	x	x	x	x	x	x	x	x	x
PT1	SOC1	x	x	x	x	x	x	x	x	x
Etc	Etc									

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

14.3.1.1 Solicited Adverse Events

Table 150: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity, and Treatment Group

		50 µg mRNA-1273.351 (N=X)		25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)		All Subjects (N=X)	
Symptom	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**
Any Symptom	**None**						
	Mild						
	Moderate						
	Severe						
Any Systemic Symptom	**None**						
	Mild						
	Moderate						
	Severe						
Arthralgia	**None**						
	Mild						
	Moderate						
	Severe						
Fatigue	**None**						
	Mild						
	Moderate						
	Severe						
Fever[a]	**None**						
	Mild						

		50 µg mRNA-1273.351 (N=X)		25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)		All Subjects (N=X)	
Symptom	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**
	Moderate						
	Severe						
Feverishness	**None**						
	Mild						
	Moderate						
	Severe						
Headache	**None**						
	Mild						
	Moderate						
	Severe						
Myalgia	**None**						
	Mild						
	Moderate						
	Severe						
Nausea	**None**						
	Mild						
	Moderate						
	Severe						
Any Local Symptom	**None**						
	Mild						

		50 µg mRNA-1273.351 (N=X)		25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)		All Subjects (N=X)	
Symptom	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**
	Moderate						
	Severe						
Erythema/Redness	**None**						
	Mild						
	Moderate						
	Severe						
Erythema/Redness Measurement (mm)	**None**						
	Mild						
	Moderate						
	Severe						
Induration/Swelling	**None**						
	Mild						
	Moderate						
	Severe						
Induration/Swelling Measurement (mm)	**None**						
	Mild						
	Moderate						
	Severe						
Pain	**None**						
	Mild						

		50 µg mRNA-1273.351 (N=X)		25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)		All Subjects (N=X)	
Symptom	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**
	Moderate						
	Severe						

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

Table 151: Summary of Solicited Events by Days Post Treatment, Symptom, and Treatment Group – 50 µg mRNA-1273.351

		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 Symptom	**None**																						
	Mild																						
	Moderate																						
	Severe																						
Any Systemic Symptom	**None**																						
	Mild																						
	Moderate																						
	Severe																						
Arthralgia	**None**																						
	Mild																						
	Moderate																						
	Severe																						
Fatigue	**None**																						
	Mild																						
	Moderate																						
	Severe																						
Fever	**None**																						
	Mild																						
	Moderate																						
	Severe																						
Feverishness	**None**																						

		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**	**%**
	Mild																						
	Moderate																						
	Severe																						
Headache	**None**																						
	Mild																						
	Moderate																						
	Severe																						
Myalgia	**None**																						
	Mild																						
	Moderate																						
	Severe																						
Nausea	**None**																						
	Mild																						
	Moderate																						
	Severe																						
Any Local Symptom	**None**																						
	Mild																						
	Moderate																						
	Severe																						
Erythema/Redness	**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																						
Erythema/Redness Measurement (mm)	**None**																						
	Mild																						
	Moderate																						
	Severe																						
Induration/Swelling	**None**																						
	Mild																						
	Moderate																						
	Severe																						
Induration/Swelling Measurement (mm)	**None**																						
	Mild																						
	Moderate																						
	Severe																						
Pain	**None**																						
	Mild																						
	Moderate																						
	Severe																						

Notes: N=Number of subjects in the Safety Population.
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", or "Severe" as their maximum severity for any day. A subject may be counted in more than one of these categories.

Table with Similar Format:

Implementation note: For any symptoms or days with missing data, add a "Not Reported" row.

Table 152: Summary of Solicited Events by Days Post Treatment, Symptom, and Treatment Group – 25 µg mRNA-1273 + 25 µg mRNA-1273.351

Table 153: Summary of Duration of Solicited Symptoms by Treatment Group - All Subjects

Variable	Statistic	50 µg mRNA-1273.351 (N=X)	25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)	All Subjects (N=X)
Any Symptom	n			
	Mean			
	Standard Deviation			
	Median			
	Minimum			
	Maximum			
Any Systemic Symptom	n			
	Mean			
	Standard Deviation			
	Median			
	Minimum			
	Maximum			
Arthralgia	n			
	Mean			
	Standard Deviation			
	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			
Headache	n			
	Mean			
	Standard Deviation			
	Median			
	Minimum			
	Maximum			
Myalgia	n			
	Mean			
	Standard Deviation			

	Median			
	Minimum			
	Maximum			
Nausea	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			
	Mean			
	Standard Deviation			
	Median			

	Minimum			
	Maximum			
Pain	n			
	Mean			
	Standard Deviation			
	Median			
	Minimum			
	Maximum			
Notes: N=Number of subjects in the Safety Population. n=Number of solicited adverse events.				

14.3.1.2 Unsolicited Adverse Events

Table 154: All Adverse Events Cross-Classified by MedDRA System Organ Class, Severity, Relationship to Study Treatment, and Treatment Group

			Relationship to Vaccination		
Treatment Group	**MedDRA System Organ Class**	**Severity**	**Not Related (n)**	**Related (n)**	**Not Yet Determined (n)**
50 µg mRNA-1273.351 (N=X)	Any SOC	Mild			
		Moderate			
		Severe			
	[Repeat for all reported SOC]	Mild			
		Moderate			
		Severe			
25 µg mRNA-1273 + 25 µg mRNA-1273.351 (N=X)	Any SOC	Mild			
		Moderate			
		Severe			
	[Repeat for all reported SOC]	Mild			
		Moderate			
		Severe			
All Subjects (N=X)	Any SOC	Mild			
		Moderate			
		Severe			
	[Repeat for all reported SOC]	Mild			
		Moderate			
		Severe			

			Relationship to Vaccination		
Treatment Group	**MedDRA System Organ Class**	**Severity**	**Not Related (n)**	**Related (n)**	**Not Yet Determined (n)**
Notes: N=Number of subjects in the Safety Population. n=Number of events.					

Table 155: Summary of All Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Severity, Relationship, and Treatment Group

				Severity			Relationship to Study Vaccination		
Treatment Group	**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)**
50 µg mRNA-1273 (N=X)	Any SOC	Any PT							
	Gastrointestinal disorders	Any PT							
		Flatulence							
		Vomiting							
	[Repeat for all reported SOC]	Any PT							
		[Repeat for all reported PT]							
25 µg mRNA-1273 + 25 µg mRNA-1273.351 (N=X)	Any SOC	Any PT							
	[Repeat for all reported SOC]	Any PT							
		[Repeat for all reported PT]							
All Subjects (N=X)	Any SOC	Any PT							
	[Repeat for all reported SOC]	Any PT							
		[Repeat for all reported PT]							

Notes: N=Number of subjects in the Safety Population.
n=Number of events.

Table 156: Number and Percentage of Subjects Experiencing Unsolicited Adverse Events by MedDRA® System Organ Class and Preferred Term, Severity, Relationship, and Treatment Group

					Severity						Relationship to Study Vaccination			
			Any Incidence		Mild		Moderate		Severe		Not Related		Related	
Treatment Group	**MedDRA System Organ Class**	**MedDRA Preferred Term**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
50 µg mRNA-1273.351 (N=X)	Any SOC	Any PT												
	[Repeat for all reported SOC]	Any PT												
		[Repeat for all reported PT]												
25 µg mRNA-1273 + 25 µg mRNA-1273.351 (N=X)	Any SOC	Any PT												
	[Repeat for all reported SOC]	Any PT												
		[Repeat for all reported PT]												
All Subjects (N=X)	Any SOC	Any PT												
	[Repeat for all reported SOC]	Any PT												
		[Repeat for all reported PT]												

Note: N=Number of subjects in the Safety Population.
n=Number of subjects reporting event with the specified SOC.
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.

14.3.2 Listing of Deaths, Other Serious and Significant Adverse Events

Table 157: Listing of Serious Adverse Events

Adverse Event	No. of Days Post Associated Dose (Duration)	No. of Days Post Dose the Event Became Serious	Reason Reported as an SAE	Severity	Relationship to Study Treatment	If Not Related, Alternative Etiology	Action Taken with Study Treatment	Subject Discontinued Due to AE	Outcome	MedDRA System Organ Class	MedDRA Preferred Term
Subject ID: , Treatment Group: , AE Number: , 20-0003 Cohort:											
Comments:											
Subject ID: , Treatment Group: , AE Number: , 20-0003 Cohort:											
Comments:											

Table 158: Listing of Non-Serious, Unsolicited, Moderate or Severe Adverse Events

Adverse Event	No. of Days Post 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: , 20-0003 Cohort:										
Comments:										
Treatment Group: , Dose #: :, Subject ID, AE Number: , 20-0003 Cohort:										
Comments:										

Table 159: Listing of MAAEs and NOCMCs

Subject ID	Treatment Group	Event Description	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)

14.3.6 Displays of Vital Signs

Table 160: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group, Any Assessment – All Subjects

		50 µg mRNA-1273.351 (N=X)		25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)		All Subjects (N=X)	
Time Point	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**
Baseline	**None**						
	Mild						
	Moderate						
	Severe						
Day 15	**None**						
	Mild						
	Moderate						
	Severe						
Day 29	**None**						
	Mild						
	Moderate						
	Severe						
Day 91	**None**						
	Mild						
	Moderate						
	Severe						
Day 181	**None**						
	Mild						

		50 µg mRNA-1273.351 (N=X)		25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)		All Subjects (N=X)	
Time Point	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**
	Moderate						
	Severe						
Day 366	**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 161: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group, Systolic Blood Pressure – All Subjects

Table 162: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group, Diastolic Blood Pressure – All Subjects

Table 163: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group, Pulse Rate – All Subjects

Table 164: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group, Temperature – All Subjects

14.4 Summary of Concomitant Medications

Table 165: Number and Percentage of Subjects with Prior and Concurrent Medications by WHO Drug Classification and Treatment Group – All Subjects

[Implementation Note: Table below contains example medications.]

		50 µg mRNA-1273.351 (N=X)		25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)		All Subjects (N=X)	
WHO Drug Code Level 1, Anatomic Group	**WHO Drug Code Level 2, Therapeutic Group**	**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						

		50 µg mRNA-1273.351 (N=X)		25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)		All Subjects (N=X)	
WHO Drug Code Level 1, Anatomic Group	**WHO Drug Code Level 2, Therapeutic Group**	**n**	**%**	**n**	**%**	**n**	**%**
	Vitamins						
Antiinfectives For Systemic Use	**Any Level 2 Codes**						
	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						

		50 µg mRNA-1273.351 (N=X)		25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)		All Subjects (N=X)	
WHO Drug Code Level 1, Anatomic Group	**WHO Drug Code Level 2, Therapeutic Group**	**n**	**%**	**n**	**%**	**n**	**%**
	Cardiac Therapy						
	Diuretics						
	Lipid Modifying Agents						
	Vasoprotectives						
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						

		50 µg mRNA-1273.351 (N=X)		25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)		All Subjects (N=X)	
WHO Drug Code Level 1, Anatomic Group	**WHO Drug Code Level 2, Therapeutic Group**	**n**	**%**	**n**	**%**	**n**	**%**
Genito Urinary System And Sex Hormones	**Any Level 2 Codes**						
	Gynecological Antiinfectives And Antiseptics						
	Other Gynecologicals						
	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						

		50 µg mRNA-1273.351 (N=X)		25 µg mRNA -1273 + 25 µg mRNA -1273.351 (N=X)		All Subjects (N=X)	
WHO Drug Code Level 1, Anatomic Group	**WHO Drug Code Level 2, Therapeutic Group**	**n**	**%**	**n**	**%**	**n**	**%**
	Psychoanaleptics						
	Psycholeptics						
Respiratory System	**Any Level 2 Codes**						
	Antihistamines For Systemic Use						
	Cough And Cold Preparations						
	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						

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

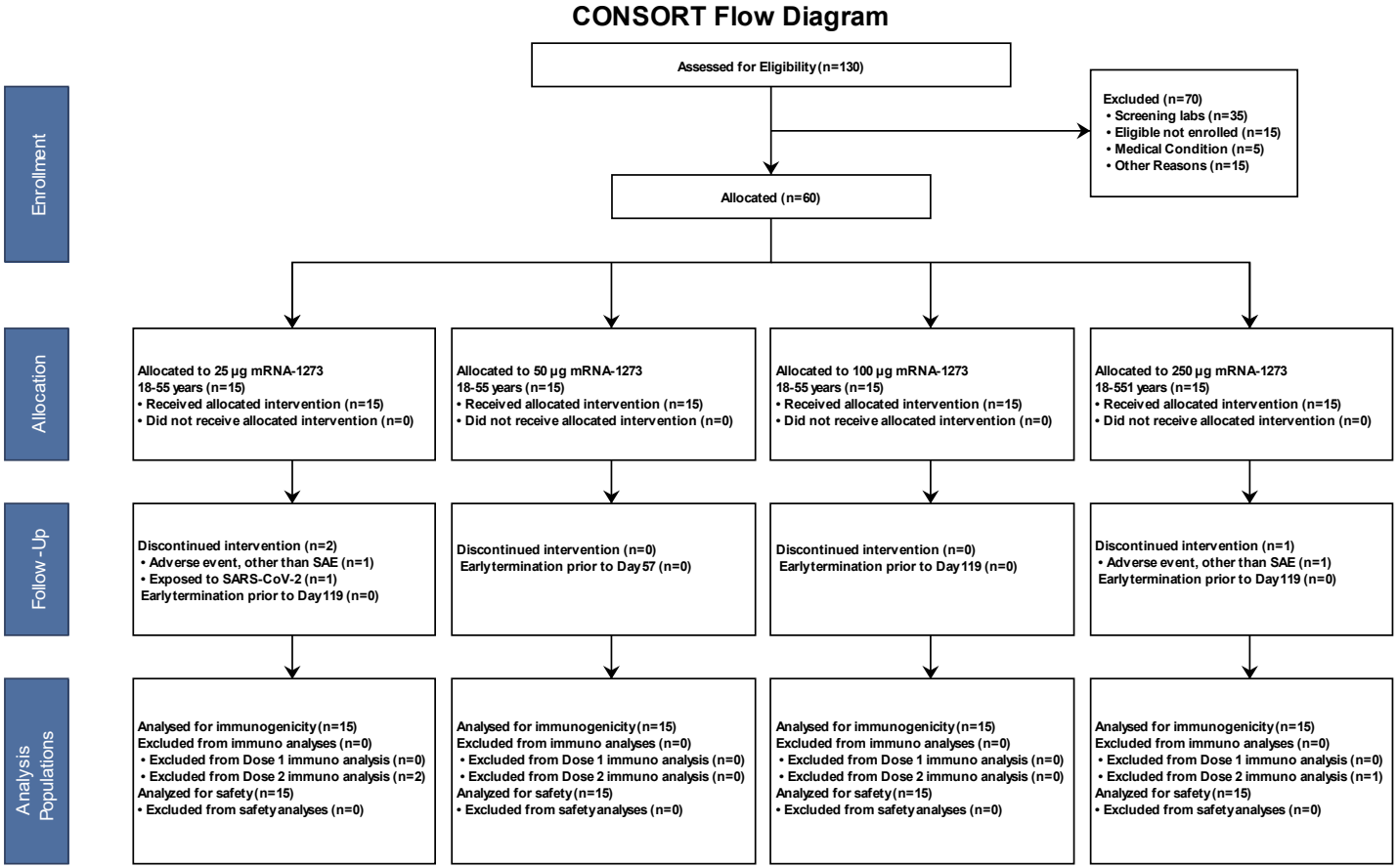
APPENDIX 2. FIGURE MOCK-UPS

LIST OF FIGURES

10.1 Disposition of Subjects

Figure 1: CONSORT Flow Diagram

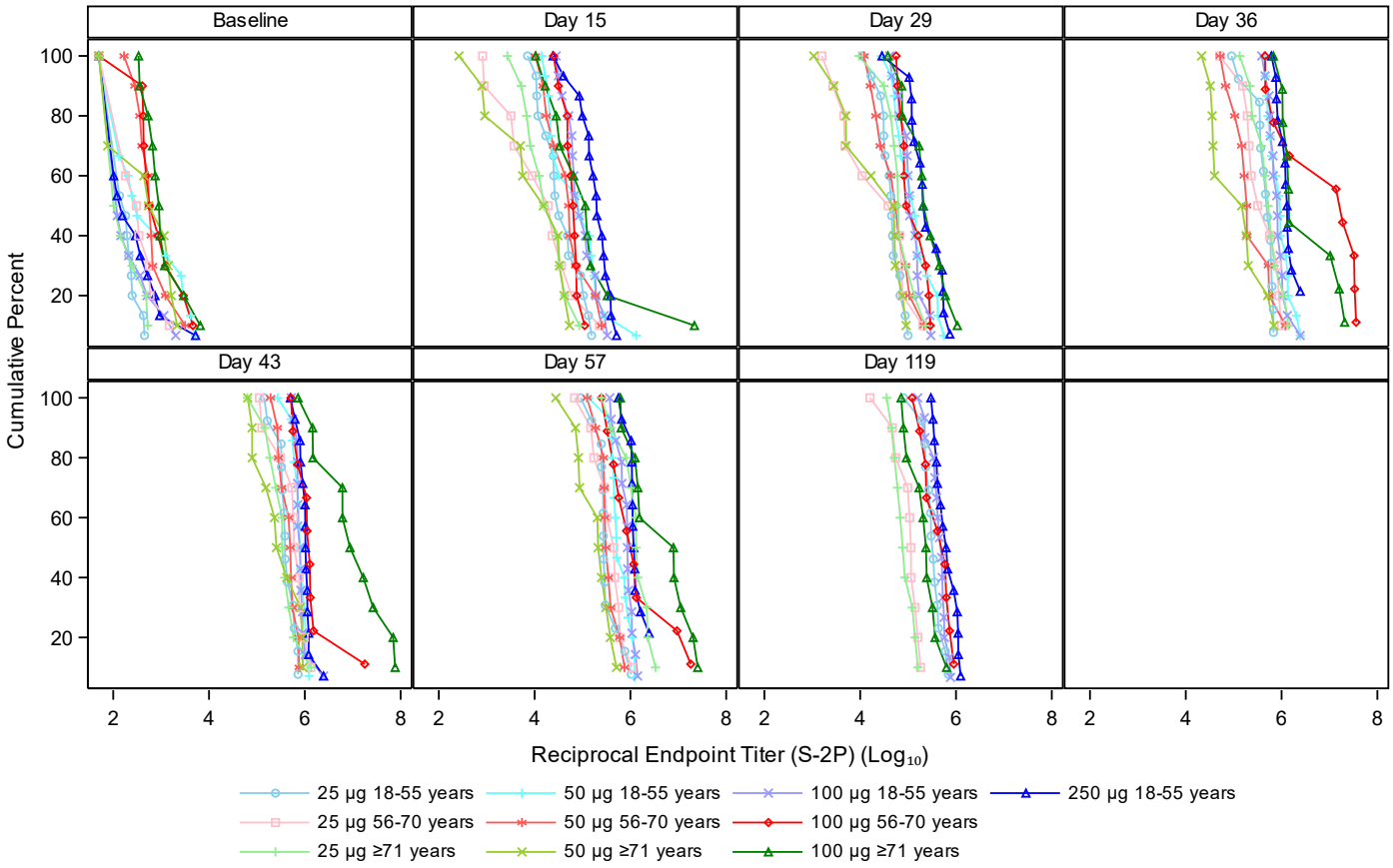
[Implementation Note: Below is an example CONSORT diagram. The final CONSORT will include the two cohort 1 groups.]



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

Figure 2: Reverse Cumulative Distribution of Serum IgG ECLIA Arbitrary Units/mL by Time Point and Treatment Group - S-2P–Wa-1, mITT Population

[Implementation Note: Below is an example figure. Lines will only be shown for the two cohort 1 groups.]



Figures with Similar Format:

Figure 3: Reverse Cumulative Distribution of Serum IgG ECLIA Arbitrary Units/mL by Time Point and Treatment Group – S-2P–Wa-1, Per Protocol Population

Figure 4: Reverse Cumulative Distribution of Serum IgG ECLIA Arbitrary Units/mL by Time Point and Treatment Group – RBD–Wa-1, mITT Population

Figure 5: Reverse Cumulative Distribution of Serum IgG ECLIA Arbitrary Units/mL by Time Point and Treatment Group – RBD–Wa-1, Per Protocol Population

Figure 6: Reverse Cumulative Distribution of Serum IgG ECLIAv2 Arbitrary Units/mL by Time Point and Treatment Group – S-2P–Wa-1, mITT Population

Figure 7: Reverse Cumulative Distribution of Serum IgG ECLIAv2 Arbitrary Units/mL by Time Point and Treatment Group – S-2P–Wa-1, Per Protocol Population

Figure 8: Reverse Cumulative Distribution of Serum IgG ECLIAv2 Arbitrary Units/mL by Time Point and Treatment Group – S-2P– B.1.351, mITT Population

Figure 9: Reverse Cumulative Distribution of Serum IgG ECLIAv2 Arbitrary Units/mL by Time Point and Treatment Group – RBD– B.1.351, Per Protocol Population

Figure 10: Reverse Cumulative Distribution of Serum IgG ECLIAv2 Arbitrary Units/mL by Time Point and Treatment Group – RBD– B.1.351, mITT Population

Figure 11: Reverse Cumulative Distribution of Serum IgG ECLIAv2 Arbitrary Units/mL by Time Point and Treatment Group – S-2P– B.1.351, Per Protocol Population

Figure 12: Reverse Cumulative Distribution of Serum IgG ECLIAv2 International Units by Time Point and Treatment Group – S-2P–Wa-1, mITT Population

Figure 13: Reverse Cumulative Distribution of Serum IgG ECLIAv2 International Units by Time Point and Treatment Group – S-2P–Wa-1, Per Protocol Population

Figure 14: Reverse Cumulative Distribution of Serum IgG ECLIAv2 Area Under the Curve by Time Point and Treatment Group – S-2P–Wa-1, mITT Population

Figure 15: Reverse Cumulative Distribution of Serum IgG ECLIAv2 Area Under the Curve by Time Point and Treatment Group – S-2P–Wa-1, Per Protocol Population

Figure 16: Reverse Cumulative Distribution of Serum IgG ECLIAv2 Area Under the Curve by Time Point and Treatment Group – S-2P–B.1.351, mITT Population

Figure 17: Reverse Cumulative Distribution of Serum IgG ECLIAv2 Area Under the Curve by Time Point and Treatment Group – S-2P–B.1.351, Per Protocol Population

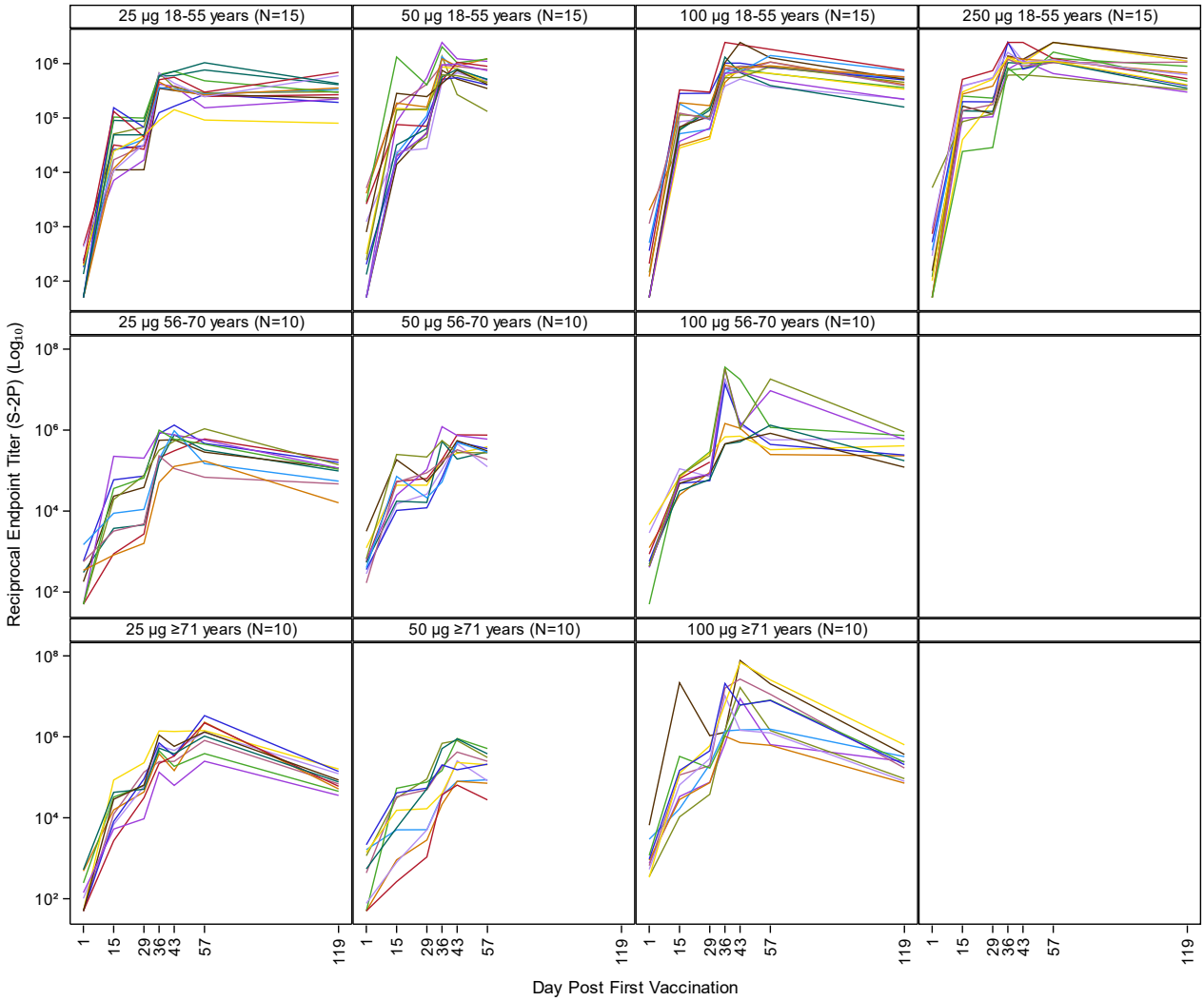
Figure 18: Reverse Cumulative Distribution of Serum IgG ECLIAv2 Area Under the Curve by Time Point and Treatment Group – S-2P–B.1.617.2, mITT Population

Figure 19: Reverse Cumulative Distribution of Serum IgG ECLIAv2 Area Under the Curve by Time Point and Treatment Group – S-2P–B.1.617.2, Per Protocol Population

Figure 20: Reverse Cumulative Distribution of Serum IgG ECLIAv2 Area Under the Curve by Time Point and Treatment Group – S-2P–P.1, mITT Population

Figure 24: Serum IgG ECLIA Arbitrary Units/mL by Time Point and Treatment Group – S-2P–Wa-1, mITT Population

[Implementation Note: Below is an example figure. Panels will only be shown for the two cohort 1 groups.]



Implementation note: y-axis label should read "Arbitrary Units/mL (S-2P-Wa-1) (log_{10})" and x-axis should read "Day Post Vaccination."

Figures with Similar Format:

Figure 25: Serum IgG ECLIA Arbitrary Units/mL by Time Point and Treatment Group – S-2P–Wa-1, Per Protocol Population

Figure 26: Serum IgG ECLIA Arbitrary Units/mL by Time Point and Treatment Group – RBD–Wa-1, mITT Population

Figure 27: Serum IgG ECLIA Arbitrary Units/mL by Time Point and Treatment Group – RBD–Wa-1, Per Protocol Population

Figure 28: Serum IgG ECLIAv2 Arbitrary Units/mL by Time Point and Treatment Group – S-2P–Wa-1, mITT Population

Figure 29: Serum IgG ECLIAv2 Arbitrary Units/mL by Time Point and Treatment Group – S-2P–Wa-1, Per Protocol Population

Figure 30: Serum IgG ECLIAv2 Arbitrary Units/mL by Time Point and Treatment Group – S-2P–B.1.351, mITT Population

Figure 31: Serum IgG ECLIAv2 Arbitrary Units/mL by Time Point and Treatment Group – S-2P–B.1.351, Per Protocol Population

Figure 32: Serum IgG ECLIAv2 Arbitrary Units/mL by Time Point and Treatment Group – RBD–B.1.351, mITT Population

Figure 33: Serum IgG ECLIAv2 Arbitrary Units/mL by Time Point and Treatment Group – RBD–B.1.351, Per Protocol Population

Figure 34: Serum IgG ECLIAv2 International Units by Time Point and Treatment Group – S-2P–Wa-1, mITT Population

Figure 35: Serum IgG ECLIAv2 International Units by Time Point and Treatment Group – S-2P–Wa-1, Per Protocol Population

Figure 36: Serum IgG ECLIAv2 Area Under the Curve by Time Point and Treatment Group – S-2P–Wa-1, mITT Population

Figure 37: Serum IgG ECLIAv2 Area Under the Curve by Time Point and Treatment Group – S-2P–Wa-1, Per Protocol Population

Figure 38: Serum IgG ECLIAv2 Area Under the Curve by Time Point and Treatment Group – S-2P– B.1.351, mITT Population

Figure 39: Serum IgG ECLIAv2 Area Under the Curve by Time Point and Treatment Group – S-2P– B.1.351, Per Protocol Population

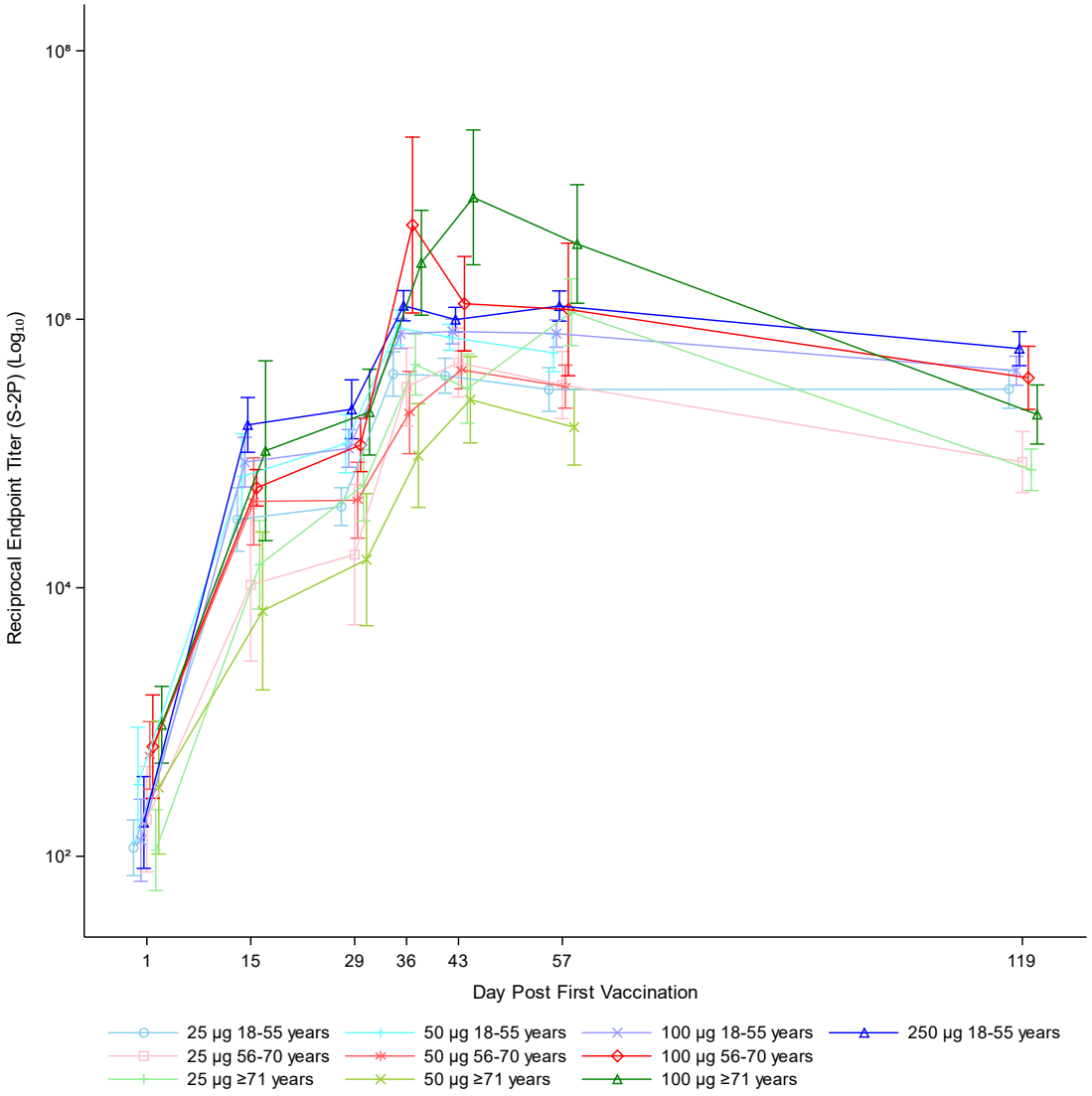
Figure 40: Serum IgG ECLIAv2 Area Under the Curve by Time Point and Treatment Group – S-2P– B.1.617.2, mITT Population

Figure 41: Serum IgG ECLIAv2 Area Under the Curve by Time Point and Treatment Group – S-2P– B.1.617.2, Per Protocol Population

Figure 42: Serum IgG ECLIAv2 Area Under the Curve by Time Point and Treatment Group – S-2P– P.1, mITT Population

Figure 46: Geometric Mean Serum IgG ECLIA Arbitrary Units/mL by Time Point and Treatment Group – S-2P–Wa-1, mITT Population

[Implementation Note: Below is an example figure. Lines will only be shown for the two cohort 1 groups.]



Figures with Similar Format:

Figure 47: Geometric Mean Serum IgG ECLIA Arbitrary Units/mL by Time Point and Treatment Group – S-2P–Wa-1, Per Protocol Population

Figure 48: Geometric Mean Serum IgG ECLIA Arbitrary Units/mL by Time Point and Treatment Group – RBD–Wa-1, mITT Population

Figure 49: Geometric Mean Serum IgG ECLIA Arbitrary Units/mL by Time Point and Treatment Group – RBD–Wa-1, Per Protocol Population

Figure 50: Geometric Mean Serum IgG ECLIAv2 Arbitrary Units/mL by Time Point and Treatment Group – S-2P–Wa-1, mITT Population

Figure 51: Geometric Mean Serum IgG ECLIAv2 Arbitrary Units/mL by Time Point and Treatment Group – S-2P–Wa-1, Per Protocol Population

Figure 52: Geometric Mean Serum IgG ECLIAv2 Arbitrary Units/mL by Time Point and Treatment Group – S-2P– B.1.351, mITT Population

Figure 53: Geometric Mean Serum IgG ECLIAv2 Arbitrary Units/mL by Time Point and Treatment Group – S-2P– B.1.351, Per Protocol Population

Figure 54: Geometric Mean Serum IgG ECLIAv2 Arbitrary Units/mL by Time Point and Treatment Group – RBD– B.1.351, mITT Population

Figure 55: Geometric Mean Serum IgG ECLIAv2 Arbitrary Units/mL by Time Point and Treatment Group – RBD– B.1.351, Per Protocol Population

Figure 56: Geometric Mean Serum IgG ECLIAv2 International Units by Time Point and Treatment Group – S-2P–Wa-1, mITT Population

Figure 57: Geometric Mean Serum IgG ECLIAv2 International Units by Time Point and Treatment Group – S-2P–Wa-1, Per Protocol Population

Figure 58: Geometric Mean Serum IgG ECLIAv2 Area Under the Curve by Time Point and Treatment Group – S-2P–Wa-1, mITT Population

Figure 59: Geometric Mean Serum IgG ECLIAv2 Area Under the Curve by Time Point and Treatment Group – S-2P–Wa-1, Per Protocol Population

Figure 60: Geometric Mean Serum IgG ECLIAv2 Area Under the Curve by Time Point and Treatment Group – S-2P– B.1.351, mITT Population

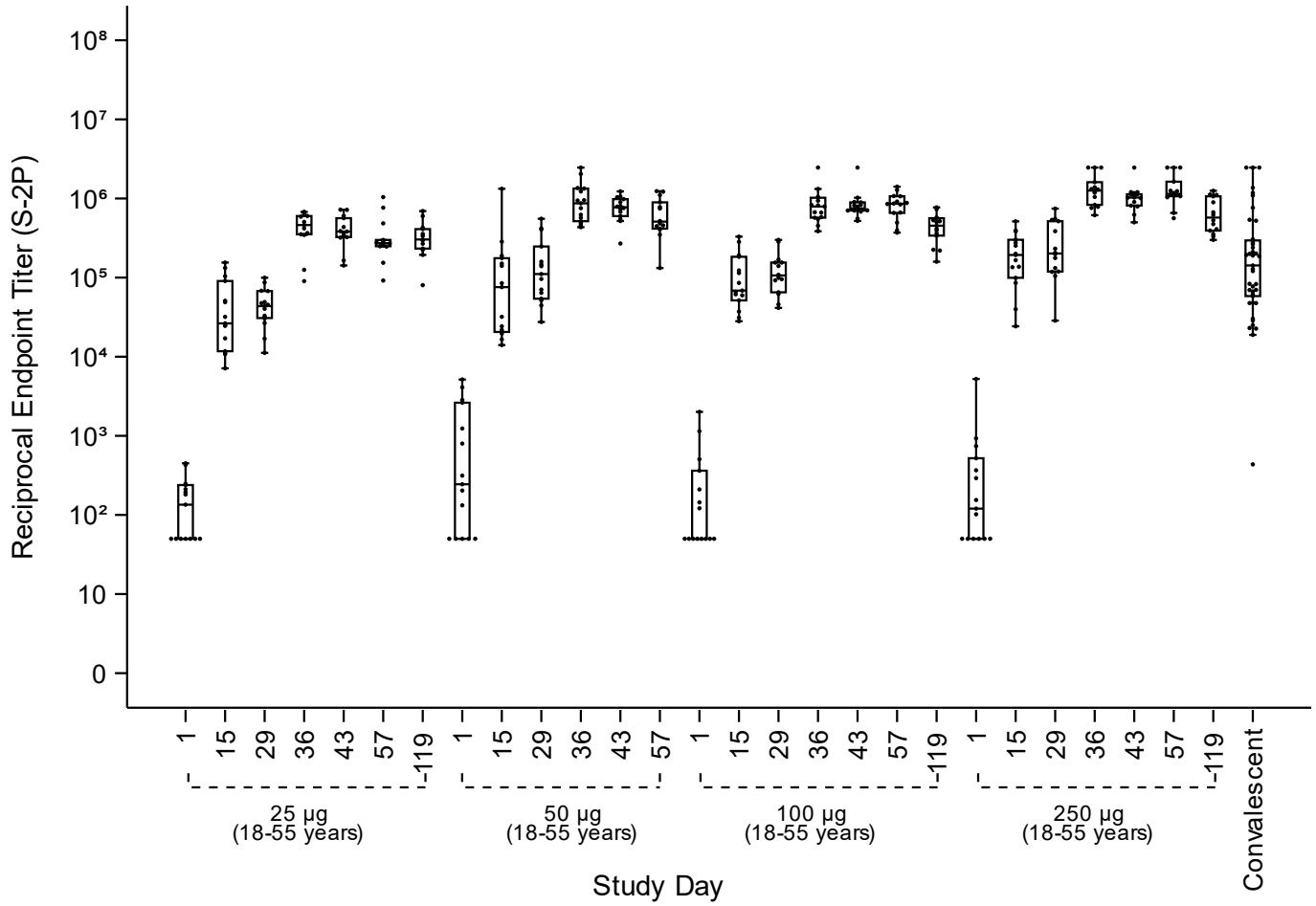
Figure 61: Geometric Mean Serum IgG ECLIAv2 Area Under the Curve by Time Point and Treatment Group – S-2P– B.1.351, Per Protocol Population

Figure 62: Geometric Mean Serum IgG ECLIAv2 Area Under the Curve by Time Point and Treatment Group – S-2P– B.1.617.2, mITT Population

Figure 63: Geometric Mean Serum IgG ECLIAv2 Area Under the Curve by Time Point and Treatment Group – S-2P– B.1.617.2, Per Protocol Population

Figure 64: Geometric Mean Serum IgG ECLIAv2 Area Under the Curve by Time Point and Treatment Group – S-2P– P.1, mITT Population

Figure 108: Distribution of Serum IgG ECLIA Arbitrary Units/mL by Time Point and Treatment Group – S-2P–Wa-1, mITT Population



Figures with Similar Format:

Figure 109: Distribution of Serum IgG ECLIA Arbitrary Units/mL by Time Point and Treatment Group – S-2P–Wa-1, Per Protocol Population

Figure 110: Distribution of Serum IgG ECLIA Arbitrary Units/mL by Time Point and Treatment Group – RBD–Wa-1, mITT Population

Figure 111: Distribution of Serum IgG ECLIA Arbitrary Units/mL by Time Point and Treatment Group – RBD–Wa-1, Per Protocol Population

Figure 112: Distribution of Serum IgG ECLIAv2 Arbitrary Units/mL by Time Point and Treatment Group – S-2P–Wa-1, mITT Population

Figure 113: Distribution of Serum IgG ECLIAv2 Arbitrary Units/mL by Time Point and Treatment Group – S-2P–Wa-1, Per Protocol Population

Figure 114: Distribution of Serum IgG ECLIAv2 Arbitrary Units/mL by Time Point and Treatment Group – S-2P– B.1.351, mITT Population

Figure 115: Distribution of Serum IgG ECLIAv2 Arbitrary Units/mL by Time Point and Treatment Group – S-2P–Wa-1, Per Protocol Population

Figure 116: Distribution of Serum IgG ECLIAv2 Arbitrary Units/mL by Time Point and Treatment Group – RBD– B.1.351, mITT Population

Figure 117: Distribution of Serum IgG ECLIAv2 Arbitrary Units/mL by Time Point and Treatment Group – RBD– B.1.351, Per Protocol Population

Figure 118: Distribution of Serum IgG ECLIAv2 International Units by Time Point and Treatment Group – S-2P–Wa-1, mITT Population

Figure 119: Distribution of Serum IgG ECLIAv2 International Units by Time Point and Treatment Group – S-2P–Wa-1, Per Protocol Population

Figure 120: Distribution of Serum IgG ECLIAv2 Area Under the Curve by Time Point and Treatment Group – S-2P–Wa-1, mITT Population

Figure 121: Distribution of Serum IgG ECLIAv2 Area Under the Curve by Time Point and Treatment Group – S-2P–Wa-1, Per Protocol Population

Figure 122: Distribution of Serum IgG ECLIAv2 Area Under the Curve by Time Point and Treatment Group – S-2P– B.1.351, mITT Population

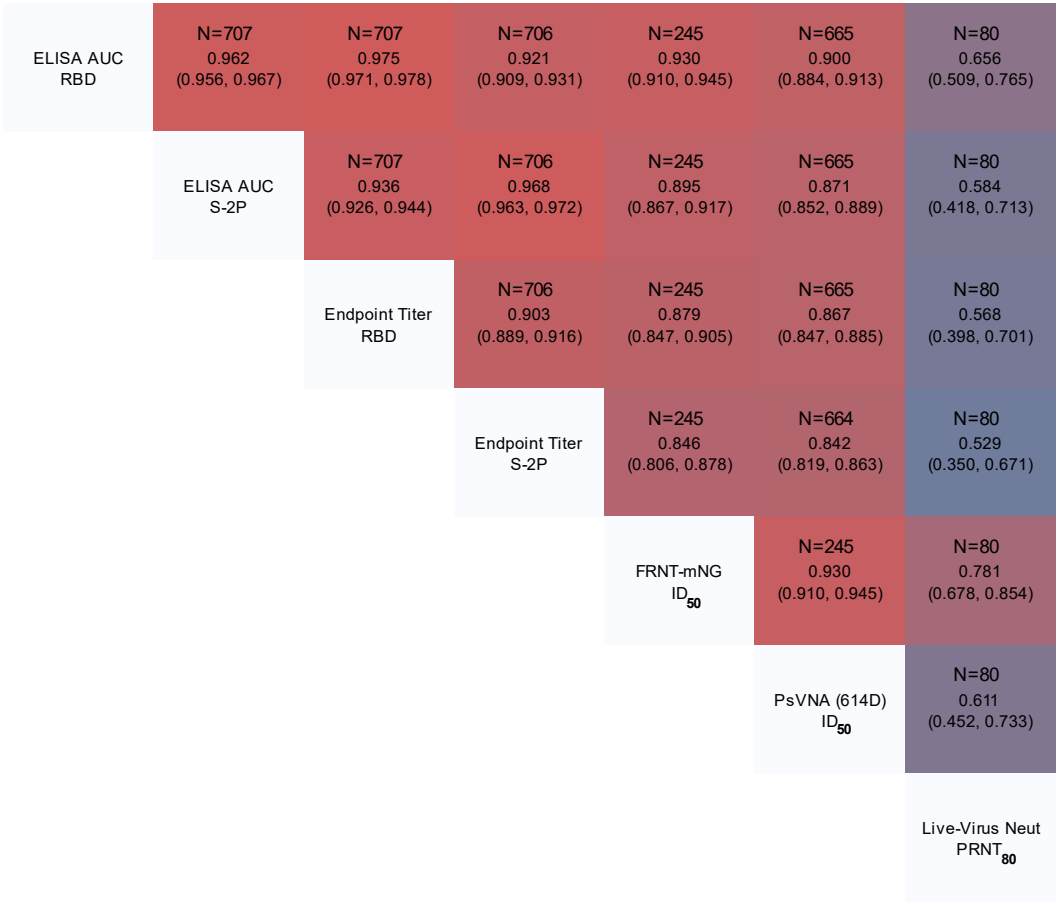
Figure 123: Distribution of Serum IgG ECLIAv2 Area Under the Curve by Time Point and Treatment Group – S-2P– B.1.351, Per Protocol Population

Figure 124: Distribution of Serum IgG ECLIAv2 Area Under the Curve by Time Point and Treatment Group – S-2P– B.1.617.2, mITT Population

Figure 125: Distribution of Serum IgG ECLIAv2 Area Under the Curve by Time Point and Treatment Group – S-2P– B.1.617.2, Per Protocol Population

Figure 126: Distribution of Serum IgG ECLIAv2 Area Under the Curve by Time Point and Treatment Group – S-2P– P.1, mITT Population

Figure 170: Correlation Heatmap, D614G – mITT Population



Figures with Similar Format:

Figure 171: Correlation Heatmap, D614G – Per Protocol Population

Figure 172: Correlation Heatmap, B.1.351 – mITT Population

Figure 173: Correlation Heatmap, B.1.351 – Per Protocol Population

Figure 174: Correlation Heatmap, B.1.617.2 – mITT Population

Figure 175: Correlation Heatmap, B.1.617.2 – Per Protocol Population

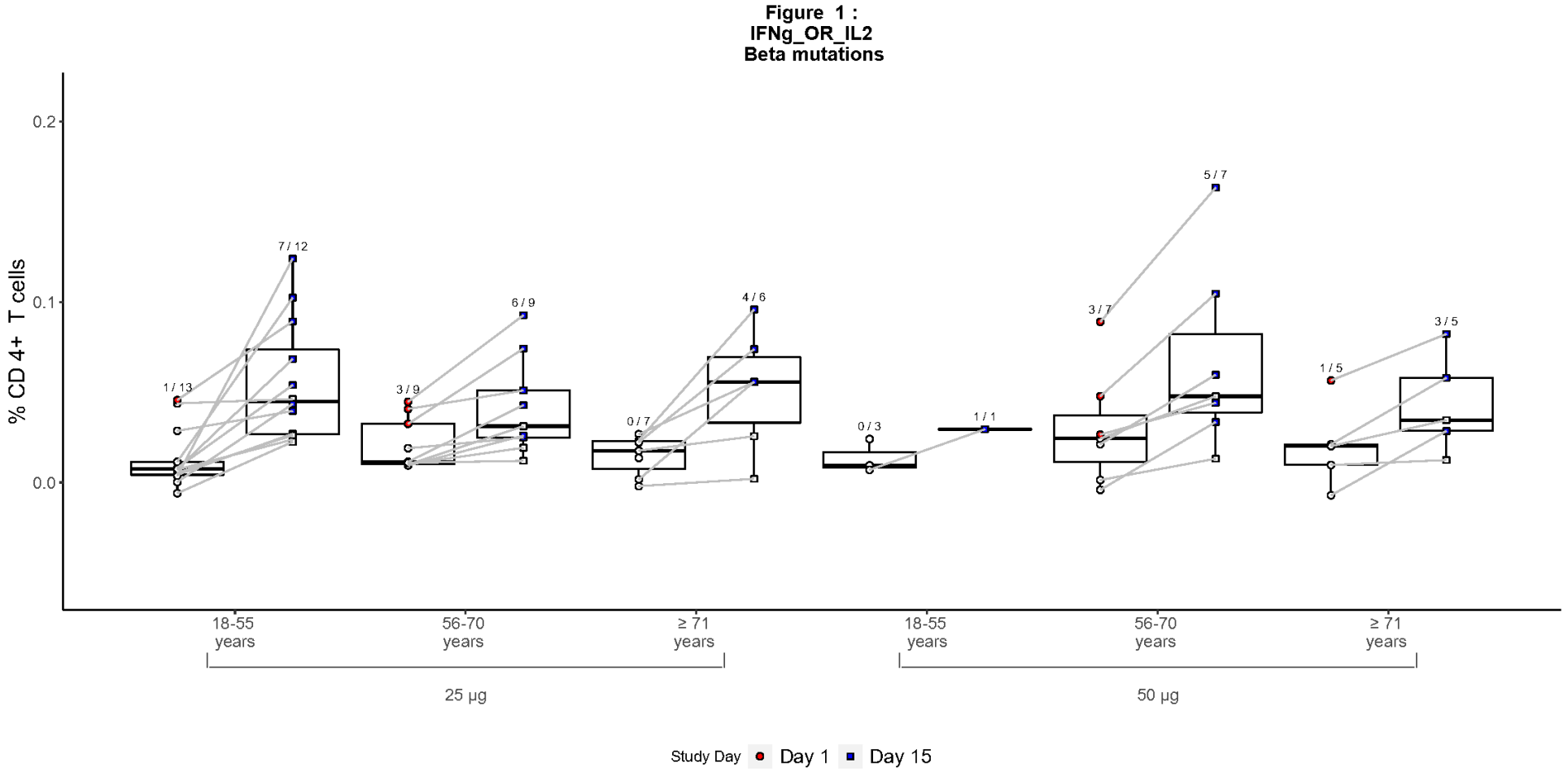
Figure 176: Correlation Heatmap, P.1 – mITT Population

Figure 177: Correlation Heatmap, P.1 – Per Protocol Population

Figure 178: Correlation Heatmap, B.1.1.7 – mITT Population

Figure 179: Correlation Heatmap, B.1.1.7 – Per Protocol Population

Figure 180: Percentages of CD4 T Cells Expressing IFNγ or IL-2, Beta Mutations

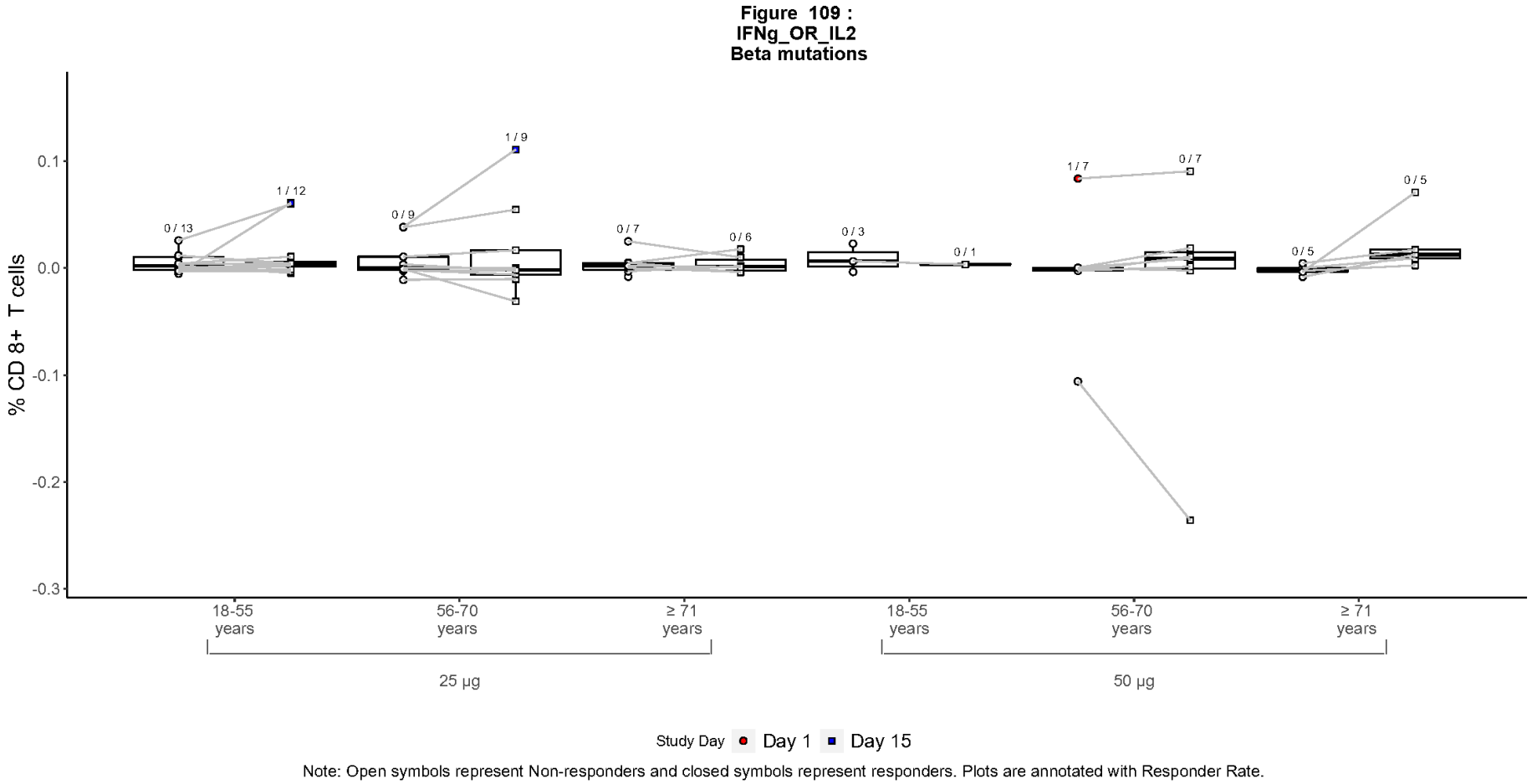


Note: Open symbols represent Non-responders and closed symbols represent responders. Plots are annotated with Responder Rate.

Implementation note: Please include all study groups and study time points.

Figures with Similar Format:

Figure 270: Percentages of CD8 T Cells Expressing IFNγ or IL-2, Beta Mutations



Note: Open symbols represent Non-responders and closed symbols represent responders. Plots are annotated with Responder Rate.

Implementation note: Do not include a graph for "Responder Rate" and please include all study groups and study time points.

Figures with Similar Format:

14.3.1.1 Solicited Adverse Events

Figure 300: Maximum Severity of Solicited Systemic Symptoms by Days Post Vaccination and Treatment Group

[Implementation Note: Panels will only be shown for the two Cohort 1 groups.]

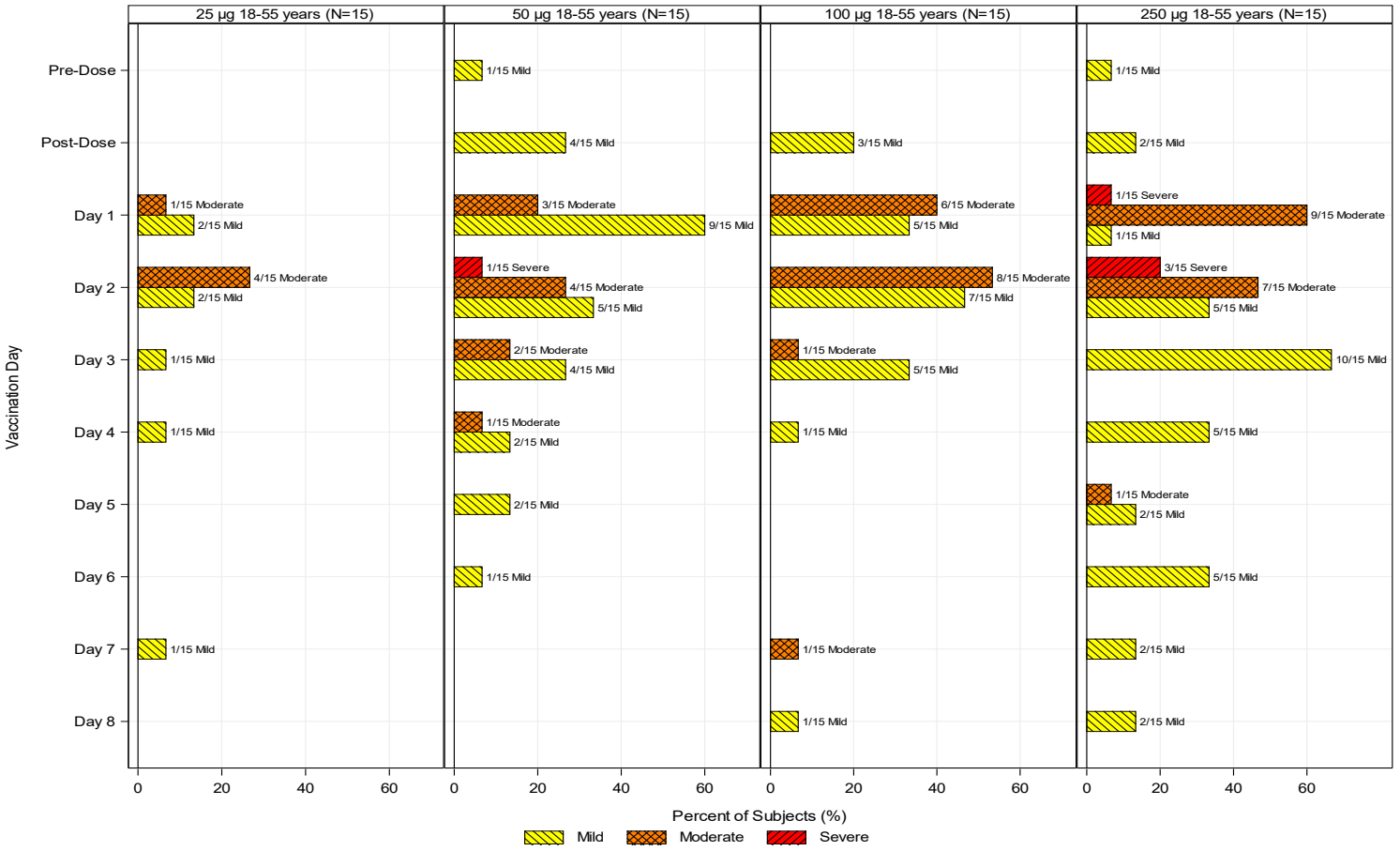


Figure 301: Maximum Severity of Solicited Local Symptoms by Days Post Vaccination and Treatment Group

[Implementation Note: Panels will only be shown for the two Cohort 1 groups.]

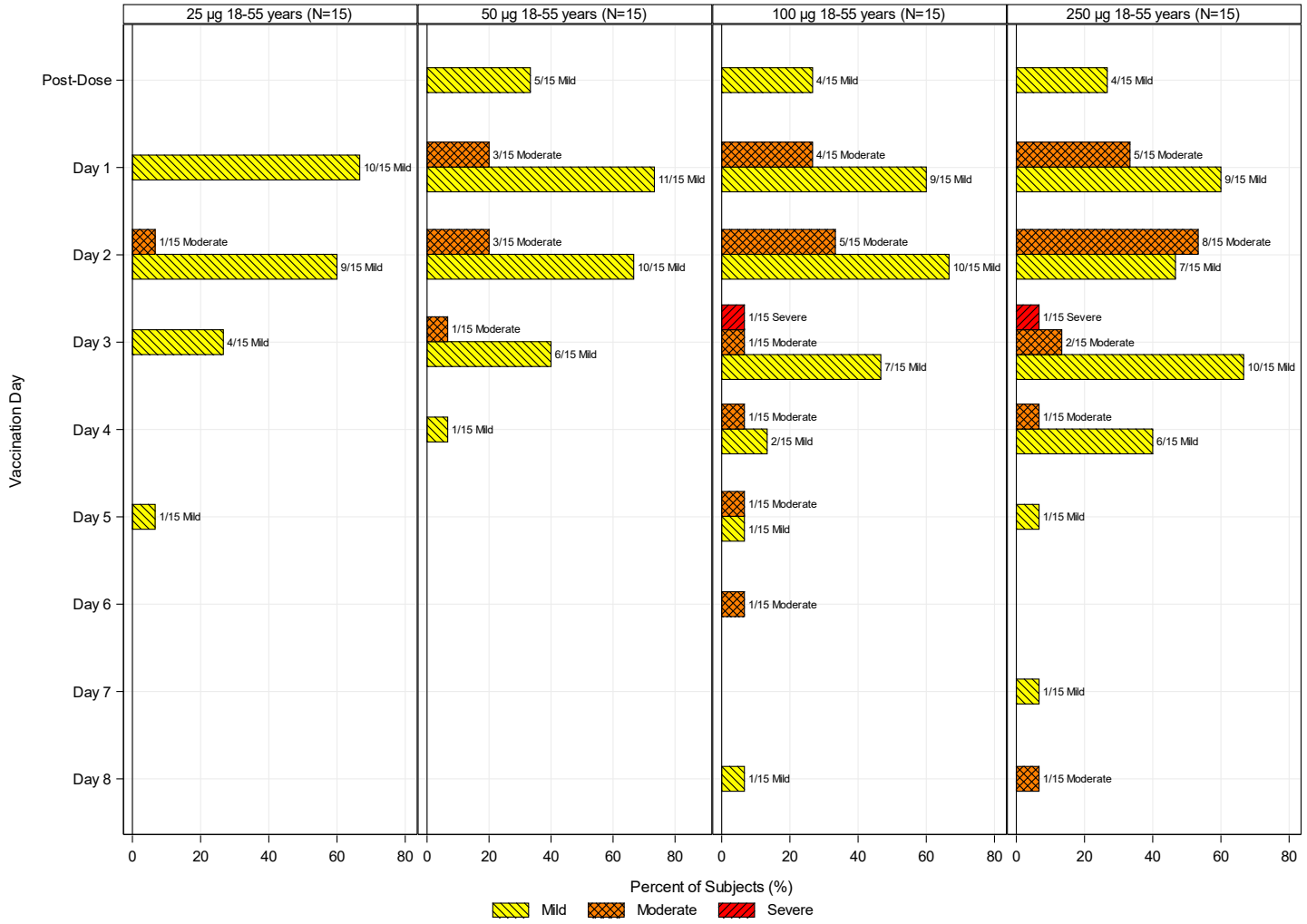


Figure 302: Onset of Solicited Systemic Symptoms by Days Post Vaccination and Treatment Group

[Implementation Note: Panels will only be shown for the two Cohort 1 groups.]

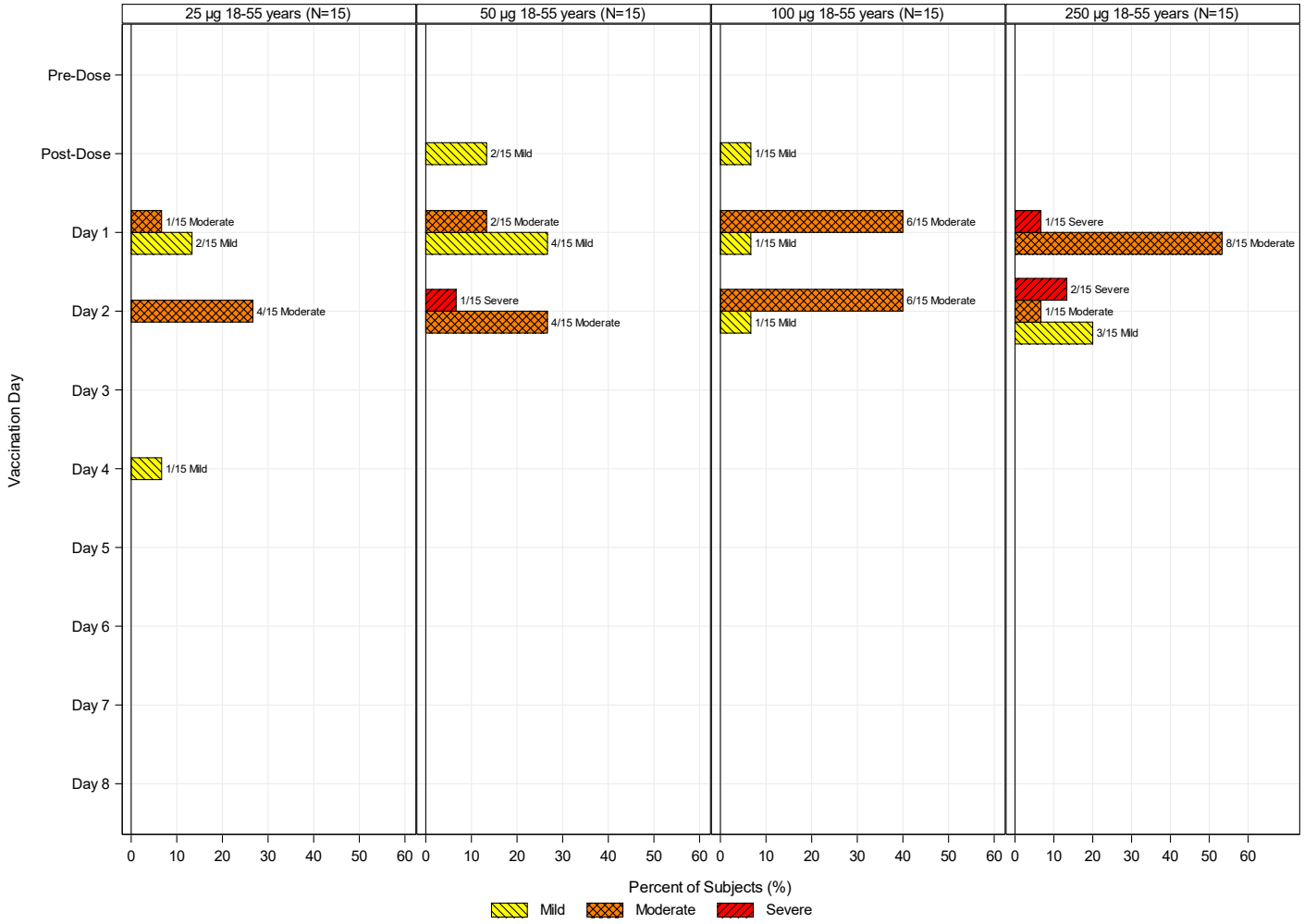


Figure with Similar Format:

Figure 303: Onset of Solicited Local Symptoms by Days Post Vaccination and Treatment Group

Figure 304: Solicited Symptoms by Days Post Vaccination and Treatment Group– Arthralgia

Implementation Note: Figure should be a single column with results from the third dose only.

Figures with Similar Format:

Figure 305: Solicited Symptoms by Days Post Vaccination and Treatment Group– Chills

Figure 306: Solicited Symptoms by Days Post Vaccination and Treatment Group– Erythema

Figure 307: Solicited Symptoms by Days Post Vaccination and Treatment Group– Erythema (mm)

Figure 308: Solicited Symptoms by Days Post Vaccination and Treatment Group– Fatigue

Figure 309: Solicited Symptoms by Days Post Vaccination and Treatment Group– Fever

Figure 310: Solicited Symptoms by Days Post Vaccination and Treatment Group– Headache

Figure 311: Solicited Symptoms by Days Post Vaccination and Treatment Group– Induration

Figure 312: Solicited Symptoms by Days Post Vaccination and Treatment Group– Induration (mm)

Figure 313: Solicited Symptoms by Days Post Vaccination and Treatment Group– Myalgia

Figure 314: Solicited Symptoms by Days Post Vaccination and Treatment Group– Nausea

Figure 315: Solicited Symptoms by Days Post Vaccination and Treatment Group– Pain

14.3.1.2 Unsolicited Adverse Events

Figure 316: Frequency of Adverse Events by MedDRA System Organ Class and Severity

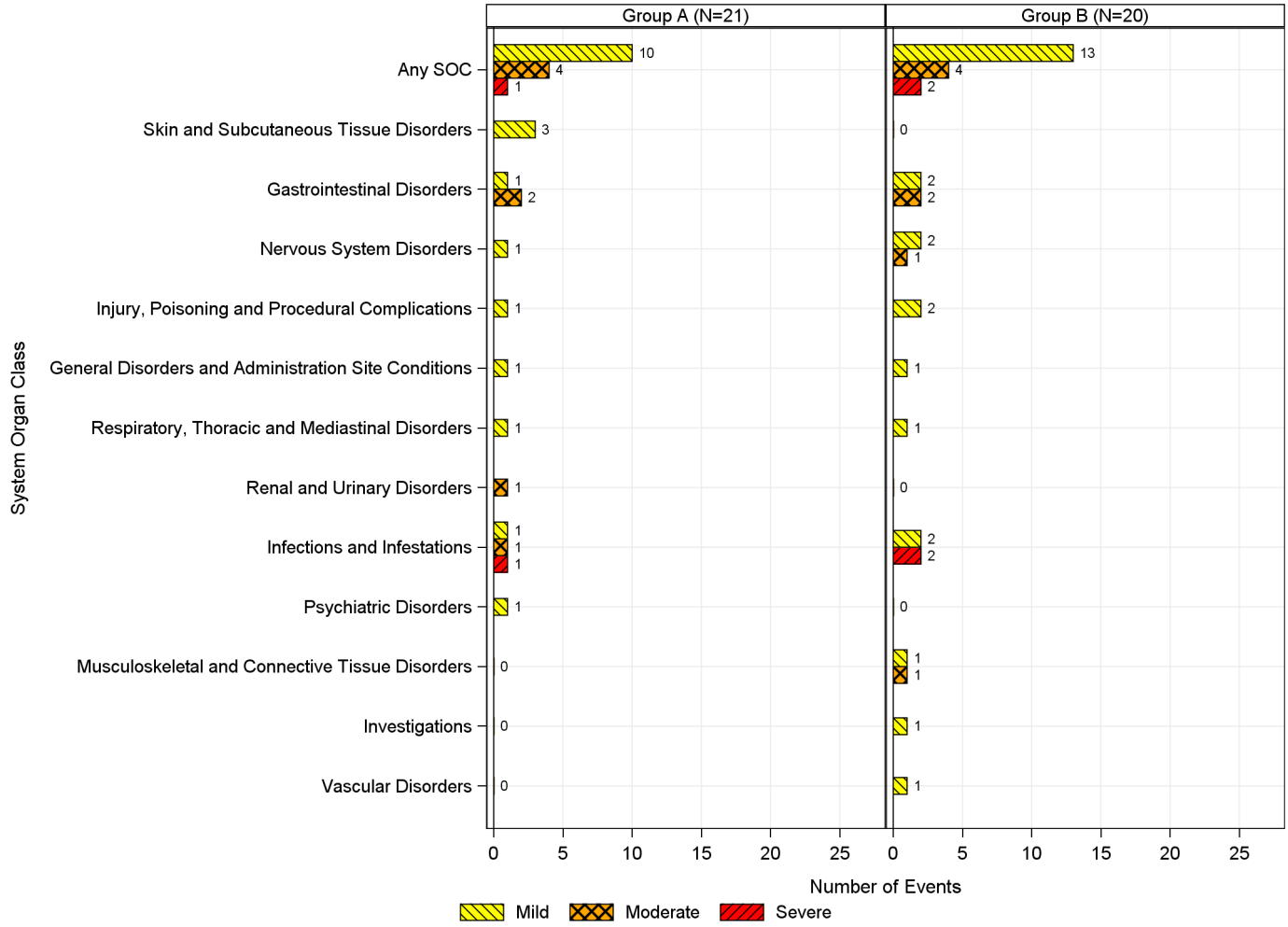
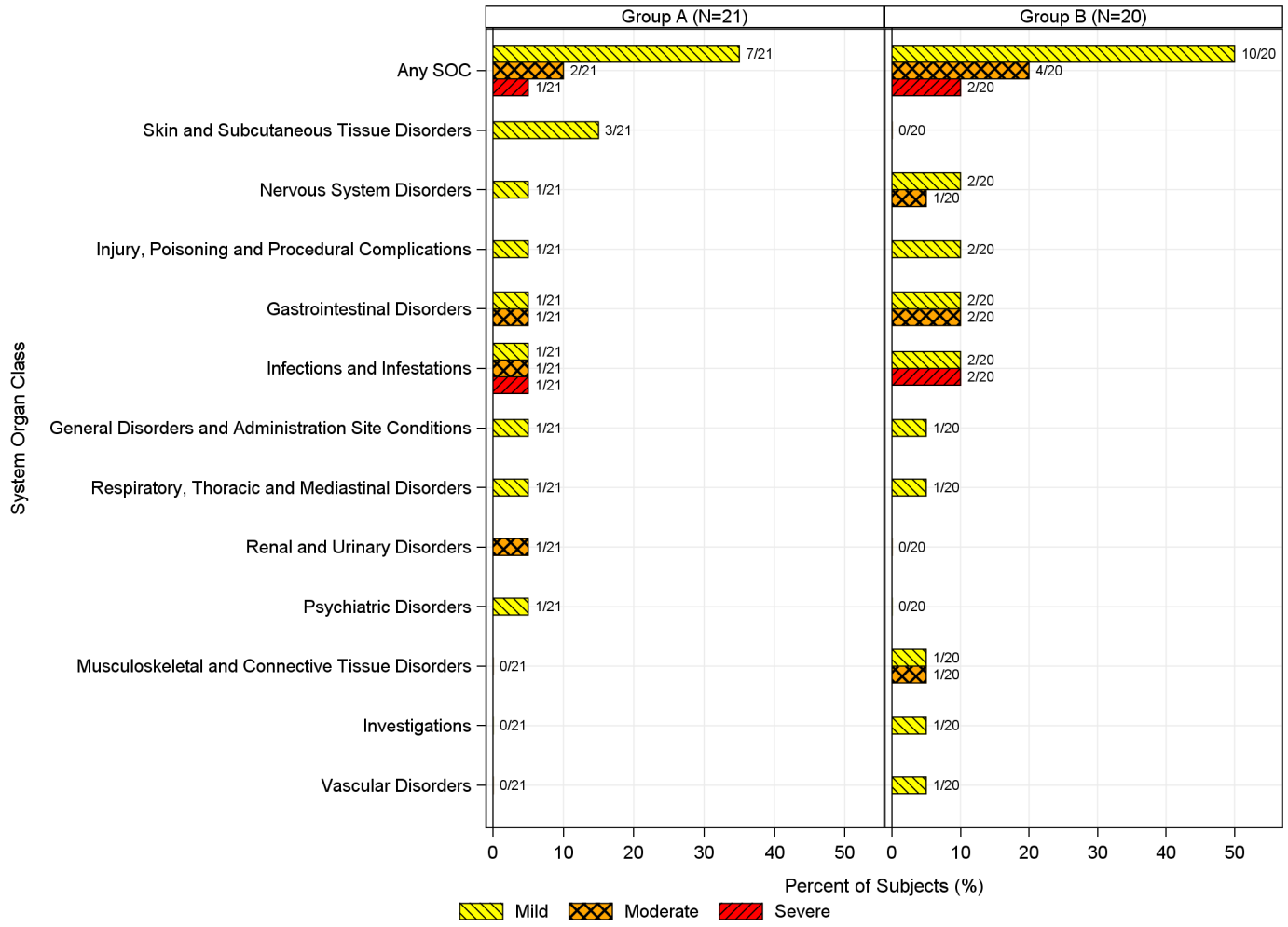


Figure 317: Incidence of Adverse Events by MedDRA® System Organ Class and Maximum Severity



14.3.5 Displays of Laboratory Results

Not Applicable.

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	Time Between Dose 2 and Dose 3 (Days)

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	Units	Results

Listing 9: 16.2.6: Individual T-cell Response Data

Treatment Group	Subject ID	Planned Time Point	Actual Study Day	T-Cell	Peptide Pool	Cytokine	Adjusted Percent	Responder (Y/N)

16.2.7 Adverse Events

Listing 10: 16.2.7.1: Solicited Events – Systemic Symptoms

Treatment Group	Subject ID	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	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

Not Applicable.

16.2.9 Vital Signs and Physical Exam Findings

Listing 13: 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 14: 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 15: 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 16: 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 17: 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 18: 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 19: 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 20: 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