CLINICAL RESEARCH IN INFECTIOUS DISEASES

STATISTICAL ANALYSIS PLAN
for
DMID Protocol: 21-0012
Janssen - Ad26.COV2.S

Study Title:
A Phase 1/2 Study of Delayed Heterologous SARS-CoV-2 Vaccine Dosing (Boost) after Receipt of EUA Vaccines: Janssen - Ad26.COV2.S Delayed Booster Vaccination

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STUDY TITLE

Protocol Number Code:	**DMID Protocol: 21-0012**
Development Phase:	Phase 1/2
Products:	Ad26.COV2.S
Form/Route:	Intramuscular (IM) 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:	May 28, 2021
Clinical Trial Completion Date:	ongoing
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Version Number:	3.0

This study was performed in compliance with Good Clinical Practice.

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LIST OF ABBREVIATIONS

ACIP	Advisory Committee on Immunization Practices
ATC	Anatomical Therapeutic Classification
AE	Adverse Event
AESI	Adverse Event of Special Interest
AU	Arbitrary Units
BAU	Binding Antibody Units
C	Celsius
CDC	Centers for Disease Control and Prevention
CI	Confidence Interval
CRF	Case Report Form
CONSORT	Consolidated Standards of Reporting Trials
COVID-19	Coronavirus Disease 2019
CSR	Clinical Study Report
DMID	Division of Microbiology and Infectious Diseases
EUA	Emergency Use Authorization
F	Fahrenheit
FDA	Food and Drug Administration
FRNT	Focus Reduction Neutralization Test
GM	Geometric Mean
GMT	Geometric Mean Titer
GMFR	Geometric Mean Fold Rise
GMR	Geometric Mean Ratio
ICH	International Conference on Harmonisation
ID	Infective Dose
IDCRC	Infectious Diseases Clinical Research Consortium
IgA	Immunoglobulin A
IgG	Immunoglobulin G
IM	Intramuscular
IND	Investigational New Drug
IRB	Institutional Review Board

List of Abbreviations *(continued)*

L	Liter
LLOD	Lower Limit of Detection
LLOQ	Lower Limit of Quantification
MAAE	Medically Attended Adverse Events
MCAR	Missing Completely at Random
mcg	Microgram
MedDRA	Medical Dictionary for Regulatory Activities
mg	Milligram
mITT	Modified Intention to Treat
mL	Milliliter
mRNA	Messenger Ribonucleic Acid
N	Number (typically refers to participants)
NOCMC	New Onset Chronic Medical Conditions
NIH	National Institutes of Health
PI	Principal Investigator
PP	Per Protocol
PT	Preferred Term
PsVNA	Pseudovirus Neutralization Assay
RLU	Relative Luminescence Units
SAE	Serious Adverse Event
SAGE	Strategic Advisory Group of Experts on Immunization
SAP	Statistical Analysis Plan
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus
SD	Standard Deviation
SMC	Safety Monitoring Committee
SOC	System Organ Class
U	Units
UK	United Kingdom
ULOQ	Upper Limit of Quantification
VRBPAC	Vaccines and Related Biological Products Advisory Committee
WHO	World Health Organization

1. PREFACE

The Statistical Analysis Plan (SAP) for "A Phase 1/2 Study of Delayed Heterologous SARS-CoV-2 Vaccine Dosing (Boost) after Receipt of EUA Vaccines: Janssen - Ad26.COV2.S Delayed Booster Vaccination"(DMID Protocol 21-0012) describes and expands upon the statistical information presented in the protocol for the Cohort 1 participants who received the Janssen – Ad26.COV2.S booster vaccine.

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. Any deviation from this SAP will be described in the CSR, as appropriate. The reader of this SAP is encouraged to also review the study protocol for details on conduct of the study and the operational aspects of clinical assessments.

2. INTRODUCTION

The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) was first detected in Wuhan, Hubei Province, China in December 2019. The corresponding illness designation, coronavirus disease 2019 (COVID-19), was declared as a pandemic respiratory illness in March 2020 [1].

The optimization and distribution of SARS-CoV-2 vaccines is of critical public health priority. The inability to mass-vaccinate the world's population in a timely fashion is resulting in ongoing high-level transmission and accelerated emergence of variants with mutations in the S protein. Moreover, the evolution of variant strains may favor immune escape or reinfection among previously infected or vaccinated individuals. 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 [2]. The emergence of variant strains has raised concerns about the breadth of immunity and protection achieved by the current vaccines. WHO SAGE and CDC ACIP have identified the safety and immunogenicity of mixed schedules as a critical and immediate research priority to inform policy on the use of mixed schedules.

Prime-boost strategies may enhance immunogenicity through complementary stimulation of humoral and T cell immune pathways. In contrast, the immune response to booster doses of certain vaccines, such as the adenovirus vector vaccines, may be limited by pre-existing antibody and/or enhanced by longer dosing intervals. Thus, the order of delivery of heterologous SARS-CoV-2 vaccine platforms may result in immune responses that are greater or less than homologous regimens of the same vaccine.

Knowledge of the safety, tolerability, and immunogenicity of a delayed heterologous boost vaccine incorporating a similar or variant spike administered following EUA dosing regimens might induce immunity to variant circulating strains and improve upon breadth and durability of protection. Utilizing one of the EUA-dosed COVID-19 vaccines available (Ad26.COV2.S), we evaluated innate, mucosal, cellular, and humoral immune responses elicited from different booster vaccines. This was part of a larger study and the results of one (Ad26.CoV2.S) subsection are included in this particular SAP. As part of an adaptive design, we added groups with variant-lineage spike proteins and other vaccine platforms, subject to availability.

2.1. Purpose of the Analyses

The analyses described in the SAPs for DMID 21-0012 will assess the immunogenicity and safety of delayed heterologous or homologous vaccine doses after EUA dosed vaccines and will be included in the clinical study report. Results from the DMID 21-0012 study will be reported in five complementary CSRs with each CSR having a corresponding SAP as described below:

- DMID 21-0012 CSR for Janssen – Ad26.COV2.S: will focus on Cohort 1 study groups 4E, 5E, 6E (Janssen Ad26.COV2.S boost).
- DMID 21-0012 CSR for Moderna – mRNA-1273: will focus on Cohort 1 study groups 1E, 2E, 3E (Moderna- mRNA-1273 100 mcg boost), 10E, 11E (Moderna- mRNA-1273.211), 12E, 13E, 14E (Moderna- mRNA-1273 50 mcg boost)
- DMID 21-0012 CSR for Pfizer - BNT162b2: will focus on Cohort 1 study groups 7E, 8E, 9E (Pfizer/BioNTech –BNT162b2 boost)
- DMID 21-0012 CSR for Novavax - NVX-CoV2373: will focus on Cohort 1 study groups 15E, 16E, 17E (Novavax NVX-CoV2373 boost)

- DMID 21-0012 CSR for Moderna – mRNA-1273, Cohort 2: will focus on Cohort 2 participants (Moderna- mRNA-1273 100 mcg prime, Moderna – 50 mcg mRNA-1273 first boost and Moderna – 50 mcg mRNA-1273.222 second boost

This SAP describes the statistical analysis that will be included in the DMID 21-0012 CSR for Janssen – Ad26.COV2.S. Specifically, the analyses will assess the co-primary objectives of DMID 21-0012, related to the safety and immunogenicity of Janssen Ad26.COV2.S vaccine administered as a booster after receipt of Moderna (Group 4E), Janssen (Group 5E) or Pfizer (Group 6E) EUA vaccinations.

3. STUDY OBJECTIVES AND ENDPOINTS

3.1. Study Objectives and Endpoints

OBJECTIVES	ENDPOINTS (OUTCOME MEASURES)
Primary	
• To evaluate the safety and reactogenicity of delayed heterologous or homologous vaccine doses after EUA dosed vaccines	• Local and systemic solicited adverse events for 7 days following the delayed boost dose. • Adverse Events from Dose 1 to 28 days following each vaccination and delayed boost dose. • MAAEs, SAEs, NOCMCs, and AESIs from Dose 1 to end of planned study participation.
• To evaluate the breadth of the humoral immune responses of heterologous and homologous delayed boost regimens following EUA dosing	• 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.
Secondary	
• None	• None
*Exploratory	
• To assess, in at least a subset of samples, the B cell immune response following EUA vaccination and delayed boost	• Magnitude, phenotype and percentage of SARS-CoV-2 specific B cells, as measured by flow cytometry and targeted B cell subset analysis at time points postvaccination and/or delayed boost.
• To assess, in at least a subset of samples, the SARS-CoV-2 protein-specific T cell responses following EUA vaccination and delayed boost	• Magnitude, phenotype, and percentage of cytokine producing S protein T cells as measured by flow cytometry at time points post-vaccination and/or delayed boost.
• To evaluate breakthrough symptomatic SARS-CoV-2 infection and sequence strains to assess for variant spike lineage	• To perform sequence analysis on breakthrough NAAT-confirmed COVID- 19 strains to assess for variant spike lineage
• To assess, in at least a subset of samples, mucosal (salivary and nasal) SARS-CoV- 2 spike protein-specific IgG and IgA responses	• Magnitude and percentage of SARS-CoV- 2 spike protein specific IgA and IgG and correlation with serologic antibody response

*Assays for exploratory endpoints may be performed and the data provided as described in Section 9.4 of the protocol, if available from the research laboratory.

3.2. Study Definitions and Derived Variables

For individual participants, the fold rise in immunogenicity endpoints (such as Binding Antibody concentration or Antibody Neutralization Titers) will be calculated by dividing levels observed at post-vaccination visits by levels observed at pre-vaccination, as obtained at Day 1 prior to dose administration.

Also related to immunogenicity endpoints, participants achieving a 4-Fold rise at post-vaccination timepoints/visits are defined as those for whom a 4-fold or higher increase in antibody levels from baseline are observed.

4. INVESTIGATIONAL PLAN

4.1. Overall Study Design and Plan

This is a phase 1/2, open-label clinical trial in individuals, 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 a delayed (>12 weeks) vaccine boost after primary vaccination with one of the EUA COVID-19 vaccines (mRNA-1273 manufactured by ModernaTX, Inc.; BNT162b2 manufactured by Pfizer/BioNTech; or Ad26.COV2.S manufactured by Janssen Pharmaceuticals/Johnson & Johnson).

This is an adaptive design and added study groups (and increased sample size) as vaccines were awarded EUA and/or variant lineage spike vaccines were manufactured or became available. Enrollment occurred at twelve domestic clinical research sites.

This study includes two cohorts. Cohort 1 provides rapid information about the safety, reactogenicity, and immunogenicity of delayed boost in a previously EUA-dosed group. This cohort can inform near term public health decisions if the variant virus becomes more widespread. Cohort 2 is an adaptive cohort that evaluates, in a prospective fashion, the safety, reactogenicity and immunogenicity of EUA-dosed vaccine followed by delayed boost. Pools of participants are recruited to receive EUA-dosed vaccine and are assigned, at a later date, to a delayed booster vaccine based on availability of vaccine product, to enable rapid implementation based on situational assessment of need. This cohort may take longer to provide information on the immunogenicity of delayed boost, but it may assume priority in enrollment as it is important to inform future public health strategies and as access to COVID-19 vaccine becomes more widespread. As Cohorts 1 and 2 are in different populations, they can enroll in parallel or prioritized as determined by DMID/IDCRC needs.

Cohort 1 includes participants greater than 18 years of age and older, stratified into two age strata (18-55 years and > 56 years) who received previously received COVID-19 vaccine at EUA dosing (two vaccinations of mRNA-1273 at the 100 mcg dose, two vaccinations of BNT162b2 at the 30 mcg dose, or one vaccination of Ad26.COV2.S at the $5x10^{10}$ vp dose). Those participants are offered enrollment into this study >12 weeks after they received the last dose of their EUA vaccine. Participants receive an open-label delayed vaccine boost that is assigned to each of the approximately twelve domestic trial sites as described below. Study groups that are the focus of this SAP are shown in bold font

1. Previously EUA-dosed vaccination with Janssen (one or two doses for Group 15E) – Ad26.COV2.S at $5x10^{10}$ vp followed by:

   Group 1E – A 100-mcg dose of mRNA-1273

   Group 4E – A $5x10^{10}$ vp dose of Ad26.COV2.S*

   Group 7E – A 30-mcg dose of BNT162b2

   Group 10E –A 100-mcg dose of mRNA-1273.211

   Group 12E – A 50-mcg dose of mRNA-1273

   Group 15E – A dose of NVX-CoV2373 (5 mcg Prototype SARS-CoV-2 rS vaccine with 50 mcg Matrix-M)*

2. Previously EUA-dosed vaccination with Moderna – mRNA-1273 at 100 mcg for two doses followed by:

   Group 2E – A 100-mcg dose of mRNA-1273

   Group 5E – A $5x10^{10}$ vp dose of Ad26.COV2.S

   Group 8E –A 30-mcg dose of BNT162b2

   Note: There is no boost with mRNA-1273.211 to avoid duplication of trial efforts with DMID 21-0003.

   Group 13E – A 50-mcg dose of mRNA-1273

   Group 16E – A dose of NVX-CoV2373 (5 mcg Prototype SARS-CoV2 rS vaccine with 50 mcg Matrix-M)*

3. Previously EUA-dosed vaccination with Pfizer/BioNTech - BNT162b2 at 30 mcg for two doses followed by:

   Group 3E – A 100-mcg dose of mRNA-1273

   Group 6E – A $5x10^{10}$ vp dose of Ad26.COV2.S

   Group 9E – A 30-mcg dose of BNT162b2

   Group 11E – A 100-mcg dose of mRNA-1273.211

   Group 14E – A 50-mcg dose of mRNA-1273

   Group 17E – A dose of NVX-CoV2373 (5 mcg Prototype SARS-CoV2 rS vaccine with 50 mcg Matrix-M)*

Refer to Table 1 for a full description of study groups covered in this SAP.

The anticipated sample size of each group is approximately 25 participants 18 through 55 years of age and approximately 25 participants 56 years of age and older for a total of 50 participants per group.

***Note** - Groups 15E-17E is planned to include 60 participants, split (approximately evenly) between age strata as able. As the use of 2 doses of Ad26COV2.S without additional vaccines is relatively infrequent in the population (and 1 dose without additional vaccines is even less frequent), participants who are enrolled and remain active in Group 4E (homologous prime-boost with Ad26COV2.S) are offered the opportunity to roll into Group 15E, if eligible. Data collected on these participants after their enrollment in Group 15E will not be included in Group 4E analyses.

Participants in Cohort 1 receive a single IM injection of the designated delayed booster vaccine and are followed through 12 months after vaccination. A telephone visit is performed at Day 8 and in-person follow-up visits occur on Days 15 and 29, as well as 3, 6, 9, and 12 months after the vaccination.

Cohort 2 is planned to include approximately 250 participants per group aged > 18 years of age who have not received a COVID-19 vaccine and have no known history of COVID-19 or SARS-CoV-2 infection. Participants are assigned to receive COVID-19 vaccine under EUA dosing as programmatically outlined in Table 9 of the protocol. Additional pools of participants are included as needed as additional COVID-19 vaccines are awarded EUA. These pools of participants are assigned a novel homologous or heterologous variant boost or heterologous platform boost at a minimum of 12 weeks following receipt of EUA dosing and followed through 12 months after the last vaccination. All Cohort 2 volunteers are offered a booster of mRNA-1273 at the approved 50 mcg dose at Day 181 (+/- 30 days) following dose 2 of their primary series. A telephone visit is performed one week after each primary EUA vaccination and one week after the booster

dose. In person follow-up visits occur on 14 days following completion of EUA vaccinations and on days 14, and 28 days after the booster dose, as well as 3, 6, and 12 months post the booster vaccination. A fourth dose of COVID-19 vaccine is administered to participants using the Moderna mRNA-1273.222 bivalent vaccine at an interval of 4 to 12 months after the third dose (1st booster). In addition to the other immunologic assays planned for earlier parts of the study (including innate, cellular and humoral responses), samples are also collected to measure mucosal immune responses before the booster dose and on days 14 and 28, and at 3 months and 6 months after the fourth dose (2nd booster). Due to the surge of the Omicron variant and breakthrough infections, volunteers who contract symptomatic or asymptomatic COVID-19 between completion of their EUA primary series and the scheduled booster dose are allowed to continue in the study. The interval between the COVID-19 infection and booster dosing should be a minimum of 28 days.

For both Cohorts 1 and 2, reactogenicity is assessed at the above-mentioned visits and blood is drawn for immunogenicity assays at the in-person follow-up visits.

After activation of the IND, IRB review and approval, and site activation, recruitment outreach efforts are initiated at the participating sites, which included fliers, letters, telephone calls, etc. Information regarding this trial can be provided to potential participants who have previously participated in other vaccine trials conducted at the participating site. Other forms and/or mechanisms of recruitment can be used. The recruitment process and all materials are approved by the IRB prior to use. Screening can occur up to 28 days prior to the first dose or on Day 1 prior to administration of Dose 1.

Schedules of assessments are found in Table 2.

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

This phase 1/2 clinical trial is designed as an open-label study, without administration of a placebo formulation. An open-label study facilitates the need for rapid review and dissemination of study data for public health reasons.

4.3. Selection of Study Population

Two cohorts are enrolled. For Cohort 1, approximately 880 individuals (50 participants/group; Groups 1E-14E, and 60 participants/group; Groups 15E-17E) 18 years of age and older, stratified into two age groups (18-55 years and >56 years at 1:1 ratio), who are in good health and received EUA dosed vaccinations of mRNA-1273, BNT162b2 or Ad26.COV2.S are intended to be enrolled in this study.

For Cohort 2, approximately 250 individuals (250 participants/group), >18 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 meet all eligibility criteria are intended to be enrolled. The target population should reflect the community at large.

The estimated time from initiation of enrollment to complete enrollment in each group within this clinical trial is approximately 2-4 weeks (though could take longer). However, owing to the adaptive nature of the design, new groups may be added to Cohort 1 or 2 dependent upon manufacture of variant lineage spike protein-based vaccine constructs or vaccines newly awarded EUA. An optional screening period can occur up to 28 days prior to the first vaccination, or can be completed on Day 1, prior to dosing.

Participant Inclusion and Exclusion Criteria must be confirmed by a study clinician, licensed to make medical diagnoses and listed on the Form FDA 1572. No exemptions are granted on Participant Inclusion or Exclusion Criteria in DMID-sponsored studies.

4.4. Treatments

4.4.1. Treatments Administered

The three study groups considered in this SAP include participants who received different EUA dosing schemes, with all participants being administered (after enrollment) one dose of Ad26.COV2.S booster vaccine.

- 4E: Evaluates the same strain and homologous platform strategy of administering Janssen – Ad26.COV2.S booster vaccine to participants previously doses with Janssen – Ad26.COV2.S
- 5E: Evaluates the same strain and heterologous platform strategy of administering Janssen – Ad26.COV2.S booster vaccine to participants previously doses with Moderna – mRNA-1273
- 6E: Evaluates the same strain and heterologous platform strategy of administering Janssen – Ad26.COV2.S booster vaccine to participants previously doses with Pfizer/BioNTech – BTN162b2

All groups received a single dose of $5x10^{10}$ vp dose Ad26.COV2.S via IM injection on Day 1.

4.4.2. Identity of Investigational Product(s)

Janssen - Ad26.COV2.S (0.5 mL) is formulated to contain $5x10^{10}$ virus particles of the Ad26 vector encoding the S glycoprotein of SARS-CoV-2. Each dose may also contain residual amounts of host cell proteins (≤0.15 mcg) and/or host cell DNA (≤3 ng). The Ad26.COV2.S vaccine is a colorless to slightly yellow, clear to very opalescent suspension. Each vial contains five doses.

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

Participants in Cohorts 1 and 2 were not randomized to study intervention. The study was open label and for each stage, a unique booster was made available. Volunteers were competitively enrolled across trial sites until targets were met for each sequential stage.

4.4.4. Selection of Doses in the Study

The Phase 1/2a study of the Ad26.COV2.S vaccine is evaluating two dosage levels ($5x10^{10}$ vp and $1x10^{11}$ vp) based upon prior vaccine studies with the Ad26 platform [3]. Both formulations administered as a single dose had favorable safety and immunogenicity profiles [4], yielding high and comparable humoral and cellular immune response rates. The lower dose had a more favorable reactogenicity profile and was selected for Phase 3 trial evaluation that demonstrated its protective efficacy [3]. As with the mRNA vaccines, upon review of risks, benefits, and immunogenicity of a second dose of Ad26.COV2.S [5], the VRBPAC advisory committee to the FDA (15 October 2021), affirmed by the ACIP (21 October 2021), recommended a homologous booster vaccine or a heterologous booster vaccine for Ad26.COV2.S, 2 months after completion of the primary vaccine in those aged 18 years or greater.

4.4.5. Blinding

The study is unblinded.

4.4.6. Prior and Concomitant Therapy

Per the protocol, collection of concomitant medications is intended to include only prescription medications through 28 days after each study vaccination and COVID-19 vaccines received outside of the study at any time during study participation. At each study visit, if there are new SAEs, Protocol Specified AESIs, MAAEs, or NOCMCs, concomitant medications are recorded on the appropriate CRF.

4.4.7. Treatment Compliance

All participants are to receive a single dose of a delayed booster vaccine administered in the clinic. Enrolled participants who do not receive the boost dose will be presented in a listing (Listing 3).

5. SAMPLE SIZE CONSIDERATIONS

This is a phase 1/2, open-label, multi-site clinical trial that is not designed to test a specific hypothesis. Rather, it is intended to obtain preliminary estimates in healthy adults of the safety, reactogenicity, and immunogenicity of delayed heterologous SARS-CoV-2 vaccine dosing (boost) after receipt of EUA vaccines.

Although rare AEs are not demonstrable in a clinical study of this size, there is a good chance of observing AEs of relatively low frequency (Table 3). With approximately 50 participants in each group there is a 99.5% chance of observing at least one AE of probability 10%. Similarly, with approximately 25 participants in each of the age subgroups, there is a 92.8% chance of observing at least one AE of probability 10%. Therefore, if no AEs of a given type occur in a Cohort 1 group, one can be relatively confident that they will occur in fewer than 10% of people once the vaccine is implemented.

Due to the surge in Omicron variant cases at the time of the writing of protocol version 6.0, it is anticipated that a non-negligible proportion of vaccinated individuals may be prone to asymptomatic breakthrough infections. To allow for potential larger numbers of participants enrolled in Stage 6 (Groups 15E-17E) that would subsequentially be found to have serological evidence of prior infection, the sample size is expanded to N=60/group (approximately 1:1 age strata) for these groups.

The precision with which the geometric mean titer (GMT) can be estimated from observed data depends on the standard deviation (SD) of the measurements, on the logarithmic scale, and the sample size. Table 4 displays two-sided 95% confidence intervals for the GMT for several values of the observed antibody titer assuming up to 10% attrition.

6. GENERAL STATISTICAL CONSIDERATIONS

6.1. General Principles

Unless otherwise specified, all continuous variables will be summarized using the following descriptive statistics: n (non-missing sample size), mean, standard deviation, median, maximum and minimum. The frequency and percentages (based on the non-missing sample size) of observed levels will be reported for all categorical measures. In general, all data will be listed, sorted by study group and participant, and when appropriate by visit number within participant. All summary tables will be structured with a column or row for each study group in the following order:

- Group 4E [Dosed Janssen, Boost Janssen]
- Group 5E [Dosed Moderna, Boost Janssen]
- Group 6E [Dosed Pfizer, Boost Janssen]

All tables will be annotated with the total population size relevant to that table/treatment, including any missing observations.

6.2. Timing of Analyses

Early reports summarizing safety, reactogenicity, and immunologic response endpoints, including data cumulated up to predefine timepoints, may be done, as needed (see Section 6.5).

The final analysis will be performed after the final data lock and the CSR will be completed when all primary safety endpoint data and all secondary immunogenicity endpoint data are available. Any available data from the exploratory immunogenicity endpoints may also be included in the CSR. Remaining exploratory immunogenicity endpoint data may be included in an addendum to the CSR, publication of manuscript(s), or other report(s).

6.3. Analysis Populations

Analyses in the plan will only include participants who received the delayed Janssen- Ad26.COV2.S booster vaccine, study groups 4E, 5E and 6E. Participants will be grouped based on their initial EUA vaccination received for all analyses.

6.3.1. Safety Population

The Safety Population includes all participants who received at least one dose of the delayed Janssen-Ad26.COV2.S booster vaccine.

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

The modified intent-to-treat (mITT) population includes all enrolled participants who received the delayed Janssen- Ad26.COV2.S booster vaccine and contributed both pre- and at least one post-vaccination boost venous blood sample for the corresponding immunogenicity endpoint testing and for which valid results were reported.

6.3.3. Modified Intention-to-Treat (mITT) Subset Population

The mITT Subset Population is used for live-virus neutralization and T-cell response endpoints and includes a set of 20 participants per study group that were randomly selected among participants with adequate availability of PBMC samples at Day 1 and Day 15, stratified by age (10 participants per age group) while also allowing for replacement to ensure representation from sites with low enrollment. The live-virus neutralization mITT analyses will be based on this population.

6.3.4. 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 participants in the mITT subset with the following exclusions:

- Data from all available visits for participants found to be ineligible at enrollment.
- 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 (i.e., 2x window):
  - Before Day 6 or after Day 10 for Day 8 Visit (Study Visit 2)
  - Before Day 11 or after Day 19 for Day 15 Visit (Study Visit 3)
  - Before Day 25 or after Day 33 for Day 29 Visit (Study Visit 4)
  - Before Day 77 or after Day 105 for Day 91 Visit (Study Visit 5)
  - Before Day 153 or after Day 209 for Day 181 Visit (Study Visit 6)
  - Before Day 217 or after Day 329 for Day 273 Visit (Study Visit 7)
  - Before Day 310 or after Day 422 for Day 366 Visit (Study Visit 8)

Additional criteria, which do not strictly constitute protocol deviations, will also be applied for exclusion of participants or observations in the PP analysis of immunogenicity endpoints, as follows:

- Receipt of non-study COVID-19 vaccine any time after study vaccination.
- Receipt of seasonal influenza vaccine within 14 days after study vaccination.
- Breakthrough COVID-19 infection either self-reported or Positive N-antibody test.

The live-virus neutralization PP analyses will be based on a subset of 20 participants per study group that were randomly selected, stratified by age for this assay and who meet all criteria of the PP population.

6.4. Covariates and Subgroups

The protocol does not define any formal subgroup analyses, and the study is not adequately powered to perform subgroup analyses. However, immunogenicity analyses will be summarized by age group (18-55 years old and 56+ years old).

6.5. Missing Data and Censoring

There will be no imputations planned for missing data. A complete-case analysis approach will be used, and summaries will be reported for participants with non-missing values only.

For binding antibody and FRNT endpoints, values below the lower limit of quantification (LLOQ) will be kept as reported by the corresponding laboratory if actual numerical values are provided. If actual values below the LLOQ are not provided, the observations will be replaced with a value equivalent LLOQ/2. Values that are greater than the upper limit of quantification (ULOQ) will be kept when actual values are reported from the corresponding laboratory. If actual values above the ULOQ are not provided, observations will be replaced with a value equivalent to the ULOQ.

For live-neutralization endpoint, any values below the lower limit of detection (LLOD) will be assigned a value equivalent to one-half the lower limit of detection for analysis purposes, and any values reported as greater than or equal to the upper limit of detection (and no absolute value is available) will be assigned a value equivalent to the upper limit of detection value. Levels that are reported as above the LLOD but below the LLOQ will be kept as reported by the corresponding laboratory if actual numerical values are provided. If a value is reported to be between the LLOD and LLOQ, but the value was not provided, the observations will be replaced with a value equivalent to the midpoint between LLOD and LLOQ (i.e., [LLOD +LLOQ]/2). If actual values below the LLOQ are not provided, the observations will be replaced with a value equivalent LLOQ/2. Values that are greater than the ULOQ will be kept when actual values are reported from the corresponding laboratory. If actual values above the ULOQ are not provided, observations will be replaced with a value equivalent to the ULOQ.

6.6. Interim Analyses and Data Monitoring

No formal interim analyses that include sequential testing of a statistical hypothesis will be conducted. Therefore, P-value adjustment will not be made to any analyses.

However, given the need for rapid review and dissemination of study data for formulating public health policies, early reports summarizing safety and immunogenicity endpoints and from data cumulated up to pre-defined timepoints, may be produced. These reports may be disseminated to public health officials and partners as needed and included in publications and presentations to inform the global scientific community. None of the analyses included in these reports include any formal statistical hypothesis testing; therefore, no adjustment of the significance level will be done.

6.6.1. Safety Monitoring Committee Reports

Given the need for rapid review and dissemination of study data for public health reasons, AEs and SAEs may be reviewed as necessary outside of SMC reviews. The SMC may not need to meet (unless halting rules are met), and materials are provided electronically. Documentation of review and any concerns noted is solicited electronically.

Prior to Protocol Version 4.0, scheduled SMC reviews for Cohort 1 Groups were targeted after participants within a Study Group have completed Day 8. At the time of the writing of Version 1.0 of the SAP, a SMC report after Day 8 had only been produced for Groups 1E, 2E and 3E. From Protocol Version 4.0 onwards, the protocol specifies that the SMC will review separate cumulative AE data reports after all participants within each booster vaccine group of Cohort 1 are dosed and complete Day 29 within Cohort 1.

For Cohort 2 there are no scheduled mandatory reviews by the SMC after participants in this cohort receive the prime, first boost or second boost vaccinations. This is due to the safety database known for EUA vaccines and vaccinations being administered in accordance with CDC guidelines. SMC reviews for Cohort 2 occur if halting rules are triggered, or as requested by the sponsor or PI.

6.6.2. Immunogenicity Review

Data review of immunogenicity endpoints are performed as often as needed to inform public health decisions. These reviews may be performed when participants have completed key immunogenicity visits and the data is available. The analyses are conducted on the mITT analysis set.

Study groups that are concurrently enrolled and planned to receive the same delayed vaccine boost can be included in a single report. The planned summaries and analyses for immunogenicity reports are described in detail in Section 8. The timing of the reports, along with key milestone visits determining the cumulative data to be included in the reports, are informed by the Central Assay Plan and/or 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.

6.7. 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.

6.8. Multiple Comparisons/Multiplicity

The study is not designed to test any specific null hypothesis, and as such no adjustment for multiple comparisons will be performed.

7. STUDY SUBJECTS

7.1. Disposition of Participants

Table 9 will present a summary of the reasons that participants were screened but not enrolled.

The composition of analysis populations, including reasons for participant exclusion, by study group, is presented in Table 8. A listing of participants excluded from analysis populations is also provided in Listing 6.

The disposition of participants in the study will be tabulated by study group (Table 7). The table shows the total number of participants screened, enrolled, received the first/second prime vaccination, received delayed boost dose, terminated from study follow-up, and the number completing the study.

A flowchart showing the disposition of study participants, adapted from the Consolidated Standards of Reporting Trials (CONSORT) Statement [6] will be included (Figure 1). This figure will present the number of participants screened, enrolled, lost to follow-up, and analyzed, by study group.

A listing of participants 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 participant-specific protocol deviations will be presented by the reason for the deviation and study group for all participants (Table 5). This table will also include deviations that were collected in the data system as non-participant specific for which a participant ID was provided. A summary of major participant-specific protocol deviations is provided in Table 6. All participant-specific protocol deviations will be included in Appendix 3 as a data listing (Listing 4). All non-participant specific deviations will be presented in Listing 5.

8. IMMUNOGENICITY EVALUATION

8.1. Primary Immunogenicity Analysis

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. See Section 9 for the planned analyses of the co-primary endpoint related to safety.

Serum antibody binding will be measured by two types of Electrochemiluminescence Immunoassay (ECLIA) formats. The first is a 4-plex assay that reports arbitrary units/mL (AU/mL). Results from the 4-plex assay for S-2P-Wa-1 will also be reported in Binding Antibody Units/mL (BAU/mL) as bridged to the WHO International Reference Standard. Conversion from AU/mL to BAU/mL units will be done using conversion factor of 0.0090 for the S-2P-WA-1 variant. Second, a 10-plex assay is a fit for purpose assay that reports area under the curve (AUC) and is used to rapidly assess antibody binding targeting specific variants of concern. Antigens presented in the CSR are S-2P-Wa-1,S-2P-B.1.351, and RDB-B.1.351 for the 4-plex ECLIA and S-2P-Wa-1, S-2P-B.1.617.2, and S-2P-B.1.351 and S-2P-B.1.1.529 for the 10-plex ECLIA (AUC).

Geometric mean (GM), geometric mean fold rise (GMFR) and 4-fold rise rates of SARS-CoV-2 specific antibody binding levels will be calculated at Study Days 1 (GM only), 15, 29, 91, 181, 273, and 366 by study group and will include both tabular and graphical summaries. Note that only timepoints with available results will be reported. Number of participants with non-missing data (n), range, minimum, maximum, GM, GMFR, and 4-fold rise rates will be presented. Corresponding 95% confidence interval (CI) estimates will be presented for GM, GMFR, and 4-fold rise (using Student's t-distribution for GM and GMFR and the Clopper-Pearson binomial method for 4-fold rise rate) at each post vaccination timepoint by study group and age group (starting with Table 13 ending with Table 28). Graphical displays will include boxplots showing the distribution of responses over time by study group (starting with Figure 2 ending with Figure 17) and by study group and age group (starting with Figure 34 ending with Figure 49).

Neutralization assays using a validated SARS-CoV-2 pseudovirus neutralization assay (PsVNA) and fit-for-purpose focus reduction neutralization test (FRNT) will be performed using serial dilutions of sera against available variants. Neutralization titers are the serum dilution at which relative luminescence units (RLU; PsVNA) or fluorescent foci (FRNT) are reduced by either 50% (ID_{50}) or 80% (ID_{80}) compared to virus control wells after subtraction of background. Each serum sample will be tested for neutralizing antibodies against each of the pseudoviruses (D614G, B.1.617.2, B.1.351, and B.1.1.529).

ID_{50} and ID_{80} will be calculated using methodology such as a 4-parameter non-linear regression model for FRNT and 5-parameter logistic regression model for PsVNA. If multiple results are reported for a sample, a geometric mean of the two results will be used for subsequent analyses. Of one of the reported values for a sample is less than LLOQ, LLOQ/2 will be used in the calculation of the sample geometric mean. ID_{50} results will be summarized by study group using number of participants with non-missing data, minimum, maximum, range, GM, GMFR, and 4-fold rise rate while ID_{80} results will be reported in the immunogenicity responses listing only. 95% CI for GM, GMFR, GMR, and 4-fold rise rate will also be presented (using Student's t-distribution for GM, GMFR, GMR and using Clopper Pearson for 4-fold rise rate) at each post vaccination timepoint by study group and age group starting with Table 29 ending with Table 36 for PsVNA and starting with Table 37 ending with Table 44 for FRNT. Graphical displays for PsVNA and FRNT will include boxplots showing the distribution of responses over time by study group (starting with Figure 18 ending with Figure 25 for PsVNA and starting with Figure 26 ending with Figure 33 for FRNT) and by study group and age group (starting with Figure 50 ending with Figure 57 for PsVNA and starting with Figure 58 ending with Figure 65 for FRNT).

Individual immunogenicity responses are shown in Listing 9.

8.2. Secondary Immunogenicity Analyses

Not Applicable.

8.3. Exploratory Immunogenicity Analyses

Details of analysis of COVID-19 sequencing and N-Protein Ab ELISA are provided in the SAP and results will be reported in the CSR. Details of other exploratory endpoints such as B cell immune response and SARS-CoV-2 protein-specific T cell responses provided below will not be reported in the CSR but may be reported in a manuscript or other immunogenicity reports.

8.3.1. COVID-19 Sequencing Data

The Simon and Bakel labs at the Icahn School of Medicine at Mount Sinai will analyze nasopharyngeal swab specimens collected from participants who experienced a SARS-CoV-2 breakthrough infection, for whom a positive test result is reported in the corresponding eCRF and a nasopharyngeal specimen is collected. The analysis aims to provide data on SARS-CoV-2 copy numbers and SARS-CoV-2 genotype/lineage.

The SARS-CoV-2 breakthrough positive nasopharyngeal specimens are provided either as a dry swab or resuspended in viral transport media (both specimen types cryo-preserved at –80C). Biospecimen are accessioned and processed according to the SOPs developed in collaboration with Dr. Greninger [7]. Briefly, each specimen undergoes RNA extraction, Reverse Transcriptase quantitative real time PCR (RT qPCR) and cDNA synthesis, whole-genome amplification followed by library preparation and next generation Illumina sequencing if the amount of SARS-CoV-2 passes the minimum requirements (e.g., less than threshold cycle 32). SARS-CoV-2 genomes are assembled and subjected to quality control using the lab's custom vRAPID pipeline [8]. The final average sequencing depth per genome ranged between 40k and 760k reads. Genomes with at least 95% coverage and 100X depth across all regions are considered complete. Genotypic analysis and clade/lineage assignment of complete genomes will be performed using the Nextclade CLI (v2.13.1), pangolin (v2.4) and pangoLEARN (v1.19) pipelines. Samples will be traced to their ancestral lineage assignments by obtaining the first letter and first numerical character of the lineage aliases provided by Nextclade.

A summary of variant PANGO calls is provided in Table 45, Table 46, and Table 47 for those participants in the mITT population with a positive test and specimen collected. A visual summary is provided in Figure 66, Figure 67, and Figure 68.

8.3.2. N-Protein Ab ELISA

Number and percentage of participants with positive N-Protein Ab ELISA among those with available results along with history of N-Protein Ab ELISA results will be reported (Table 48). The number and percentage of participants with reported SARS-CoV-2 positive tests and receipt of COVID-19 vaccine boost outside of the study will be reported in Table 49.

8.3.3. B Cell Immune Response

SARS-CoV-2 specific B cell response to vaccination/boost by analytical flow cytometry will be evaluated for subsets of participants in Cohort 1 Study Groups. Both D614G ("WT") and BA.1 ("Omicron") variant probes will be used to identify WT-specific and cross-reactive cells elicited by vaccination. Summaries (including number of observations, median, IQR and range) will be reported at each timepoint for the following markers of B-cell response:

- Percent S2P WT+ (Total S-2P) of all IgG and IgA memory B cells.
- Percent S2P WT+/S2P Omicron+ (Cross-reactive S-2P) of all IgG and IgA memory B cells.
- Percent S2P WT+/S2P Omicron- (WT-only S-2P) of all IgG and IgA memory B cells.
- Percent RBD WT+ (Total RBD) of all IgG and IgA memory B cells.
- Percent RBD WT+/RBD Omicron+ (Cross-reactive RBD) of all IgG and IgA memory B cells.
- Percent RBD WT+/RBD Omicron- (WT-only RBD) of all IgG and IgA memory B cells.
- Percent S2P NTD WT_Omicron+ (Total NTD) of all IgG and IgA memory B cells
- Percent RBD WT-/NTD WT_Omicron-/S2P WT+ (Total S-2P-only) of all IgG and IgA memory B cells.
- Percent RBD WT-/NTD WT_Omicron-/S2P WT+/S2P Omicron+ (Cross-reactive S-2P-only) of all IgG and IgA memory B cells.
- Percent RBD WT-/NTD WT_Omicron-/S2P WT+/S2P Omicron- (WT-only S-2P-only) of all IgG and IgA memory B cells.
- Percent RBD WT+ or NTD WT_Omicron+ or S2P WT+ (Any Probe) of all IgG and IgA memory B cells.

For B cell response characterization, further subsampling selection will be performed, randomly selecting 12 participants (with 6 per Age Group) among the original subset of 20 participants selected for testing of T cell and live-virus neutralization in each boosting group.

8.3.4. SARS-CoV-2 Protein-Specific T Cell Responses

SARS-CoV-2 CD4+ and CD8+ T cell responses, as obtained from a validated 27-color ICS/Flow cytometry assay, will be reported for a subset of participants. Specimens were stimulated with two peptide pools (15 amino acids overlapping by 11 amino acids) covering the S1 and S2 regions of the original Wuhan strain, along with variant peptides for the D614G mutation. Results for the following markers will be reported:

- Percent of CD4+ Cells Expressing IL-2 and/or IFN-g
- Percent of CD4+ Cells Expressing IL-2 and/or IFN-g and/or CD154
- Percent of CD4+ Cells Expressing IL-4 and/or IL-5/IL-13 and CD154
- Percent of CD8+ Cells Expressing IL-2 and/or IFN-g

Summaries for these markers include number of participants with successfully assayed samples, proportion of participants with positive response and, both overall and among those with positive response, the median, IQR and range of the percent CD4+/CD8+ expressing specific cells.

9. SAFETY EVALUATION

Summaries and analysis of safety data will be presented for the Safety Population. Safety summaries will be presented overall and grouped by study group.

Solicited AEs will be summarized by severity for each day post vaccination (Days 1-8) and as the maximum severity over all 8 days. Solicited AEs that were ongoing beyond Day 8 will be summarized in the Day 8+ and maximum post baseline columns. 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 participants reporting each symptom, any local symptom, and any systemic symptom.

Unsolicited non-serious AEs will be collected from the time of the delayed boost vaccination through 28 days after 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 delayed boost vaccination through the end of planned study participation. The information collected on SAEs, AESIs, NOCMCs, and MAAEs will be reported in detailed listings showing the event description, MedDRA preferred term and SOC, relevant dates (study boost vaccination and onset/resolution of AEs), severity, relatedness, and outcome for each event. Non-serious unsolicited AEs will be summarized as number and percentage of participants reporting at least one event in each MedDRA preferred term and SOC, cross tabulated by severity and relationship to study vaccination. Additionally, the proportion of participants 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, race, height, weight, and BMI will be presented by study group (Table 10 and Table 11). Age, height, weight, and BMI will be summarized as continuous variables. Ethnicity is categorized as Hispanic or Latino, not Hispanic and not Latino, Not Reported, or Unknown. Race is categorized as American Indian or Alaskan Native, Asian, Black or African American, Native Hawaiian or other Pacific Islander, White, or Other. Participants self-designated as belonging to more than one race are categorized for the analysis as Multi-Racial and participants who refuse to identify a race are categorized as Unknown.

Individual participant listings will be presented for all demographic characteristics collected (Listing 7).

9.1.1. Prior and Concurrent Medical Conditions

Summaries of participants' pre-existing medical conditions will be presented by treatment group (Table 12).

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

9.1.2. Prior and Concomitant Medications

Summaries of medications that were started prior to dosing and continuing at the time of dosing will be presented by WHO Drug Anatomical Therapeutic Chemical (ATC) classification levels 1 and 2 and study group (Table 68). This table will only include medications collected per protocol and meeting the protocol concomitant medications reporting criteria.

Individual participant listings will be presented for all concomitant medications collected in the study including medications that did not meet the reporting criteria will be presented (Listing 16).

9.2. Measurements of Treatment Compliance

Only one study vaccination is expected (delayed boost at least 12 weeks after EUA vaccination). Any participants who were enrolled but not vaccinated will be presented by study group as part of the participant disposition table (Table 7).

9.3. Adverse Events

When calculating the incidence of adverse events (i.e., on a per participant basis), each participant will only be counted once and any repetitions of adverse events within a participant will be ignored; the denominator will be the total population size. All adverse events reported will be included in the summaries and analyses. A summary of all adverse events is provided in Table 50. A summary of those events that occurred in ≥5% of participants in any study group is provided in Table 51. Frequency of adverse events will be defined as the total number of adverse events including all repetitions of adverse events within a participant.

9.3.1. Solicited Events and Symptoms

Systemic solicited adverse events were collected pre-vaccination, and systemic and local solicited adverse events were collected 30 minutes post-vaccination and then daily for 7 days after vaccination and graded on a scale of 0 (none), 1 (mild), 2 (moderate) and 3 (severe), and 4 (potentially life-threatening). Systemic events include fatigue, headache, myalgia, arthralgia, nausea, chills, and fever. Local events include injection site pain, injection site erythema, and injection site edema/induration. Erythema and induration measurements between 0 and 2.5 cm were reported in the data system as not gradable but will be summarized as having a severity of none since their measurement were below the criteria for mild severity.

The proportion of participants 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 52). For each systemic and local event, any systemic event, any local event, and any solicited event, the maximum severity over 7 days after study vaccination will be summarized for the Safety Population. The number and percentage of participants reporting each event will be summarized by the maximum severity and study group. For each event, the denominator is the number of participants with non-missing data for the specific event (Table 52).

The number of participants reporting a solicited adverse event will be summarized for each day post vaccination in a summary table (Table 53, Table 54, and Table 55) and graphically in a bar chart (Figure 69 and Figure 70).

Solicited adverse events by participant will be presented in Listing 10 and Listing 11.

9.3.2. Unsolicited Adverse Events

The proportion of participants reporting at least one unsolicited adverse event will be summarized by MedDRA SOC and PT. Denominators for percentages are the number of participants who received the delayed boost vaccination. For participants reporting multiple events within the same MedDRA term, the maximum severity grade will be counted.

The following summaries for unsolicited adverse events will be presented by MedDRA SOC, PT, and study group:

- Incidence of unsolicited adverse events with 95% CIs by study group (Table 56);
    - Incidence of unsolicited adverse events by MedDRA SOC, PT, maximum severity, and relationship to study vaccination (Table 57);
    - Incidence of unsolicited adverse events by MedDRA SOC and PT (Table 58);
    - Participant listing of non-serious unsolicited adverse events of moderate or greater severity (Table 61);
    - Bar chart displaying frequency of adverse events by severity and MedDRA SOC (Figure 71);
    - Bar chart displaying incidence of adverse events by severity and MedDRA SOC (Figure 72);
    - Bar chart displaying frequency of adverse events by MedDRA SOC and relationship to study vaccination (Figure 73);
    - Bar chart displaying incidence of adverse events by MedDRA SOC and relationship to study vaccination (Figure 74)

Adverse events by participant will be presented in Listing 12.

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

SAEs will be summarized by MedDRA SOC and PT (Table 59). The following listings will be presented including Participant ID, Adverse Event Description, Adverse Event Onset Date/Days Post Dose, Severity, Reason Reported as an SAE, Relationship to Study Vaccination, Alternate Etiology if not Related, Outcome, and Duration of Event (days), MedDRA SOC and PT:

- Deaths and Serious Adverse Events (Table 60);
- Protocol specified Adverse Events of Special Interest (AESIs); New Onset Chronic Medical Conditions (NOCMCs); Medically Attended Adverse Events (MAAEs) (Table 62)

9.5. Pregnancies

For any participants in the Safety Population who became pregnant during the study, every attempt will made to follow these participants 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 17, Listing 18, Listing 19, Listing 20, and Listing 21).

9.6. Clinical Laboratory Evaluations

For this study, no local clinical laboratory data is collected during follow-up. A listing of SARS-CoV-2 test results is provided in Listing 13.

9.7. Vital Signs and Physical Evaluations

Vital sign measurements included systolic blood pressure, diastolic blood pressure, heart rate, and oral temperature. Vital signs were assessed at Day 1, Day 15 and Day 29. Vital signs will be tabulated by visit and study group in Table 63, Table 64, Table 65, Table 66, and Table 67. Individual vital signs data will also be listed in Listing 14.

Physical Examinations were only to be performed if clinically indicated at Study Days 1, 15, 29, 91, 181, 273, and 366. The following body systems will be assessed: Abdomen, Cardiovascular/heart Extremities, General Appearance, HEENT, Lymph nodes, Musculoskeletal, Neck, Neurological, Pulmonary/Chest, and Skin. Abnormal physical examination findings are presented (Listing 15).

9.8. Concomitant Medications

Concomitant medications will be coded to the Anatomical Therapeutic Classification (ATC) using the WHO Drug Dictionary. The use of prior and concomitant medications taken during the study will be recorded on the CRFs. The use of concomitant medications during the study collected per protocol and meeting the protocol concomitant medications reporting criteria will be summarized by ATC1, ATC2 code and study group for the Safety population (Table 68). A by-participant listing of all concomitant medications collected in the study including medications that did not meet the reporting criteria will be presented (Listing 16).

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 rounded to one more decimal place 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

15.1. Changes from Version 1.0 to Version 2.0

- SAP updated to align with protocol changes that occurred after Version 1.0 of SAP (protocol updated from Version 4.0 to Version 9.0). Minor changes to wording throughout document.
- Exploratory endpoints were added.
- Analysis sets updated in Section 3.1. Details specific to Cohort 2 added to Sections 3.2, 6.3, and 7.3. SMC reports updated in Section 4.1. “Other Safety Measures” section moved from 9.6 to 12, SMC reports moved from 9.7 to 9.6.
- Additional details added to Section 10.4. Section 10.5 “Random selection of participants” created, and “Early Immunogenicity Reports” renumbered from 10.5 to 10.6. Section 11 expanded. Section 12 added.

15.2. Changes from Version 2.0 to Version 3.0

- SAP updated to align with DMID template.
- Updated the SAP to focus the analyses on data from study groups 4E, 5E, 6E which include only participants who received the delayed Janssen booster vaccine.
- Added shells for tables, figures, listings.
- Added intext references for the tables, figures, listings.
- Removed analyses of exploratory endpoints that will not be reported in the CSR.

16. REFERENCES

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17. LISTING OF TABLES, FIGURES, AND LISTINGS

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

APPENDICES

APPENDIX 1. TABLE MOCK-UPS

LIST OF TABLES

9.1 Overall Study Design and Plan Description

Table 1: Study Design (Study Groups 4E, 5E, 6E Only)

Group	Sample Size*	EUA Dosing Scheme	Interval(weeks)	Delayed Booster Vaccination	Strategy Tested
4E	**50**	Previously dosed Janssen – Ad26.COV2-S	≥12	Janssen – Ad26.COV2.S	 Control - Same Strain & platform
5E	**50**	Previously dosed Moderna – mRNA-1273	≥12	Janssen – Ad26.COV2.S	 Same Strain Heterologous platform
6E	**50**	Previously dosed Pfizer/BioNTech – BNT162b2	≥12	Janssen – Ad26.COV2.S	 Same Strain Heterologous platform

9.5.1 Immunogenicity and Safety Measurements Assessed and Flow Chart

Table 2: Schedule of Study Procedures

Study Day	D-28 to D-1	1	8[b]	15	29	91	181	273	366	Illness/ Unscheduled Visit	Early Termination Visit
Visit Number	00[a]	1	2	3	4	5	6	7	8		
Window (+/-)		0	1	2	2	7	14	28	28		
Informed Consent[a]	X										
Eligibility Criteria	X	X									
Medical History	X	X									
Vaccination[c]		**X**									
Concomitant Meds		X	X	X	X						
Interim History		X	X	X	X	X	X	X	X	X	X
Physical Exam - Targeted	X	X		X	X	X	X	X	X	X	X
Vital Signs[d]	X	X		X	X					X	X
Height/Weight (BMI)[a]	X										
Urine β-HCG[e]		X									
Memory Aid, Solicited AEs		X	X	X[f]							
Unsolicited AEs		X	X	X	X						
SAEs, Protocol specified AESIs, MAAEs, and NOCMCs			X	X	X	X	X	X	X	X	X
Nasal or NP swab for PCR & Sequencing										X[g]	
Immunoassays											
Serum- Humoral Assays		32		32	32	32	32	32	32		32
PBMC Cellular Assays & plasma		64		64			64		64		64
Daily Volume (mL)		96		96	32	32	96	32	96		96
Cumulative Volume (mL)		96		192	224	256	352	384	480		

[a] Optional screening visit – informed consent and height/weight only performed at screening or Day 1
[b] Telephone visit
[c] Delayed booster dose based upon assignment to Groups 1E-3E (and/or future groups added as adaptive design)
[d] Vital signs before and after booster vaccination. Otherwise, only as clinically indicated
[e] For women of childbearing potential, a negative urine pregnancy on Day 1 will be performed with negative results confirmed before dosing
[f] Review 7-day Memory Aid data.
[g] Collect nasal or NP swab for PCR (x2). Sequencing will be performed on all Illness visit-confirmed SARS-CoV-2 specimens.

9.7.1 Sample Size

Table 3: Probability of Observing an Adverse Event for Various Event Rates in One Vaccine Schedule Group (or Age Subgroup), Assuming No Attrition (N = 50 or N = 25) or Approximately 10% Attrition (N = 45 or N = 22)

N	"True" Event Rate	Probability of Observing ≥ 1 Events (%)	N	"True" Event Rate	Probability of Observing ≥ 1 Events (%)
50	0.1%	4.9	45	0.1%	4.4
	0.5%	22.2		0.5%	20.2
	1.0%	39.5		1.0%	36.4
	2.0%	63.6		2.0%	59.7
	3.0%	78.2		3.0%	74.6
	4.0%	87.0		4.0%	84.1
	5.0%	92.3		5.0%	90.1
	10.0%	99.5		10.0%	99.1
	15.0%	>99.9		15.0%	99.9
	20.0%	>99.9		20.0%	>99.9
	30.0%	>99.9		30.0%	>99.9
N	**"True" Event Rate**	**Probability of Observing ≥ 1 Events (%)**	**N**	**"True" Event Rate**	**Probability of Observing ≥ 1 Events (%)**
25	0.1%	2.5	22	0.1%	2.2
	0.5%	11.8		0.5%	10.4
	1.0%	22.2		1.0%	19.8
	2.0%	39.7		2.0%	35.9
	3.0%	53.3		3.0%	48.8
	4.0%	64.0		4.0%	59.3
	5.0%	72.3		5.0%	67.6
	10.0%	92.8		10.0%	90.2
	15.0%	98.3		15.0%	97.2
	20.0%	99.6		20.0%	99.3
	30.0%	>99.9		30.0%	>99.9

Table 4: Two-Sided 95% Confidence Intervals Based on Observing a Particular Average Log_e-Antibody Titer in Participants' Vaccine Groups and Age Subgroups

Observed Average Log_e-Antibody Titer	SD of Log_e-Antibody Titer	95% Confidence Interval of GMT in Vaccine Group		95% Confidence Interval of GMT in Age Subgroup	
		N = 50	N = 45[a]	N = 25	N = 22[a]
log_e (5)	0.5	(4.3, 5.8)	(4.3, 5.8)	(4.1, 6.1)	(4, 6.2)
log_e (20)		(17.4, 23.1)	(17.2, 23.2)	(16.3, 24.6)	(16, 25)

$\log_e$ (50)		(43.4, 57.6)	(43, 58.1)	(40.7, 61.5)	(40.1, 62.4)
$\log_e$ (100)		(86.8, 115.3)	(86.1, 116.2)	(81.4, 122.9)	(80.1, 124.8)
$\log_e$ (250)		(216.9, 288.2)	(215.1, 290.5)	(203.4, 307.3)	(200.3, 312)
$\log_e$ (500)		(433.8, 576.3)	(430.3, 581)	(406.8, 614.6)	(400.6, 624.1)
$\log_e$ (1000)		(867.5, 1152.7)	(860.5, 1162.1)	(813.5, 1229.2)	(801.2, 1248.2)
$\log_e$ (5)	1.0	(3.8, 6.6)	(3.7, 6.8)	(3.3, 7.6)	(3.2, 7.8)
$\log_e$ (20)		(15.1, 26.6)	(14.8, 27)	(13.2, 30.2)	(12.8, 31.2)
$\log_e$ (50)		(37.6, 66.4)	(37, 67.5)	(33.1, 75.6)	(32.1, 77.9)
$\log_e$ (100)		(75.3, 132.9)	(74, 135)	(66.2, 151.1)	(64.2, 155.8)
$\log_e$ (250)		(188.2, 332.2)	(185.1, 337.6)	(165.5, 377.8)	(160.5, 389.5)
$\log_e$ (500)		(376.3, 664.3)	(370.2, 675.2)	(330.9, 755.5)	(320.9, 779)
$\log_e$ (1000)		(752.6, 1328.7)	(740.5, 1350.4)	(661.8, 1511)	(641.9, 1558)

[a] Assumes approximately 10% attrition.

10.2 Protocol Deviations

Table 5: Distribution of Protocol Deviations by Type and Study Group, All Enrolled Participants

Deviation Type	Group 4E [Dosed Janssen, Boost Janssen] (N=X)		Group 5E [Dosed Moderna, Boost Janssen] (N=X)		Group 6E [Dosed Pfizer, Boost Janssen] (N=X)		All Participants (N=X)	
	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.
Any type								
Inappropriate enrollment	x	x	x	x			x	x
Failure to follow randomization or blinding procedures								
Study product management deviation								
Study product dispensing error								
Study product use/non-use deviation								
Conduct of non-protocol procedure								
Improper AE/SAE								
Unreported AE								
Unreported SAE/AESI								
Breach of confidentiality								
Physical assessment deviation								
Lab assessment deviation								
Mishandled lab specimen								
Staff performing duties that they are not qualified to perform								
Use of non-IRB/EC-approved materials								
Use of excluded concomitant mediations, devices, or non-study products								
Informed consent process deviation								
Visit completed outside of window								

Deviation Type	Group 4E [Dosed Janssen, Boost Janssen] (N=X)		Group 5E [Dosed Moderna, Boost Janssen] (N=X)		Group 6E [Dosed Pfizer, Boost Janssen] (N=X)		All Participants (N=X)	
	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.
Too few aliquots obtained								
Required procedure not conducted								
Other								
Note: N= Number of participants enrolled.								

Table with similar format:

Table 6: Distribution of Major Protocol Deviations by Type and Study Group, All Enrolled Participants

14.1 Description of Study Participants

14.1.1 Disposition of Participants

Table 7: Participant Disposition by Study Group, All Enrolled Participants

Participant Disposition	Group 4E [Dosed Janssen, Boost Janssen] (N=X)		Group 5E [Dosed Moderna, Boost Janssen] (N=X)		Group 6E [Dosed Pfizer, Boost Janssen] (N=X)		All Participants (N=X)	
	n	%	n	%	n	%	n	%
Screened	--	--	--	--	--	--	x	--
Enrolled	x	100	x	100	x	100	x	100
Received delayed boost dose	x	xx	x	xx	x	xx	x	xx
Early Termination[a]								
[Early term reason 1]								
[Early term reason 2]								
[Early term reason 3]								
Other								
Completed Study								

Note: N=Number of participants enrolled.
[a] Refer to Listing 16.2.1 for reasons participants discontinued or terminated early.

Table 8: Analysis Populations by Study Group, All Enrolled Participants

[Implementation note: Other exclusion criteria described in Section 6.3.4 will be added to the per protocol sections of this table when applicable.]

Analysis Populations	Reason Participants Excluded	Group 4E [Dosed Janssen, Boost Janssen] (N=X)		Group 5E [Dosed Moderna, Boost Janssen] (N=X)		Group 6E [Dosed Pfizer, Boost Janssen] (N=X)		All Participants (N=X)	
		%	n	%	n			%	n
Safety	Did not receive one dose of the delayed boost vaccine	x	xx	x	xx			x	xx
Modified Intent-To-Treat	Any Reason								
	Did not contribute a pre-vaccination blood sample for which valid immunogenicity results were reported								
	Did not contribute at least one post-vaccination blood sample for which valid immunogenicity results were reported								
Per Protocol, Any Timepoint	Any Reason								
	Found to be ineligible at enrollment[a]								
	Protocol deviation considered to affect the science[b]								
	Visit occurred substantially out of window[c]								
Per Protocol, Day 1	Any Reason								
	Found to be ineligible at enrollment[a]								
	Protocol deviation considered to affect the science[b]								
	Visit occurred substantially out of window[c]								
Per Protocol, Day 15	Any Reason								
	Found to be ineligible at enrollment[a]								
	Protocol deviation considered to affect the science[b]								
	Visit occurred substantially out of window[c]								
Repeat Per Protocol rows for Days 29, 91, 181, 273, 366.									

Notes: N=Number of participants enrolled.
n=Number of participants meeting the criteria.
Participants may be excluded from an analysis population for multiple reasons.
[a] Participant data from all visits are excluded from the per protocol analyses. All instances of exclusion are summarized in this table.
[b] Participant data are excluded from the per protocol analyses at all timepoints that occur at or after this protocol deviation. All instances of exclusion are summarized in this table. Participant data collected up to the time the exclusionary criterion is met is eligible for analysis.
[c] Only data from the out of window visit are excluded from the per protocol analyses.

Table 9: Ineligibility Summary of Screen Failures

Inclusion/Exclusion Category	Inclusion/Exclusion Criterion	n[a]	%[b]
Inclusion and Exclusion	Number of participants 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 participant.
[b] Denominator for percentages is the total number of screen failures.

14.1.2 Demographic Data by Study Group

Table 10: Summary of Categorical Demographic and Baseline Characteristics by Study Group, All Enrolled Participants

Variable	Characteristic	Group 4E [Dosed Janssen, Boost Janssen] (N=X)		Group 5E [Dosed Moderna, Boost Janssen] (N=X)		Group 6E [Dosed Pfizer, Boost Janssen] (N=X)		All Participants (N=X)	
		n	%	n	%	n	%	n	%
Sex	Male	x	xx	x	xx	x	xx	x	xx
	Female								
Ethnicity	Not Hispanic or Latino	x	xx	x	xx	x	xx	x	xx
	Hispanic or Latino								
	Not Reported								
	Unknown								
Race	American Indian or Alaska Native	x	xx	x	xx	x	xx	x	xx
	Asian								
	Native Hawaiian or Other Pacific Islander								
	Black or African American								
	White								
	Multi-Racial								
	Unknown								
	Other								

Note: N=Number of participants enrolled.

Table 11: Summary of Continuous Demographic and Baseline Characteristics by Study Group, All Enrolled Participants

Variable	Statistic	Group 4E [Dosed Janssen, Boost Janssen] (N=X)	Group 5E [Dosed Moderna, Boost Janssen] (N=X)	Group 6E [Dosed Pfizer, Boost Janssen] (N=X)	All Participants (N=X)
Age (Years)	Mean	xx	xx	xx	xx
	Standard Deviation	xx	xx	xx	xx
	Median	x	x	x	x
	Minimum	x	x	x	x
	Maximum	x	x	x	x
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				
Note: N=Number of participants enrolled.					

14.1.3 Prior and Concurrent Medical Conditions

Table 12: Summary of Participants with Pre-Existing Medical Conditions by MedDRA System Organ Class and Study Group, Safety Analysis Population

MedDRA System Organ Class	Group 4E [Dosed Janssen, Boost Janssen] (N=X)		Group 5E [Dosed Moderna, Boost Janssen] (N=X)		Group 6E [Dosed Pfizer, Boost Janssen] (N=X)		All Participants (N=X)	
	n	%	n	%			n	%
Any SOC	x	xx	x	xx			x	xx
[SOC 1]								
[SOC 2]								
[SOC 3]								

Note: N=Number of participants in the Safety Population; n = Number of participants reporting medical history within the specified SOC. A participant is only counted once per SOC.

14.2 Immunogenicity Data

Table 13: Summaries of Serum IgG Binding Assay Arbitrary Units/mL Measured by 4-plex ECLIA by Time Point, Age Group, and Study Group, S-2P–Wa-1 – mITT Population

Planned Time Point	Statistic	Group 4E [Dosed Janssen, Boost Janssen] (N=X)			Group 5E [Dosed Moderna, Boost Janssen] (N=X)			Group 6E [Dosed Pfizer, Boost Janssen] (N=X)			All Participants (N=X)		
		Age 18-55 (N=X)	Age ≥ 56 (N=X)	Overall (N=X)	Age 18-55 (N=X)	Age ≥ 56 (N=X)	Overall (N=X)	Age 18-55 (N=X)	Age ≥ 56 (N=X)	Overall (N=X)	Age 18-55 (N=X)	Age ≥ 56 (N=X)	Overall (N=X)
Day 1, Pre-Dose	n												
	Range (min, max)												
	GM (95% CI)												
Day 15	n												
	Range (min, max)												
	GM (95% CI)												
	GMFR (95% CI)												
	4-Fold Rise - % (95% CI)												
Day 29	n												
	Range (min, max)												
	GM (95% CI)												
	GMFR (95% CI)												
	4-Fold Rise - % (95% CI)												
Day 91	n												
	Range (min, max)												
	GM (95% CI)												
	GMFR (95% CI)												
	4-Fold Rise - % (95% CI)												

Planned Time Point	Statistic	Group 4E [Dosed Janssen, Boost Janssen] (N=X)			Group 5E [Dosed Moderna, Boost Janssen] (N=X)			Group 6E [Dosed Pfizer, Boost Janssen] (N=X)			All Participants (N=X)		
		Age 18-55 (N=X)	Age ≥ 56 (N=X)	Overall (N=X)	Age 18-55 (N=X)	Age ≥ 56 (N=X)	Overall (N=X)	Age 18-55 (N=X)	Age ≥ 56 (N=X)	Overall (N=X)	Age 18-55 (N=X)	Age ≥ 56 (N=X)	Overall (N=X)
Day 181	n												
	Range (min, max)												
	GM (95% CI)												
	GMFR (95% CI)												
	4-Fold Rise - % (95% CI)												
Day 273	n												
	Range (min, max)												
	GM (95% CI)												
	GMFR (95% CI)												
	4-Fold Rise - % (95% CI)												
Day 366	n												
	Range (min, max)												
	GM (95% CI)												
	GMFR (95% CI)												
	4-Fold Rise - % (95% CI)												

Notes: N=Number of participants in the mITT population.
n=Number of participants with results available at time point.
GM=Geometric Mean, GMFR=Geometric Mean Fold Rise, NE=Not Estimable.
The GMFR was calculated by dividing the result at each day by the result at Day 1 and then calculating the geometric mean.
4-Fold Rise is the proportion of participants with results available with a 4-fold increase or higher in the result relative to Day 1.
Confidence intervals of the GM and GMFR were calculated with the Student's t distribution on log-transformed data.
Confidence intervals of 4-Fold Rise are exact binomial confidence intervals calculated using the Clopper-Pearson method.

Tables with similar format:

Table 14: Summaries of Serum IgG Binding Assay Arbitrary Units/mL Measured by 4-plex ECLIA by Time Point, Age Group, and Study Group, S-2P–Wa-1 – Per Protocol Population

Table 15: Summaries of Serum IgG Binding Assay Arbitrary Units/mL Measured by 4-plex ECLIA by Time Point, Age Group, and Study Group, S-2P–B.1.351 – mITT Population

Table 16: Summaries of Serum IgG Binding Assay Arbitrary Units/mL Measured by 4-plex ECLIA by Time Point, Age Group, and Study Group, S-2P– B.1.351 – Per Protocol Population

Table 17: Summaries of Serum IgG Binding Assay Arbitrary Units/mL Measured by 4-plex ECLIA by Time Point, Age Group, and Study Group, RDB–B.1.351 – mITT Population

Table 18: Summaries of Serum IgG Binding Assay Arbitrary Units/mL Measured by 4-plex ECLIA by Time Point, Age Group, and Study Group, RDB– B.1.351 – Per Protocol Population

Table 19: Summaries of Serum IgG Binding Assay Binding Antibody Units/mL Measured by 4-plex ECLIA by Time Point, Age Group, and Study Group, S-2P–Wa-1 – mITT Population

Table 20: Summaries of Serum IgG Binding Assay Binding Antibody Units/mL Measured by 4-plex ECLIA by Time Point, Age Group, and Study Group, S-2P–Wa-1 – Per Protocol Population

Table 21: Summaries of Serum IgG Binding Assay Area under the Curve Measured by 10-plex ECLIA by Time Point, Age Group, and Study Group, S-2P–Wa-1 – mITT Population

Table 22: Summaries of Serum IgG Binding Assay Area under the Curve Measured by 10-plex ECLIA by Time Point, Age Group, and Study Group, S-2P–Wa-1 – Per Protocol Population

Table 23: Summaries of Serum IgG Binding Assay Area under the Curve Measured by 10-plex ECLIA by Time Point, Age Group, and Study Group, S-2P–B.1.617.2– mITT Population

Table 24: Summaries of Serum IgG Binding Assay Area under the Curve Measured by 10-plex ECLIA by Time Point, Age Group, and Study Group, S-2P– B.1.617.2 – Per Protocol Population

Table 25: Summaries of Serum IgG Binding Assay Area under the Curve Measured by 10-plex ECLIA by Time Point, Age Group, and Study Group, S-2P–B.1.351– mITT Population

Table 26: Summaries of Serum IgG Binding Assay Area under the Curve Measured by 10-plex ECLIA by Time Point, Age Group, and Study Group, S-2P– B.1.351 – Per Protocol Population

Table 27: Summaries of Serum IgG Binding Assay Area under the Curve Measured by 10-plex ECLIA by Time Point, Age Group, and Study Group, S-2P–B.1.1.529– mITT Population

Table 28: Summaries of Serum IgG Binding Assay Area under the Curve Measured by 10-plex ECLIA by Time Point, Age Group, and Study Group, S-2P– B.1.1.529– Per Protocol Population

Table 29: Summaries of Pseudovirus Neutralization Assay ID_{50} Titers by Time Point, Age Group, and Study Group, D614G – mITT Population

[Implementation note: If the assay results are reported on the mITT subset population, update the analysis population used in the title and footnote to reflect that.]

Planned Time Point	Statistic	Group 4E [Dosed Janssen, Boost Janssen] (N=X)			Group 5E [Dosed Moderna, Boost Janssen] (N=X)			Group 6E [Dosed Pfizer, Boost Janssen] (N=X)			All Participants (N=X)		
		Age 18-55 (N=X)	Age ≥ 56 (N=X)	Overall (N=X)	Age 18-55 (N=X)	Age ≥ 56 (N=X)	Overall (N=X)	Age 18-55 (N=X)	Age ≥ 56 (N=X)	Overall (N=X)	Age 18-55 (N=X)	Age ≥ 56 (N=X)	Overall (N=X)
Day 1, Pre-Dose	n												
	Range (min, max)												
	GM (95% CI)												
Day 15	n												
	Range (min, max)												
	GM (95% CI)												
	GMFR (95% CI)												
	4-Fold Rise - % (95% CI)												
Day 29	n												
	Range (min, max)												
	GM (95% CI)												
	GMFR (95% CI)												
	4-Fold Rise - % (95% CI)												
Day 91	n												
	Range (min, max)												
	GM (95% CI)												
	GMFR (95% CI)												
	4-Fold Rise - % (95% CI)												

Planned Time Point	Statistic	Group 4E [Dosed Janssen, Boost Janssen] (N=X)			Group 5E [Dosed Moderna, Boost Janssen] (N=X)			Group 6E [Dosed Pfizer, Boost Janssen] (N=X)			All Participants (N=X)		
		Age 18-55 (N=X)	Age ≥ 56 (N=X)	Overall (N=X)	Age 18-55 (N=X)	Age ≥ 56 (N=X)	Overall (N=X)	Age 18-55 (N=X)	Age ≥ 56 (N=X)	Overall (N=X)	Age 18-55 (N=X)	Age ≥ 56 (N=X)	Overall (N=X)
Day 181	n												
	Range (min, max)												
	GM (95% CI)												
	GMFR (95% CI)												
	4-Fold Rise - % (95% CI)												
Day 273	n												
	Range (min, max)												
	GM (95% CI)												
	GMFR (95% CI)												
	4-Fold Rise - % (95% CI)												
Day 366	n												
	Range (min, max)												
	GM (95% CI)												
	GMFR (95% CI)												
	4-Fold Rise - % (95% CI)												

Notes: N=Number of participants in the mITT population.
n=Number of participants with results available at time point.
GM=Geometric Mean, GMFR=Geometric Mean Fold Rise, NE=Not Estimable.
The GMFR was calculated by dividing the result at each day by the result at Day 1 and then calculating the geometric mean.
4-Fold Rise is the proportion of participants with results available with a 4-fold increase or higher in the result relative to Day 1.
Confidence intervals of the GM and GMFR were calculated with the Student's t distribution on log-transformed data.
Confidence intervals of 4-Fold Rise are exact binomial confidence intervals calculated using the Clopper-Pearson method.

Table with similar format:

Table 30: Summaries of Pseudovirus Neutralization Assay ID_{50} Titers by Time Point, Age Group, and Study Group, D614G – Per Protocol Population

Table 31: Summaries of Pseudovirus Neutralization Assay ID_{50} Titers by Time Point, Age Group, and Study Group, B.1.617.2 – mITT Population

Planned Time Point	Statistic	Group 4E [Dosed Janssen, Boost Janssen] (N=X)			Group 5E [Dosed Moderna, Boost Janssen] (N=X)			Group 6E [Dosed Pfizer, Boost Janssen] (N=X)			All Participants (N=X)		
		Age 18-55 (N=X)	Age ≥ 56 (N=X)	Overall	Age 18-55 (N=X)	Age ≥ 56 (N=X)	Overall	Age 18-55 (N=X)	Age ≥ 56 (N=X)	Overall	Age 18-55 (N=X)	Age ≥ 56 (N=X)	Overall
Day 1, Pre-Dose	n												
	Range (min, max)												
	GM (95% CI)												
Day 15	n												
	Range (min, max)												
	GM (95% CI)												
	GMR (95% CI)												
	GMFR (95% CI)												
	4-Fold Rise - % (95% CI)												
Day 29	n												
	Range (min, max)												
	GM (95% CI)												
	GMR (95% CI)												
	GMFR (95% CI)												
	4-Fold Rise - % (95% CI)												
Day 91	n												
	Range (min, max)												
	GM (95% CI)												
	GMR (95% CI)												
	GMFR (95% CI)												
	4-Fold Rise - % (95% CI)												

Planned Time Point	Statistic	Group 4E [Dosed Janssen, Boost Janssen] (N=X)			Group 5E [Dosed Moderna, Boost Janssen] (N=X)			Group 6E [Dosed Pfizer, Boost Janssen] (N=X)			All Participants (N=X)		
Day 181	n												
	Range (min, max)												
	GM (95% CI)												
	GMR (95% CI)												
	GMFR (95% CI)												
	4-Fold Rise - % (95% CI)												
Day 273	n												
	Range (min, max)												
	GM (95% CI)												
	GMR (95% CI)												
	GMFR (95% CI)												
	4-Fold Rise - % (95% CI)												
Day 366	n												
	Range (min, max)												
	GM (95% CI)												
	GMR (95% CI)												
	GMFR (95% CI)												
	4-Fold Rise - % (95% CI)												

Notes: N=Number of participants in the mITT population.
n=Number of participants with results available at time point.
GM=Geometric Mean, GMFR=Geometric Mean Fold Rise, GMR=Geometric Mean Ratio, NE=Not Estimable.
The GMFR was calculated by dividing the result at each day by the result at Day 1 and then calculating the geometric mean.
The GMR was calculated by dividing the result for each variant by the result for the D614G variant and then calculating the geometric mean.
4-Fold Rise is the proportion of participants with results available with a 4-fold increase or higher in the result relative to Day 1.
Confidence intervals of the GM, GMFR, and GMR were calculated with the Student's t distribution on log-transformed data.
Confidence intervals of 4-Fold Rise are exact binomial confidence intervals calculated using the Clopper-Pearson method.

Tables with similar format:

Table 32: Summaries of Pseudovirus Neutralization Assay ID_{50} Titers by Time Point, Age Group, and Study Group, B.1.617.2 – Per Protocol Population

Table 33: Summaries of Pseudovirus Neutralization Assay ID_{50} Titers by Time Point, Age Group, and Study Group, B.1.351 – mITT Population

Table 34: Summaries of Pseudovirus Neutralization Assay ID_{50} Titers by Time Point, Age Group, and Study Group, B.1.351 – Per Protocol Population

Table 35: Summaries of Pseudovirus Neutralization Assay ID_{50} Titers by Time Point, Age Group, and Study Group, B.1.1.529 – mITT Population

Table 36: Summaries of Pseudovirus Neutralization Assay ID_{50} Titers by Time Point, Age Group, and Study Group, B.1.1.529 – Per Protocol Population

Table 37: Summaries of Focus Reduction Neutralization Test ID_{50} Titers by Time Point, Age Group, and Study Group, D614G – mITT Population

Planned Time Point	Statistic	Group 4E [Dosed Janssen, Boost Janssen] (N=X)			Group 5E [Dosed Moderna, Boost Janssen] (N=X)			Group 6E [Dosed Pfizer, Boost Janssen] (N=X)			All Participants (N=X)		
		Age 18-55 (N=X)	Age ≥ 56 (N=X)	Overall (N=X)	Age 18-55 (N=X)	Age ≥ 56 (N=X)	Overall (N=X)	Age 18-55 (N=X)	Age ≥ 56 (N=X)	Overall (N=X)	Age 18-55 (N=X)	Age ≥ 56 (N=X)	Overall (N=X)
Day 1, Pre-Dose	n												
	Range (min, max)												
	GM (95% CI)												
Day 15	n												
	Range (min, max)												
	GM (95% CI)												
	GMFR (95% CI)												
	4-Fold Rise - % (95% CI)												
Day 29	n												
	Range (min, max)												
	GM (95% CI)												
	GMFR (95% CI)												
	4-Fold Rise - % (95% CI)												
Day 91	n												
	Range (min, max)												
	GM (95% CI)												
	GMFR (95% CI)												
	4-Fold Rise - % (95% CI)												

Planned Time Point	Statistic	Group 4E [Dosed Janssen, Boost Janssen] (N=X)			Group 5E [Dosed Moderna, Boost Janssen] (N=X)			Group 6E [Dosed Pfizer, Boost Janssen] (N=X)			All Participants (N=X)		
		Age 18-55 (N=X)	Age ≥ 56 (N=X)	Overall (N=X)	Age 18-55 (N=X)	Age ≥ 56 (N=X)	Overall (N=X)	Age 18-55 (N=X)	Age ≥ 56 (N=X)	Overall (N=X)	Age 18-55 (N=X)	Age ≥ 56 (N=X)	Overall (N=X)
Day 181	n												
	Range (min, max)												
	GM (95% CI)												
	GMFR (95% CI)												
	4-Fold Rise - % (95% CI)												
Day 273	n												
	Range (min, max)												
	GM (95% CI)												
	GMFR (95% CI)												
	4-Fold Rise - % (95% CI)												
Day 366	n												
	Range (min, max)												
	GM (95% CI)												
	GMFR (95% CI)												
	4-Fold Rise - % (95% CI)												

Notes: N=Number of participants in the mITT population.
n=Number of participants with results available at time point.
GM=Geometric Mean, GMFR=Geometric Mean Fold Rise, NE=Not Estimable.
The GMFR was calculated by dividing the result at each day by the result at Day 1 and then calculating the geometric mean.
4-Fold Rise is the proportion of participants with results available with a 4-fold increase or higher in the result relative to Day 1.
Confidence intervals of the GM and GMFR were calculated with the Student's t distribution on log-transformed data.
Confidence intervals of 4-Fold Rise are exact binomial confidence intervals calculated using the Clopper-Pearson method.

Table with similar format:

Table 38: Summaries of Focus Reduction Neutralization Test ID_{50} Titers by Time Point, Age Group, and Study Group, D614G – Per Protocol Population

Table 39: Summaries of Focus Reduction Neutralization Test ID_{50} Titers by Time Point, Age Group, and Study Group, B.1.617.2 – mITT Population

Planned Time Point	Statistic	Group 4E [Dosed Janssen, Boost Janssen] (N=X)			Group 5E [Dosed Moderna, Boost Janssen] (N=X)			Group 6E [Dosed Pfizer, Boost Janssen] (N=X)			All Participants (N=X)		
		Age 18-55 (N=X)	Age ≥ 56 (N=X)	Overall	Age 18-55 (N=X)	Age ≥ 56 (N=X)	Overall	Age 18-55 (N=X)	Age ≥ 56 (N=X)	Overall	Age 18-55 (N=X)	Age ≥ 56 (N=X)	Overall
Day 1, Pre-Dose	n												
	Range (min, max)												
	GM (95% CI)												
Day 15	n												
	Range (min, max)												
	GM (95% CI)												
	GMR (95% CI)												
	GMFR (95% CI)												
	4-Fold Rise - % (95% CI)												
Day 29	n												
	Range (min, max)												
	GM (95% CI)												
	GMR (95% CI)												
	GMFR (95% CI)												
	4-Fold Rise - % (95% CI)												
Day 91	n												
	Range (min, max)												
	GM (95% CI)												
	GMR (95% CI)												
	GMFR (95% CI)												
	4-Fold Rise - % (95% CI)												

Planned Time Point	Statistic	Group 4E [Dosed Janssen, Boost Janssen] (N=X)			Group 5E [Dosed Moderna, Boost Janssen] (N=X)			Group 6E [Dosed Pfizer, Boost Janssen] (N=X)			All Participants (N=X)		
Day 181	n												
	Range (min, max)												
	GM (95% CI)												
	GMR (95% CI)												
	GMFR (95% CI)												
	4-Fold Rise - % (95% CI)												
Day 273	n												
	Range (min, max)												
	GM (95% CI)												
	GMR (95% CI)												
	GMFR (95% CI)												
	4-Fold Rise - % (95% CI)												
Day 366	n												
	Range (min, max)												
	GM (95% CI)												
	GMR (95% CI)												
	GMFR (95% CI)												
	4-Fold Rise - % (95% CI)												

Notes: N=Number of participants in the mITT population.
n=Number of participants with results available at time point.
GM=Geometric Mean, GMFR=Geometric Mean Fold Rise, GMR=Geometric Mean Ratio, NE=Not Estimable.
The GMFR was calculated by dividing the result at each day by the result at Day 1 and then calculating the geometric mean.
The GMR was calculated by dividing the result for each variant by the result for the D614G variant and then calculating the geometric mean.
4-Fold Rise is the proportion of participants with results available with a 4-fold increase or higher in the result relative to Day 1.
Confidence intervals of the GM, GMFR, and GMR were calculated with the Student's t distribution on log-transformed data.
Confidence intervals of 4-Fold Rise are exact binomial confidence intervals calculated using the Clopper-Pearson method.

Tables with similar format:

Table 40: Summaries of Focus Reduction Neutralization Test ID_{50} Titers by Time Point, Age Group, and Study Group, B.1.617.2 – Per Protocol Population

Table 41: Summaries of Focus Reduction Neutralization Test ID_{50} Titers by Time Point, Age Group, and Study Group, B.1.351 – mITT Population

Table 42: Summaries of Focus Reduction Neutralization Test ID_{50} Titers by Time Point, Age Group, and Study Group, B.1.351 – Per Protocol Population

Table 43: Summaries of Focus Reduction Neutralization Test ID_{50} Titers by Time Point, Age Group, and Study Group, B.1.1.529 – mITT Population

Table 44: Summaries of Focus Reduction Neutralization Test ID_{50} Titers by Time Point, Age Group, and Study Group, B.1.1.529 – Per Protocol Population

Table 45: Number of Participants with Breakthrough Infections by PANGO Call and Study Group, mITT Population

[Implementation Note: Listed PANGO calls (variants) are examples only, the sequenced variants will be included in the table. Percentages are based on the number of sequenced samples available during the interval.]

Interval	PANGO Call	Group 4E [Dosed Janssen, Boost Janssen] (N=X)	Group 5E [Dosed Moderna, Boost Janssen] (N=X)	Group 6E [Dosed Pfizer, Boost Janssen] (N=X)	All Participants (N=X)
Day 1 to Day 8 (n=x)	D614G	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	Beta	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	Delta	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	BA.1	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	BA.4/5	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	XBB.1	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Day 9 to Day 15 (n=x)	D614G	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	Beta	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	Delta	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	BA.1	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	BA.4/5	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	XBB.1	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Day 16 to Day 29 (n=x)	D614G	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	Beta	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	Delta	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	BA.1	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	BA.4/5	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	XBB.1	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Day 30 to Day 91 (n=x)	D614G	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	Beta	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	Delta	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	BA.1	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	BA.4/5	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	XBB.1	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Day 92 to Day 181 (n=x)	D614G	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	Beta	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	Delta	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	BA.1	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	BA.4/5	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	XBB.1	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)

Interval	PANGO Call	Group 4E [Dosed Janssen, Boost Janssen] (N=X)	Group 5E [Dosed Moderna, Boost Janssen] (N=X)	Group 6E [Dosed Pfizer, Boost Janssen] (N=X)	All Participants (N=X)
Day 182 to Day 273 (n=x)	D614G	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	Beta	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	Delta	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	BA.1	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	BA.4/5	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	XBB.1	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Day 274 to Day 366 (n=x)	D614G	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	Beta	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	Delta	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	BA.1	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	BA.4/5	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	XBB.1	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Any Time Point (n=x)	D614G	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	Beta	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	Delta	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	BA.1	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	BA.4/5	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
	XBB.1	x (xx.x%)	x (xx.x%)	x (xx.x%)	x (xx.x%)
Note: N=Number of participants in the Per Protocol population with sequencing done. n=Number of participants with reported infections and sequencing available at a given visit.					

Tables with Similar Format:

Table 46: Number Participants with Breakthrough Infections by PANGO Call and Study Group, Infected (by Self-Report or N-Protein) Cohort – mITT Population

[Implementation note: Update footnotes for N and n to state 'N=Number of infected participants in the Per Protocol population with sequencing done.' And 'n=Number of infected participants with reported infections and sequencing available at a given visit.']

Table 47: Number of Participants with Breakthrough Infections by PANGO Call and Study Group, Uninfected (by Self-Report or N-Protein) Cohort – mITT Population

[Implementation note: Update footnotes for N and n to state 'N=Number of uninfected participants in the Per Protocol population with sequencing done.' And 'n=Number of uninfected participants with reported infections and sequencing available at a given visit.']

Table 48: Summary of N-Protein Ab ELISA Results by Study Group – All Enrolled Participants

	Group 4E [Dosed Janssen, Boost Janssen] (N=X)	Group 5E [Dosed Moderna, Boost Janssen] (N=X)	Group 6E [Dosed Pfizer, Boost Janssen] (N=X)	All Participants (N=X)
Positive N-Protein Ab ELISA Among Those with Available Results[a]				
Day 1 - n/M (%)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Day 91 - n/M (%)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Day 181 - n/M (%)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Day 273 - n/M (%)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
Day 366 - n/M (%)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
History of N-Protein Ab ELISA Results (D1-D91-D181-D273-D366) Among Participants with Complete Panel[b]				
NNNN - p/Q (%)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
NNNNP - p/Q (%)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
NNNPN - p/Q (%)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
NNPNN - p/Q (%)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
NPNNN - p/Q (%)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
PNNNN - p/Q (%)	x/x (x)	x/x (x)	x/x (x)	x/x (x)
[Repeat for all 32 combinations of N and P at the 5 timepoints. Delete rows for combinations that are not observed in the study.]				
Participants with Missing Observations				
Last observed negative at Day 91 (XN_) - m	x	x	x	x
Last observed negative at Day 181 (XXN_) - m	x	x	x	x
Last observed negative at Day 273 (XXXN_) – m	x	x	x	x
Last observed negative at Day 1[c] – m	x	x	x	x
No observed negative at Day 1[d]– m	x	x	x	x

Notes: N = Number of enrolled participants. N = Number of participants with Positive N-Protein Ab ELISA at the corresponding visit. M= Number of participants with available N-Protein Ab ELISA data at the corresponding visit.
P = Number of participants meeting the row criteria for the corresponding D1-D91-D181-D273-D366 N-Protein Ab ELISA panel.
Q = Number of participants with D1-D91-D181-D273-D366 complete panel for N-Protein Ab ELISA.
M = Number of participants with missing observations.
[a] Percentages are calculated based on the number of participants with available N-Protein Ab ELISA data at each visit.
[b] Coded as Negative (N), Positive (P), Either Positive or Negative (X) or Missing (_) result at Day 1, Day 91, Day 181, Day 273, and Day 366 visits (e.g. "NPP" denotes a participants with a first positive result at Day 91, "NN_" denotes a participant with missing result at Day 181, while "XXN_" denotes a participant with missing result at Day 273 but with either a positive or negative result at Days 1 and 91 and with a negative result at Day 181). It includes all observed histories in Cohort 1. Percentages are calculated based on the total enrolled participants.
[c] Number of participants with missing observations at any post Day 1 timepoints with a last negative result observed at Day 1.
[d] Number of participants with missing observations at any post Day 1 timepoints with a positive or missing result observed at Day 1.

Table 49: Participants with Reported SARS-CoV-2 Positive Tests and Receipt of COVID-19 Vaccine Boost Outside of the Study – All Enrolled Participants

	Group 4E [Dosed Janssen, Boost Janssen] (N=X)	Group 5E [Dosed Moderna, Boost Janssen] (N=X)	Group 6E [Dosed Pfizer, Boost Janssen] (N=X)	All Participants (N=X)
	n (%)	n (%)	n (%)	n (%)
Reported Positive SARS-CoV-2 test				
Anytime	x (x)	x (x)	x (x)	x (x)
At or before Day 29	x (x)	x (x)	x (x)	x (x)
After Day 29, before or at Day 91	x (x)	x (x)	x (x)	x (x)
After Day 91, before or at Day 181	x (x)	x (x)	x (x)	x (x)
After Day 181, before or at Day 273	x (x)	x (x)	x (x)	x (x)
After Day 273, before or at Day 366	x (x)	x (x)	x (x)	x (x)
Reported Receiving Outside COVID-19 Boost Vaccine				
Before or at Day 29	x (x)	x (x)	x (x)	x (x)
Before or at Day 91	x (x)	x (x)	x (x)	x (x)
Before or at Day 181	x (x)	x (x)	x (x)	x (x)
Before or at Day 273	x (x)	x (x)	x (x)	x (x)
Before or at Day 366	x (x)	x (x)	x (x)	x (x)
Remaining participants with no evidence of infection/boost	x (x)	x (x)	x (x)	x (x)

Note: N = Number of participants enrolled. n = Number of participants meeting the row criteria.

14.3 Safety Data

14.3.1 Displays of Adverse Events

Table 50: Overall Summary of Adverse Events

	Group 4E [Dosed Janssen, Boost Janssen] (N=X)		Group 5E [Dosed Moderna, Boost Janssen] (N=X)		Group 6E [Dosed Pfizer, Boost Janssen] (N=X)		All Participants (N = xx)	
Participants[a] with	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
At least one local solicited adverse event	x	x	x	x	x	x	x	x
At least one systemic solicited adverse event	x	x	x	x	x	x	x	x
At least one unsolicited adverse event	x	x	x	x	x	x	x	x
At least one related unsolicited adverse event	x	x	x	x	x	x	x	x
Mild (Grade 1)	x	x	x	x	x	x	x	x
Moderate (Grade 2)	x	x	x	x	x	x	x	x
Severe (Grade 3)	x	x	x	x	x	x	x	x
At least one severe (Grade 3) unsolicited adverse event	x	x	x	x	x	x	x	x
Related	x	x	x	x	x	x	x	x
Unrelated	x	x	x	x	x	x	x	x
At least one serious adverse event[b]	x	x	x	x	x	x	x	x
At least one related, serious adverse event	x	x	x	x	x	x	x	x
At least one medically attended adverse event	x	x	x	x	x	x	x	x
At least one new onset chronic medical condition	x	x	x	x	x	x	x	x
At least one adverse event of special interest								

N = Number of participants in the Safety Population
[a] Participants are counted once for each category regardless of the number of events.
[b] A listing of Serious Adverse Events is included in Table 57.

Table 51: Adverse Events Occurring in 5% of Participants in Any Study Group by MedDRA System Organ Class and Preferred Term, and Study Group - Safety Population

MedDRA System Organ Class	Preferred Term	Group 4E [Dosed Janssen, Boost Janssen] (N=X)			Group 5E [Dosed Moderna, Boost Janssen] (N=X)			Group 6E [Dosed Pfizer, Boost Janssen] (N=X)			All Participants (N=X)		
		n	%	Events	n	%	Events	n	%	Events	n	%	Events
Any Adverse Event[a]													
All	All	x	x	x	x	x	x	x	x	x	x	x	x
Non-serious Adverse Events													
All	All	x	x	x	x	x	x	x	x	x	x	x	x
SOC1	PT1	x	x	x	x	x	x	x	x	x	x	x	x
Etc.	Etc.												
Solicited Adverse Events													
All	All	x	x	x	x	x	x	x	x	x	x	x	x
SOC1	PT1	x	x	x	x	x	x	x	x	x	x	x	x
Etc.	Etc.												

N = number of participants in the Safety Population (number of participants at risk).
n= number of participants reporting event.
Events= total frequency of events reported.
Solicited events ongoing past Day 8 are included as unsolicited events.
[a] Includes only non-serious adverse events and solicited adverse events that met the 5% threshold.

14.3.1.1 Solicited Adverse Events

Table 52: Number and Percentage of Participants Experiencing Solicited Events with 95% Confidence Intervals by Symptom, Dose, and Study Group, Safety Population

		Group 4E [Dosed Janssen, Boost Janssen] (N=X)			Group 5E [Dosed Moderna, Boost Janssen] (N=X)			Group 6E [Dosed Pfizer, Boost Janssen] (N=X)			All Participants (N=X)		
Symptom	**Severity**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
Any Symptom	None												
	Mild												
	Moderate												
	Severe												
	Potentially Life-threatening												
Any Systemic Symptom	None												
	Mild												
	Moderate												
	Severe												
	Potentially Life-threatening												
Arthralgia	None												
	Mild												
	Moderate												
	Severe												
	Potentially Life-threatening												
Fatigue	None												
	Mild												
	Moderate												
	Severe												
	Potentially Life-threatening												

		Group 4E [Dosed Janssen, Boost Janssen] (N=X)			Group 5E [Dosed Moderna, Boost Janssen] (N=X)			Group 6E [Dosed Pfizer, Boost Janssen] (N=X)			All Participants (N=X)		
Symptom	**Severity**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
Fever	None												
	Mild												
	Moderate												
	Severe												
	Potentially Life-threatening												
Chills	None												
	Mild												
	Moderate												
	Severe												
	Potentially Life-threatening												
Headache	None												
	Mild												
	Moderate												
	Severe												
	Potentially Life-threatening												
Myalgia	None												
	Mild												
	Moderate												
	Severe												
	Potentially Life-threatening												

		Group 4E [Dosed Janssen, Boost Janssen] (N=X)			Group 5E [Dosed Moderna, Boost Janssen] (N=X)			Group 6E [Dosed Pfizer, Boost Janssen] (N=X)			All Participants (N=X)		
Symptom	**Severity**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
Nausea	None												
	Mild												
	Moderate												
	Severe												
	Potentially Life-threatening												
Any Local Symptom	None												
	Mild												
	Moderate												
	Severe												
	Potentially Life-threatening												
Erythema	None												
	Mild												
	Moderate												
	Severe												
	Potentially Life-threatening												
Erythema Measurement Grade[a]	None												
	Mild												
	Moderate												
	Severe												
	Potentially Life-threatening												

		Group 4E [Dosed Janssen, Boost Janssen] (N=X)			Group 5E [Dosed Moderna, Boost Janssen] (N=X)			Group 6E [Dosed Pfizer, Boost Janssen] (N=X)			All Participants (N=X)		
Symptom	**Severity**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**	**n**	**%**	**95% CI**
Induration/Edema	None												
	Mild												
	Moderate												
	Severe												
	Potentially Life-threatening												
Induration/Edema Measurement Grade[a]	None												
	Mild												
	Moderate												
	Severe												
	Potentially Life-threatening												
Pain	None												
	Mild												
	Moderate												
	Severe												
	Potentially Life-threatening												

Severity is the maximum severity reported over all solicited symptoms post dosing for each participant.
N = Number of participants in the Safety Population.
n = Number of participants reporting event.
95% CI estimated using Clopper-Pearson exact method.
[a] Induration and erythema measurements graded based on the FDA Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials.

Table 53: Summary of Solicited Events by Days Post Delayed Boost Vaccination and Symptom – Study Group 4E [Dosed Janssen, Boost Janssen], Safety Population

		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+ [a] (N=X)		Any Post-Dose[b] (N=X)	
Symptom	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Any Symptom	None																						
	Mild																						
	Moderate																						
	Severe																						
	Potentially Life-threatening																						
Any Systemic Symptom	None																						
	Mild																						
	Moderate																						
	Severe																						
	Potentially Life-threatening																						
Arthralgia	None																						
	Mild																						
	Moderate																						
	Severe																						
	Potentially Life-threatening																						
Fatigue	None																						
	Mild																						
	Moderate																						
	Severe																						
	Potentially Life-threatening																						

		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+ [a] (N=X)		Any Post-Dose[b] (N=X)	
Symptom	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Fever	None																						
	Mild																						
	Moderate																						
	Severe																						
	Potentially Life-threatening																						
Chills	None																						
	Mild																						
	Moderate																						
	Severe																						
	Potentially Life-threatening																						
Headache	None																						
	Mild																						
	Moderate																						
	Severe																						
	Potentially Life-threatening																						
Myalgia	None																						
	Mild																						
	Moderate																						
	Severe																						
	Potentially Life-threatening																						
Nausea	None																						
	Mild																						
	Moderate																						
	Severe																						
	Potentially Life-threatening																						

		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+ [a] (N=X)		Any Post-Dose[b] (N=X)	
Symptom	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Any Local Symptom	None																						
	Mild																						
	Moderate																						
	Severe																						
	Potentially Life-threatening																						
Erythema	None																						
	Mild																						
	Moderate																						
	Severe																						
	Potentially Life-threatening																						
Erythema Measurement Grade[c]	None																						
	Mild																						
	Moderate																						
	Severe																						
	Potentially Life-threatening																						
Induration/Edema	None																						
	Mild																						
	Moderate																						
	Severe																						
	Potentially Life-threatening																						
Induration/Edema Measurement Grade[c]	None																						
	Mild																						
	Moderate																						
	Severe																						
	Potentially Life-threatening																						

		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+ [a] (N=X)		Any Post-Dose[b] (N=X)	
Symptom	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Pain	None																						
	Mild																						
	Moderate																						
	Severe																						
	Potentially Life-threatening																						

Notes: N=Number of participants in the Safety Population.
Severity is the maximum severity reported post dosing for each participant for each day.
[a] Day 8+ includes the maximum severity of each symptom reported on or after Day 8 (includes ongoing symptoms)
[b] Indicates how many participants had "None", "Mild", "Moderate", "Severe", or "Potentially Life-threatening" as their maximum severity for any day. A participant may be counted in more than one of these categories.
[c] Induration and erythema measurements graded based on the FDA Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials.

Tables with similar format:

Table 54: Summary of Solicited Events by Days Post Delayed Boost Vaccination and Symptom – Study Group 5E [Dosed Moderna, Boost Janssen], Safety Population

Table 55: Summary of Solicited Events by Days Post Delayed Boost Vaccination and Symptom – Study Group 6E [Dosed Pfizer, Boost Janssen], Safety Population

14.3.1.2 Unsolicited Adverse Events

Table 56: Number and Percentage of Participants Experiencing Unsolicited Events with 95% Confidence Intervals by Study Group, Safety Population

	Group 4E [Dosed Janssen, Boost Janssen] (N=X)			Group 5E [Dosed Moderna, Boost Janssen] (N=X)			Group 6E [Dosed Pfizer, Boost Janssen] (N=X)			All Participants (N = xx)		
Participants[a] with	n	%	95% CI	n	%	95% CI	n	%	95% CI	n	%	95% CI
At least one related unsolicited adverse event	x	x	x, x	x	x	x, x	x	x	x, x	x	x	x, x
Mild or higher	x	x	x, x	x	x	x, x	x	x	x, x	x	x	x, x
Moderate or higher	x	x	x, x	x	x	x, x	x	x	x, x	x	x	x, x
Severe or higher	x	x	x, x	x	x	x, x	x	x	x, x	x	x	x, x
At least one unsolicited adverse event	x	x	x, x	x	x	x, x	x	x	x, x	x	x	x, x
Mild or higher	x	x	x, x	x	x	x, x	x	x	x, x	x	x	x, x
Moderate or higher	x	x	x, x	x	x	x, x	x	x	x, x	x	x	x, x
Severe or higher	x	x	x, x	x	x	x, x	x	x	x, x	x	x	x, x

N = Number of participants in the Safety Population. n=Number of participants meeting the row criteria.
95% CI estimated using Clopper-Pearson exact method.
[a] Participants are counted once for each category regardless of the number of events.

Table 57: Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Maximum Severity, Relationship, and Study Group, Safety Population

MedDRA System Organ Class	Preferred Term	Severity	Group 4E [Dosed Janssen, Boost Janssen] (N=X)						Group 5E [Dosed Moderna, Boost Janssen] (N=X)						Group 6E [Dosed Pfizer, Boost Janssen] (N=X)					
			Related		Not Related		Total		Related		Not Related		Total		Related		Not Related		Total	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Any SOC	Any PT	Any Severity	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Potentially Life-threatening	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Death	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
SOC 1	PT 1	Any Severity	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Potentially Life-threatening	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Death	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	PT 2	Any Severity	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Potentially Life-threatening	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Death	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx

Notes: N = Number of participants in the Safety Population. n = Number of participants reporting event.

Table 58: Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term and Study Group, Safety Population

		Group 4E [Dosed Janssen, Boost Janssen] (N=X)			Group 5E [Dosed Moderna, Boost Janssen] (N=X)			Group 6E [Dosed Pfizer, Boost Janssen] (N=X)		
MedDRA System Organ Class	**Preferred Term**	**n**	**% (95% CI)**	**Events**	**n**	**% (95% CI)**	**Events**	**n**	**% (95% CI)**	**Events**
Any SOC	Any PT	x	xx (xx, xx)	x	x	xx (xx, xx)	x	x	xx (xx, xx)	x
[SOC 1]	Any PT									
	[PT 1]									
	[PT 2]									
[SOC 2]	Any PT									
	[PT 1]									
	[PT 2]									

Notes: N = Number of participants in the Safety Population. n = Number of participants reporting event.
Events = Total frequency of events reported.
95% CI estimated using Clopper-Pearson exact method.

Table with similar format:

Table 59: Serious Adverse Events by MedDRA System Organ Class and Preferred Term and Study Group, Safety Population

14.3.2 Listing of Deaths, Other Serious and Significant Adverse Events

Table 60: Listing of Serious Adverse Events

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

Table 61: Listing of Non-Serious, Unsolicited, Moderate or Severe Adverse Events

Adverse Event	Day of Onset (Duration)	Severity	Relationship to Study Vaccination	If Not Related, Alternative Etiology	Action Taken with Study Vaccination	Outcome	MedDRA System Organ Class	MedDRA Preferred Term
Participant ID: , Study Group: , AE Number:								
Comments:								
Participant ID: , Study Group: , AE Number:								
Comments:								

Table 62: Listing of AESIs, MAAEs, and NOCMCs

Participant ID	Study Group	Event Description	Date of Product Administration[a]	Duration of Event	Day of Onset	MedDRA® Sytem Organ Class	MedDRA® Preferred Term	Severity	AESI?	MAAE?	NOCMC?	Relationship	Outcome

14.3.3 Narratives of Deaths, Other Serious and Significant Adverse Events

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

14.3.4 Abnormal Laboratory Value Listings (by Participant)

Not Applicable.

14.3.5 Displays of Laboratory Results

Not Applicable.

14.3.6 Displays of Vital Signs

Table 63: Vital Signs by Assessment, Maximum Severity, Time Point, and Study Group – Any Assessment, Safety Population

Time Point	Severity[a]	Group 4E [Dosed Janssen, Boost Janssen] (N=X)		Group 5E [Dosed Moderna, Boost Janssen] (N=X)		Group 6E [Dosed Pfizer, Boost Janssen] (N=X)		All Participants (N=X)	
		n	%	n	%	n	%	n	%
Day 1	None	x	xx	x	xx	x	xx	x	xx
	Mild	x	xx	x	xx	x	xx	x	xx
	Moderate	x	xx	x	xx	x	xx	x	xx
	Severe	x	xx	x	xx	x	xx	x	xx
	Missing	x	xx	x	xx	x	xx	x	xx
Day 15	None								
	Mild								
	Moderate								
	Severe								
	Missing								
Day 29	None								
	Mild								
	Moderate								
	Severe								
	Missing								
Max Severity Post Baseline	None								
	Mild								
	Moderate								
	Severe								
	Missing								

Note: The "Max Post Baseline" rows indicate the maximum severity experienced by each participant at any time point post baseline, including unscheduled assessments.
N = Number of participants in the Safety Population.
[a] Vital signs graded based on the FDA Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials.

Tables with similar format:

Table 64: Vital Signs by Assessment, Maximum Severity, Time Point, and Study Group – Systolic Blood Pressure, Safety Population

Table 65: Vital Signs by Assessment, Maximum Severity, Time Point, and Study Group – Diastolic Blood Pressure, Safety Population

Table 66: Vital Signs by Assessment, Maximum Severity, Time Point, and Study Group – Heart Rate, Safety Population

Table 67: Vital Signs by Assessment, Maximum Severity, Time Point, and Study Group – Oral Temperature, Safety Population

14.4 Summary of Concomitant Medications

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

WHO Drug Code Level 1, Anatomic Group	WHO Drug Code Level 2, Therapeutic Subgroup	Group 4E [Dosed Janssen, Boost Janssen] (N=X)		Group 5E [Dosed Moderna, Boost Janssen] (N=X)		Group 6E [Dosed Pfizer, Boost Janssen] (N=X)		All Participants (N=X)	
		n	%	n	%	n	%	n	%
Any Level 1 Codes	Any Level 2 Codes	x	xx	x	xx	x	xx	x	xx
[ATC Level 1 - 1]	Any [ATC 1 – 1]								
	[ATC 2 - 1]								
	[ATC 2 - 2]								
	[ATC 2 - 3]								
[ATC Level 1 – 2]	[ATC 2 - 1]								
	[ATC 2 - 2]								
	[ATC 2 - 3]								

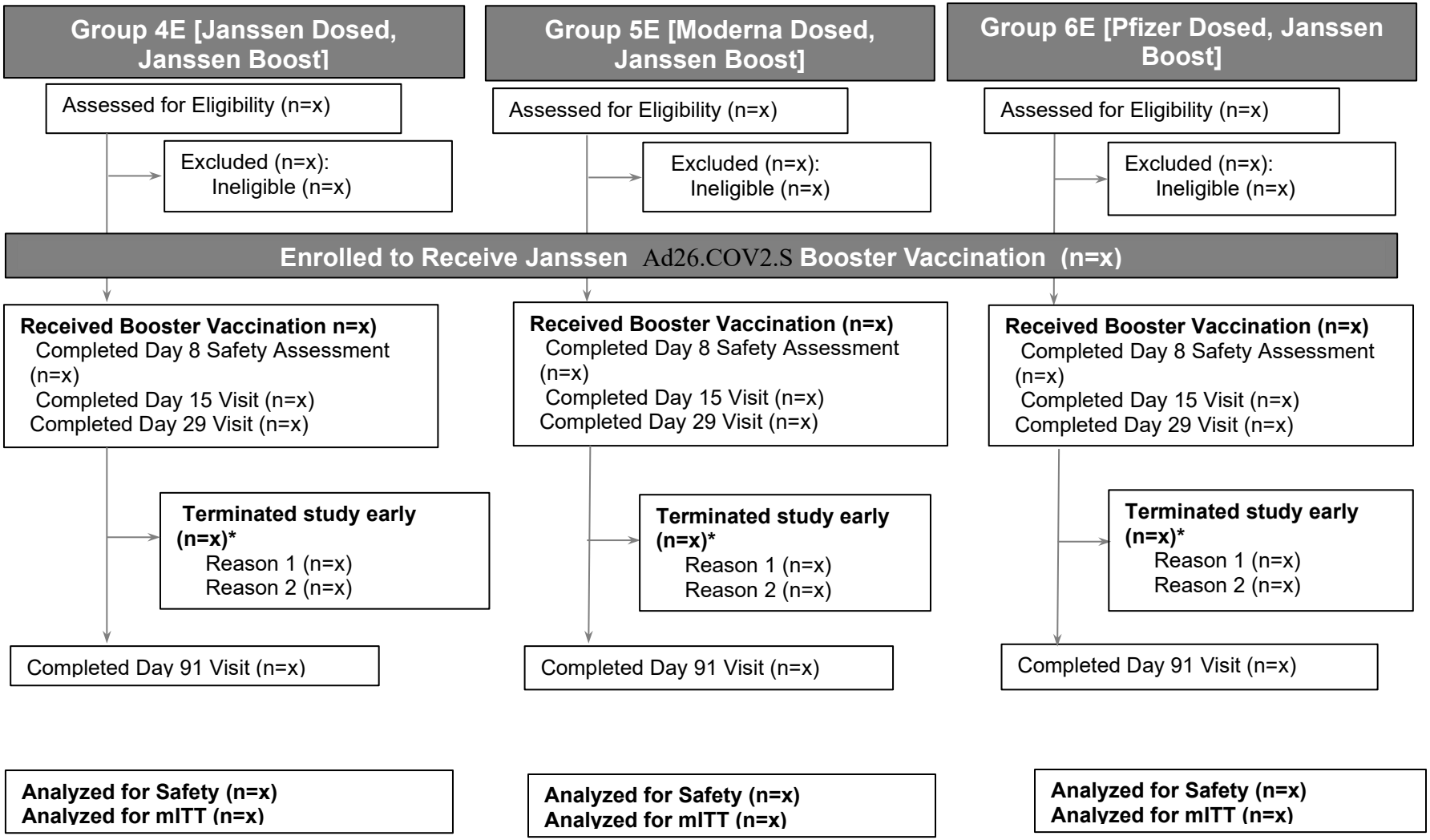
Notes: N = Number of participants in the Safety Population. n = Number of participants reporting taking at least one medication in the specific WHO Drug Class.

APPENDIX 2. FIGURE MOCK-UPS

LIST OF FIGURES

10.1 Disposition of Participants

Figure 1: CONSORT Flow Diagram

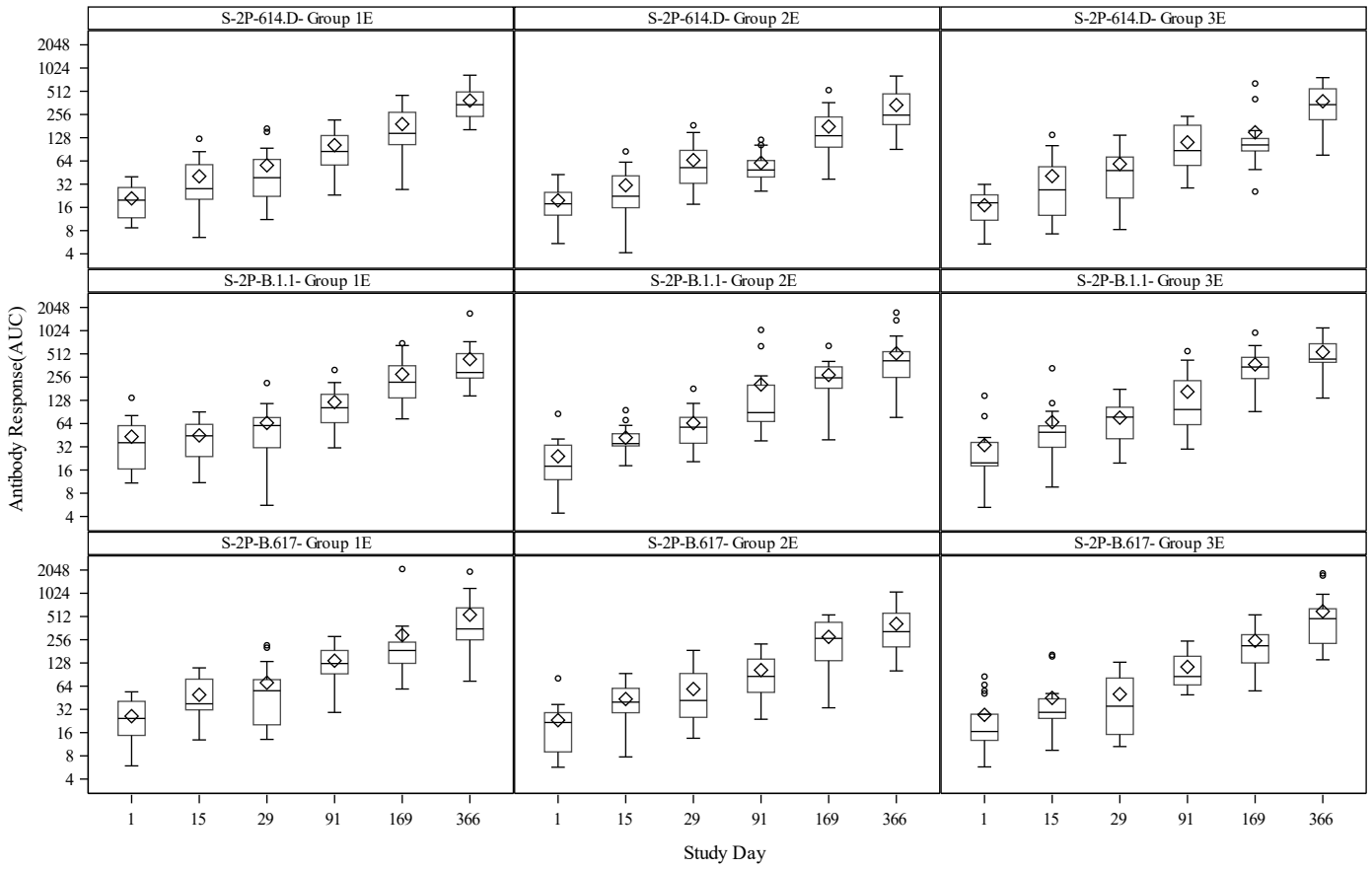


** Participants with (i) early termination recorded before Day 91 or (ii) early termination recorded after Day 91 but with last completed visit before Day*

14.2.2 Immunogenicity Response Figures by Measure, Study Group, and Time Point

Figure 2: Distribution of Serum IgG ECLIA (4-plex) Arbitrary Units/mL by Time Point and Study Group, S-2P–Wa-1 – mITT Population

[Implementation Note: A generic sample figure is shown below. The box plots should be presented in a single figure with three separate panels for each study group. Study group labels should be included in the panel headers. Within each panel individual box plot should be used for each study day (1 (Baseline), 15, 29, 91, 181, 273, and 366 post delayed vaccination boost).Update y-axis label to display Antibody Response (AU/mL)]



Figures with similar format:

Figure 3: Distribution of Serum IgG ECLIA (4-plex) Arbitrary Units/mL by Time Point and Study Group, S-2P–Wa-1 – Per Protocol Population

Figure 4: Distribution of Serum IgG ECLIA (4-plex) Arbitrary Units/mL by Time Point and Study Group, S-2P–B.1.351– mITT Population

Figure 5: Distribution of Serum IgG ECLIA (4-plex) Arbitrary Units/mL by Time Point and Study Group, S-2P–B.1.351– Per Protocol Population

Figure 6: Distribution of Serum IgG ECLIA (4-plex) Arbitrary Units/mL by Time Point and Study Group, RDB–B.1.351– mITT Population

Figure 7: Distribution of Serum IgG ECLIA (4-plex) Arbitrary Units/mL by Time Point and Study Group, RDB–B.1.351– Per Protocol Population

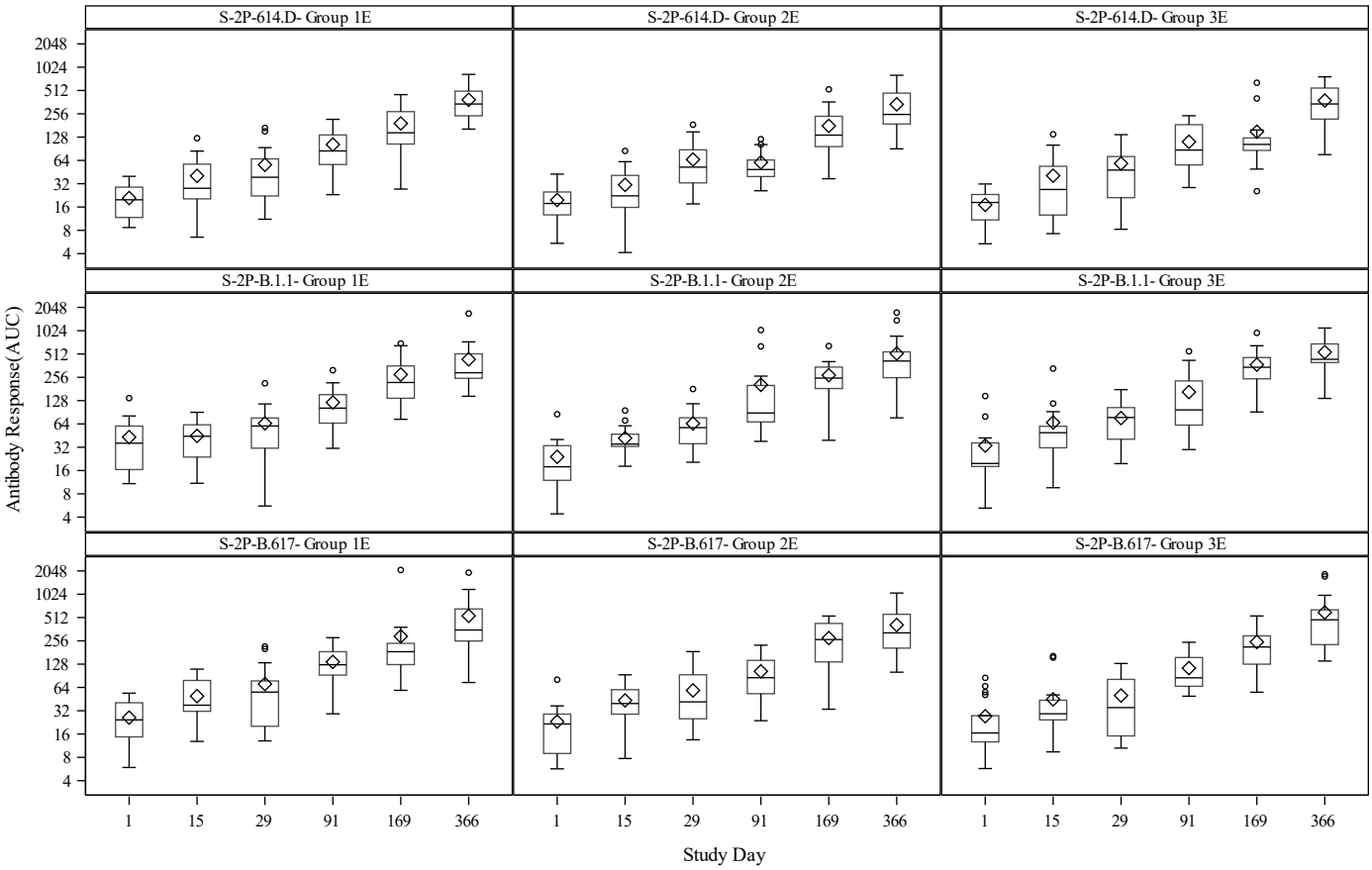
Figure 8: Distribution of Serum IgG ECLIA (4-plex) Binding Antibody Units/mL by Time Point and Study Group, S-2P-Wa-1– mITT Population

[Implementation note: Update y-axis label to display Antibody Response (BAU/mL).]

Figure 9: Distribution of Serum IgG ECLIA (4-plex) Binding Antibody Units/mL by Time Point and Study Group, S-2P-Wa-1– Per Protocol Population

[Implementation note: Update y-axis label to display Antibody Response (BAU/mL).]

Figure 10: Distribution of Serum IgG ECLIA (10-plex) Area under the Curve by Time Point and Study Group, S-2P–Wa-1– mITT Population



Figures with similar format:

Figure 11: Distribution of Serum IgG ECLIA (10-plex) Area under the Curve by Time Point and Study Group, S-2P–Wa-1– Per Protocol Population

Figure 12: Distribution of Serum IgG ECLIA (10-plex) Area under the Curve by Time Point and Study Group, S-2P–B.1.617.2– mITT Population

Figure 13: Distribution of Serum IgG ECLIA (10-plex) Area under the Curve by Time Point and Study Group, S-2P–B.1.617.2– Per Protocol Population

Figure 14: Distribution of Serum IgG ECLIA (10-plex) Area under the Curve by Time Point and Study Group, S-2P–B.1.351– mITT Population

Figure 15: Distribution of Serum IgG ECLIA (10-plex) Area under the Curve by Time Point and Study Group, S-2P–B.1.351– Per Protocol Population

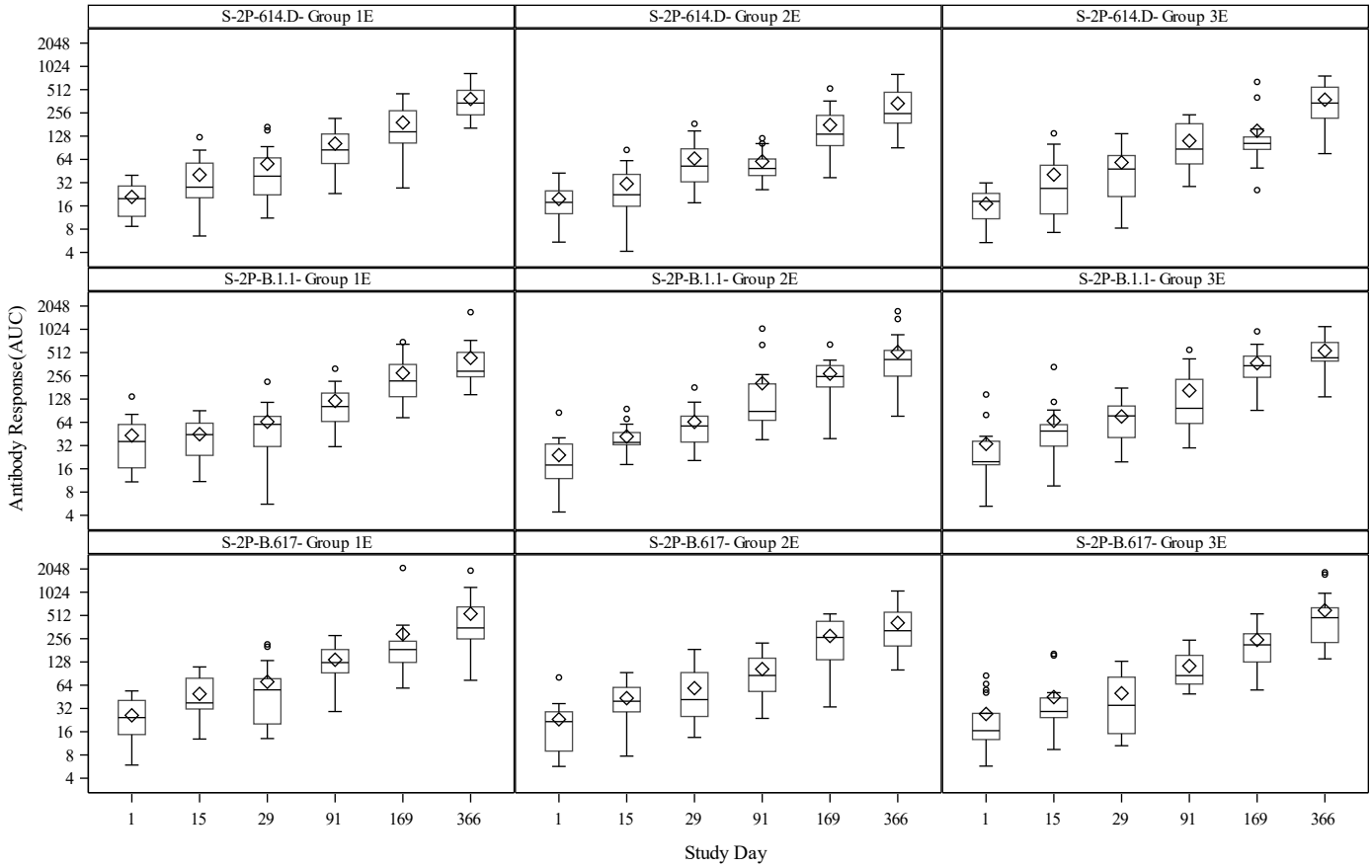
Figure 16: Distribution of Serum IgG ECLIA (10-plex) Area under the Curve by Time Point and Study Group, S-2P–B.1.1.529– mITT Population

Figure 17: Distribution of Serum IgG ECLIA (10-plex) Area under the Curve by Time Point and Study Group, S-2P–B.1.1.529– Per Protocol Population

Figure 18: Distribution of Pseudovirus Neutralization Assay ID_{50} Titers by Time Point and Study Group, D614G– mITT Population

[Update y-axis label to display Antibody Response (Titer).]

[Implementation note: If the assay results are reported on the mITT subset population, update the analysis population used in the title to reflect that.]



Figures with similar format:

Figure 19: Distribution of Pseudovirus Neutralization Assay ID_{50} Titers by Time Point and Study Group, D614G – Per Protocol Population

Figure 20: Distribution of Pseudovirus Neutralization Assay ID_{50} Titers by Time Point and Study Group, B.1.617.2– mITT Population

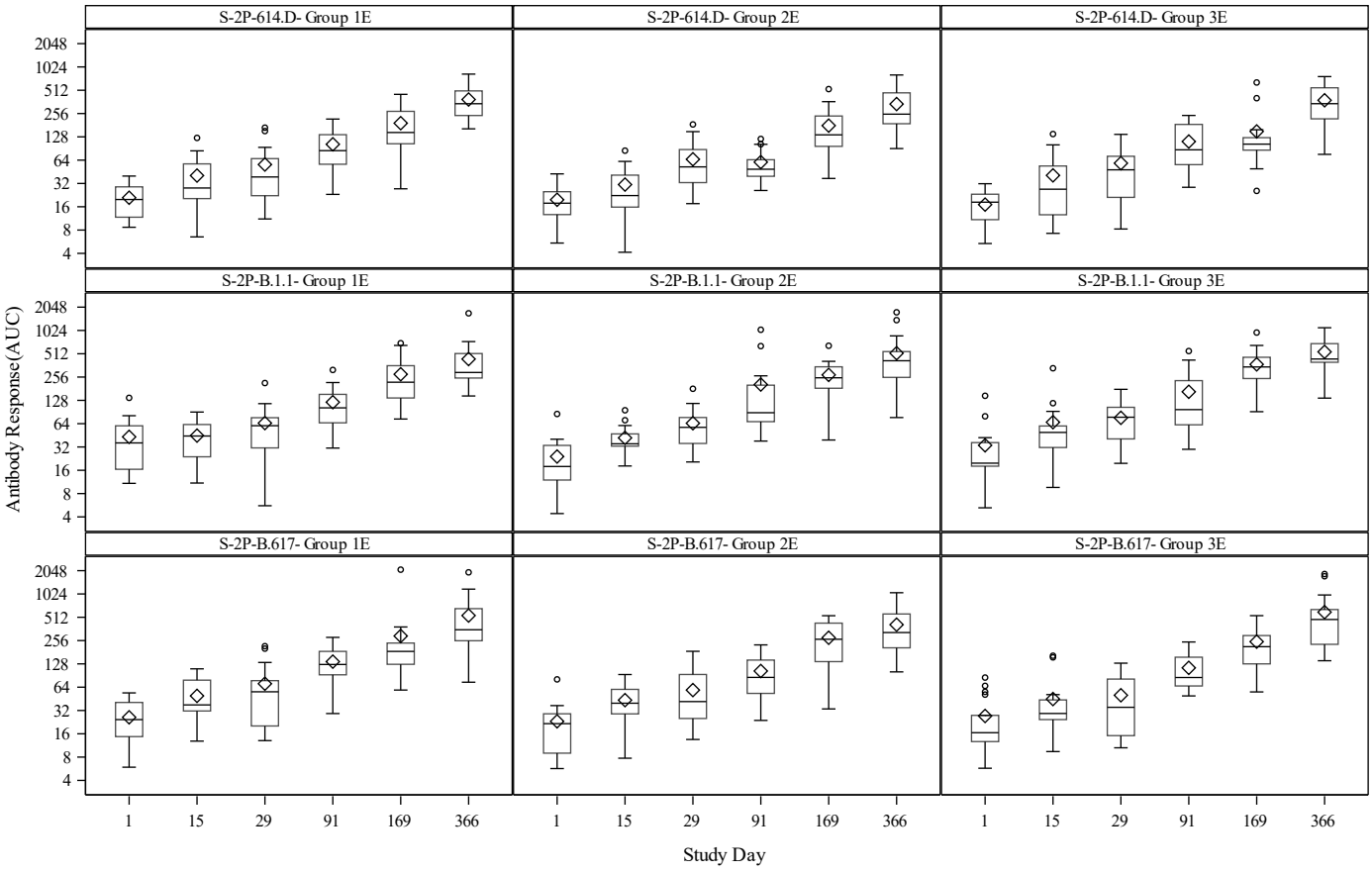
Figure 21: Distribution of Pseudovirus Neutralization Assay ID_{50} Titers by Time Point and Study Group, B.1.617.2 – Per Protocol Population

Figure 22: Distribution of Pseudovirus Neutralization Assay ID_{50} Titers by Time Point and Study Group, B.1.351– mITT Population

Figure 23: Distribution of Pseudovirus Neutralization Assay ID_{50} Titers by Time Point and Study Group, B.1.351 – Per Protocol Population

Figure 34: Distribution of Serum IgG ECLIA (4-plex) Arbitrary Units/mL by Time Point, Age Group, and Study Group, S-2P–Wa-1 – mITT Population

[Implementation Note: A generic sample figure is shown below. The box plots should be presented in a single figure with six panels for each study group and age group combinations. Study group/Age group labels should be included in the panel headers. Within each panel individual boxplots should be used for each study day ((1 (Baseline), 15, 29, 91, 181, 273, and 366 post delayed vaccination boost). Update y-axis label to display Antibody Response (AU/mL)]



Figures with similar format:

Figure 35: Distribution of Serum IgG ECLIA (4-plex) Arbitrary Units/mL by Time Point, Age Group, and Study Group, S-2P–Wa-1 – Per Protocol Population

Figure 36: Distribution of Serum IgG ECLIA (4-plex) Arbitrary Units/mL by Time Point, Age Group, and Study Group, S-2P–B.1.351– mITT Population

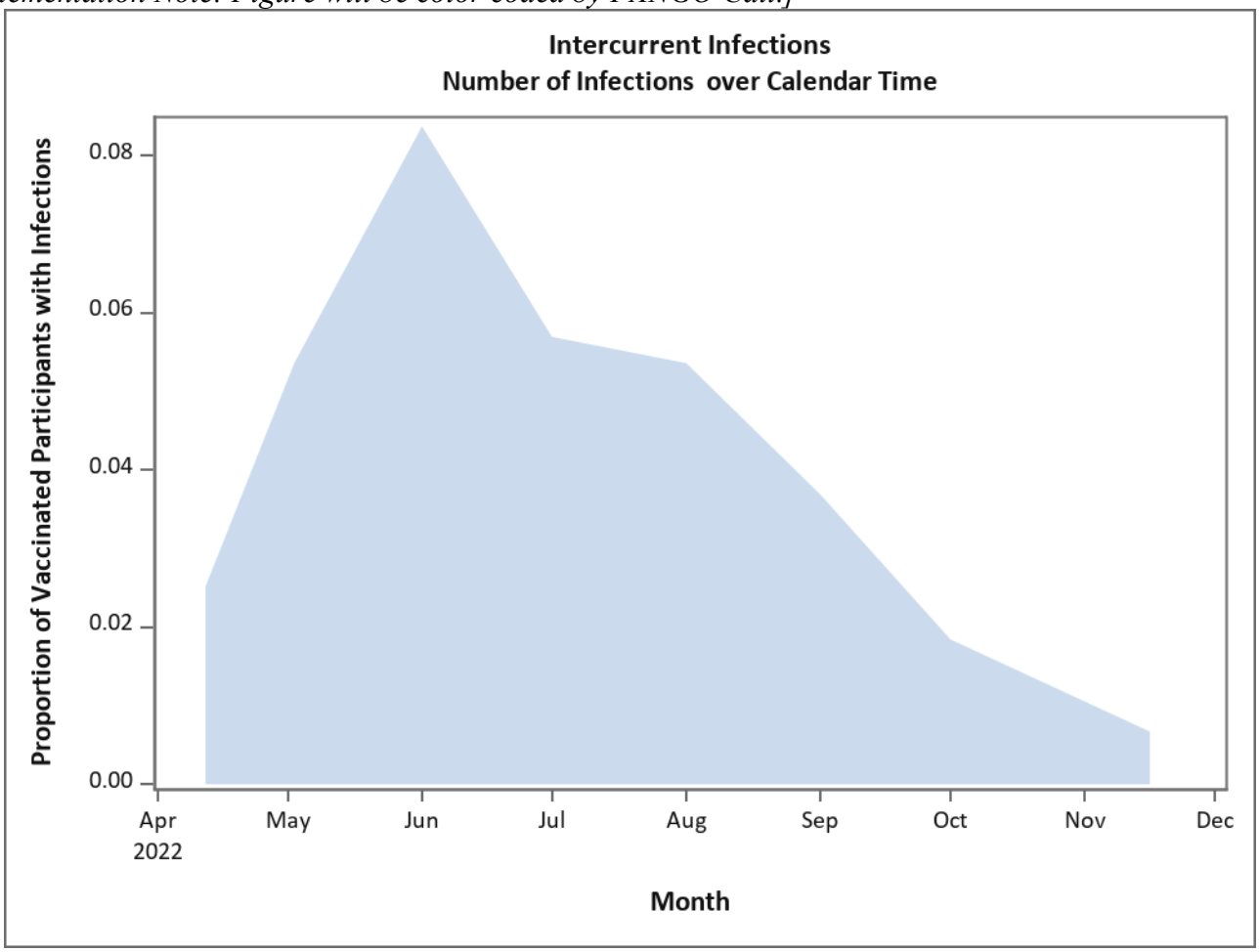
Figure 37: Distribution of Serum IgG ECLIA (4-plex) Arbitrary Units/mL by Time Point, Age Group, and Study Group, S-2P–B.1.351– Per Protocol Population

Figure 38: Distribution of Serum IgG ECLIA (4-plex) Arbitrary Units/mL by Time Point, Age Group, and Study Group, RDB–B.1.351– mITT Population

Figure 39: Distribution of Serum IgG ECLIA (4-plex) Arbitrary Units/mL by Time Point, Age Group, and Study Group, RDB–B.1.351– Per Protocol Population

Figure 66: Summary of Breakthrough Infections by PANGO Call and Study Group – Group 4E [Dosed Janssen, Boost Janssen], mITT Population

[Implementation Note: Figure will be color coded by PANGO Call.]



Figures with similar format:

Figure 67: Summary of Breakthrough Infections by PANGO Call and Study Group – Group 5E [Dosed Moderna, Boost Janssen], mITT Population

Figure 68: Summary of Breakthrough Infections by PANGO Call and Study Group – Group 6E [Dosed Pfizer, Boost Janssen], mITT Population

14.3.1.1 Solicited Adverse Events

Figure 69: Maximum Severity of Solicited Systemic Symptoms by Days Post Delayed Vaccination Boost

*[Implementation Note: A Generic figure is shown below. A **horizontal** bar chart should be presented in 1 image file with separate panels for each study group (3 panels). Axes should be labeled as follows: y-axis label: Study Day, x-axis label: Percentage of Participants (%). The study groups should be indicated in the panel headers including "(N=X)", where N = the number of participants in the in the Safety Population. Participants are counted at most once at the maximum severity across all systemic events reported for the specified time point]*

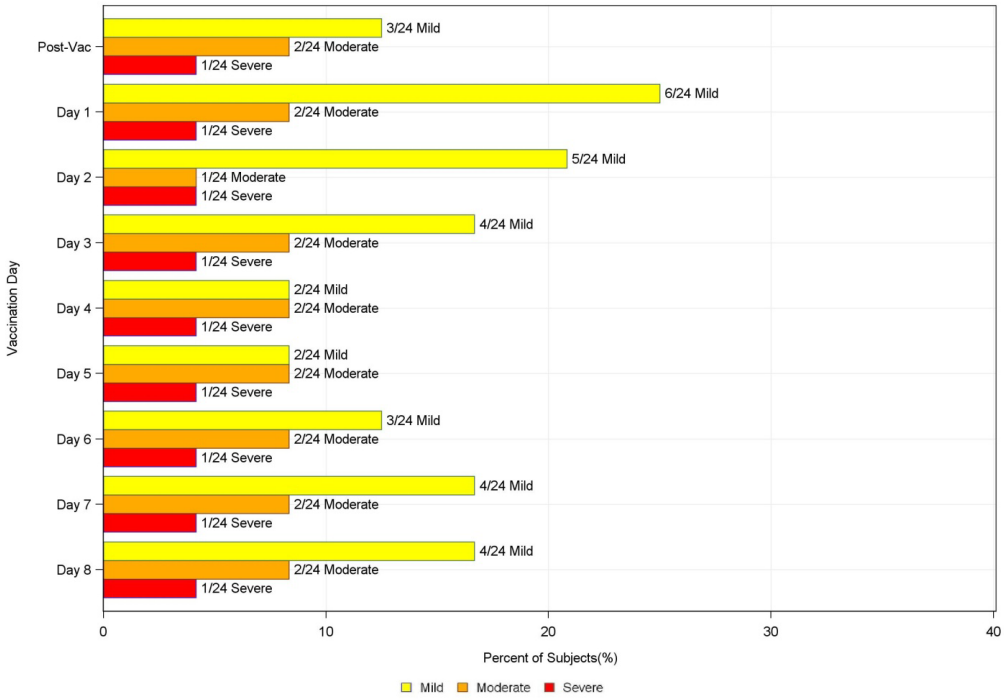


Figure with similar format:

Figure 70: Maximum Severity of Solicited Local Symptoms by Days Post Delayed Vaccination Boost

14.3.1.2 Unsolicited Adverse Events

Figure 71: Frequency of Adverse Events by MedDRA System Organ Class and Maximum Severity

*[Implementation Note: A Generic figure is shown below. This figure includes all unsolicited events. A **horizontal** bar chart should be presented in 1 image file separate panels for each study group (3 panels). Axes should be labeled as follows: y-axis label: System Organ Class, x-axis label: Number of Events. The study groups should be indicated in the panel headers including "(N=X)", where N = the number of participants in the in the Safety Population. The y-axis should present all SOCs reported by at least 1 participant and an "All Events" category. Y-axis should be sorted with "All Events first, then in decreasing order of total frequency]*

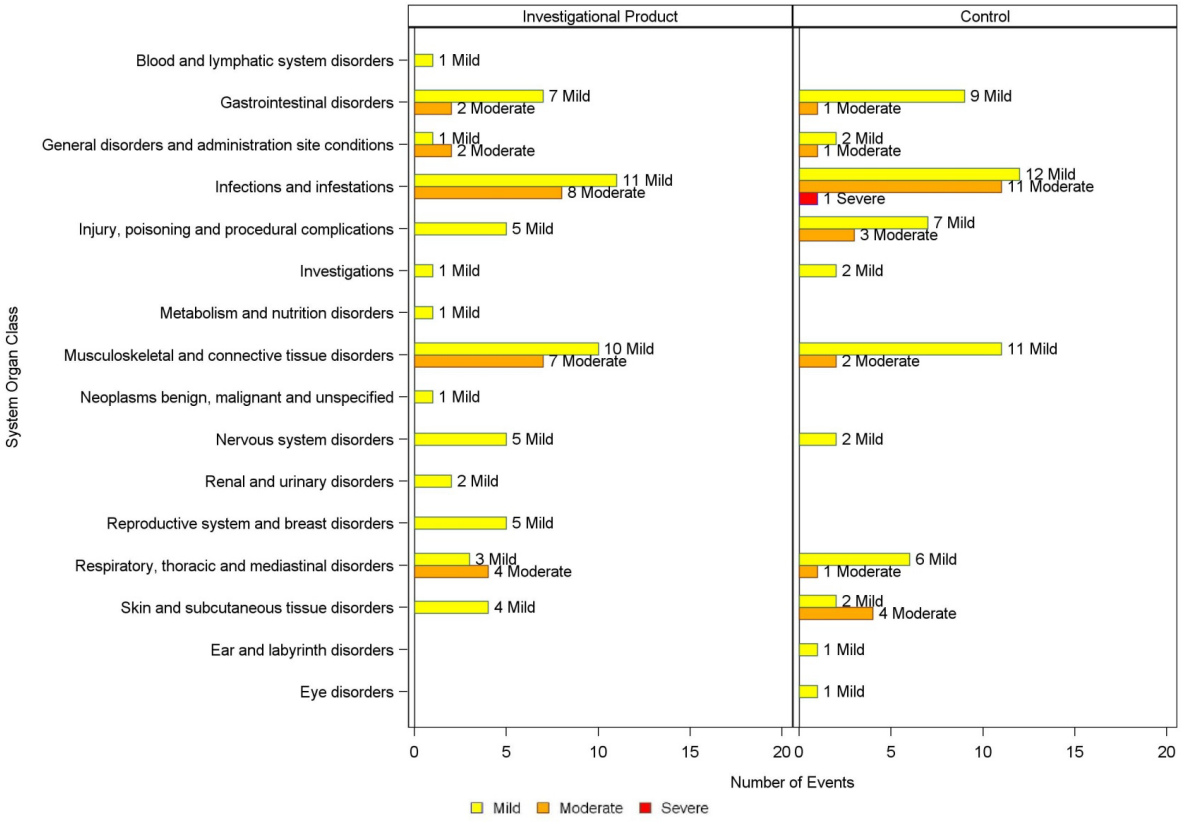


Figure 72: Incidence of Adverse Events by MedDRA® System Organ Class and Maximum Severity

*[Implementation Note: A Generic figure is shown below. This figure includes all unsolicited events. A **horizontal** bar chart should be presented in 1 image file separate panels for each study group (3 panels). Axes should be labeled as follows: y-axis label: System Organ Class, x-axis label: Number of Events. The study groups should be indicated in the panel headers including "(N=X)", where N = the number of participants in the in the Safety Population. The y-axis should present all SOCs reported by at least 1 participant and an "All Events" category. Y-axis should be sorted with "All Events first, then in decreasing order of total incidence]*

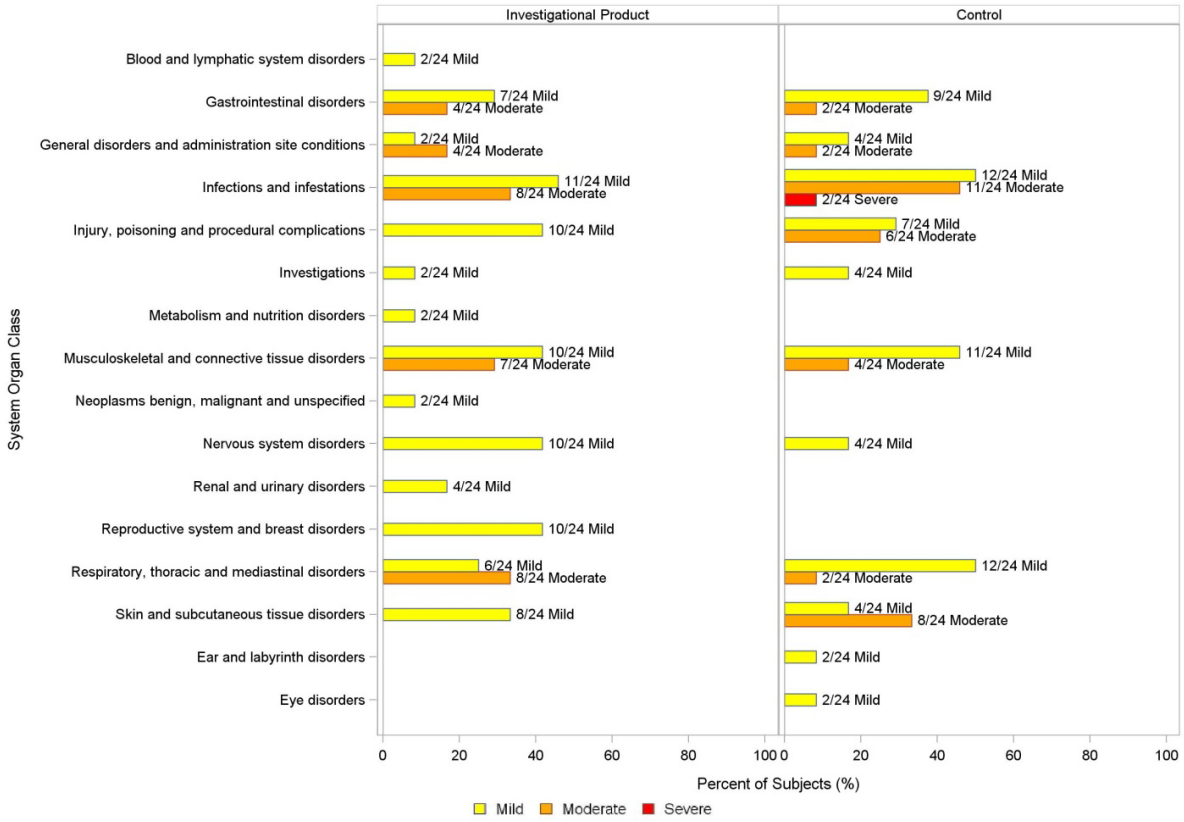


Figure 73: Frequency of Adverse Events by MedDRA System Organ Class and Relationship to Study Vaccination

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

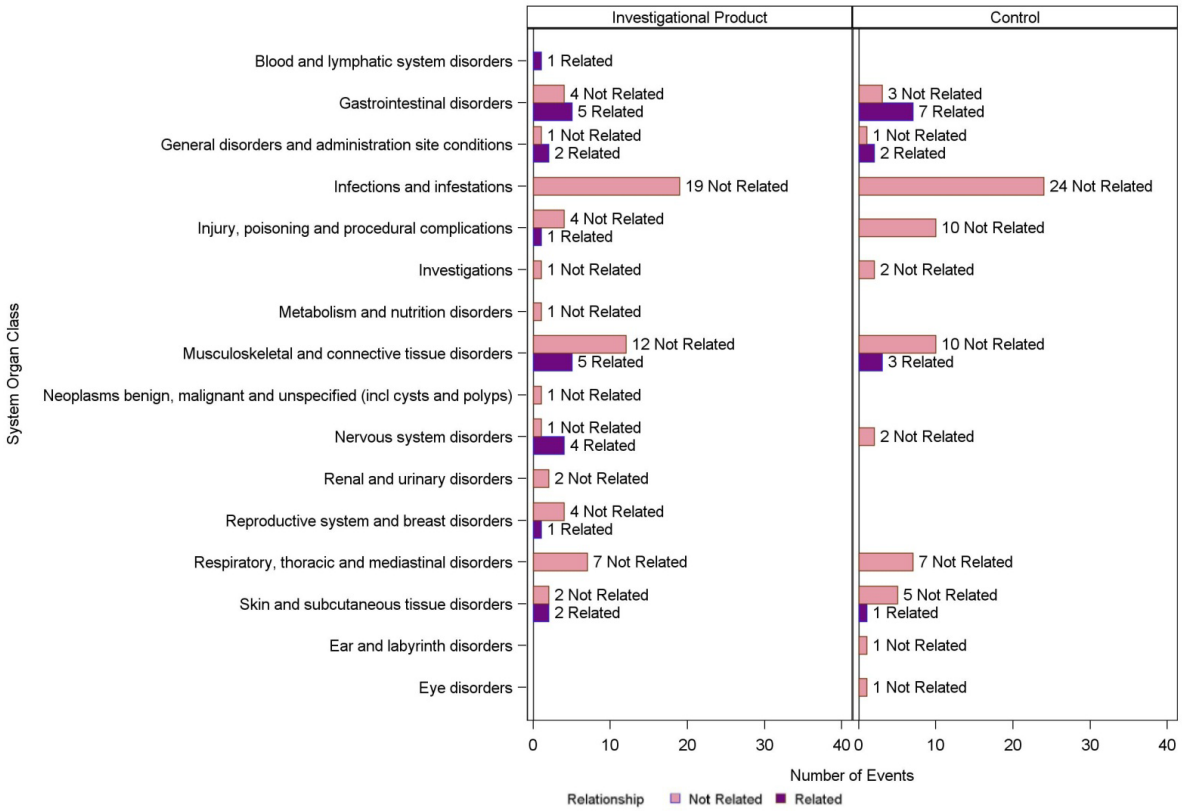
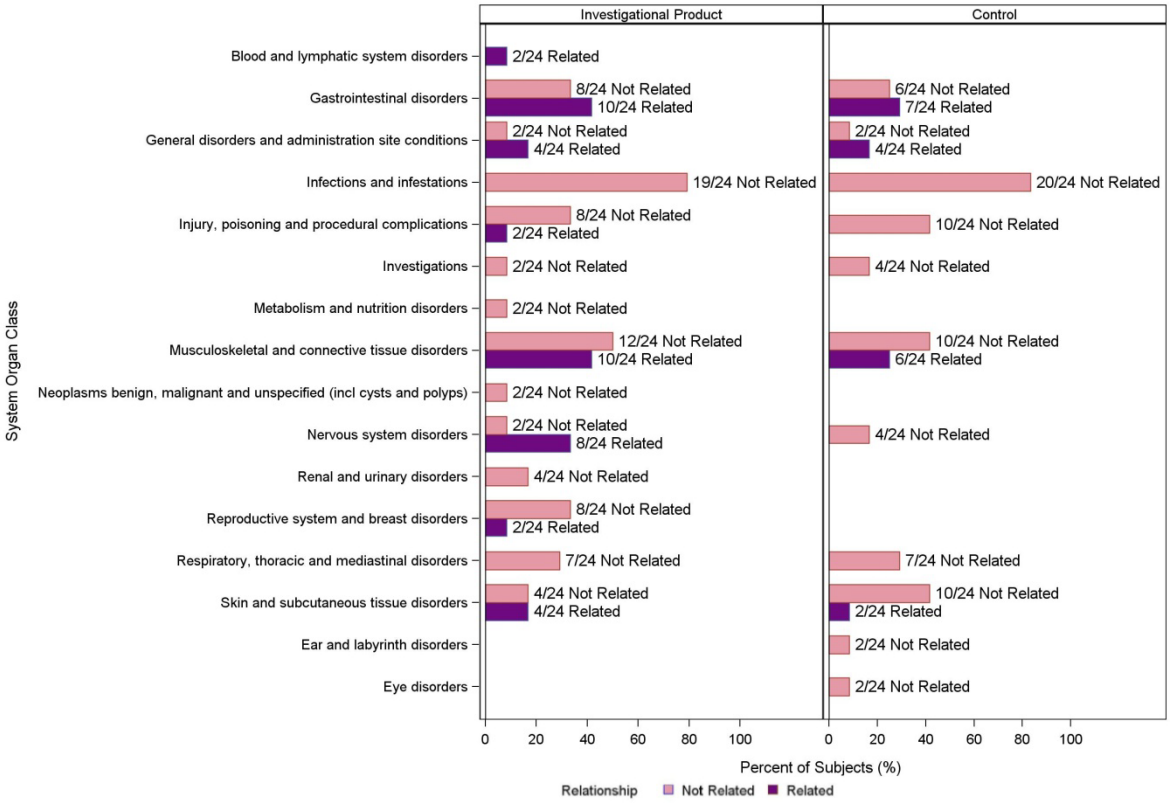


Figure 74: Incidence of Adverse Events by MedDRA System Organ Class and Relationship to Study Vaccination

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



14.3.5 Displays of Laboratory Results

Not Applicable.

APPENDIX 3. LISTINGS MOCK-UPS

LISTINGS

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

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

16.2 Database Listings by Participant

16.2.1 Discontinued Participants

Listing 2: 16.2.1.1: Early Terminations

[Implementation Note: Sort the listing by study group and participant ID.]

Study Group	Participant ID	Reason for Early Termination	Study Day

Listing 3: 16.2.1.2: Enrolled but Not Vaccinated

[Implementation Note: Sort the listing by study group and participant ID.]

Study Group	Participant ID	Reason Enrolled but not Vaccinated	Study Day

16.2.2 Protocol Deviations

Listing 4: 16.2.2.1: Participant-Specific Protocol Deviations

[Implementation Note: Sort the listing by study group, participant ID, and DV number]

Study Group	Participant ID	DV Number	Study Day	Deviation Type	Description of Deviation	Deviation Reported to IRB/EC?

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

[Implementation Note: Sort the listing by site and deviation date.]

Site	Deviation Date	Deviation	Description of Deviation

16.2.3 Participants Excluded from the Efficacy Analysis

Listing 6: 16.2.3: Participants Excluded from Analysis Populations

[Implementation Note: Sort the listing by study group and participant ID.]

Study Group	Participant ID	Analyses in which Participant is Included	Analyses from which Participant is Excluded	Results Available?	Reason Participant 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 7: 16.2.4.1: Demographic Data

[Implementation Note: Sort the listing by study group and participant ID.]

Study Group	Participant ID	Sex	Age at Enrollment (years)	Ethnicity	Race	Weight (kg)	Height (cm)	BMI (kg/m^2)

Listing 8: 16.2.4.2: Pre-Existing and Concurrent Medical Conditions

[Implementation Note: Sort the listing by study group, participant ID, and MH number.]

Study Group	Participant 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 9: 16.2.6: Individual Immunogenicity Response Data

[Implementation Note: Sort the listing by study group, participant ID, Assay, Variant, and Planned Time Point..]

Study Group	Participant ID	Planned Time Point	Actual Study Day	Assay	Variant	Units	Results

16.2.7 Adverse Events

Listing 10: 16.2.7.1: Solicited Events – Systemic Symptoms

[Implementation Note: Sort the listing by study group, participant ID, symptom, and post dose day. For temperature, include severity in parentheses.]

Study Group	Participant ID	Post Dose Day	Symptom	Severity

Listing 11: 16.2.7.2: Solicited Events – Local Symptoms

[Implementation note: For erythema and induration, include measurements in parentheses for severity.

Sort the listing by study group, participant ID, symptom, and post dose day.]

Treatment Group	Participant ID	Symptom	Post Dose Day	Severity

Listing 12: 16.2.7.3: Unsolicited Adverse Events

[Implementation note: Sort the listing by study group, participant ID, and AE number.]

Adverse Event	Day of Onset (Duration)	Severity	SAE?	AESI?	NOCMC?	MAAE?	Unanticipated Problem?	Relationship to Study Vaccination	In Not Related, Alternative Etiology	Action Taken with Study Vaccination	Action Taken to Treat AE	Outcome	MedDRA System Organ Class	MedDRA Preferred Term
Study Group: , Participant ID: , AE Number:														
Comments:														
Comments:														
Study Group: , Participant ID: , AE Number:														
Comments:														
Note: For additional details about SAEs, see Table: 60.														

16.2.8 Individual Laboratory Measurements

Listing 13: 16.2.8.1: SARS-CoV-2 Test Results

[Implementation note: Sort the listing by study group, participant ID, symptom, and post dose day.]

Treatment Group	Participant ID	Specimen Collection Date	Test Type	Test Result

16.2.9 Vital Signs and Physical Exam Findings

Listing 14: 16.2.9.1: Vital Signs

[Implementation note: Sort the listing by study group, participant ID, and planned time point.]

Study Group	Participant 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 15: 16.2.9.2: Abnormal Physical Exam Findings

[Implementation note: Only include abnormal physical exam findings. Sort the listing by study group, participant ID, planned time point and body system.]

Study Group	Participant ID	Planned Time Point	Actual Study Day	Body System	Abnormal Finding

16.2.10 Concomitant Medications

Listing 16: 16.2.10: Concomitant Medications

[Implementation note: Sort the listing by study group, participant ID, and CM number.]

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

16.2.11 Pregnancy Reports

Listing 17: 16.2.11.1: Pregnancy Reports – Maternal Information

[Implementation note: Sort the listing by study group, participant ID, and pregnancy number.]

Study Group	Participant ID	Pregnancy Number	Study Day of onset of last menstrual period	Amenorrheic for Past 6 Months	Estimated Day of Delivery	Source of Information to Estimate Date of Delivery	Study Day of Ultrasound	First Pregnancy Since Enrollment?
Note: Maternal Complications are included in the Adverse Event listing. Medications taken during pregnancy are included in the Concomitant Medications Listing.								

Listing 18: 16.2.11.2: Pregnancy Reports – Gravida and Para

	Live Births												
Participant ID	Number of Extremely PLBs[a]	Number of Very PLBs[a]	Number of Early PLBs[a]	Number of Late PLBs[a]	Number of Early TLBs[b]	Number of Full TLBs[b]	Number of Late TLBs[b]	Number of Post TLBs[b]	Number of Spontaneous Fetal Deaths and/or Still Births	Number Spontaneous Abortions	Number Elective or Therapeutic Abortions	Number of Ectopic Pregnancies	Pregnancy Complications or Fetal/Infant Congenital Anomalies?
Note: Gravida includes the current pregnancy, para events do not. [a] Preterm Live Birth [b] Term Live Birth													

Listing 19: 16.2.11.3: Pregnancy Reports – Live Birth Outcomes

Participant 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?	Non-delivery Related Complications?
Note: Congenital Anomalies are included in the Adverse Event listing.												

Listing 20: 16.2.11.4: Pregnancy Reports – Still Birth Outcomes

Participant ID	Date of Initial Report	Fetus Number	Pregnancy Outcome (for this Fetus)	Autopsy Performed?	If Autopsy, Reason for Still Birth/Intrauterine Fetal Demise Determined?

Listing 21: 16.2.11.5: Pregnancy Reports – Spontaneous, Elective, or Therapeutic Abortion Outcomes

Participant 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