CLINICAL RESEARCH IN INFECTIOUS DISEASES

STATISTICAL ANALYSIS PLAN
for
DMID Protocol: 20-0034
Study Title:

A Phase 1 Trial to Evaluate the Safety, Immunogenicity, and Reactogenicity of Heterologous and Homologous Chimpanzee Adenovirus and Self-Amplifying mRNA Prime-Boost Prophylactic Vaccines Against SARS-CoV-2 in Healthy Adults

NCT04776317

Version 1.0

DATE: 29 November 2023

RESTRICTED

STUDY TITLE

Protocol Number Code:	**DMID Protocol: 20-0034**
Development Phase:	Phase 1
Products:	GRT-C907, GRT-R908, GRT-C909, GRT-R910
Form/Route:	Injection
Indication Studied:	2019-nCoV
Sponsor:	Division of Microbiology and Infectious Diseases National Institute of Allergy and Infectious Diseases National Institutes of Health
Clinical Trial Initiation Date:	01MAR2021
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Version Number:	1.0

This study was performed in compliance with Good Clinical Practice.

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LIST OF ABBREVIATIONS

AE	Adverse Event
AESI	Adverse Event of Special Interest
ALP	Alkaline Phosphatase
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
BMI	Body Mass Index
BP	Blood Pressure
C	Celsius
CDC	Centers for Disease Control and Prevention
CFR	Code of Federal Regulations
ChAd	Chimpanzee Adenovirus
CI	Confidence Interval
CK	Creatine Kinase
COVID-19	Coronavirus Disease 2019
Cr	Creatinine
CRF	Case Report Form
CSR	Clinical Study Report
DMID	Division of Microbiology and Infectious Diseases
DSMB	Data and Safety Monitoring Board
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
ELISA	Enzyme-linked Immunosorbent Assay
ELISpot	Enzyme-linked Immunospot
EUA	Emergency Use Authorization
F	Fahrenheit
GBS	Guillain-Barré Syndrome
GMT	Geometric Mean Titer
GMFR	Geometric Mean Fold Rise
HgB	Hemoglobin

List of Abbreviations *(continued)*

ICF	Informed Consent Form
ICH	International Conference on Harmonisation
ICS	Intracellular Cytokine Staining
IDCRC	Infectious Diseases Clinical Research Consortium
IFN	Interferon
IgG	Immunoglobulin G
IRB	Institutional Review Board
ITT	Intention to Treat
IQR	Interquartile range
L	Liter
LLN	Lower Limit of Normal
MAAE	Medically Attended Adverse Event
mcg	Microgram
MedDRA	Medical Dictionary for Regulatory Activities
mEq	Milliequivalent
mg	Milligram
mITT	Modified Intention to Treat
mL	Milliliter
mmHg	Millimeters of Mercury
mRNA	Messenger Ribonucleic Acid
N	Number (typically refers to participants)
NIH	National Institutes of Health
NOCMC	New Onset Chronic Medical Conditions
PBMC	Peripheral Blood Mononuclear Cell
PCR	Polymerase Chain Reaction
PI	Principal Investigator
PIMMC	Potentially Immune-Mediated Medical Condition
PLT	Platelets
PP	Per Protocol
PT	Preferred Term

List of Abbreviations *(continued)*

RBC	Red Blood Cell
RBD	Ribosomal binding domain
RCD	Reverse Cumulative Distribution
SAE	Serious Adverse Event
SAM	Self-Amplifying mRNA
SAP	Statistical Analysis Plan
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
SD	Standard Deviation
SDCC	Statistical and Data Coordinating Center
SMC	Safety Monitoring Committee
SOC	System Organ Class
SOP	Standard Operating Procedures
T Bili	Total Bilirubin
TCE	T Cell Epitope
Th1	T Helper Cell Type 1
Th2	T Helper Cell Type 2
TTS	Thrombosis with Thrombocytopenia Syndrome
U	Units
ULN	Upper Limit of Normal
VITT	Vaccine-Induced Immune Thrombotic Thrombocytopenia
WBC	White Blood Cell
WHO	World Health Organization
YO	Years Old

1. PREFACE

The Statistical Analysis Plan (SAP) for "A Phase 1 Trial to Evaluate the Safety, Immunogenicity, and Reactogenicity of Heterologous and Homologous Chimpanzee Adenovirus and Self-Amplifying mRNA Prime-Boost Prophylactic Vaccines Against SARS-CoV-2 in Healthy Adults" (DMID Protocol 20-0034) describes and expands upon the statistical information presented in the protocol.

This document describes all planned analyses and provides reasons and justifications for these analyses. It also includes sample tables, figures, and listings (TFLs) 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 TFLs. Within the TFL mock-ups (Appendices 1, 2, and 3), references to CSR sections are included. Any deviation from this SAP will be described and justified in protocol amendments and/or in the CSR, as appropriate. The reader of this SAP is encouraged to also review the study protocol for details on conduct of the study and the operational aspects of clinical assessments.

2. INTRODUCTION

This phase 1 clinical trial will explore the ability of novel vectors (notably self-amplifying mRNA or SAM), a novel schedule (heterologous or homologous prime-boost), and novel SARS-CoV-2 epitope cassettes (extending COVID antigenic vaccine content beyond Spike) to safely drive strong, broad, durable immune responses to SARS-CoV-2. Cassette S contains a codon optimized Spike and will be assessed during Stage 1. An additional Spike-T Cell Epitope (S-TCE) cassette will also be studied in Stage 1 as well as in Stage 2.

The successful emergency use authorization (EUA)/licensed COVID-19 vaccine roll-out campaign has resulted in a diminishing domestic naïve population. Most of the population has received an EUA/licensed mRNA COVID-19 vaccine; to optimize homogeneity of study groups, we focus on the enrollment of EUA/licensed mRNA COVID-19 vaccine experienced participants into the majority of Stage 2 Groups. Due to the rare cases of Thrombosis and Thrombocytopenia Syndrome (TTS) associated with the approved AstraZeneca and EUA Johnson & Johnson/Janssen adenovirus vectored COVID-19 vaccines in patients primarily <50 years old, we will focus on boosting participants >60 years old with Chimpanzee Adenovirus (ChAd)-S-TCE. In addition, ChAd-S-TCE vaccine may be a stronger T cell response inducer than the SAM-S-TCE vaccine, particularly in the elderly, which further supports boosting of participants >60 years old.

Because the EUA/licensed COVID-19 vaccines encode only the Spike protein, a single boost with ChAd-S-TCE or SAM-S-TCE will boost spike-specific T cell immunity yet may only prime a TCE-specific response in previously vaccinated participants. Ongoing studies suggest increased receipt of additional doses of mRNA COVID-19 vaccines may increase reactogenicity in persons previously vaccinated with mRNA COVID-19 vaccines. Therefore, participants who previously received two EUA/licensed mRNA COVID-19 vaccines will receive one boost of SAM-S-TCE, whereas participants previously given at least one dose of the Johnson & Johnson/Janssen Ad26 COVID-19 EUA plus one booster dose of EUA/licensed mRNA COVID-19 vaccine will receive two boosts of SAM-S-TCE to determine whether the TCE-specific response can be enhanced.

The vector, antigenic cassette, schedule, and dose that generates the strongest T and B cell responses to SARS-CoV-2 will be identified during this phase 1 clinical trial for subsequent phase 2/3 testing and will also provide proof-of-concept that we can mix and match genetic and viral vector platforms, which will provide much needed information with the limited available doses of mRNA and adenoviral-vectored vaccines.

2.1. Purpose of the Analyses

These analyses will assess the safety, reactogenicity, and immunogenicity of different doses of homologous prime-boost (SAM-S x 2 and SAM-S-TCE x 2), heterologous prime-boost (ChAd-S + SAM-S) regimens in COVID-19 infection and vaccination naïve individuals, as well as single and double boosting participants previously given EUA/licensed COVID-19 vaccination(s), in healthy adults 18-60 years old and >60 years old. Analyses will be included in the clinical study report.

3. STUDY OBJECTIVES AND ENDPOINTS

The table below presents the study objectives and endpoints.

Table 1: Objectives and Endpoints

Objectives	Endpoints (Outcome Measures)
Primary	
• To assess the safety and tolerability of different doses of ChAd-S or ChAd-S-TCE, and SAM-S or SAM-S-TCE when administered as: – prime-boost in healthy naïve adult participants – boost in healthy adult participants previously vaccinated with an EUA/licensed mRNA or adenoviral-vectored COVID-19 vaccine	• Occurrence of solicited local reactogenicity signs and symptoms for 7 days following each study vaccination • Occurrence of solicited systemic reactogenicity signs and symptoms for 7 days following each study vaccination • Occurrence of unsolicited AEs for 28 days following each study vaccination • Change from baseline for clinical safety laboratory parameters 7 days after each study vaccination • Occurrence of SAEs and AESIs, including PIMMCs, MAAEs and NOCMCs, throughout the entire study following the first study vaccination
Secondary	
• To assess the humoral immunogenicity of ChAd-S or ChAd-S-TCE, and SAM-S or SAM-S-TCE	• Response rate, and magnitude of SARS-CoV-2-specific antibody binding and neutralization titers (including against emergent viral strains, e.g., B.1.1.7) in serum samples will be assessed via a range of assays measuring total Spike-specific IgG (ELISA-based), and function (neutralization, RBD binding, or similar) in serum on the following days: For Stage 1, Groups 1 and 3A: Days 1 and 29 post Dose 1; then Days 29, 181, and 366 post Dose 2 For Stage 1, Groups 3B and 4: Days 1, 29, 57, and 85-130 post Dose 1; then Days 15, 29, 85, 181, and 366 post Dose 2 For Stage 2, Groups 5-7A*, 7B*, 9, 10A, 10B, and 11A, 11B, and 13-15: Days 1, 15, 29, 85, 181, and 366 post study vaccination For Stage 2, Groups 8A*, 8B* and 12A*, 12B*: Days 1, 15, 29, and 57 post Dose 1; then Days 15, 29, 85, 181, and 366 post Dose 2
• To assess T cell responses to ChAd-S or ChAd-S-TCE, and SAM-S or SAM-S-TCE	• Response rate, magnitude, and functional profiling of SARS-CoV-2 specific T cells stimulated with overlapping 15mers covering Spike and TCE regions from all participants at pre- and post-treatment timepoints will be analyzed by IFN-γ ELISpot: For Stage 1, Groups 1 and 3A: Days 1 and 29 post Dose 1; then Days 29, 181, and 366 post Dose 2 For Stage 1, Groups 3B and 4: Days 1, 29, and 85-130 post Dose 1; then Days 15, 29, 85, 181, and 366 post Dose 2 For Stage 2, Groups 5-7A*, 7B*, 9, 10A, 10B, 11A, 11B, and 13-15: Days 1, 15, 29, 85, 181, and 366 post study vaccination

Objectives	Endpoints (Outcome Measures)
	For Stage 2, Groups 8A*, 8B*, and 12A*, 12B*: Days 1, 15, 29, and 57 post Dose 1; then Days 15, 29, 85, 181, and 366 post Dose 2 And by Intracellular Cytokine Staining (ICS): For Stage 1, Groups 1 and 3A: Days 1 and 29 post Dose 1; then Day 29 post Dose 2 For Stage 1, Groups 3B and 4: Days 1, 29, and 85-130 post Dose 1; then Day 15 post Dose 2 For Stage 2, Groups 5-7A*, 7B*, 9, 10A, 10B, 11A, 11B, and 13-15: Days 1 and 15 post study vaccination For Stage 2, Groups 8A*, 8B*, and 12A*, 12B*: Days 1, 15, and 57 post Dose 1; then Day 15 post Dose 2 • ELISpot supernatants from 4-week post-boost timepoints from a subset of participants will be assessed for Th1/Th2 cytokine balance of T cell response by measuring IL-2, TNF-α, IL-4, IL-10, and IL-13
Exploratory	
• To assess memory B cell responses to ChAd-S or ChAd-S-TCE, and SAM-S or SAM-S-TCE	• Antigen-specificity of memory B cells at late timepoints (6- and/or 12-month follow-up) in a subset of participants will be assessed by Spike multimer binding (flow cytometry-based assay) and/or IgG ELISpot
• To assess antibody responses to the ChAd68 vector	• Response rate and magnitude of ChAd68-specific neutralization titers in serum, pre- and post study vaccination, in participants who receive the ChAd-S and ChAd-S-TCE vaccines, at the following timepoints: For Groups 1, 13, 14, and 15: Days 1 and 29 post Dose 1
* After protocol version 9.0 was implemented, it was decided not to enroll participants into Groups 7 and 8 because of competing priorities and predicted difficulties enrolling into these two groups. Group 12 was also not enrolled.	

3.1. Study Definitions and Derived Variables

Vital signs, including oral temperature, pulse, and blood pressure (BP), and clinical laboratory parameters obtained prior to the first study vaccination will be considered as baseline. Blood drawn for cellular immunology assays, antibody assays, and transcriptomal assays (groups 5-11, 13-15 only) prior to the first dose of study product will be considered as baseline in immunogenicity analyses.

4. INVESTIGATIONAL PLAN

4.1. Overall Study Design and Plan

This is a multicenter, US-only, phase 1, open-label, dose escalation, non-randomized study of the safety, tolerability, and immunogenicity of investigational ChAd and SAM SARS-CoV-2 vaccines in healthy adult participants. Homologous and heterologous prime-boost vaccination schedules (Stage 1), as well as boost(s) after receipt of EUA/licensed COVID-19 vaccines (Stage 2) will be examined. Participants' willingness to receive ChAd vaccines will be assessed and documented at the time of informed consent and considered to determine group assignments.

This phase 1 study will enroll 17 Stage 1 and up to 118 Stage 2 participants. Eligible participants will be enrolled in different groups based on their age (18-60 years old and >60 years old) and their EUA/licensed COVID-19 vaccination status. A sentinel approach with 72-hour (Stage 1, and Stage 2, Groups 5, 6, 8*-10, 12*, 13-15) or 7-day observation times (Groups 7* and 11) will be used before recruiting the remainder of each dose escalation group. Decisions about dose escalation will be determined by the Study Steering Committee (SSC) with consultation with the Data and Safety Monitoring Board (DSMB) as needed after all participants in each group have been observed through Day 8 post first study vaccination. All participants will be followed through 12 months after their last study vaccination. Vaccinated participants will be carefully monitored for exposure and infection to SARS-CoV-2 throughout the study.

Escalation to the highest dose (10 µg) of SAM-S-TCE in younger participants will proceed only following safety assessments of the 10 µg dose in older participants for a period of 28 days post-vaccination.

In addition, the dosage of SAM-S-TCE given as a double boost to participants previously vaccinated with the Johnson & Johnson/Janssen Ad26 COVID-19 EUA vaccine in Groups 8A*, 8B*, and 12A*, 12B* will be determined based on the dose escalation reactogenicity and immunogenicity results in Groups 5-7* and 9-11, respectively.

See Table 2, Figure 1, Table 3, and Section 4.4 for details on group assignments, study vaccines, and doses to be administered.

* After protocol version 9.0 was implemented, it was decided not to enroll participants into Groups 7 and 8 because of competing priorities and predicted difficulties enrolling into these groups. Group 12 was also not enrolled for the same reasons.

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

No control groups were used.

4.3. Selection of Study Population

The study population will include healthy adults aged 18 years and older, who are naïve or previously vaccinated with a COVID-19 EUA vaccine. In addition, participants that have experienced prior infection with SARS-CoV-2 or those not previously infected will be studied. However, participants with recent (within the last 4 months of enrollment) or acute infection (PCR positive) will be excluded.

The study will enroll participants from at least 4 US-based Infectious Diseases Clinical Research Consortium (IDCRC) sites.

4.4. Treatments

4.4.1. Treatments Administered

The following vaccinations will be administered.

Table 2: Vaccination Arms

Stage	Study Population	Group	Sample Size	Vaccination(s)	Day of Dosing/ Interval Between Doses (Days)
1*	Naïve (18-60 yo)	1	4	5 x 10^{10} vp ChAd-S/ 30 µg SAM-S	28
		3A	3	30 µg SAM-S/ 30 µg SAM-S	28
		3B	7	30 µg SAM-S/ 3 µg SAM-S	84-129
		4	3	10 µg SAM-S-TCE/ 3 µg SAM-S-TCE	84-129
2**	SAM-S-TCE Boosts after EUA/licensed mRNA (Groups 5-7) and Ad26 (Group 8) COVID-19 Vaccines (18-60 yo)	5	10	3 µg SAM-S-TCE	≥112
		6	10	6 µg SAM-S-TCE	≥112
		7A&B#	8-12	10 µg SAM-S-TCE	≥112
		8A&B#	8-12	10 µg SAM-S-TCE/ 10 µg SAM-S-TCE***	≥112/ 56***
	SAM-S-TCE Boosts after approved/licensed mRNA (Groups 9-11) and Ad26 (Group 12) COVID-19 Vaccines (>60 yo)	9	8	3 µg SAM-S-TCE	≥112
		10A&B#	8-12	6 µg SAM-S-TCE	≥112
		11A&B#	8-12	10 µg SAM-S-TCE	≥112
		12A&B#	8-12	10 µg SAM-S-TCE/ 10 µg SAM-S-TCE***	≥112/ 56***
	ChAd-S-TCE Boosts after approved/licensed mRNA COVID-19 Vaccines (>60 yo)	13	7-10	5 x 10^{10} vp ChAd-S-TCE	≥112
		14	7-10	1 x 10^{11} vp ChAd-S-TCE	≥112
		15	7-10	5 x 10^{11} vp ChAd-S-TCE	≥112

*Were enrolled prior to protocol version 5.0. No further enrollment will occur in Stage 1. Group 1A, as noted in protocol version 4.0, is noted above as Group 1. Groups 1B and 2, as noted in protocol version 4.0, have been eliminated, due to anticipated challenges with enrollment of naïve participants.

**Will be enrolled under protocol versions 5.0 and later; Stage 2 was redesigned in version 5.0 to focus on participants previously given primary vaccination series of mRNA or Ad26 COVID-19 vaccines and has now been redesigned to also include those given recommended COVID-19 booster vaccinations. All Stage 2 participants will receive single or double boosts of SAM-S-TCE or a single boost with ChAd-S-TCE. Groups 5, 6, 8, 9, 10, 12, and 13-15 are dose escalations with 3 sentinels/group (irrespective of subgroup) who will be followed for 72 hours post vaccination. After all 3 sentinels are evaluated for 72 hours and no safety issues are observed, the remainder of the group will be enrolled and followed through Day 8 after study vaccination before dose escalation. Dosing in Groups 7 and 11 (10 µg SAM-S-TCE) will proceed with 3 sentinels/group (irrespective of subgroup) monitored for 7 days post vaccination prior to enrollment of the remainder of the group; enrollment into Group 7 will depend on all safety data from Group 11 generated through 28 days of follow up post-vaccination.

***Will administer the highest tolerable dose as determined by the dose escalations. For the SAM-S-TCE double boosting groups, the interval after the last EUA/licensed COVID-19 vaccination will be ≥112 days and the interval between the 2 SAM-S-TCE boosts will be 56 days.

#Participants in Groups 7, 8, 10, 11, and 12 will be enrolled in two subgroups: A (vaccinated, but no prior infection history) and B (vaccinated, and history or evidence of infection, but not within 4 months before enrollment), and the numbers of noninfected and infected participants will not be pre-specified. For Groups 13-15, 7-10 participants will be enrolled into each group that have been previously infected with SARS-CoV-2 at least 4 months earlier or not, and the numbers of noninfected and infected participants to be enrolled will not be pre-specified. Enrollment into Groups 7, 8, and 12 did not occur due to competing priorities and predicted difficulties enrolling into these groups.

4.4.2. Identity of Investigational Product(s)

GRT-C907

GRT-C907 (ChAdV68) is a replication-defective, E1, E3 E4Orf2-4 deleted adenoviral vector based on chimpanzee adenovirus 68 (C68, 68/SadV-25, originally designated as Pan 9), which belongs to the sub-group E adenovirus family. The vector contains a spike expression cassette, introduced into the deleted viral E1 region, expressing SARS-CoV-2 spike protein (D614G variant) with a cytomegalovirus (CMV) promoter located at the 5′ end and the SV-40 polyadenylation signal at the 3′ end of the cassette sequence within the ChAdV vector. The vector was designed such that the CMV promoter sequence and SV-40 polyadenylation signal sequence remain part of the vector backbone. Therefore, the cassette is synthesized and inserted into the vector backbone to generate the GRT-C907 vaccine.

GRT-R908

GRT-R908 (SAM-LNP) is a SAM vector based on VEEV. In order to generate GRT-R908, sequences encoding the structural proteins of VEEV were deleted and replaced by an expression cassette encoding spike protein, the same spike protein as expressed in the GRT-C907 vaccine vector. The GRT-R908 vector encodes the VEEV proteins as well as the 5′ and 3′ RNA sequences required for RNA replication, but encodes no structural proteins, so no infectious viral particle is formed. The VEEV sub-genomic 26S promoter located 5′ of the inserted cassette drives expression of the spike cassette. The cassette is inserted into the SAM backbone vector to produce the GRT-R908 vaccine. The SAM is formulated in LNP composed of 4 lipids: an ionizable amino lipid, a phosphatidylcholine, cholesterol, and a polyethylene glycol (PEG)-based coat lipid to encapsulate the SAM and form LNPs.

GRT-C909

GRT-C909 (ChAdV68) is a replication-defective, E1, E3 E4Orf2-4 deleted adenoviral vector based on chimpanzee adenovirus 68 (C68, 68/SadV-25, originally designated as Pan 9), which belongs to the sub-group E adenovirus family. The vector contains a modified spike protein and a separate TCE expression cassette, introduced into the deleted viral E1 region, expressing SARS-CoV-2 antigens with a CMV promoter located at the 5′ end and the SV-40 polyadenylation signal at the 3′ end of the spike cassette sequence within the ChAdV vector. The vector was designed such that the CMV promoter sequence and SV-40 polyadenylation signal sequence remains part of the vector backbone. Therefore, the spike cassette is synthesized and inserted into the vector backbone. The spike D614G protein is modified so that the furin cleavage site at amino acids position 682-685 (RRAR) is replaced with a non-cleavable amino acid sequence (GSAS). In addition, two proline amino acids are substituted at amino acid positions 896 and 897 (K896P, V897P). The TCE cassette is expressed using an additional CMV promoter and a BGH polyA driving expression of a TCE cassette and the CMV promoter. TCE5 cassette and BGH were cloned as a single DNA fragment downstream of the SV40 polyadenylation signal to generate the GRT-C909 vaccine.

GRT-R910

GRT-R910 (SAM-LNP) is a SAM vector based on VEEV. In order to generate GRT-R910, sequences encoding the structural proteins of VEEV were deleted and replaced by an expression cassette encoding a spike protein and T cell epitope, the same spike protein and T cell epitope as expressed in the GRT-C909 vaccine vector. The GRT-R910 vector encodes the VEEV proteins as well as the 5′ and 3′ RNA sequences required for RNA replication, but encodes no structural proteins, so no infectious viral particle is formed. The VEEV sub-genomic 26S promoter located 5′ of the inserted TCE cassette and this is followed by a second VEEV sub-genomic 26S promoter driving expression of the spike cassette. The spike cassettes and the second sub-genomic promoter driving the TCE expression are inserted into the SAM backbone vector to produce the

GRT-R910 vaccine. The spike D614G protein is modified so that the furin cleavage site at amino acids position 682-685 (RRAR) is replaced with a non-cleavable amino acid sequence (GSAS). In addition, two proline amino acids are substituted at amino acid positions 896 and 897 (K896P, V897P). The SAM is formulated in LNPs composed of 4 lipids: an ionizable amino lipid, a phosphatidylcholine, cholesterol, and a PEG-based coat lipid to encapsulate the SAM and form LNPs.

Diluent: 0.9% Sodium Chloride, USP (Normal Saline)

The diluent used for this study will be 0.9% Sodium Chloride Injection, USP, and is a sterile, nonpyrogenic, isotonic solution of sodium chloride and water for injection. Each milliliter (mL) contains sodium chloride 9 mg. It contains no bacteriostat, antimicrobial agent or added buffer and is supplied only in single-dose containers to dilute or dissolve drugs for injection. 0.308 mOsmol/mL (calc.). 0.9% Sodium Chloride Injection, USP contains no preservatives. The solution may contain hydrochloric acid and/or sodium hydroxide for pH adjustment (pH 5.3 [4.5 to 7.0]).

4.4.3. Method of Assigning Participants to Vaccination arms (Randomization)

Prior to version 3.0 of the protocol, participants 18-60 years old were randomized in a 1:1 ratio to Groups 1 and 3A. After protocol version 3.0, no random assignment to groups is planned or will be conducted. As of the writing of protocol version 5.0, Groups 1, 3A, 3B and 4 will not enroll any additional participants, and no further enrollments are planned for Stage 1. After protocol version 9.0 was implemented, it was decided Groups 7A, 7B, 8A and 8B in Stage 2 will not be opened to enroll participants. Group 12 was also not enrolled.

Participants enrolled into Stage 2 may elect not to receive ChAd-S-TCE, in which case the participant will only be considered for enrollment into SAM-S-TCE single or double boosted vaccination groups. Participants that consent to receiving a ChAd vaccine may enroll into groups that do not provide ChAd vaccine, but enrollment into groups providing a ChAd vaccine will be prioritized.

As of the writing of protocol version 5.0, participants will be enrolled into the different groups according to 1) age (see Table 1 of the protocol), 2) whether the participant consented to ChAd vaccine, and 3) dose escalation dependencies (as specified in the protocol Section 8.1.6). In protocol version 8.0 Stage 2 Groups 7-8 and 10-12 will enroll 8-12 participants that are vaccinated, with either no prior infection history or evidence of infection at least 4 months previously into A & B subgroups, respectively. Groups 13-15 will allow sample sizes of 7-10 participants total with no prespecified ratio for infected vs noninfected.

4.4.4. Selection of Doses in the Study

Table 3: Dosing and Administration

Group	Product Name	Dose	Route	Volume	Frequency of Administration
Stage 1					
1	GRT-C907	$5x10^{10}$ vp	IM	0.5 mL	D1
	GRT-R908	30 µg	IM	0.5 mL	D29
3A	GRT-R908	30 µg	IM	0.5 mL	D1, D29
3B	GRT-R908	30 µg	IM	0.5 mL	D1
	GRT-R908	3 µg	IM	0.25 mL	D85-130
4	GRT-R910	10 µg	IM	0.5 mL	D1

Group	Product Name	Dose	Route	Volume	Frequency of Administration
	GRT-R910	3 µg	IM	0.25 mL	D85-130
Stage 2					
5	GRT-R910	3 µg	IM	0.25 mL	D1
6	GRT-R910	6 µg	IM	0.25 mL	D1
7A	GRT-R910	10 µg	IM	0.5 mL	D1
7B	GRT-R910	10 µg	IM	0.5 mL	D1
8A	GRT-R910	10 µg	IM	0.5 mL	D1, D57
8B	GRT-R910	10 µg	IM	0.5mL	D1, D57
9	GRT-R910	3 µg	IM	0.25 mL	D1
10A	GRT-R910	6 µg	IM	0.25 mL	D1
10B	GRT-R910	6 µg	IM	0.25 mL	D1
11A	GRT-R910	10 µg	IM	0.5 mL	D1
11B	GRT-R910	10 µg	IM	0.5 mL	D1
12A	GRT-R910	10 µg	IM	0.5 mL	D1, D57
12B	GRT-R910	10 µg	IM	0.5 mL	D1, D57
13	GRT-C909	$5x10^{10}$ vp	IM	0.5 mL	D1
14	GRT-C909	$1x10^{11}$ vp	IM	0.5 mL	D1
15	GRT-C909	$5x10^{11}$ vp	IM	1.0 mL	D1

4.4.5. Selection and Timing of Dose for Each Participant

Groups 1 and 3A will receive vaccinations on Days 1 and 29+/-3 post-enrollment. Groups 3B and 4 will receive vaccinations on Days 1 and 85+45. The remaining groups 5, 6, 9-11, 13-15 will receive a single vaccine on Day 1.

4.4.6. Blinding

Participants and site staff will be unblinded to participants' vaccination arm assignments in Stage 1 and Stage 2.

4.4.7. Prior and Concomitant Therapy

Concomitant medications will include all current medications and medications taken in the 30 days prior to signing the informed consent form (ICF) for the duration of the study. Medications reported in the electronic case report form (eCRF) are limited to those taken within 30 days prior to the first study vaccination and for 12 months after the last study vaccination. Prescription and over-the-counter drugs will be included as well as herbals, vitamins, and supplements. In addition, receipt of any non-study vaccines will be solicited for the entire duration of the study and reported in the eCRF. Use of a new medication should prompt evaluation for the occurrence of any medication associated adverse effects, including a new diagnosis of chronic medical disease or condition.

Medications that might interfere with the evaluation of the investigational product(s) should not be used during the trial-reporting period (until approximately 12 months after the last study vaccination) unless clinically indicated as part of the participant's health care. Medications in this category include the prohibited medications per the Participant Exclusion Criteria (see protocol Section 5.1.3). In addition, the site PI or appropriate sub-investigator may identify other medications that should not be used due to a risk to participant safety or assessment of reactogenicity and immunogenicity.

Concomitant medications will be reviewed at each study visit/contact, from screening to the Study Day 394 for groups 1 and 3A, Study Day 450 for groups 3B and 4, and Study Day 366 for groups 5, 6, 9-11, and 13-15. Interim medical history will also be reviewed at each visit, including an assessment for new medical conditions requiring the use of concomitant medications. Participants will be provided with a Memory Aid and other study-related materials to record daily oral temperature, solicited injection site and systemic reactions, unsolicited AEs, and concomitant medications. Memory Aids will be reviewed with the participants via telephone, email, or text for contact visits. Based on the information collected, participants may be asked to return to the clinic for an evaluation. Administration of any medications, therapies or vaccines will be recorded on the appropriate DCF.

4.4.8. Treatment Compliance

Participants will be directly observed at the time of dosing by a member of the clinical research team who is licensed to administer the study product. Administration will be documented on the appropriate data collection form and entered on the eCRF.

4.5. Immunogenicity and Safety Variables

Immunogenicity

Humoral Immunogenicity Assays

The following humoral immunogenicity assays may be performed:

- IgG ELISA antibody binding assays to SARS-CoV-2 proteins (may include nucleocapsid protein, and multiple variant receptor binding domains and variant spike proteins).
- Neutralization assays using SARS-CoV-2 variant specific S-pseudotyped viruses.
- Neutralization assays using different strains of live SARS-CoV-2 (focus reduction neutralization test).
- ChAd68-specific neutralization assay in participants who receive the ChAd-S and ChAd-S-TCE vaccines.

Data at the following time points, or a subset, may be analyzed:

- Stage 1, Groups 1 and 3A: Days 1 and 29 post Dose 1 and Days 29, 181, and 366 post Dose 2
- Stage 1, Groups 3B and 4: Days 1, 29, 57, and 85-130 post Dose 1 and Days 15, 29, 85, 181, and 366 post Dose 2
- Stage 2, Groups 5-7A*, 7B*, 9, 10A, 10B, and 11A, 11B, and 13-15: Days 1, 15, 29, 85, 181, and 366 post study vaccination

- Stage 2, Groups 8A*, 8B* and 12A*, 12B*: Days 1, 15, 29, and 57 post Dose 1 and Days 15, 29, 85, 181, and 366 post Dose 2

  ** After protocol version 9.0 was implemented, it was decided not to enroll participants into Groups 7 and 8 because of competing priorities and predicted difficulties enrolling into these two groups. Group 12 was also not enrolled.*

Cellular Immunology Assays

This trial may investigate T cell immune responses using the IFN-γ ELISpot assay and Intracellular Cytokine Staining (ICS). Time points analyzed may include the following or a subset:

ICS

- Stage 1, Groups 1 and 3A: Days 1 and 29 post Dose 1 and Day 29 post Dose 2
- Stage 1, Groups 3B and 4: Days 1, 29, and 85-130 post Dose 1 and Day 15 post Dose 2
- Stage 2, Groups 5-7A*, 7B*, 9, 10A, 10B, 11A, 11B, and 13-15: Days 1 and 15 post study vaccination
- Stage 2, Groups 8A*, 8B*, and 12A*, 12B*: Days 1, 15, and 57 post Dose 1 and Day 15 post Dose 2

ELISpot

- Stage 1, Groups 1 and 3A: Days 1 and 29 post Dose 1 and Days 29, 181, and 366 post Dose 2
- Stage 1, Groups 3B and 4: Days 1, 29, and 85-130 post Dose 1 and Days 15, 29, 85, 181, and 366 post Dose 2
- Stage 2, Groups 5-7A*, 7B*, 9, 10A, 10B, 11A, 11B, and 13-15: Days 1, 15, 29, 85, 181, and 366 post study vaccination
- Stage 2, Groups 8A*, 8B*, and 12A*, 12B*: Days 1, 15, 29, and 57 post Dose 1 and Days 15, 29, 85, 181, and 366 post Dose 2

The antigen-specificity of memory B cell responses may also be assessed at late timepoints (6 and/or 12 months post-vaccination) using a Spike multimer binding assay and/or IgG ELISpot.

** After protocol version 9.0 was implemented, it was decided not to enroll participants into Groups 7 and 8 because of competing priorities and predicted difficulties enrolling into these two groups. Group 12 was also not enrolled.*

Safety

All safety endpoints for this trial are obtained by reporting of adverse events (solicited or unsolicited) and clinical laboratory results.

Adverse Events

AE means any untoward medical occurrence associated with the use of an intervention in humans, whether or not considered intervention-related [21 CFR 312.32 (a)]. An AE can therefore be any unfavorable and unintended sign, symptom or disease temporally associated with the use of medicinal (investigational) product.

Any medical condition that is present at the time that the participant is screened will be considered as baseline and not reported as an AE. However, if the severity of any pre-existing medical condition increases, it will be recorded as an AE.

AEs can be further divided into solicited AEs and unsolicited AEs. Solicited AEs are those that are described in the package insert as local or systemic reactogenicity occurring in the first 7 days after vaccination. Unsolicited AEs are those events that the participant reports occurring without being queried about the specific event.

AEs will be assessed for severity and relationship to study intervention. Reporting of all AEs, solicited and unsolicited, will occur during the period from study product administration on Day 1 through 28 days after each vaccination. After 28 days post last vaccination through the end of study, only SAEs, protocol specified AESIs (including PIMMCs, MAAEs, and NOCMCs), and AEs leading to withdrawal from the study will be reported.

All AEs, solicited and unsolicited, will be captured on the appropriate DCF. Solicited AEs will be regarded as related to the study product and will not require separate entry into the AE log. Information to be collected for unsolicited AEs includes event description, date of onset, assessment of severity, relationship to study product and alternate etiology (assessed only by those with the training and authority to make a diagnosis and listed on the Form FDA 1572 as the participating site PI or appropriate sub-investigator), date of resolution, seriousness, and outcome. AEs occurring during the study-collection and reporting period will be documented appropriately regardless of relationship.

AEs will be followed to resolution or stabilization.

Solicited Adverse Events

Solicited AEs are anticipated local and systemic AEs for which consistent collection of information is desired. Study clinicians will follow and collect resolution information for any reactogenicity symptoms that are not resolved within 7 days.

Solicited AEs will be collected using a memory aid and confirmed data recorded on the appropriate DCF from the time of each vaccination through 7 days post each vaccination.

For this study, solicited AEs will be:

- Injection site Pain
- Injection site Tenderness
- Injection site Erythema
- Injection site Edema/Induration
- Headache
- Fatigue
- Malaise
- Myalgia
- Arthralgia
- Nausea
- Fever
- Chills
- Diarrhea

Unsolicited Adverse Events

All AEs spontaneously reported by the participant and/or in response to an open question from study staff or revealed by observation, physical examination or other diagnostic procedures must be recorded on the appropriate DCF.

Unsolicited AEs of all severities will be reported from the time of study product administration through 28 days post each vaccination.

After 28 days post last vaccination through the end of study, only SAEs, AESIs (including PIMMCs, NOCMCs, and MAAEs), and AEs leading to withdrawal from the study will be reported.

Serious Adverse Events

An SAE is defined in 21 CFR 312.32 as follows: "An AE or suspected adverse reaction is considered serious if, in the view of either the participating site PI or appropriate sub-investigator or the sponsor, it results in any of the following outcomes:

- Death
- a life-threatening AE
- inpatient hospitalization or prolongation of existing hospitalization
- a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions
- or a congenital anomaly/birth defect

Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the patient or participant and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse."

"Life-threatening" refers to an AE that at occurrence represents an immediate risk of death to a participant. An event that may cause death if it occurs in a more severe form is not considered life-threatening. Similarly, a hospital admission for an elective procedure is not considered an SAE.

All SAEs, as with any AE, will be assessed for severity and relationship to study intervention.

All SAEs will be recorded on the appropriate SAE DCF.

All SAEs will be followed through resolution or stabilization by a study clinician, licensed to make medical diagnoses and listed on the Form FDA 1572 as the participating site PI or appropriate sub-investigator.

All SAEs will be reviewed and evaluated by DMID and will be sent to the DSMB (for periodic review unless related) and IRB/IEC as needed.

Adverse Events of Special Interest (AESIs)

An adverse event of special interest (serious or nonserious) is one of scientific and medical concern specific to the sponsor's product or program, for which ongoing monitoring and rapid communication by the investigator to the sponsor can be appropriate. Such an event might warrant further investigation in order to characterize and understand it. Depending on the nature of the event, rapid communication by the trial sponsor to other parties (e.g., regulators) might also be warranted. For this study, protocol specified AESIs are serologically or

virologically confirmed SARS-CoV-2 infection, severe COVID-19 to evaluate for potential episodes of vaccine-induced immune disease enhancement, myocarditis/pericarditis, Guillain-Barré Syndrome (GBS), and (Thrombosis with Thrombocytopenia Syndrome) TTS/Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT). Protocol-specified AESIs also include Medical Dictionary for Regulatory Activities (MedDRA®) Preferred Terms (PTs) and text strings as proposed by the Centers for Disease Control and Prevention (CDC) for surveillance of TTS events [1]. In addition, specified AESIs include any PTs included in the Standard MedDRA Query (SMQ) "embolic and thrombotic events", including the PTs listed under the following SMQs, active as of 15JUL2021 in MedDRA dictionary 24.0: Embolic and thrombotic events, arterial; Embolic and thrombotic events, venous; and Embolic and thrombotic events, vessel type unspecified and mixed arterial and venous. These AESIs also include PTs incorporated into Section 4.6 of the CDC Vaccine Adverse Event Reporting System (VAERS) Standard Operating Procedures for COVID-19 [2], and the Brighton Collaboration AESIs relevant to vaccination that are listed below:

- New Onset Chronic Medical Conditions (NOCMCs) – defined as any new ICD diagnosis (per current International Statistical Classification of Diseases and Related Health Problems) that is applied to the participant during the course of the study, after receipt of the study agent, that is expected to continue for at least 3 months and requires continued health care intervention.
- Medically Attended Adverse Events (MAAEs) – defined as hospitalization, an emergency room visit or an otherwise unscheduled visit to or from medical personnel for any reason.
- Potentially Immune-Mediated Medical Conditions (PIMMCs) – These constitute a group of AEs that includes diseases which are clearly autoimmune in etiology and other inflammatory and/or neurologic disorders which may or may not have autoimmune etiology. PIMMCs that are of special interest for this study are Brighton Collaboration AESIs relevant to vaccination that include: seizures, GBS, acute disseminated encephalomyelitis, vasculitides, anaphylaxis, vaccine-associated enhanced respiratory disease, myocarditis/pericarditis, thrombocytopenia, and thrombotic events.

All AESIs are assessed, recorded, and followed as described above under AEs.

Clinical Laboratory Assessments

Clinical safety laboratory parameters evaluated after receipt of study product will include white blood cells (WBC), hemoglobin (HgB), platelets (PLT), alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), total bilirubin (T Bili), creatine kinase (CK), and creatinine (Cr). These evaluations will be performed prior to vaccination and approximately 7 days after each study vaccination. Results will be graded using the FDA Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventative Vaccine Clinical Trials [4] and recorded by severity as mild/grade 1, moderate/grade 2, severe/grade 3, and potentially life threatening/grade 4, in addition to low (below normal range) and high (above normal range).

Time Period and Frequency for Event Assessment and Follow-Up

For this study, solicited adverse events will be collected for 7 days following each vaccine dose; unsolicited AEs will be collected until 28 days after each vaccination; AESIs (including PIMMCs, NOCMCs and MAAEs), SAEs, and AEs leading to withdrawal from the study will be collected from Day 1 through the end of the study. Clinical safety laboratory assessments are collected at Day 1 and 7 days post-vaccination for each dose.

5. SAMPLE SIZE CONSIDERATIONS

The targeted sample size for each of the study groups was determined based on previous phase 1 studies. The study is targeted to enroll up to 135 participants, with up to 12 participants in each group.

Sample size calculations for safety

The goal of the safety evaluation for this study is to identify safety concerns associated with product administration. The ability of the study to detect SAEs (see Section 4.5) can be expressed by the true event rate above which at least 1 SAE would likely be observed and the true event rate below which no events would likely be observed in each of the groups.

Specifically, in each sentinel group of 3 participants, there is a 48.8% chance of observing at least 1 event if the true rate of such event is 20% or higher; and there is at least a 72.9% chance of observing no events if the true event rate is 10% or less. For each group of 7 participants, there is a 79% chance of observing at least 1 event if the true rate is 20% or higher, and there is at least 47.8% chance of observing no events if the true event is 10% or less. For each group of 10 participants, there is an 89.3% chance of observing at least 1 event if the true rate is 20% or higher, and there is at least 34.9% chance of observing no events if the true event is 10% or less. For each group of 12 participants, there is a 93.1% chance of observing at least 1 event if the true rate is 20% or higher, and there is at least 28.2% chance of observing no events if the true event is 10% or less.

Binomial probabilities of observing 0, 1 or more, and 2 or more events among groups of size 3, 7, 10 or 12 are presented in Table 4 for a range of possible true adverse event rates. These calculations provide a more complete picture of the sensitivity of the study design to identify potential safety problems with the vaccine.

Table 4: Probability of observing 0 events, 1 or more events, and 2 or more events, among groups of size 3, 10, for different true event rates

True Event Rate (%)	Group Size (N)	Pr(0 Events)	Pr(1+ Events)	Pr(2+ Events)
1	3	97	3	<0.1
	7	93.2	6.8	0.2
	10	90.4	9.6	0.4
	12	88.6	11.4	0.6
4	3	88.5	11.5	0.5
	7	75.1	24.9	2.9
	10	66.5	33.5	5.8
	12	61.3	38.7	8.1
10	3	72.9	27.1	2.8
	7	47.8	52.2	15
	10	34.9	65.1	26.4
	12	28.2	71.8	34.1
20	3	51.2	48.8	10.4
	7	21.0	79.0	42.3

True Event Rate (%)	Group Size (N)	Pr(0 Events)	Pr(1+ Events)	Pr(2+ Events)
	10	10.7	89.3	62.4
	12	6.9	93.1	72.5

Sample size calculations for SARS-CoV-2-specific antibody binding and neutralization titer in serum

A secondary endpoint of this study is to evaluate the magnitude of SARS-CoV-2-specific antibody binding and neutralization titers in serum samples. This endpoint is descriptive in nature and will be accomplished by estimating the geometric mean titer (GMT) at each timepoint when samples are collected.

The precision with which a true GMT can be estimated from observed data depends on the standard deviation (SD) of the measurements, in the logarithmic scale, and the sample size. Table 5 displays two-sided 95% confidence intervals for the GMT for several values of the observed antibody titer.

Table 5: Two-sided 95% confidence intervals based on observing a particular average loge-antibody titer in participants' groups, taking 0% or 20% attrition into consideration (n = 12, 10, 8, 7)

Observed average $\log_e$ antibody titer	SD of $\log_e$ antibody titer	95% confidence interval			
		n=12	n = 10	n = 8	n=7
$\log_e(5)$	0.5	(3.6, 6.9)	(3.5, 7.2)	(3.3, 7.6)	(3.1,7.9)
$\log_e(20)$		(14.6, 27.5)	(14, 28.6)	(13.2, 30.4)	(12.6,31.8)
$\log_e(50)$		(36.4, 68.7)	(35, 71.5)	(32.9, 75.9)	(31.5,79.4)
$\log_e(100)$		(72.8, 137.4)	(69.9, 143)	(65.8, 151.9)	(63,158.8)
$\log_e(250)$		(182, 343.5)	(174.8, 357.5)	(164.6, 379.7)	(157.4,397)
$\log_e(500)$		(363.9, 687)	(349.6, 715)	(329.2, 759.5)	(314.9,794)
$\log_e(1000)$		(727.8, 1373.9)	(699.3, 1430)	(658.4, 1518.9)	(629.8,1587.9)
$\log_e(5)$	1.0	(2.6, 9.4)	(2.4, 10.2)	(2.2, 11.5)	(2,12.6)
$\log_e(20)$		(10.6, 37.8)	(9.8, 40.9)	(8.7, 46.1)	(7.9,50.4)
$\log_e(50)$		(26.5, 94.4)	(24.5, 102.2)	(21.7, 115.4)	(19.8,126.1)
$\log_e(100)$		(53, 188.8)	(48.9, 204.5)	(43.3, 230.7)	(39.7,252.1)
$\log_e(250)$		(132.4, 471.9)	(122.3, 511.2)	(108.4, 576.8)	(99.1,630.4)
$\log_e(500)$		(264.9, 943.9)	(244.5, 1022.5)	(216.7, 1153.6)	(198.3,1260.7)
$\log_e(1000)$		(529.7, 1887.7)	(489, 2044.9)	(433.4, 2307.2)	(396.6,2521.5)

6. GENERAL STATISTICAL CONSIDERATIONS

6.1. General Principles

Unless otherwise noted, 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.

6.2. Timing of Analyses

After the last participant completes their last visit and all data is received by the Statistical and Data Coordinating Center (SDCC), data cleaning and locking processes will be completed. The final analysis will be performed after data lock.

Prior to the final analysis, data may be disseminated to public health officials and partners as needed and included in publications and presentations to inform the global scientific community. Early analyses will include safety and immunogenicity. Further, the protocol team will review data periodically to confirm that no halting rules have been met as described in Section 8.6.1 of the protocol.

Cumulative safety information, study status, and endpoint results may be published, presented at a public forum, or presented as summaries aggregated by study arm at the discretion of the sponsor while the primary study is ongoing. Any ad hoc analyses, jointly developed by the protocol team, SDCC and/or Gritstone bio, Inc. (formerly known as Gritstone Oncology, Inc.), will be executed by the SDCC as needed. None of the interim analyses will include any formal statistical hypothesis testing.

Interim Safety Review

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 DSMB reviews. The DSMB will not need to meet unless halting rules are met, or as requested by the sponsor or PI, and materials will be provided electronically. Documentation of review and any concerns noted will be solicited electronically.

Safety reviews for sentinel halting rules by the protocol team and for dose escalation criteria by the SSC are described in Sections 8.5.1 and 8.1.6 of the protocol. Additional safety reviews may be conducted as necessary.

Safety Reviews by the DSMB

Given the frequency and urgency to review data, the DSMB will not need to meet to assess sentinel halting rules or dose escalation criteria unless halting rules are met or as requested by the SSC.

If any of the halting rules listed in Sections 8.5.1 and 8.5.2 of the protocol are met, cumulative safety data from all enrolled participants will be summarized for DSMB review.

If no halting rules are met, or in addition to unscheduled DSMB reviews, the DSMB will review cumulative AE data as follows:

- After all participants in Groups 1, 3A, 3B, and 4 have completed Day 8 post first study vaccination visit.
- After all participants in Groups 1, 3A, 3B and 4 have completed Day 8 post second study vaccination visit.

- After all participants in Groups 5-7, 9, 10, 11, and 13-15 have completed Day 8 post study vaccination visit.
- After all participants in Groups 8 and 12 have completed Day 8 post first study vaccination visit.

The DSMB reviews listed above do not have to occur in a sequential manner and may be combined if milestones are reached on dates that are close together.

In addition, the DSMB will meet to review available safety data after all participants in all groups enrolled in Stages 1 and 2 have completed the visit that occurs 28 days after their last study vaccination.

Ad hoc safety reports may also be prepared for DSMB review as deemed necessary and appropriate by DMID.

Materials for all DSMB reviews will be provided electronically. Documentation of review and any concerns noted will be solicited electronically.

Interim Immunogenicity Review

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

Statistical analyses of secondary immunogenicity endpoints, by vaccine schedule group, may be performed when participants have completed key immunogenicity visits. Immunogenicity reviews may be shared with the DSMB, as determined by DMID. Immunogenicity reports may be combined with safety reports if projected milestones for reports will occur close enough to each other where, in the opinion of the protocol team, producing one report, as opposed to two separate reports, is more informative regarding the safety of participants and more beneficial to the overall needs of the protocol team.

Data may be disseminated to public health officials and partners as needed. In addition, participants will be informed regarding interim aggregate antibody results after the 4-week timepoint after the last study vaccination.

6.3. Analysis Populations

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

The modified Intention-to-Treat (mITT) population includes all participants who received at least one dose of the study vaccination and contributed both pre- and at least one post-dose venous blood samples for immunogenicity testing for which valid results were reported. All analyses of the immunogenicity data will be completed for the mITT population

6.3.2. Per Protocol Population

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

1. Data from all available visits for participants found to be ineligible at baseline.
2. Data from all visits after protocol deviations that are considered to affect the analysis.
3. Data from all visits after the receipt of an out-of-study COVID-19 vaccine.
4. Data from all visits after a post-baseline COVID-19 infection.
5. Data from any visit that occurs substantially out of window.

COVID-19 infection will be determined by self-report and the ELISA SARS-CoV-2 Nucleoprotein IgG (N-Antibody) assay, which tests for antibodies to the N-protein as an indicator of previous COVID-19 infection. This assay will return a result of negative or positive for previous COVID-19 infection.

All analyses of the immunogenicity data will be completed for the per protocol population.

6.3.3. Safety Population

The safety population will consist of all participants who received at least one dose of a study vaccine. All analyses of safety data will be completed for the safety 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.

6.5. Missing Data

There are no imputations planned for missing data. For neutralization assays, any percent neutralization below zero will be imputed as zero for analyses. For assays with a lower limit of detection (LLOD) or a lower limit of quantification (LLOQ), any results below the LLOD/LLOQ will be imputed as one-half the LLOD/LLOQ. For the ICS assay, results below 0.001 will be imputed as 0.001.

6.6. Interim Analyses and Data Monitoring

See Section 6.2.

6.7. Multicenter Studies

Data will be pooled across all clinical sites for analyses. 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

No formal hypothesis testing will be conducted.

7. STUDY PARTICIPANTS

7.1. Disposition of Participants

The disposition of participants in the study will be tabulated by vaccination arm (Table 19, Table 20, Table 21, Table 22, Table 23, and Table 24). The table shows the total number of participants screened, enrolled, receiving first vaccination, receiving the second vaccination (if applicable), discontinuing treatment, terminated from study follow-up, and completing the study. The composition of analysis populations, including reasons for participant exclusion, by treatment arm, is presented in Table 25, Table 26, Table 27, Table 28, and Table 29. A summary of the reasons that participants were screened but not enrolled will be presented in Table 36. A flowchart showing the disposition of study participants, adapted from the Consort Statement [3] will be included (Figure 1 and Figure 2). This figure will present the number of participants screened, enrolled, lost to follow-up, and analyzed, by vaccination arm. 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, the deviation category, and the vaccination arm for all deviations (Table 9, Table 10, Table 11, Table 12, and Table 13) and major deviations only (Table 14, Table 15, Table 16, Table 17, and Table 18). Ineligibility or product administration deviations will be considered major deviations and reviewed for possible participant exclusion from the per protocol population. Other protocol deviations may be considered major deviations, as determined by DMID. All participant specific protocol deviations and non-participant specific protocol deviations will be included in Listing 3 and Listing 4.

8. IMMUNOGENICITY EVALUATION

8.1. Primary Immunogenicity Analysis

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

8.2. Secondary Immunogenicity Analyses

Descriptive summaries of immunogenicity data will be presented for the mITT and PP populations.

The results of three immunological assays will be analyzed to address the secondary immunogenicity endpoints. The ELISA assay is a validated assay that reports antibody concentrations and is used to assess antibody binding against SARS-CoV-2 S-2P and ribosomal binding domain (RBD). The results of the ELISA assay will be summarized for each group at each available time point by the geometric mean (GM) and geometric mean fold rise (GMFR) from baseline (Day 1) along with corresponding 95% confidence intervals (CIs). GMFR is defined as the ratio of the result at a time point divided by the result at Day 1. Summaries of the ELISA results are shown starting with Table 48 and ending with Table 71. Graphical displays will include geometric mean over time (starting with Figure 3 and ending with Figure 22), and distribution of responses over time (starting with Figure 143 and ending with Figure 162).

The SARS-CoV-2 pseudovirus neutralization assay (PsVNA) and focus reduction neutralization test (FRNT) will be run using serial dilutions against available variants (e.g. Beta, Delta, Omicron). From these assays ID50 and ID80, which estimate the amount of antibodies required for a neutralization rate of 50% or 80%, will be reported. Neutralization titers will be summarized by the GM, GMFR, geometric mean ratio (GMR) to D614G, and seropositive rate with corresponding 95% CIs, for each group at each time point. The GMR is the geometric mean of the assay result against a variant of concern divided by the result against D614G. The seropositive rate is the percentage of participants with results above the LLOD. The summaries of PsVNA results are shown starting with Table 72 and ending with Table 131, and the summaries of FRNT results are shown starting with Table 132 and ending with Table 191. Graphical displays for PsVNA and FRNT will include geometric mean over time (starting with Figure 23 and ending with Figure 142) and distributions of responses over time (starting with Figure 163 and ending with Figure 282).

T cell responses to ChAd-S or ChAd-S-TCE, and SAM-S or SAM-S-TCE will be assessed by IFN-γ ELISpot and ICS assays. The results of the IFN-γ ELISpot assay will be summarized at all available time points in tables (starting with Table 192 and ending with Table 201) by the mean with a 95% CI, median, min, and max and in figures showing the distribution of responses over time (starting with Figure 283 and ending with Figure 392). The results of the ICS assay will be summarized at all available time points in tables (starting with Table 202 and ending with Table 211) by the mean with a 95% CI, median, min, max, and response rate with a 95% CI. The distribution of results over time and the response rate will be presented in figures, starting with Figure 393 and ending with Figure 542. For the ICS assay, results below 0.001 will be imputed as 0.001.

CIs for means, GMs, GMFRs, and GMRs will be calculated using the Student's t-distribution and CIs for seropositive rates and response rates will be calculated using the Clopper-Pearson binomial method.

If additional immunological assays are determined to be necessary, then the results will be summarized in a similar manner to that of the assays described above.

Individual immunogenicity responses are shown in Listing 8.

8.3. Exploratory Immunogenicity Analyses

ChAd68-specific neutralization will be analyzed in a similar manner as the pseudovirus and live neutralization, for participants who received the ChAd-S and ChAd-S-TCE vaccines (Groups 1, 13, 14, and 15) at Study Days 1 and 29.

Memory B cell responses to ChAd-S or ChAd-S-TCE and SAM-S or SAM-S-TCE will be analyzed in a similar manner as the T cell assays with tables showing the mean with 95% CI, median, min, and max and figures illustrating the distribution of responses over time.

9. SAFETY EVALUATION

Summaries and analyses of safety data will be presented for the safety analysis population.

Solicited non serious AEs will be collected from the time of each vaccination until 7 days after. Solicited AEs will be summarized by severity for each day post each vaccination and as the maximum severity over all 8 days. Additionally, solicited AEs will be analyzed using standard techniques, such as 95% CIs (using the Clopper-Pearson method), to summarize the proportion of participants reporting each symptom, any local (vaccination site) symptom, and any systemic symptom.

9.1. Demographic and Other Baseline Characteristics

Summaries of sex, ethnicity, race, age, weight, BMI, previous COVID-19 infection, previous COVID-19 vaccinations (where applicable), and time from most recent community COVID-19 vaccination (where applicable) will be presented by vaccination arm and overall (starting with Table 37 and ending with Table 46). Ethnicity is categorized as Hispanic or Latino, or not Hispanic and not Latino. In accordance with NIH reporting policy, participants may self-designate as belonging to more than one race or may refuse to identify a race, the latter reflected in the CRF as "No" to each racial option. Summary clinical laboratory values and vital signs at baseline will be included in tables grouped by vaccination arm and overall (beginning with Table 312 and ending with Table 336).

Individual participant listings will be presented for all demographics (Listing 6). Baseline clinical laboratory values will be included in Listing 12 and Listing 13, baseline vital signs will be included in Listing 14, and baseline physical exam findings will be included in Listing 15.

9.1.1. Prior and Concurrent Medical Conditions

Complete medical history is obtained by interviewing participants at first study visit, and interim medical history will be collected at follow-up visits. Medical history is limited to significant medical disorders of the head, eyes, ears, nose, throat, mouth, cardiovascular system, blood, lymph nodes, endocrine system, lungs, gastrointestinal tract, liver, pancreas, musculoskeletal system, skin, and genital/reproductive tract. A history of any allergies, clotting or other abnormality of the coagulation system, cancer, immunodeficiency, psychiatric illness, substance abuse, and autoimmune disease are solicited.

All current illnesses and past pre-existing medical conditions will be MedDRA coded using MedDRA dictionary version 23.0 or higher. Summaries of participants' pre-existing medical conditions will be presented by vaccination arm and overall (Table 47, Table 48, Table 49, Table 50, and Table 51). Individual participant listings will be presented for all medical conditions (Listing 7).

9.1.2. Prior and Concomitant Medications

Administration of any medications, therapies, or vaccines will be recorded. Concomitant medication includes all current medications and medications taken in the 30 days prior to signing of the ICF for the duration of the study. Medications reported are limited to those taken within 30 days prior to the first study vaccination and for 12 months after the last study vaccination.

Summaries of medications that were started prior to dosing and continuing at the time of dosing will be presented by WHODrug Terms 2 and 3 and vaccination arm (Table 337, Table 338, Table 339, Table 340, and Table 341).

Individual participant listings will be presented for all concomitant medications (Listing 16).

9.2. Measurements of Treatment Compliance

All participants are to receive one or two doses of the study product administered in the clinic. Section 7 of the protocol provides summaries of key treatment compliance milestones/variables. The number of participants receiving each dose will be summarized as part of the participant disposition table. The month of first study vaccination will be tabulated by vaccination arm and overall (Table 30, Table 31, Table 32, Table 33, Table 34, and Table 35). Individual participant listings will be presented for all participants terminated early or discontinued treatment (Listing 2). Listings will be presented for all participants-specific and non-participant specific protocol deviations (Listing 3 and Listing 4).

9.3. Adverse Events

All adverse events reported will be included in the summaries and analyses. 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.

Overall summaries of adverse events are presented by vaccination arm beginning with Table 212, Table 213, Table 214, Table 215, and Table 216. Adverse events occurring in at least 5% of participants in any vaccination arm by MedDRA SOC and preferred term are presented by vaccination arm beginning with Table 217, Table 218, Table 219, Table 220, and Table 221.

9.3.1. Solicited Events and Symptoms

Systemic solicited AEs were collected pre-vaccination, and systemic and local solicited AEs were collected 30 minutes post-vaccination and then daily for 7 days after each vaccination. Solicited local events include erythema (redness), induration (hardness)/edema (swelling), pain, and tenderness. Solicited systemic events include fever, chills (feverishness), fatigue (tiredness), malaise (general unwell feeling), myalgia (body aches/muscular pain exclusive of the injection site), arthralgia (joint pain exclusive for the injection site), headache, nausea, and diarrhea. Solicited events were graded on a scale of none (absent), mild, moderate, and severe. Measurement values for erythema and induration (hardness)/edema (swelling) were collected and graded based on the FDA Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventative Vaccine Clinical Trials [4].

Solicited AEs are summarized by severity pre-vaccination (systemic solicited AEs only), post-vaccination, and each day post-study vaccination (Days 1-8). Solicited AEs are also summarized by the maximum severity over all post-vaccination measurements. The proportions of participants reporting each symptom, any local symptom, any systemic symptom, and any symptom are summarized by vaccination arm separately for each dose and both doses combined (where applicable). For each event the denominator is the number of participants with non-missing data for the event.

The following summaries for solicited adverse events are presented by maximum severity, vaccination (each dose separately and both doses combined, where applicable), and vaccination arm:

- Number and percentage of participants experiencing solicited events by symptom and maximum severity, for any symptom, local symptoms, and systemic symptoms (beginning with Table 222 and ending with Table 230)
- Number and percentage of participants experiencing any solicited event, any systemic event, any local symptom, and each symptom, by day and severity, for each vaccination (starting with Table 231 and ending with Table 250)

- Duration of solicited symptoms summarized by mean, standard deviation, median, minimum, and maximum by symptom, dose, and vaccination arm (Table 251, Table 252, Table 253, Table 254, and Table 255)
- Bar graphs of the number of participants experiencing a symptom by severity and day for systemic symptoms (beginning with Figure 543 and ending with Figure 551) and for local symptoms (beginning with Figure 552 and ending with Figure 560)
- Bar graphs of the number of participants experiencing the onset of a symptom by the severity and day for systemic symptoms (beginning with Figure 561 and ending with Figure 569) and local symptoms (beginning with Figure 570 and ending with Figure 578)
- Figures of solicited symptoms by day, dose, and vaccination arm for each participant, separated by symptom (beginning with Figure 579 and ending with Figure 653)

9.3.2. Unsolicited Adverse Events

The proportion of participants reporting at least one unsolicited adverse event are summarized by MedDRA system organ class and preferred term for each dose and both doses combined, where applicable. Denominators for percentages are the number of participants who received the vaccination.

The following summaries for unsolicited adverse events will be presented by vaccination arm:

- Frequency of AEs by MedDRA system organ class (SOC), severity, and relationship to study vaccination (beginning with Table 256 and ending with Table 272)
- Frequency of AEs by MedDRA SOC, MedDRA preferred term, severity, and relationship to study vaccination (beginning with Table 273 and ending with Table 289)
- Participant incidence of AEs (number and percentage of participants experiencing AEs) by MedDRA SOC, MedDRA preferred term, severity, and relationship to study vaccination (beginning with Table 290 and ending with Table 306)
- Frequency of AEs (number and percentage of participants experiencing AEs) by MedDRA SOC and severity (Figure 654, Figure 655, Figure 656, Figure 657, and Figure 658)
- Participant incidence of AEs (number and percentage of participants experiencing AEs) by MedDRA SOC and severity (Figure 659, Figure 660, Figure 661, Figure 662, and Figure 663)
- Participant listing of all unsolicited adverse events (Listing 11)
- Participant listing of serious adverse events (Table 307)
- Participant listing of non-serious adverse events of moderate or greater severity (Table 308)
- Participant listing of other significant adverse events, which includes AESIs, PIMMCs, MAAEs, and NOCMCs (Table 309)

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

Individual participant listings of serious adverse events and adverse events of special interest, which includes medically attended adverse events, potentially immune-mediated medical conditions, and new onset chronic medical conditions will be presented (Table 307, Table 309).

9.5. Pregnancies

Urine or serum pregnancy tests will be performed at the screening visit and within 24 hours prior to each study vaccination. Results must be negative to ensure eligibility and continuation of study treatment. For pregnancies occurring in study participants, a venous blood sample for serological assays will be collected per protocol with participant permission. Large volume blood samples for cellular immunological assays will be discontinued. The participant will be followed for the duration of the study. Efforts will be made to follow all pregnancies reported during the study to pregnancy outcome with participant permission.

The following individual participant listings will be presented for pregnancies and outcomes (Appendix 16.2.11):

- Maternal information (Listing 17)
- Gravida and para (Listing 18)
- Live birth outcomes (Listing 19)
- Still birth outcomes (Listing 20)
- Spontaneous, elective, or therapeutic abortion outcomes (Listing 21)

9.6. Clinical Laboratory Evaluations

Chemistry parameters measured include alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, total bilirubin, creatine kinase, and creatinine. Hematology parameters measure include white blood cells, hemoglobin, and platelets.

Summaries of clinical laboratory data are grouped by vaccination arm, severity for each visit, and the maximum over all post-vaccination visits. Summaries are shown for each chemistry parameter and all chemistry parameters combined (Table 312, Table 313, Table 314, Table 315, Table 316, Table 317, and Table 318) and for each hematology parameter and all hematology parameters combined (Table 325, Table 326, Table 327, and Table 328). Clinical laboratory results and change from baseline are also summarized by mean, standard deviation, median, minimum, and maximum for each chemistry parameter (Table 319, Table 320, Table 321, Table 322, Table 323, and Table 324) and for each hematology parameter (Table 329, Table 330, and Table 331). Bar graphs of clinical laboratory results by maximum severity post baseline and vaccination arm will be presented Figure 664, Figure 665, Figure 666, Figure 667, and Figure 668).

Individual participant listings for abnormal chemistry results (Table 310) and abnormal hematology results (Table 311) will be presented.

9.7. Vital Signs and Physical Evaluations

Vital signs including oral temperature, pulse, and systolic and diastolic blood pressure will be taken at each in-clinic visit. Vital signs assessed on Day 1 prior to the first study vaccination will be considered as baseline. Vital signs will be graded using the FDA Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventative Vaccine Clinical Trials [4] and recorded by severity as mild/grade 1, moderate/grade 2, severe/grade 3, and potentially life threatening/grade 4. Results will be tabulated by time point, severity, and vaccination arm for each vital sign and all vital signs combined (Table 332, Table 333, Table 334, Table 335, and Table 336).

Individual participant listings of vital signs will be presented (Listing 14).

A targeted physical examination may be performed, if indicated, based on review of interim medical history. Height and weight will be collected on Day 1 prior to the first study vaccination to calculate BMI, which will be presented with continuous demographics (Table 42, Table 43, Table 44, Table 45, and Table 46). Individual participant listings of physical exam findings will be presented (Listing 15).

9.8. Concomitant Medications

Concomitant medications will be coded to the Anatomical Therapeutic Classification using the WHODrug Dictionary. Concomitant medications are defined in Section 9.1.2 of the protocol. The use of prior and concomitant medications taken during the study will be recorded on the appropriate DCF. The use of concomitant medications during the study will be summarized by ATC1, ATC2 code, and vaccination arm (Table 337, Table 338, Table 339, Table 340, and Table 341). Individual participant listings of the use of concomitant medications during the study will be presented (Listing 16).

9.9. Other Safety Measures

No additional safety analyses are planned.

10. PHARMACOKINETICS

Not applicable.

11. IMMUNOGENICITY

See Section 8.

12. OTHER ANALYSES

Not applicable.

13. REPORTING CONVENTIONS

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

14. TECHNICAL DETAILS

SAS version 9.4 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

See the summary of changes for the protocol for changes in the conduct of the study.

16. REFERENCES

1. Shimabukuro T. Update: Thrombosis with thrombocytopenia syndrome (TTS) following COVID-19 vaccination. Advisory Committee on Immunization Practices (ACIP) Meeting Materials: Centers for Disease Control and Prevention; 2021. P. 40.
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3. Drummond R. CONSORT Revised: Improving the Reporting of Randomized Clinical Trials. JAMA. 2001; 285(15): 2006-2007.
4. Guidance for Industry: Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials. U.S. Department of Health and Human Services, Food and Drug Administration, Center for Biologics Evaluation and Research, 2007. Available from: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/toxicity-grading-scale-healthy-adult-and-adolescent-volunteers-enrolled-preventive-vaccine-clinical

17. LISTING OF TABLES, FIGURES, AND LISTINGS

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

APPENDICES

APPENDIX 1. TABLE MOCK-UPS

Notes:

Tables labelled "COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A" include Groups 1 and 3A. Column headers for the groups will be Group 1: 5 x 10^{10} vp ChAd-S/30 µg SAM-S and Group 3A: 30 µg SAM-S/30 µg SAM-S.

Tables labelled "COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4" include Groups 3B and 4. Column headers for the groups will be Group 3B: 30 µg SAM-S/3 µg SAM-S and Group 4: 10 µg SAM-S-TCE/3 µg SAM-S-TCE.

Tables labelled "COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts" include Groups 5 and 6. Column headers for the groups will be Group 5: 3µg SAM-S-TCE, Group 6: 6 µg SAM-S-TCE.

Tables labelled "COVID-19 mRNA Vaccinated, >60 years of age, SAM-S-TCE Boosts" include Groups 9, 10, and 11. Column headers for the groups will be Group 9: 3 µg SAM-S-TCE, Group 10: 6 µg SAM-S-TCE, Group 11: 10 µg SAM-S-TCE. Group 10 is Groups 10A and 10B combined. Group 11 is Groups 11A and 11B combined.

Tables labelled "COVID-19 mRNA Vaccinated, >60 years of age, ChAd-S-TCE Boosts" include Groups 13, 14, 15. Column headers for the groups will be Group 13: 5 x 10^{10} vp ChAd-S-TCE, Group 14: 1 x 10^{11} vp ChAd-S-TCE, Group 15: 5 x 10^{11} vp ChAd-S-TCE.

LIST OF TABLES

9.1 Overall Study Design and Plan Description

See Table 2.

9.5.1 Efficacy/Immunogenicity and Safety Measurements Assessed and Flow Chart

Table 6: Schedule of Activities - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A

Study Visit	**V00**	**V01**	**V02**	**V03**	**V04**	**V05**	**V06**	**V07**	**V08**	**V08A**	**V09**	**V10**	**V11**	**Unsc**	**Early Term**
Study Day post 1st Study Vaccination	**Scr-30d to -1d**	**D1**	**D2+1d**	**D4+2d**	**D8 +2d**	**D29±3d**	**D30+1d**	**D32+2d**	**D36+2d**	**D43+4wk**	**D57±3d**	**D209±14d**	**D394±14d**		
Study Day post 2nd Study Vaccination						**D1**	**D2+1d**	**D4+2d**	**D8+2d**	**D15+4wk**	**D29±3d**	**D181±14d**	**D366±14d**		
Obtain Written Informed Consent	X									X					
Review Eligibility Criteria	X	X				X				X					
Medical History	X														
Review Interim Medical History		X	X	X	X	X	X	X	X	X	X	X	X	X	X
Concomitant Medications	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Vital Signs (Oral Temp, Pulse, BP)	X	X			X	X			X	X	X	X	X	X	X
Physical Examination including Height and Weight	X														
Targeted PE, if indicated		X			X	X			X	X	X	X	X	X	X
Serum or Urine Pregnancy Test	X	X				X				X					
Nasal Swab Collection for SARS-CoV-2 PCR	X					X									
Blood Collection for Safety Labs	X[1]				X[2]	X[2]			X[2]	X[3]				X[2,4]	X[2.5]
Blood Collection for HBsAg, Anti-HCV, SARS-CoV-2 serology, HIV	X					X[6]									
Blood Collection for ELISpot		X				X					X	X	X	X	X
Blood Collection for ICS Assays		X				X					X			X	X
Blood Collection for Antibody Assays		X				X					X	X	X	X	X
Blood Collection for PBMC and Plasma Storage		X			X	X			X		X	X	X	X	X

Study Visit	**V00**	**V01**	**V02**	**V03**	**V04**	**V05**	**V06**	**V07**	**V08**	**V08A**	**V09**	**V10**	**V11**	**Unsc**	**Early Term**
Study Day post 1st Study Vaccination	**Scr-30d to -1d**	**D1**	**D2+1d**	**D4+2d**	**D8 +2d**	**D29±3d**	**D30+1d**	**D32+2d**	**D36+2d**	**D43+4wk**	**D57±3d**	**D209±14d**	**D394±14d**		
Study Day post 2nd Study Vaccination						**D1**	**D2+1d**	**D4+2d**	**D8+2d**	**D15+4wk**	**D29±3d**	**D181±14d**	**D366±14d**		
Enroll in Advantage eClinical		X													
Study Vaccination		X				X									
45 Minute Evaluation After Study Vaccination		X				X									
Distribute Memory Aid and Study Related Materials		X				X									
Review Memory Aid			X	X	X		X	X	X					X[5]	X[5]
Adverse Events		X	X	X	X	X	X	X	X		X			X[7]	X[7]
SAEs/AESIs including PIMMCs/MAAEs/NOCMCs		X	X	X	X	X	X	X	X	X[8]	X	X	X	X	X
Optional Leukapheresis[9]										X					
Saliva Collection for Antibodies		X			X				X						
Phone Call[10]			X	X			X	X							

[1] Includes WBC. HgB. PLT, ALT. AST, ALP, T Bili, CK, Cr and PT/PTT
[2] Includes WBC, HgB, PLT, ALT, AST, ALP, T Bili, CK, and Cr
[3] Safety lab per local Leukapheresis procedure
[4] If clinically indicated
[5] If within 7 days after study vaccination
[6] Includes SARS-CoV-2 serology (N-specific) only
[7] If prior to Study Visit 09
[8] SAEs only
[9] Extra screening visit may be needed prior to Leukapheresis procedure
[10] Can be phone, text, or email contact

Table 7: Schedule of Activities – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4

Study Visit	**V00**	**V01**	**V02**	**V03**	**V04**	**V05**	**V06**	**V07**	**V08**	**V09**	**V10**	**V11**	**V11A**	**V12**	**V13**	**V14**	**V15**	**Unsc**	**Early Term**
Study Day post 1st Study Vaccination	**Scr -30d to -1d**	**D1**	**D2+ 1d**	**D4+ 2d**	**D8+ 2d**	**D29± 3d**	**D57± 3d**	**D85+ 45d**	**D86+ 1d**	**D88+ 2d**	**D92+ 2d**	**D99+ 2d**	**D99+ 4wk**	**D113 ±3d**	**D169 ±3d**	**D265± 14d**	**D450± 14d**		
Study Day post 2nd Study Vaccination								**D1**	**D2+ 1d**	**D4+ 2d**	**D8+ 2d**	**D15+ 2d**	**D15 +4wk**	**D29± 3d**	**D85± 3d**	**D181± 4d**	**D366± 14d**		
Obtain Written Informed Consent	X												X						
Review Eligibility Criteria	X	X						X					X						
Medical History	X																		
Review Interim Medical History		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Concomitant Medications	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Vital Signs (Oral Temp, Pulse, BP)	X	X			X	X	X	X	X		X	X	X	X	X	X	X	X	X
Physical Examination including Height and Weight	X																		
Targeted PE, if indicated		X			X	X	X	X	X		X	X	X	X	X	X	X	X	X
Serum or Urine Pregnancy Test	X	X						X					X						
Nasal Swab Collection for SARS-CoV-2 PCR	X							X											
Blood Collection for Safety Labs	X[1]				X[2]			X[2]			X[2]		X[3]					X[2,4]	X[2,5]
Blood Collection for HBsAg, Anti-HCV, SARS-CoV-2 serology, HIV	X							X[6]											
Blood Collection for ELISpot		X				X		X				X		X	X	X	X	X	X
Blood Collection for ICS Assays		X				X		X				X						X	X
Blood Collection for Antibody Assays		X				X	X	X				X		X	X	X	X	X	X
Blood Collection for PBMC and Plasma Storage		X			X	X	X	X				X		X	X	X	X	X	X
Blood Collection for Transcriptomal Signatures								X	X		X							X	X[5]
Blood Collection for Cytokines								X	X		X							X	X
Enroll in Advantage *eClinical*		X																	

Study Visit	**V00**	**V01**	**V02**	**V03**	**V04**	**V05**	**V06**	**V07**	**V08**	**V09**	**V10**	**V11**	**V11A**	**V12**	**V13**	**V14**	**V15**	**Unsc**	**Early Term**
Study Day post 1st Study Vaccination	**Scr -30d to -1d**	**D1**	**D2+ 1d**	**D4+ 2d**	**D8+ 2d**	**D29± 3d**	**D57± 3d**	**D85+ 45d**	**D86+ 1d**	**D88+ 2d**	**D92+ 2d**	**D99+ 2d**	**D99+ 4wk**	**D113 ±3d**	**D169 ±3d**	**D265± 14d**	**D450± 14d**		
Study Day post 2nd Study Vaccination								**D1**	**D2+ 1d**	**D4+ 2d**	**D8+ 2d**	**D15+ 2d**	**D15 +4wk**	**D29± 3d**	**D85± 3d**	**D181± 4d**	**D366± 14d**		
Study Vaccination		X						X											
45 Minute Evaluation After Study Vaccination		X						X											
Distribute Memory Aid and Study Related Materials		X						X											
Review Memory Aid			X	X	X				X	X	X							X[5]	X[5]
Adverse Events		X	X	X	X	X	X	X	X	X	X	X		X				X[7]	X[7]
SAEs/AESIs including PIMMCs/MAAEs/ NOCMCs		X	X	X	X	X	X	X	X	X	X	X	X[8]	X	X	X	X	X	X
Optional Leukapheresis[9]													X						
Saliva Collection for Antibodies		X			X						X								
Phone Call[10]			X	X						X									

[1] Includes WBC, HgB. PLT, ALT, AST, ALP, T Bili, CK, Cr and PT/PTT
[2] Includes WBC, HgB, PLT, ALT, AST, ALP, T Bili, CK, and Cr
[3] Safety lab per local Leukapheresis procedure
[4] If clinically indicated
[5] If within 7 days after study vaccination
[6] Includes SARS-CoV-2 serology (N-specific) only
[7] If prior to Study Visit 12
[8] SAEs only
[9] Extra screening visit may be needed prior to Leukapheresis procedure
[10] Can be phone, text, or email contact

Table 8: Schedule of Activities – COVID-19 mRNA Vaccinated, Groups 5, 6, 9, 10, 11, 13, 14, 15

Study Visit	**V00**	**V01**	**V02**	**V03**	**V04**	**V05**	**V05A**	**V06**	**V07**	**V08**	**V09**	**Unsc**	**Early Term**
Study Day post Study Vaccination	**Scr-30 to -1d**	**D1**	**D2+1d**	**D4+2d**	**D8+2d**	**D15+2d**	**D15+4wk**	**D29±3d**	**D85±3d**	**D181±14d**	**D366±14d**		
Obtain Written Informed Consent	X						X						
Review Eligibility Criteria	X	X					X						
Medical History	X												
Review Interim Medical History		X	X	X	X	X	X	X	X	X	X	X	X
Concomitant Medications	X	X	X	X	X	X	X	X	X	X	X	X	X
Vital Signs (Oral Temp, Pulse, BP)	X	X	X		X	X	X	X	X	X	X	X	X
Physical Examination including Height and Weight	X												
Targeted PE, if indicated		X	X		X	X	X	X	X	X	X	X	X
Serum or Urine Pregnancy Test	X	X					X						
Nasal Swab Collection for SARS-CoV-2 PCR	X												
Blood Collection for Safety Labs	X[1]				X[2]		X[3]					X[2,4]	X[2,5]
Blood Collection for HBsAg, Anti-HCV, SARS-CoV-2 serology, HIV	X												
Blood Collection for ELISpot		X				X		X	X	X	X	X	X
Blood for ICS Assays		X				X						X	X
Blood Collection for Antibody Assays		X				X		X	X	X	X	X	X
Blood Collection for PBMC and Plasma Storage		X				X		X	X	X	X	X	X
Blood Collection for Transcriptomal Signatures		X	X		X							X	X[5]
Blood Collection for Cytokines		X	X		X							X	X
Enroll in Advantage *eClinical*		X											
Study Vaccination		X											
45 Minute Evaluation After Study Vaccination		X											
Distribute Memory Aid and Study Related Materials		X											
Review Memory Aid			X	X	X							X[5]	X[5]
Adverse Events		X	X	X	X	X		X				X[6]	X[6]
SAEs/AESIs including PIMMCs/MAAEs/NOCMCs		X	X	X	X	X	X[7]	X	X	X	X	X	X

Study Visit	V00	V01	V02	V03	V04	V05	V05A	V06	V07	V08	V09	Unsc	Early Term
Study Day post Study Vaccination	**Scr-30 to -1d**	**D1**	**D2+1d**	**D4+2d**	**D8+2d**	**D15+2d**	**D15+4wk**	**D29±3d**	**D85±3d**	**D181±14d**	**D366±14d**		
Optional Leukapheresis[8]							X						
Saliva Collection for Antibodies		X			X								
Phone Call[9]				X									

[1] Includes WBC, HgB. PLT, ALT, AST, ALP, T Bili, CK, Cr and PT/PTT
[2] Includes WBC, HgB, PLT, ALT, AST, ALP, T Bili, CK, and Cr
[3] Safety lab per local Leukapheresis procedure
[4] If clinically indicated
[5] If within 7 days after study vaccination
[6] If prior to Study Visit 06
[7] SAEs only
[8] Extra screening visit may be needed prior to Leukapheresis procedure
[9] Can be phone, text, or email contact
* After protocol version 9.0 was implemented, it was decided not to enroll participants into Groups 7 and 8 because of competing priorities and predicted difficulties enrolling into these two groups.

10.2 Protocol Deviations

Table 9: Distribution of Protocol Deviations by Category, Type, and Vaccination Arm - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A

Category	Deviation Type	Group 1: 5 x 10^{10} vp ChAd-S/ 30 µg SAM-S (N=X)		Group 3A: 30 µg SAM-S/ 30 µg SAM-S (N=X)		All Participants (N=X)	
		# of Ppt.	# of Dev.	# of Ppt.	# of Dev.	# of Ppt.	# of Dev.
Eligibility/enrollment	Any type	x	x	x	x	x	x
	Did not meet inclusion criterion						
	Met exclusion criterion						
	ICF not signed prior to study procedures						
	Other						
Vaccination schedule	Any type						
	Out of window visit						
	Missed visit/visit not conducted						
	Missed Vaccination						
	Delayed Vaccination						
	Other						
Follow-up visit schedule	Any type						
	Out of window visit						
	Missed visit/visit not conducted						
	Other						
Protocol procedure/assessment	Any type						
	Incorrect version of ICF signed						
	Blood not collected						
	Urine not collected						
	Other specimen not collected						
	Too few aliquots obtained						

Category	Deviation Type	Group 1: 5 x 10^{10} vp ChAd-S/ 30 µg SAM-S (N=X)		Group 3A: 30 µg SAM-S/ 30 µg SAM-S (N=X)		All Participants (N=X)	
		# of Ppt.	# of Dev.	# of Ppt.	# of Dev.	# of Ppt.	# of Dev.
	Specimen result not obtained						
	Required procedure not conducted						
	Required procedure done incorrectly						
	Specimen temperature excursion						
	Other						
Vaccine administration	Any type						
	Required procedure done incorrectly						
	Study product temperature excursion						
	Other						

Tables with similar format:

Table 10: Distribution of Protocol Deviations by Category, Type, and Vaccination Arm - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4

Table 11: Distribution of Protocol Deviations by Category, Type, and Vaccination Arm – COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts

Table 12: Distribution of Protocol Deviations by Category, Type, and Vaccination Arm – COVID-19 mRNA Vaccinated, >60 years of age, SAM-S-TCE Boosts

Table 13: Distribution of Protocol Deviations by Category, Type, and Vaccination Arm – COVID-19 mRNA Vaccinated, >60 years of age, ChAd-S-TCE Boosts

Table 14: Distribution of Major Protocol Deviations by Category, Type, and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A

Table 15: Distribution of Major Protocol Deviations by Category, Type, and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4

12.2.2 Displays of Adverse Events

All AEs or SAEs will be assessed for severity according to the toxicity grading scales in the FDA Guidance Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials [4].

12.4.1 Individual Laboratory Measurements and Abnormal Laboratory Values

All laboratory measurements will be assessed for severity according to the toxicity grading scales in the FDA Guidance Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trials [4].

14.1 Description of Study Participants

14.1.1 Disposition of Participants

Table 19: Participant Disposition by Vaccination Arm - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A

Participant Disposition	Group 1: 5 x 10^{10} vp ChAd-S/30 µg SAM-S (N=X)		Group 3A: 30 µg SAM-S/30 µg SAM-S (N=X)		All Participants (N=X)	
	n	%	n	%	n	%
Screened	-	-	-	-	x	-
Enrolled	x	x	x	x	x	x
Received the first vaccination	x	x	x	x	x	x
Received the second vaccination	x	x	x	x	x	x
Discontinued treatment[a]	x	x	x	x	x	x
Study ongoing	x	x	x	x	x	x
Early termination[a]	x	x	x	x	x	x
Completed study	x	x	x	x	x	x
Completed per protocol[b]	x	x	x	x	x	x

Note: N = Number of participants in safety analysis population
[a] Refer to Listing 2 for reasons participants discontinued or terminated early.
[b] Refer to Listing 5 for reasons participants are excluded from the Analysis populations.

Tables with similar format:

Table 20: Participant Disposition by Vaccination Arm - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4

Table 21: Participant Disposition by Vaccination Arm - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4

Table 22: Participant Disposition by Vaccination Arm - COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts

Table 23: Participant Disposition by Vaccination Arm - COVID-19 mRNA Vaccinated, >60 years of age, SAM-S-TCE Boosts

Table 24: Participant Disposition by Vaccination Arm - COVID-19 mRNA Vaccinated, >60 years of age, ChAd-S-TCE Boosts

Table 25: Analysis Populations by Vaccination Arm - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A

Analysis Populations	Reason Participants Excluded	Group 1: 5×10^{10} vp ChAd-S/ 30 µg SAM-S (N=X)		Group 3A: 30 µg SAM-S/ 30 µg SAM-S (N=X)		All Participants (N=X)	
		n	%	n	%	%	n
Safety	Any Reason	x	xx	x	xx	x	xx
	[Reason 1, for example: Did not meet eligibility criteria]						
	[Reason 2]						
	[Reason 3]						
	[Reason 4]						
Modified Intent-To-Treat	Any Reason						
	[Reason 1]						
	[Reason 2]						
Per Protocol	Any Reason						
	[Reason 1]						
	[Reason 2]						

Tables with similar format:

Table 26: Analysis Populations by Vaccination Arm - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4

Table 27: Analysis Populations by Vaccination Arm - COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts

Table 28: Analysis Populations by Vaccination Arm - COVID-19 mRNA Vaccinated, >60 years of age, SAM-S-TCE Boosts

Table 29: Analysis Populations by Vaccination Arm - COVID-19 mRNA Vaccinated, >60 years of age, ChAd-S-TCE Boosts

Table 30: Dates of First Treatment by Site – All Vaccination Arms

Dates of Dosing	Baylor College of Medicine (N=X)	Hope Clinic of the Emory Vaccine Center (N=X)	Saint Louis University (N=X)	University of Washington (N=X)	All Sites (N=X)
Total (Entire period of enrollment)					
22MAR2021-15NOV2021	x	x	x	x	x
14MAR2022 – 26SEP2022					
Note: Enrollment was paused between 15NOV2021 and 14MAR2022 (exclusive).					

Table 31: Dates of First Treatment by Vaccination Arm - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A

Dates of Dosing	Group 1: 5 x 10^{10} vp ChAd-S/30 µg SAM-S (N=X)	Group 3A: 30 µg SAM-S/30 µg SAM-S (N=X)	All Participants (N=X)
Total (Entire period of enrollment)			
March, 2021	x	x	x
April, 2021			
May, 2021			
June, 2021			

Table with similar format:

Table 32: Dates of First Treatment by Vaccination Arm - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4

Table 33: Dates of First Treatment by Vaccination Arm - COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts

Dates of Dosing	Group 5: 3µg SAM-S-TCE (N=X)	Group 6: 6 µg SAM-S-TCE (N=X)	All Participants (N=X)
Total (Entire period of enrollment)			
September, 2021			
October, 2021			
Note: There were no enrollments in these groups during months not included in the table.			

Table 34: Dates of First Treatment by Vaccination Arm - COVID-19 mRNA Vaccinated, >60 years of age, SAM-S-TCE Boosts

Dates of Dosing	Group 9: 3µg SAM-S-TCE (N=X)	Group 10: 6 µg SAM-S-TCE (N=X)	Group 11: 10 µg SAM-S-TCE (N=X)	All Participants (N=X)
Total (Entire period of enrollment)				
September, 2021				
October, 2021				
November, 2021				
March, 2022				
April, 2022				
May, 2022				
June, 2022				
July, 2022				
August, 2022				
Note: There were no enrollments in these groups during months not included in the table.				

Table 35: Dates of First Treatment by Vaccination Arm - COVID-19 mRNA Vaccinated, >60 years of age, ChAd-S-TCE Boosts

Dates of Dosing	Group 13: 5×10^{10} vp ChAd-S-TCE (N=X)	Group 14: 1×10^{11} vp ChAd-S-TCE (N=X)	Group 15: 5×10^{11} vp ChAd-S-TCE (N=X)	All Participants (N=X)
Total (Entire period of enrollment)				
September, 2021				
October, 2021				
November, 2021				
March, 2022				
April, 2022				
May, 2022				
June, 2022				
July, 2022				
August, 2022				
September, 2022				
Note: There were no enrollments in these groups during months not included in the table.				

Table 36: 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 37: Summary of Categorical Demographic and Baseline Characteristics by Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A

Demographic Category	Characteristic	Group 1: 5 x 10^{10} vp ChAd-S/ 30 µg SAM-S (N=X)		Group 3A: 30 µg SAM-S/ 30 µg SAM-S (N=X)		All Participants (N=X)	
		n	%	n	%	n	%
Sex	Male	x	x	x	x	x	x
	Female	x	x	x	x	x	x
Ethnicity	Not Hispanic or Latino	x	x	x	x	x	x
	Hispanic or Latino	x	x	x	x	x	x
	Not Reported	x	x	x	x	x	x
	Unknown	x	x	x	x	x	x
Race	American Indian or Alaska Native	x	x	x	x	x	x
	Asian	x	x	x	x	x	x
	Native Hawaiian or Other Pacific Islander	x	x	x	x	x	x
	Black or African American	x	x	x	x	x	x
	White	x	x	x	x	x	x
	Multi-Racial	x	x	x	x	x	x
	Unknown	x	x	x	x	x	x
Previous COVID-19 Infection (Self-reported or positive N-Antibody result)	Previous infection						
	No previous infection						
Previous COVID-19 vaccinations	Primary mRNA vaccination series (2 doses)						
	Primary mRNA vaccination series (2 doses) + mRNA booster						
Note: N = Number of participants in safety analysis population							

Implementation note: Only include the "Previous COVID-19 vaccinations" rows in the tables for the Stage 2 groups (COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts; COVID-19 mRNA Vaccinated, >60 years of age, SAM-S-TCE Boosts; COVID-19 mRNA Vaccinated, >60 years of age, ChAd-S-TCE Boosts)

Tables with similar format:

Table 38: Summary of Categorical Demographic and Baseline Characteristics by Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4

Table 39: Summary of Categorical Demographic and Baseline Characteristics by Vaccination Arm – COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts

Table 40: Summary of Categorical Demographic and Baseline Characteristics by Vaccination Arm – COVID-19 mRNA Vaccinated, >60 years of age, SAM-S-TCE Boosts

Table 41: Summary of Categorical Demographic and Baseline Characteristics by Vaccination Arm – COVID-19 mRNA Vaccinated, >60 years of age, ChAd-S-TCE Boosts

Table 42: Summary of Continuous Demographic and Baseline Characteristics by Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A

Variable	Statistic	Group 1: 5 x 10^{10} vp ChAd-S/30 µg SAM-S (N=X)	Group 3A: 30 µg SAM-S/30 µg SAM-S (N=X)	All Participants (N=X)
Age (years)	Mean	x.x	x.x	x.x
	Standard Deviation	x.x	x.x	x.x
	Median	x.x	x.x	x.x
	Minimum	x	x	x
	Maximum	x	x	x
Weight (kg)	Mean	x.x	x.x	x.x
	Standard Deviation	x.x	x.x	x.x
	Median	x.x	x.x	x.x
	Minimum	x	x	x
	Maximum	x	x	x
BMI (kg/m^2)	Mean	x.x	x.x	x.x
	Standard Deviation	x.x	x.x	x.x
	Median	x.x	x.x	x.x
	Minimum	x	x	x
	Maximum	x	x	x
Note: N = Number of participants in safety analysis population				

Table with similar format:

Table 43: Summary of Continuous Demographic and Baseline Characteristics by Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4

Table 44: Summary of Continuous Demographic and Baseline Characteristics by Vaccination Arm – COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts

Variable	Statistic	Group 1: 5 x 10^{10} vp ChAd-S/30 µg SAM-S (N=X)	Group 3A: 30 µg SAM-S/30 µg SAM-S (N=X)	All Participants (N=X)
Age (years)	Mean	x.x	x.x	x.x
	Standard Deviation	x.x	x.x	x.x
	Median	x.x	x.x	x.x
	Minimum	x	x	x
	Maximum	x	x	x
Weight (kg)	Mean	x.x	x.x	x.x
	Standard Deviation	x.x	x.x	x.x
	Median	x.x	x.x	x.x
	Minimum	x	x	x
	Maximum	x	x	x
BMI (kg/m^2)	Mean	x.x	x.x	x.x
	Standard Deviation	x.x	x.x	x.x
	Median	x.x	x.x	x.x
	Minimum	x	x	x
	Maximum	x	x	x
Time from previous COVID-19 vaccination (days)	Mean	x.x	x.x	x.x
	Standard Deviation	x.x	x.x	x.x
	Median	x.x	x.x	x.x
	Minimum	x	x	x
	Maximum	x	x	x
Note: N = Number of participants in safety analysis population				

Tables with similar format:

Table 45: Summary of Continuous Demographic and Baseline Characteristics by Vaccination Arm – COVID-19 mRNA Vaccinated, >60 years of age, SAM-S-TCE Boosts

Table 46: Summary of Continuous Demographic and Baseline Characteristics by Vaccination Arm – COVID-19 mRNA Vaccinated, >60 years of age, ChAd-S-TCE Boosts

14.1.3 Prior and Concurrent Medical Conditions

Table 47: Summary of Participants with Pre-Existing Medical Conditions by MedDRA System Organ Class and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A

MedDRA System Organ Class	Group 1: 5 x 10^{10} vp ChAd/ 30 µg SAM-S (N=X)		Group 3A: 30 µg SAM-S/ 30 µg SAM-S (N=X)		All Participants (N=X)	
	n	%	n	%	n	%
Any SOC	x	xx	x	xx	x	xx
[SOC 1]						
[SOC 2]						

Tables with similar format:

Table 48: Summary of Participants with Pre-Existing Medical Conditions by MedDRA System Organ Class and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4

Table 49: Summary of Participants with Pre-Existing Medical Conditions by MedDRA System Organ Class and Vaccination Arm – COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts

Table 50: Summary of Participants with Pre-Existing Medical Conditions by MedDRA System Organ Class and Vaccination Arm – COVID-19 mRNA Vaccinated, >60 years of age, SAM-S-TCE Boosts

Table 51: Summary of Participants with Pre-Existing Medical Conditions by MedDRA System Organ Class and Vaccination Arm – COVID-19 mRNA Vaccinated, >60 years of age, ChAd-S-TCE Boosts

14.2 Immunogenicity Data

Table 52: Summary of ELISA IgG Antibody Against SARS-CoV-2 S-2P by Time Point and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A, mITT Population

Time Point	Statistic	Group 1: 5 x 10^{10} vp ChAd-S/30 µg SAM-S (N=X)	Group 3A: 30 µg SAM-S/30 µg SAM-S (N=X)	All Participants (N=X)
Day 1 (Pre-Vaccination 1)	n			
	GMT			
	95% CI			
Day 29 Post Vaccination 1	n			
	GMT			
	95% CI			
Day 57 Post Vaccination 1 (29 Days Post Vaccination 2)	n			
	GMT			
	95% CI			
Day 209 Post Vaccination 1 (181 Days Post Vaccination 2)	n			
	GMT			
	95% CI			
Day 391 Post Vaccination 1 (366 Days Post Vaccination 2)	n			
	GMT			
	95% CI			

Notes: N = Number of participants enrolled
n = Number of participants in the mITT population with available results
GMT = Geometric Mean Titer

Implementation Notes:

For the Groups 1 and 3A tables, the time points should be Day 1 (Pre-Vaccination 1), Day 29 Post Vaccination 1, Day 57 Post Vaccination 1 (29 Days Post Vaccination 2), Day 209 Post Vaccination 1 (181 Days Post Vaccination 2), Day 391 Post Vaccination 1 (366 Days Post Vaccination 2.

For the Groups 3B and 4 tables, the time points should be Day 1 (Pre-Vaccination 1), Day 29 Post Vaccination 1, Day 57 Post Vaccination 1, Day 85 Post Vaccination 1, Day 99 Post Vaccination 1 (15 Days Post Vaccination 2), Day 113 Post Vaccination 1 (29 Days Post Vaccination 2), Day 169 Post Vaccination 1 (85 Days Post Vaccination 2), Day 265 Post Vaccination 1 (181 Days Post Vaccination 2), Day 450 Post Vaccination 1 (366 Days Post Vaccination 2).

For the Groups 5 and 6 tables, the time points should be: Day 1 (Pre-Vaccination), Day 15 Post Vaccination, Day 29 Post Vaccination, Day 85 Post Vaccination, Day 181 Post Vaccination, and Day 366 Post Vaccination.

For the Groups 9, 10, and 11 tables, the time points should be: Day 1 (Pre-Vaccination), Day 15 Post Vaccination, Day 29 Post Vaccination, Day 85 Post Vaccination, Day 181 Post Vaccination, and Day 366 Post Vaccination.

For the Groups 10A, 10B, 11A, and 11B tables, the time points should be: Day 1 (Pre-Vaccination), Day 15 Post Vaccination, Day 29 Post Vaccination, Day 85 Post Vaccination, Day 181 Post Vaccination, and Day 366 Post Vaccination.

For the Groups 13, 14, and 15 tables, the time points should be: Day 1 (Pre-Vaccination), Day 15 Post Vaccination, Day 29 Post Vaccination, Day 85 Post Vaccination, Day 181 Post Vaccination, and Day 366 Post Vaccination.

Tables with similar format:

Table 53: Summary of ELISA IgG Antibody Against SARS-CoV-2 S-2P by Time Point and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A, Per Protocol Population

Table 54: Summary of ELISA IgG Antibody Against SARS-CoV-2 S-2P by Time Point and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4, mITT Population

Table 55: Summary of ELISA IgG Antibody Against SARS-CoV-2 S-2P by Time Point and Vaccination Arm COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4, Per Protocol Population

Table 56: Summary of ELISA IgG Antibody Against SARS-CoV-2 S-2P by Time Point and Vaccination Arm – COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts, mITT Population

Table 57: Summary of ELISA IgG Antibody Against SARS-CoV-2 S-2P by Time Point and Vaccination Arm – COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts, Per Protocol Population

Table 58: Summary of ELISA IgG Antibody Against SARS-CoV-2 S-2P by Time Point and Vaccination Arm – COVID-19 mRNA Vaccinated, >60 years of age, SAM-S-TCE Boosts, mITT Population

Table 59: Summary of ELISA IgG Antibody Against SARS-CoV-2 S-2P by Time Point and Vaccination Arm – COVID-19 mRNA Vaccinated, >60 years of age, SAM-S-TCE Boosts, Per Protocol Population

Table 60: Summary of ELISA IgG Antibody Against SARS-CoV-2 S-2P by Time Point and Vaccination Arm – COVID-19 mRNA Vaccinated, >60 years of age, ChAd-S-TCE Boosts, mITT Population

Table 61: Summary of ELISA IgG Antibody Against SARS-CoV-2 S-2P by Time Point and Vaccination Arm – COVID-19 mRNA Vaccinated, >60 years of age, ChAd-S-TCE Boosts, Per Protocol Population

Table 62: Summary of ELISA IgG Antibody Against SARS-CoV-2 RBD by Time Point and Vaccination Arm COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A, mITT Population

Table 63: Summary of ELISA IgG Antibody Against SARS-CoV-2 RBD by Time Point and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A, Per Protocol Population

Table 72: Summary of Pseudovirus Neutralizing Antibody ID_{50} Against SARS-CoV-2 D614G by Time Point and Vaccination Arm - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A, mITT Population

Time Point	Statistic	Group 1: 5×10^{10} vp ChAd-S/30 µg SAM-S (N=X)	Group 3A: 30 µg SAM-S/30 µg SAM-S (N=X)	All Participants (N=X)
Day 1 (Pre-Vaccination 1)	n			
	GMT (95% CI)			
	Seropositive (95% CI)			
Day 29 Post Vaccination 1	n			
	GMT (95% CI)			
	GMR_{D614G} (95% CI)			
	GMFR (95% CI)			
	Seropositive (95% CI)			
Day 57 Post Vaccination 1 (29 Days Post Vaccination 2)	n			
	GMT (95% CI)			
	GMR_{D614G} (95% CI)			
	GMFR (95% CI)			
	Seropositive (95% CI)			
Day 209 Post Vaccination 1 (181 Days Post Vaccination 2)	n			
	GMT (95% CI)			
	GMR_{D614G} (95% CI)			
	GMFR (95% CI)			
	Seropositive (95% CI)			
Day 391 Post Vaccination 1 (366 Days Post Vaccination 2)	n			
	GMT (95% CI)			
	GMR_{D614G} (95% CI)			
	GMFR (95% CI)			
	Seropositive (95% CI)			

Notes: N = Number of participants enrolled
n = Number of participants in the mITT population with available results
GMT = Geometric Mean Titer, GMFR = Geometric Mean Fold Rise, GMR_{D614G} = Geometric Mean Ratio to D614G

Implementation Notes:

Remove the row and footnote for GMR_{D614G} from the tables for D614G.

For the Groups 1 and 3A tables, the time points should be Day 1 (Pre-Vaccination 1), Day 29 Post Vaccination 1, Day 57 Post Vaccination 1 (29 Days Post Vaccination 2), Day 209 Post Vaccination 1 (181 Days Post Vaccination 2), Day 391 Post Vaccination 1 (366 Days Post Vaccination 2.

For the Groups 3B and 4 tables, the time points should be Day 1 (Pre-Vaccination 1), Day 29 Post Vaccination 1, Day 57 Post Vaccination 1, Day 85 Post Vaccination 1, Day 99 Post Vaccination 1 (15 Days Post Vaccination 2), Day 113 Post Vaccination 1 (29 Days Post Vaccination 2), Day 169 Post Vaccination 1 (85 Days Post Vaccination 2), Day 265 Post Vaccination 1 (181 Days Post Vaccination 2), Day 450 Post Vaccination 1 (366 Days Post Vaccination 2).

For the Groups 5 and 6 tables, the time points should be: Day 1 (Pre-Vaccination), Day 15 Post Vaccination, Day 29 Post Vaccination, Day 85 Post Vaccination, Day 181 Post Vaccination, and Day 366 Post Vaccination.

For the Groups 9, 10, and 11 tables, the time points should be: Day 1 (Pre-Vaccination), Day 15 Post Vaccination, Day 29 Post Vaccination, Day 85 Post Vaccination, Day 181 Post Vaccination, and Day 366 Post Vaccination.

For the Groups 10A, 10B, 11A, and 11B tables, the time points should be: Day 1 (Pre-Vaccination), Day 15 Post Vaccination, Day 29 Post Vaccination, Day 85 Post Vaccination, Day 181 Post Vaccination, and Day 366 Post Vaccination.

For the Groups 13, 14, and 15 tables, the time points should be: Day 1 (Pre-Vaccination), Day 15 Post Vaccination, Day 29 Post Vaccination, Day 85 Post Vaccination, Day 181 Post Vaccination, and Day 366 Post Vaccination.

Tables with similar format:

Table 73: Summary of Pseudovirus Neutralizing Antibody ID_{50} Against SARS-CoV-2 D614G by Time Point and Vaccination Arm - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A, Per Protocol Population

Table 74: Summary of Pseudovirus Neutralizing Antibody ID_{80} Against SARS-CoV-2 D614G by Time Point and Vaccination Arm - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A, mITT Population

Table 75: Summary of Pseudovirus Neutralizing Antibody ID_{80} Against SARS-CoV-2 D614G by Time Point and Vaccination Arm - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A, Per Protocol Population

Table 76: Summary of Pseudovirus Neutralizing Antibody ID_{50} Against SARS-CoV-2 D614G by Time Point and Vaccination Arm - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4, mITT Population

Table 77: Summary of Pseudovirus Neutralizing Antibody ID_{50} Against SARS-CoV-2 D614G by Time Point and Vaccination Arm - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4, Per Protocol Population

Table 78: Summary of Pseudovirus Neutralizing Antibody ID_{80} Against SARS-CoV-2 D614G by Time Point and Vaccination Arm - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4, mITT Population

Table 79: Summary of Pseudovirus Neutralizing Antibody ID_{80} Against SARS-CoV-2 D614G by Time Point and Vaccination Arm - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4, Per Protocol Population

Table 119: Summary of Pseudovirus Neutralizing Antibody ID_{80} Against SARS-CoV-2 BA.4/5 by Time Point and Vaccination Arm - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4, Per Protocol Population

Table 120: Summary of Pseudovirus Neutralizing Antibody ID_{50} Against SARS-CoV-2 BA.4/5 by Time Point and Vaccination Arm - COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts, mITT Population

Table 121: Summary of Pseudovirus Neutralizing Antibody ID_{50} Against SARS-CoV-2 BA.4/5 by Time Point and Vaccination Arm - COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts, Per Protocol Population

Table 122: Summary of Pseudovirus Neutralizing Antibody ID_{80} Against SARS-CoV-2 BA.4/5 by Time Point and Vaccination Arm - COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts, mITT Population

Table 123: Summary of Pseudovirus Neutralizing Antibody ID_{80} Against SARS-CoV-2 BA.4/5 by Time Point and Vaccination Arm - COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts, Per Protocol Population

Table 124: Summary of Pseudovirus Neutralizing Antibody ID_{50} Against SARS-CoV-2 BA.4/5 by Time Point and Vaccination Arm - COVID-19 mRNA Vaccinated, >60 years of age, SAM-S-TCE Boosts, mITT Population

Table 125: Summary of Pseudovirus Neutralizing Antibody ID_{50} Against SARS-CoV-2 BA.4/5 by Time Point and Vaccination Arm - COVID-19 mRNA Vaccinated, >60 years of age, SAM-S-TCE Boosts, Per Protocol Population

Table 126: Summary of Pseudovirus Neutralizing Antibody ID_{80} Against SARS-CoV-2 BA.4/5 by Time Point and Vaccination Arm - COVID-19 mRNA Vaccinated, >60 years of age, SAM-S-TCE Boosts, mITT Population

Table 127: Summary of Pseudovirus Neutralizing Antibody ID_{80} Against SARS-CoV-2 BA.4/5 by Time Point and Vaccination Arm - COVID-19 mRNA Vaccinated, >60 years of age, SAM-S-TCE Boosts, Per Protocol Population

Table 128: Summary of Pseudovirus Neutralizing Antibody ID_{50} Against SARS-CoV-2 BA.4/5 by Time Point and Vaccination Arm - COVID-19 mRNA Vaccinated, >60 years of age, ChAd-S-TCE Boosts, mITT Population

Table 129: Summary of Pseudovirus Neutralizing Antibody ID_{50} Against SARS-CoV-2 BA.4/5 by Time Point and Vaccination Arm - COVID-19 mRNA Vaccinated, >60 years of age, ChAd-S-TCE Boosts, Per Protocol Population

Table 130: Summary of Pseudovirus Neutralizing Antibody ID_{80} Against SARS-CoV-2 BA.4/5 by Time Point and Vaccination Arm - COVID-19 mRNA Vaccinated, >60 years of age, ChAd-S-TCE Boosts, mITT Population

Table 131: Summary of Pseudovirus Neutralizing Antibody ID_{80} Against SARS-CoV-2 BA.4/5 by Time Point and Vaccination Arm - COVID-19 mRNA Vaccinated, >60 years of age, ChAd-S-TCE Boosts, Per Protocol Population

Table 192: Summary of T Cells Expressing IFNγ as measured by the ELISpot Assay in Spot Forming Units (SFU) per Million by Time Point and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A, mITT Population

Overlapping Peptide	Time Point	Statistic	Group 1: 5×10^{10} vp ChAd-S/30 µg SAM-S (N=4)	Group 3A: 30 µg SAM-S/30 µg SAM-S (N=3)
15mer OLPs Spanning Membrane Frame	Day 1 (Pre-Vaccination 1)	n	x	x
		Mean (95% CI)	x.xx (x.xx, x.xx)	x.xx (x.xx, x.xx)
		Median	x.xx	x.xx
		Min, Max	x.x, x.x	x.x, x.x
	Day 29 Post Vaccination 1	n		
		Mean (95% CI)		
		Median		
		Min, Max		
	Day 57 Post Vaccination 1 (29 Days Post Vaccination 2)	n		
		Mean (95% CI)		
		Median		
		Min, Max		
15mer OLPa Spanning Nucleocapsid Frame	Day 1 (Pre-Vaccination 1)	n		
		Mean (95% CI)		
		Median		
		Min, Max		
	Day 29 Post Vaccination 1	n		
		Mean (95% CI)		
		Median		
		Min, Max		
	Day 57 Post Vaccination 1 (29 Days Post Vaccination 2)	n		
		Mean (95% CI)		
		Median		
		Min, Max		

Overlapping Peptide	Time Point	Statistic	Group 1: 5 x 10^{10} vp ChAd-S/30 µg SAM-S (N=4)	Group 3A: 30 µg SAM-S/30 µg SAM-S (N=3)
15mer OLPs spanning Open Reading Frame 3a	Day 1 (Pre-Vaccination 1)	n		
		Mean (95% CI)		
		Median		
		Min, Max		
	Day 29 Post Vaccination 1	n		
		Mean (95% CI)		
		Median		
		Min, Max		
	Day 57 Post Vaccination 1 (29 Days Post Vaccination 2)	n		
		Mean (95% CI)		
		Median		
		Min, Max		
Consensus Spike (Wuhan-1) whole protein, 1st of 4 OLP pools	Day 1 (Pre-Vaccination 1)	n		
		Mean (95% CI)		
		Median		
		Min, Max		
	Day 29 Post Vaccination 1	n		
		Mean (95% CI)		
		Median		
		Min, Max		
	Day 57 Post Vaccination 1 (29 Days Post Vaccination 2)	n		
		Mean (95% CI)		
		Median		
		Min, Max		

Overlapping Peptide	Time Point	Statistic	Group 1: 5 x 10^{10} vp ChAd-S/30 µg SAM-S (N=4)	Group 3A: 30 µg SAM-S/30 µg SAM-S (N=3)
Consensus Spike (Wuhan-1) whole protein, 2nd of 4 OLP pools	Day 1 (Pre-Vaccination 1)	n		
		Mean (95% CI)		
		Median		
		Min, Max		
	Day 29 Post Vaccination 1	n		
		Mean (95% CI)		
		Median		
		Min, Max		
	Day 57 Post Vaccination 1 (29 Days Post Vaccination 2)	n		
		Mean (95% CI)		
		Median		
		Min, Max		
Consensus Spike (Wuhan-1) whole protein, 3rd of 4 OLP pools	Day 1 (Pre-Vaccination 1)	n		
		Mean (95% CI)		
		Median		
		Min, Max		
	Day 29 Post Vaccination 1	n		
		Mean (95% CI)		
		Median		
		Min, Max		
	Day 57 Post Vaccination 1 (29 Days Post Vaccination 2)	n		
		Mean (95% CI)		
		Median		
		Min, Max		

Overlapping Peptide	Time Point	Statistic	Group 1: 5 x 10^{10} vp ChAd-S/30 µg SAM-S (N=4)	Group 3A: 30 µg SAM-S/30 µg SAM-S (N=3)
Consensus Spike (Wuhan-1) whole protein, 4th of 4 OLP pools	Day 1 (Pre-Vaccination 1)	n		
		Mean (95% CI)		
		Median		
		Min, Max		
	Day 29 Post Vaccination 1	n		
		Mean (95% CI)		
		Median		
		Min, Max		
	Day 57 Post Vaccination 1 (29 Days Post Vaccination 2)	n		
		Mean (95% CI)		
		Median		
		Min, Max		
S1	Day 1 (Pre-Vaccination 1)	n		
		Mean (95% CI)		
		Median		
		Min, Max		
	Day 29 Post Vaccination 1	n		
		Mean (95% CI)		
		Median		
		Min, Max		
	Day 57 Post Vaccination 1 (29 Days Post Vaccination 2)	n		
		Mean (95% CI)		
		Median		
		Min, Max		

Overlapping Peptide	Time Point	Statistic	Group 1: 5 x 10^{10} vp ChAd-S/30 µg SAM-S (N=4)	Group 3A: 30 µg SAM-S/30 µg SAM-S (N=3)
S2	Day 1 (Pre-Vaccination 1)	n		
		Mean (95% CI)		
		Median		
		Min, Max		
	Day 29 Post Vaccination 1	n		
		Mean (95% CI)		
		Median		
		Min, Max		
	Day 57 Post Vaccination 1 (29 Days Post Vaccination 2)	n		
		Mean (95% CI)		
		Median		
		Min, Max		
Spike	Day 1 (Pre-Vaccination 1)	n		
		Mean (95% CI)		
		Median		
		Min, Max		
	Day 29 Post Vaccination 1	n		
		Mean (95% CI)		
		Median		
		Min, Max		
	Day 57 Post Vaccination 1 (29 Days Post Vaccination 2)	n		
		Mean (95% CI)		
		Median		
		Min, Max		

Implementation Notes:

For the Groups 1 and 3A tables, the time points should be Day 1 (Pre-Vaccination), Day 29 Post Vaccination 1, Day 57 Post Vaccination 1 (29 Days Post Vaccination 2), Day 209 Post Vaccination 1 (181 Days Post Vaccination 2), Day 391 Post Vaccination 1 (366 Days Post Vaccination 2.

For the Groups 3B and 4 tables, the time points should be Day 1 (Pre-Vaccination), Day 29 Post Vaccination 1, Day 85 Post Vaccination 1, Day 99 Post Vaccination 1 (15 Days Post Vaccination 2), Day 113 Post Vaccination 1 (29 Days Post Vaccination 2), Day 169 Post Vaccination 1 (85 Days Post Vaccination 2), Day 265 Post Vaccination 1 (181 Days Post Vaccination 2), Day 450 Post Vaccination 1 (366 Days Post Vaccination 2).

For the Groups 5 and 6 tables, the time points should be: Day 1 (Pre-Vaccination), Day 15 Post Vaccination, Day 29 Post Vaccination, Day 85 Post Vaccination, Day 181 Post Vaccination, and Day 366 Post Vaccination.

For the Groups 9, 10, and 11 tables, the time points should be: Day 1 (Pre-Vaccination), Day 15 Post Vaccination, Day 29 Post Vaccination, Day 85 Post Vaccination, Day 181 Post Vaccination, and Day 366 Post Vaccination.

For the Groups 10A, 10B, 11A, and 11B tables, the time points should be: Day 1 (Pre-Vaccination), Day 15 Post Vaccination, Day 29 Post Vaccination, Day 85 Post Vaccination, Day 181 Post Vaccination, and Day 366 Post Vaccination.

For the Groups 13, 14, and 15 tables, the time points should be: be Day 1 (Pre-Vaccination), Day 15 Post Vaccination, Day 29 Post Vaccination, Day 85 Post Vaccination, Day 181 Post Vaccination, and Day 366 Post Vaccination.

Tables with similar format:

Table 193: Summary of T Cells Expressing IFNγ as measured by the ELISpot Assay in Spot Forming Units (SFU) per Million by Time Point and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A, Per Protocol Population

Table 194: Summary of T Cells Expressing IFNγ as measured by the ELISpot Assay in Spot Forming Units (SFU) per Million by Time Point and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4, mITT Population

Table 195: Summary of T Cells Expressing IFNγ as measured by the ELISpot Assay in Spot Forming Units (SFU) per Million by Time Point and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4, Per Protocol Population

Table 196: Summary of T Cells Expressing IFNγ as measured by the ELISpot Assay in Spot Forming Units (SFU) per Million by Time Point and Vaccination Arm – COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts, mITT Population

Table 197: Summary of T Cells Expressing IFNγ as measured by the ELISpot Assay in Spot Forming Units (SFU) per Million by Time Point and Vaccination Arm – COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts, Per Protocol Population

Table 198: Summary of T Cells Expressing IFNγ as measured by the ELISpot Assay in Spot Forming Units (SFU) per Million by Time Point and Vaccination Arm – COVID-19 mRNA Vaccinated, >60 years of age, SAM-S-TCE Boosts, mITT Population

Table 202: Summary of T Cells Expressing Cytokines as measured by the ICS Assay by Time Point and Vaccination Arm - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A, mITT Population

TCELL Sub	Peptide Pool	Cell Type	Time Point	Statistic	Group 1: 5 x 10^{10} vp ChAd-S/30 µg SAM-S (N=4)	Group 3A: 30 µg SAM-S/30 µg SAM-S (N=3)
CD4	ANY COV2 S	IFNg_OR_IL2	Day 1 (Pre-Vaccination 1)	n	x	x
				Mean	x.xxx	x.xxx
				95% CI	x.xxx, x.xxx	x.xxx, x.xxx
				Response Rate	x/n (xx%)	x/n (xx%)
				95% CI	xx.x%, xx.x%	xx.x%, xx.x%
			Day 29 Post Vaccination 1	n		
				Mean		
				95% CI		
				Response Rate		
				95% CI		
			Day 57 Post Vaccination 1 (29 Days Post Vaccination 2)	n		
				Mean		
				95% CI		
				Response Rate		
				95% CI		
		IL4_OR_IL5_OR_IL13_AND_154	Day 1 (Pre-Vaccination 1)	n		
				Mean		
				95% CI		
				Response Rate		
				95% CI		
			Day 29 Post Vaccination 1	n		
				Mean		

TCELL Sub	Peptide Pool	Cell Type	Time Point	Statistic	Group 1: 5 x 10^{10} vp ChAd-S/30 µg SAM-S (N=4)	Group 3A: 30 µg SAM-S/30 µg SAM-S (N=3)
				95% CI		
				Response Rate		
				95% CI		
			Day 57 Post Vaccination 1 (29 Days Post Vaccination 2)	n		
				Mean		
				95% CI		
				Response Rate		
				95% CI		
CD8	ANY COV2 S	IFNg_OR_IL2	Day 1 (Pre-Vaccination 1)	n		
				Mean		
				95% CI		
				Response Rate		
				95% CI		
			Day 29 Post Vaccination 1	n		
				Mean		
				95% CI		
				Response Rate		
				95% CI		
			Day 57 Post Vaccination 1 (29 Days Post Vaccination 2)	n		
				Mean		
				95% CI		
				Response Rate		
				95% CI		

Notes: N = Number of participants in the mITT population
n = Number of participants in the mITT population with available results

Implementation Notes:

For the Groups 1 and 3A tables, the time points should be Day 1 (Pre-Vaccination), Day 29 Post Vaccination 1, Day 57 Post Vaccination 1 (29 Days Post Vaccination 2).

For the Groups 3B and 4 tables, the time points should be Day 1 (Pre-Vaccination), Day 29 Post Vaccination 1, Day 85 Post Vaccination 1, Day 99 Post Vaccination 1 (15 Days Post Vaccination 2).

For the Groups 5 and 6 tables, the time points should be: Day 1 (Pre-Vaccination), Day 15 Post Vaccination.

For the Groups 9, 10, and 11 tables, the time points should be: Day 1 (Pre-Vaccination), Day 15 Post Vaccination.

For the Groups 10A, 10B, 11A, and 11B tables, the time points should be: Day 1 (Pre-Vaccination), Day 15 Post Vaccination.

For the Groups 13, 14, and 15 tables, the time points should be: Day 1 (Pre-Vaccination), Day 15 Post Vaccination

Tables with similar format:

Table 203: Summary of T Cells Expressing Cytokines as measured by the ICS Assay by Time Point and Vaccination Arm - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A, Per Protocol Population

Table 204: Summary of T Cells Expressing Cytokines as measured by the ICS Assay by Time Point and Vaccination Arm - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4, mITT Population

Table 205: Summary of T Cells Expressing Cytokines as measured by the ICS Assay by Time Point and Vaccination Arm - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4, Per Protocol Population

Table 206: Summary of T Cells Expressing Cytokines as measured by the ICS Assay by Time Point and Vaccination Arm - COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts, mITT Population

Table 207: Summary of T Cells Expressing Cytokines as measured by the ICS Assay by Time Point and Vaccination Arm - COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts, Per Protocol Population

Table 208: Summary of T Cells Expressing Cytokines as measured by the ICS Assay by Time Point and Vaccination Arm - COVID-19 mRNA Vaccinated, >60 years of age, SAM-S-TCE Boosts, mITT Population

Table 209: Summary of T Cells Expressing Cytokines as measured by the ICS Assay by Time Point and Vaccination Arm - COVID-19 mRNA Vaccinated, >60 years of age, SAM-S-TCE Boosts, Per Protocol Population

Table 210: Summary of T Cells Expressing Cytokines as measured by the ICS Assay by Time Point and Vaccination Arm - COVID-19 mRNA Vaccinated, >60 years of age, ChAd-S-TCE Boosts, mITT Population

Table 211: Summary of T Cells Expressing Cytokines as measured by the ICS Assay by Time Point and Vaccination Arm - COVID-19 mRNA Vaccinated, >60 years of age, ChAd-S-TCE Boosts, Per Protocol Population

14.3 Safety Data

14.3.1 Displays of Adverse Events

Table 212: Overall Summary of Adverse Events by Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A

Participants[a] with		Group 1: 5 x 10^{10} vp ChAd-S/30 µg SAM-S (N=X)		Group 3A: 30 µg SAM-S/30 µg SAM-S (N=X)		All Participants (N=X)	
Category 1	**Category 2**	**n**	**%**	**n**	**%**	**n**	**%**
At least one local solicited adverse event	NA						
At least one systemic solicited adverse event	NA						
At least one unsolicited adverse event	NA						
At least one related unsolicited adverse event	Any Grade						
	Mild (Grade 1)						
	Moderate (Grade 2)						
	Severe (Grade 3)						
At least one severe (Grade 3) unsolicited adverse event	Any relationship						
Related	Related						
Unrelated	Unrelated						
At least one serious adverse event[b]	Any relationship						
	Related						
At least one adverse event leading to early termination[c]	NA						
At least one adverse event leading to treatment discontinuation	NA						
Any laboratory Adverse Event	NA						

Participants[a] with		Group 1: 5 x 10^{10} vp ChAd-S/30 µg SAM-S (N=X)		Group 3A: 30 µg SAM-S/30 µg SAM-S (N=X)		All Participants (N=X)	
Category 1	**Category 2**	**n**	**%**	**n**	**%**	**n**	**%**
Any Vital Signs Adverse Event	NA						
At least one medically attended adverse event	NA						
At least one new onset chronic medical condition	NA						

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 307.
[c]As reported on the Adverse Event eCRF.

Implementation Notes:

For the Groups 5-15 tables, do not include the "At least one adverse event leading to treatment discontinuation" row, as those groups have only one study vaccination.]

Tables with similar format:

Table 213: Overall Summary of Adverse Events by Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4

Table 214: Overall Summary of Adverse Events by Vaccination Arm – COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts

Table 215: Overall Summary of Adverse Events by Vaccination Arm – COVID-19 mRNA Vaccinated, >60 years of age, SAM-S-TCE Boosts

Table 216: Overall Summary of Adverse Events by Vaccination Arm – COVID-19 mRNA Vaccinated, >60 years of age, ChAd-S-TCE Boosts

Table 217: Adverse Events Occurring in 5% of Participants in Any Vaccination Arm by MedDRA System Organ Class and Preferred Term, and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A

Preferred Term	MedDRA System Organ Class	Group 1: 5 x 1010 vp ChAd-S/30 µg SAM-S (N=X)			Group 3A: 30 µg SAM-S/30 µg SAM-S (N=X)			All Participants (N=X)		
		n	%	Events	n	%	Events	n	%	Events
Serious Adverse Events										
All	All	x	x	x	x	x	x	x	x	x
PT1	SOC1	x	x	x	x	x	x	x	x	x
Etc.	Etc.									
Non-serious Adverse Events										
All	All	x	x	x	x	x	x	x	x	x
PT1	SOC1	x	x	x	x	x	x	x	x	x
Etc.	Etc.									
Solicited Adverse Events										
All	All	x	x	x	x	x	x	x	x	x
PT1	SOC1	x	x	x	x	x	x	x	x	x
Etc.	Etc.									
Any Adverse Event										
All	All	x	x	x	x	x	x	x	x	x

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.

Tables with Similar Format:

Table 218: Adverse Events Occurring in 5% of Participants in Any Vaccination Arm by MedDRA System Organ Class and Preferred Term, and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4

Table 219: Adverse Events Occurring in 5% of Participants in Any Vaccination Arm by MedDRA System Organ Class and Preferred Term, and Vaccination Arm – COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts

Table 220: Adverse Events Occurring in 5% of Participants in Any Vaccination Arm by MedDRA System Organ Class and Preferred Term, and Vaccination Arm – COVID-19 mRNA Vaccinated, >60 years of age, SAM-S-TCE Boosts

Table 221: Adverse Events Occurring in 5% of Participants in Any Vaccination Arm by MedDRA System Organ Class and Preferred Term, and Vaccination Arm – COVID-19 mRNA Vaccinated, >60 years of age, ChAd-S-TCE Boosts

14.3.1.1 Solicited Adverse Events

Table 222: Number and Percentage of Participants Experiencing Solicited Events by Symptom, Maximum Severity, Dose, and Vaccination Arm - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A – Dose 1

		Group 1: 5×10^{10} vp ChAd-S/30 µg SAM-S (N=X)		Group 3A: 30 µg SAM-S/30 µg SAM-S (N=X)		All Participants (N=X)	
Symptom	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**
Any Symptom	**None**						
	Mild						
	Moderate						
	Severe						
Any Systemic Symptom	**None**						
	Mild						
	Moderate						
	Severe						
Arthralgia	**None**						
	Mild						
	Moderate						
	Severe						
Diarrhea	**None**						
	Mild						
	Moderate						
	Severe						
Fatigue	**None**						
	Mild						
	Moderate						
	Severe						

		Group 1: 5 x 10^{10} vp ChAd-S/30 µg SAM-S (N=X)		Group 3A: 30 µg SAM-S/30 µg SAM-S (N=X)		All Participants (N=X)	
Symptom	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**
Fever[a]	**None**						
	Mild						
	Moderate						
	Severe						
Feverishness	**None**						
	Mild						
	Moderate						
	Severe						
Headache	**None**						
	Mild						
	Moderate						
	Severe						
Malaise	**None**						
	Mild						
	Moderate						
	Severe						
Myalgia	**None**						
	Mild						
	Moderate						
	Severe						
Nausea	**None**						
	Mild						
	Moderate						
	Severe						

		Group 1: 5 x 10^{10} vp ChAd-S/30 µg SAM-S (N=X)		Group 3A: 30 µg SAM-S/30 µg SAM-S (N=X)		All Participants (N=X)	
Symptom	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**
Any Local Symptom	**None**						
	Mild						
	Moderate						
	Severe						
Erythema/Redness	**None**						
	Mild						
	Moderate						
	Severe						
Erythema/Redness Measurement (mm)	**None**						
	Mild						
	Moderate						
	Severe						
Induration/Swelling	**None**						
	Mild						
	Moderate						
	Severe						
Induration/Swelling Measurement (mm)	**None**						
	Mild						
	Moderate						
	Severe						
Pain	**None**						
	Mild						
	Moderate						
	Severe						

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

Tables with similar format:

Table 223: Number and Percentage of Participants Experiencing Solicited Events by Symptom, Maximum Severity, Dose, and Vaccination Arm - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A – Dose 2

Table 224: Number and Percentage of Participants Experiencing Solicited Events by Symptom, Maximum Severity, Dose, and Vaccination Arm - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A – Any Dose

Table 225: Number and Percentage of Participants Experiencing Solicited Events by Symptom, Maximum Severity, Dose, and Vaccination Arm - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4 – Dose 1

Table 226: Number and Percentage of Participants Experiencing Solicited Events by Symptom, Maximum Severity, Dose, and Vaccination Arm - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4 – Dose 2

Table 227: Number and Percentage of Participants Experiencing Solicited Events by Symptom, Maximum Severity, Dose, and Vaccination Arm - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4 – Any Dose

Table 228: Number and Percentage of Participants Experiencing Solicited Events by Symptom, Maximum Severity, Dose, and Vaccination Arm - COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE

Table 229: Number and Percentage of Participants Experiencing Solicited Events by Symptom, Maximum Severity, Dose, and Vaccination Arm - COVID-19 mRNA Vaccinated, >60 years of age, SAM-S-TCE Boosts

Table 230: Number and Percentage of Participants Experiencing Solicited Events by Symptom, Maximum Severity, Dose, and Vaccination Arm - COVID-19 mRNA Vaccinated, >60 years of age, ChAd-S-TCE Boosts

Table 231: Summary of Solicited Events by Days Post Vaccination and Vaccination Arm, Dose 1 – Group 1

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

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

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

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

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

Tables with similar format:

Table 232: Summary of Solicited Events by Days Post Vaccination and Vaccination Arm, Dose 2 – Group 1

Table 233: Summary of Solicited Events by Days Post Vaccination and Vaccination Arm, Any Dose – Group 1

Table 234: Summary of Solicited Events by Days Post Vaccination and Vaccination Arm, Dose 1 – Group 3A

Table 235: Summary of Solicited Events by Days Post Vaccination and Vaccination Arm, Dose 2 – Group 3A

Table 236: Summary of Solicited Events by Days Post Vaccination and Vaccination Arm, Any Dose – Group 3A

Table 251: Summary of Duration of Solicited Symptoms by Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A

		Group 1: 5 x 10^{10} vp ChAd-S/30 µg SAM-S (N=X)			Group 3A: 30 µg SAM-S/30 µg SAM-S (N=X)			All Participants (N=X)		
Variable	**Statistic**	**Dose 1**	**Dose 2**	**All**	**Dose 1**	**Dose 2**	**All**	**Dose 1**	**Dose 2**	**All**
Any Symptom	n									
	Mean									
	Standard Deviation									
	Median									
	Minimum									
	Maximum									
Any Systemic Symptom	n									
	Mean									
	Standard Deviation									
	Median									
	Minimum									
	Maximum									
Arthralgia	n									
	Mean									
	Standard Deviation									
	Median									
	Minimum									
	Maximum									
Diarrhea	n									
	Mean									
	Standard Deviation									
	Median									

		Group 1: 5 x 10^{10} vp ChAd-S/30 µg SAM-S (N=X)			Group 3A: 30 µg SAM-S/30 µg SAM-S (N=X)			All Participants (N=X)		
Variable	**Statistic**	**Dose 1**	**Dose 2**	**All**	**Dose 1**	**Dose 2**	**All**	**Dose 1**	**Dose 2**	**All**
	Minimum									
	Maximum									
Fatigue	n									
	Mean									
	Standard Deviation									
	Median									
	Minimum									
	Maximum									
Fever	n									
	Mean									
	Standard Deviation									
	Median									
	Minimum									
	Maximum									
Feverishness	n									
	Mean									
	Standard Deviation									
	Median									
	Minimum									
	Maximum									
Headache	n									
	Mean									
	Standard Deviation									
	Median									

		Group 1: 5 x 10^{10} vp ChAd-S/30 µg SAM-S (N=X)			Group 3A: 30 µg SAM-S/30 µg SAM-S (N=X)			All Participants (N=X)		
Variable	**Statistic**	**Dose 1**	**Dose 2**	**All**	**Dose 1**	**Dose 2**	**All**	**Dose 1**	**Dose 2**	**All**
	Minimum									
	Maximum									
Malaise	n									
	Mean									
	Standard Deviation									
	Median									
	Minimum									
	Maximum									
Myalgia	n									
	Mean									
	Standard Deviation									
	Median									
	Minimum									
	Maximum									
Nausea	n									
	Mean									
	Standard Deviation									
	Median									
	Minimum									
	Maximum									
Any Local Symptom	n									
	Mean									
	Standard Deviation									
	Median									

		Group 1: 5 x 10^{10} vp ChAd-S/30 µg SAM-S (N=X)			Group 3A: 30 µg SAM-S/30 µg SAM-S (N=X)			All Participants (N=X)		
Variable	**Statistic**	**Dose 1**	**Dose 2**	**All**	**Dose 1**	**Dose 2**	**All**	**Dose 1**	**Dose 2**	**All**
	Minimum									
	Maximum									
Erythema	n									
	Mean									
	Standard Deviation									
	Median									
	Minimum									
	Maximum									
Edema /Induration	n									
	Mean									
	Standard Deviation									
	Median									
	Minimum									
	Maximum									
Pain	n									
	Mean									
	Standard Deviation									
	Median									
	Minimum									
	Maximum									
Tenderness	n									
	Mean									
	Standard Deviation									
	Median									

		Group 1: 5 x 10^{10} vp ChAd-S/30 µg SAM-S (N=X)			Group 3A: 30 µg SAM-S/30 µg SAM-S (N=X)			All Participants (N=X)		
Variable	**Statistic**	**Dose 1**	**Dose 2**	**All**	**Dose 1**	**Dose 2**	**All**	**Dose 1**	**Dose 2**	**All**
	Minimum									
	Maximum									

Notes: N=Number of participants in the Safety Population.
n=Number of participants experiencing the solicited symptom.
Statistics calculated using participants that experienced symptoms only.
The duration of a symptom is the number of days the symptom occurred with a severity of mild or greater.

Implementation Note:

For the Group 5-15 tables, do not split the group columns into doses (have one column under each group).

Tables with similar format:

Table 252: Summary of Duration of Solicited Symptoms by Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4

Table 253: Summary of Duration of Solicited Symptoms by Vaccination Arm – COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts

Table 254: Summary of Duration of Solicited Symptoms by Vaccination Arm – COVID-19 mRNA Vaccinated, >60 years of age, SAM-S-TCE Boosts

Table 255: Summary of Duration of Solicited Symptoms by Vaccination Arm – COVID-19 mRNA Vaccinated, >60 years of age, ChAd-S-TCE Boosts

14.3.1.2 Unsolicited Adverse Events

Table 256: All Adverse Events Cross-Classified by MedDRA System Organ Class, Severity, and Relationship to Study Vaccination, and Vaccination Arm – Group 1 (N=X)

		Relationship to Study Vaccination	
MedDRA System Organ Class	Severity	Not Related (n)	Related (n)
Any SOC	Mild		
	Moderate		
	Severe		
Blood And Lymphatic System Disorders	Mild		
	Moderate		
	Severe		
Cardiac Disorders	Mild		
	Moderate		
	Severe		
Ear And Labyrinth Disorders	Mild		
	Moderate		
	Severe		
Eye Disorders	Mild		
	Moderate		
	Severe		
Gastrointestinal Disorders	Mild		
	Moderate		
	Severe		
General Disorders and Administration Site Conditions	Mild		
	Moderate		
	Severe		

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

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

Implementation Note:

"N" in the table title should be the number of participants enrolled in the group and receiving at least one dose of the vaccine. Table names with a specific group number (e.g. Group 1) will only contain the participants in that group. Table names with multiple groups (e.g. COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts) will pool the participants in those groups.

The SOC shown in the example table shell are examples only. Only SOC reported in the relevant groups will be included in the table.

Tables with similar format:

Table 257: All Adverse Events Cross-Classified by MedDRA System Organ Class, Severity, and Relationship to Study Vaccination, and Vaccination Arm – Group 3A (N=X)

Table 258: All Adverse Events Cross-Classified by MedDRA System Organ Class, Severity, and Relationship to Study Vaccination, and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A (N=X)

Table 259: All Adverse Events Cross-Classified by MedDRA System Organ Class, Severity, and Relationship to Study Vaccination, and Vaccination Arm – Group 3B (N=X)

Table 260: All Adverse Events Cross-Classified by MedDRA System Organ Class, Severity, and Relationship to Study Vaccination, and Vaccination Arm – Group 4 (N=X)

Table 261: All Adverse Events Cross-Classified by MedDRA System Organ Class, Severity, and Relationship to Study Vaccination, and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4 (N=X)

Table 262: All Adverse Events Cross-Classified by MedDRA System Organ Class, Severity, and Relationship to Study Vaccination, and Vaccination Arm – Group 5 (N=X)

Table 263: All Adverse Events Cross-Classified by MedDRA System Organ Class, Severity, and Relationship to Study Vaccination, and Vaccination Arm – Group 6 (N=X)

Table 264: All Adverse Events Cross-Classified by MedDRA System Organ Class, Severity, and Relationship to Study Vaccination, and Vaccination Arm – COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts (N=X)

Table 265: All Adverse Events Cross-Classified by MedDRA System Organ Class, Severity, and Relationship to Study Vaccination, and Vaccination Arm – Group 9 (N=X)

Table 266: All Adverse Events Cross-Classified by MedDRA System Organ Class, Severity, and Relationship to Study Vaccination, and Vaccination Arm – Group 10 (N=X)

Table 267: All Adverse Events Cross-Classified by MedDRA System Organ Class, Severity, and Relationship to Study Vaccination, and Vaccination Arm – Group 11 (N=X)

Table 268: All Adverse Events Cross-Classified by MedDRA System Organ Class, Severity, and Relationship to Study Vaccination, and Vaccination Arm – COVID-19 mRNA Vaccinated, >60 years of age, SAM-S-TCE Boosts (N=X)

Table 269: All Adverse Events Cross-Classified by MedDRA System Organ Class, Severity, and Relationship to Study Vaccination, and Vaccination Arm – Group 13 (N=X)

Table 273: Summary of All Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Severity, Relationship, and Vaccination Arm – Group 1 (N=X)

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

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

Implementation Note:

"N" in the table title should be the number of participants enrolled in the group and receiving at least one dose of the vaccine. Table names with a specific group number (e.g. Group 1) will only contain the participants in that group. Table names with a specific group number (e.g. Group 1) will only contain the participants in that group. Table names with multiple groups (e.g. COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts) will pool the participants in those groups. The SOC shown in the example table shell are examples only. Only SOC reported in the relevant groups will be included in the table.

Tables with similar format:

Table 274: Summary of All Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Severity, Relationship, and Vaccination Arm – Group 3A (N=X)

Table 275: Summary of All Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Severity, Relationship, and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A

Table 276: Summary of All Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Severity, Relationship, and Vaccination Arm – Group 3B (N=X)

Table 290: Number and Percentage of Participants Experiencing Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Severity, Relationship, and Vaccination Arm – Group 1 (N=X)

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

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

Implementation Note:

Count each participant once per table row in the column of their highest severity and closest relationship. "N" in the table title should be the number of participants enrolled in the group and receiving at least one dose of the vaccine. Table names with a specific group number (e.g. Group 1) will only contain the participants in that group. Table names with a specific group number (e.g. Group 1) will only contain the participants in that group. Table names with multiple groups (e.g. COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts) will pool the participants in those groups. The SOC shown in the example table shell are examples only. Only SOC reported in the relevant groups will be included in the table.

Tables with similar format:

Table 291: Number and Percentage of Participants Experiencing Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Severity, Relationship, and Vaccination Arm – Group 3A (N=X)

Table 292: Number and Percentage of Participants Experiencing Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Severity, Relationship, and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A (N=X)

Table 293: Number and Percentage of Participants Experiencing Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Severity, Relationship, and Vaccination Arm – Group 3B (N=X)

Table 294: Number and Percentage of Participants Experiencing Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Severity, Relationship, and Vaccination Arm – Group 4 (N=X)

Table 295: Number and Percentage of Participants Experiencing Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Severity, Relationship, and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4 (N=X)

Table 296: Number and Percentage of Participants Experiencing Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Severity, Relationship, and Vaccination Arm – Group 5 (N=X)

Table 297: Number and Percentage of Participants Experiencing Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Severity, Relationship, and Vaccination Arm – Group 6 (N=X)

Table 298: Number and Percentage of Participants Experiencing Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Severity, Relationship, and Vaccination Arm – COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts (N=X)

Table 299: Number and Percentage of Participants Experiencing Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Severity, Relationship, and Vaccination Arm – Group 9 (N=X)

Table 300: Number and Percentage of Participants Experiencing Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Severity, Relationship, and Vaccination Arm – Group 10 (N=X)

Table 301: Number and Percentage of Participants Experiencing Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Severity, Relationship, and Vaccination Arm – Group 11 (N=X)

Table 302: Number and Percentage of Participants Experiencing Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Severity, Relationship, and Vaccination Arm – COVID-19 mRNA Vaccinated, >60 years of age, SAM-S-TCE Boosts (N=X)

Table 303: Number and Percentage of Participants Experiencing Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Severity, Relationship, and Vaccination Arm – Group 13 (N=X)

Table 304: Number and Percentage of Participants Experiencing Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Severity, Relationship, and Vaccination Arm – Group 14 (N=X)

Table 305: Number and Percentage of Participants Experiencing Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Severity, Relationship, and Vaccination Arm – Group 15 (N=X)

Table 306: Number and Percentage of Participants Experiencing Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Severity, Relationship, and Vaccination Arm – COVID-19 mRNA Vaccinated, >60 years of age, ChAd-S-TCE Boosts (N=X)

14.3.2 Listing of Deaths, Other Serious and Significant Adverse Events

Table 307: Listing of Serious Adverse Events

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

Table 308: Listing of Non-Serious, Unsolicited, Moderate or Severe Adverse Events

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

Table 309: Listing of Other Significant Adverse Events

Adverse Event	Number of Doses Received at Time of Event	No. of Days Post Associated Dose	Duration of Event	Severity	MedDRA System Organ Class	AESI Type	Relationship	Outcome
Participant ID: , Vaccination Arm: , AE Number:								
Comments:								
Participant ID: , Vaccination Arm: , AE Number:								
Comments:								

Implementation Note:

The column AESI Type will contain PIMMC, MAAE, or NOCMC if the AESI is classified as one of those three categories, otherwise it will state the PT of the AESI.

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)

Table 310: Listing of Abnormal Laboratory Results - Chemistry

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

Table 311: Listing of Abnormal Laboratory Results - Hematology

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

14.3.5 Displays of Laboratory Results

14.3.5.1 Chemistry Results

Table 312: Laboratory Results by Parameter, Maximum Severity, Time Point, and Vaccination Arm – Any Chemistry Parameter

Time Point	Vaccination Arm	N	None		Mild/ Grade 1 (Low)		Mild/ Grade 1 (High)		Moderate/ Grade 2 (Low)		Moderate/ Grade 2 (High)		Severe/ Grade 3 (Low)		Severe/ Grade 3 (High)		Missing	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Baseline	Group 1: 5 x 10^{10} vp ChAd/ 30 µg SAM-S	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Group 3A: 30 µg SAM-S/ 30 µg SAM-S																	
	Group 3B: 30 µg SAM-S/ 3 µg SAM-S																	
	Group 4: 10 µg SAM-S-TCE/ 3 µg SAM-S-TCE																	
	Group 5: 3 µg SAM-S-TCE																	
	Group 6: 6 µg SAM-S-TCE																	
	Group 9: 3 µg SAM-S-TCE																	
	Group 10: 6 µg SAM-S-TCE																	
	Group 11: 10 µg SAM-S-TCE																	
	Group 13: 5 x 10^{10} vp ChAd-S-TCE																	
	Group 14: 1 x 10^{11} vp ChAd-S-TCE																	
	Group 15: 5 x 10^{11} vp ChAd-S-TCE																	
	All Participants																	

Time Point	Vaccination Arm	N	None		Mild/ Grade 1 (Low)		Mild/ Grade 1 (High)		Moderate/ Grade 2 (Low)		Moderate/ Grade 2 (High)		Severe/ Grade 3 (Low)		Severe/ Grade 3 (High)		Missing	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Day 8	…																	
Day 29 (pre-dose 2 for Groups 1 and 3A)	…																	
Day 36 (8 days post-dose 2 for Groups 3A and 4)																		
Day 85 (pre-dose 2 for Groups 3B and 4)	…																	
Day 92 (8 days post-dose 2 for Groups 3B and 4)																		
Max Severity Post-Baseline	…																	

Note: The "Maximum 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 safety population

Implementation Note:

The vaccination arms receiving one dose will be shown at Days 1 and 8 only. Groups 1 and 3A will be shown at Days 1, 8, 29, and 36. Groups 3B and 4 will be shown at Days 1, 8, 85, and 92). All vaccination arms will be shown in the Max Severity Post-Baseline row.

Tables with similar format:

Table 313: Laboratory Results by Parameter, Maximum Severity, Study Day, and Vaccination Arm – Alanine Aminotransferase

Table 314: Laboratory Results by Parameter, Maximum Severity, Study Day, and Vaccination Arm – Aspartate Aminotransferase

Table 315: Laboratory Results by Parameter, Maximum Severity, Study Day, and Vaccination Arm – Alkaline Phosphatase

Table 316: Laboratory Results by Parameter, Maximum Severity, Study Day, and Vaccination Arm – Total Bilirubin

Table 317: Laboratory Results by Parameter, Maximum Severity, Study Day, and Vaccination Arm – Creatine Kinase

Table 318: Laboratory Results by Parameter, Maximum Severity, Study Day, and Vaccination Arm – Creatinine

Table 319: Laboratory Summary Statistics by Parameter, Time Point, and Vaccination Arm – Alanine Aminotransferase

Time Point	Vaccination Arm	N	Mean	Standard Deviation	Median	Min, Max
Baseline	Group 1: 5 x 10^{10} vp ChAd/ 30 µg SAM-S	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Group 3A: 30 µg SAM-S/ 30 µg SAM-S					
	Group 3B: 30 µg SAM-S/ 3 µg SAM-S					
	Group 4: 10 µg SAM-S-TCE/ 3 µg SAM-S-TCE					
	Group 5: 3 µg SAM-S-TCE					
	Group 6: 6 µg SAM-S-TCE					
	Group 9: 3 µg SAM-S-TCE					
	Group 10: 6 µg SAM-S-TCE					
	Group 11: 10 µg SAM-S-TCE					
	Group 13: 5 x 10^{10} vp ChAd-S-TCE					
	Group 14: 1 x 10^{11} vp ChAd-S-TCE					
	Group 15: 5 x 10^{11} vp ChAd-S-TCE					
	All Participants					
Day 8	…					
Day 8, Change from Baseline	…					
Day 29 (pre-dose 2 for Groups 1 and 3A)	…					
Day 29, Change from Baseline						
Day 36 (8 days post-dose 2 for Groups 3A and 4)						
Day 36, Change from Baseline						
Day 85 (pre-dose 2 for Groups 3B and 4)						
Day 85, Change from Baseline						
Day 92 (8 days post-dose 2 for Groups 3B and 4)						
Day 92, Change from Baseline						
Note: N = Number of participants in safety population						

Implementation Note:

The vaccination arms receiving one dose will be shown at Days 1 and 8 only. Groups 1 and 3A will be shown at Days 1, 8, 29, and 36. Groups 3B and 4 will be shown at Days 1, 8, 85, and 92).

Tables with similar format:

Table 320: Laboratory Summary Statistics by Parameter, Time Point, and Vaccination Arm – Aspartate Aminotransferase

Table 321: Laboratory Summary Statistics by Parameter, Time Point, and Vaccination Arm – Alkaline Phosphatase

Table 322: Laboratory Summary Statistics by Parameter, Time Point, and Vaccination Arm – Total Bilirubin

Table 323: Laboratory Summary Statistics by Parameter, Time Point, and Vaccination Arm – Creatine Kinase

Table 324: Laboratory Summary Statistics by Parameter, Time Point, and Vaccination Arm – Creatinine

14.3.5.2 Hematology Results

Table 325: Laboratory Results by Parameter, Maximum Severity, Time Point, and Vaccination Arm – Any Hematology Parameter

Time Point	Vaccination Arm	N	None		Mild/ Grade 1 (Low)		Mild/ Grade 1 (High)		Moderate/ Grade 2 (Low)		Moderate/ Grade 2 (High)		Severe/ Grade 3 (Low)		Severe/ Grade 3 (High)		Missing	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Baseline	Group 1: 5 x 10^{10} vp ChAd/ 30 µg SAM-S	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Group 3A: 30 µg SAM-S/ 30 µg SAM-S																	
	Group 3B: 30 µg SAM-S/ 3 µg SAM-S																	
	Group 4: 10 µg SAM-S-TCE/ 3 µg SAM-S-TCE																	
	Group 5: 3 µg SAM-S-TCE																	
	Group 6: 6 µg SAM-S-TCE																	
	Group 9: 3 µg SAM-S-TCE																	
	Group 10: 6 µg SAM-S-TCE																	
	Group 11: 10 µg SAM-S-TCE																	
	Group 13: 5 x 10^{10} vp ChAd-S-TCE																	
	Group 14: 1 x 10^{11} vp ChAd-S-TCE																	
	Group 15: 5 x 10^{11} vp ChAd-S-TCE																	
	All Participants																	

Time Point	Vaccination Arm	N	None		Mild/ Grade 1 (Low)		Mild/ Grade 1 (High)		Moderate/ Grade 2 (Low)		Moderate/ Grade 2 (High)		Severe/ Grade 3 (Low)		Severe/ Grade 3 (High)		Missing	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Day 8	…																	
Day 29 (pre-dose 2 for Groups 1 and 3A)	…																	
Day 36 (8 days post-dose 2 for Groups 3A and 4)	…																	
Day 85 (pre-dose 2 for Groups 3B and 4)	…																	
Day 92 (8 days post-dose 2 for Groups 3B and 4)	…																	
Max Severity Post Baseline	…																	
Note: The "Maximum Post Baseline" rows indicate the maximum severity experienced by each vaccination group at any time point post baseline, including unscheduled assessments. N = Number of participants in the Safety Analysis Population																		

Implementation Note:

The vaccination arms receiving one dose will be shown at Days 1 and 8 only. Groups 1 and 3A will be shown at Days 1, 8, 29, and 36. Groups 3B and 4 will be shown at Days 1, 8, 85, and 92). All vaccination arms will be shown in the Max Severity Post-Baseline row.

Tables with similar format:

Table 326: Laboratory Results by Parameter, Maximum Severity, Time Point, and Vaccination Arm – White Blood Cells

Table 327: Laboratory Results by Parameter, Maximum Severity, Time Point, and Vaccination Arm – Hemoglobin

Table 328: Laboratory Results by Parameter, Maximum Severity, Time Point, and Vaccination Arm – Platelets

Table 329: Laboratory Summary Statistics by Parameter, Time Point, and Vaccination Arm – White Blood Cells

Time Point	Vaccination Arm	N	Mean	Standard Deviation	Median	Min, Max
Baseline	Group 1: 5 x 10^{10} vp ChAd/ 30 µg SAM-S	x	xx.x	xx.x	xx.x	xx.x, xx.x
	Group 3A: 30 µg SAM-S/ 30 µg SAM-S					
	Group 3B: 30 µg SAM-S/ 3 µg SAM-S					
	Group 4: 10 µg SAM-S-TCE/ 3 µg SAM-S-TCE					
	Group 5: 3 µg SAM-S-TCE					
	Group 6: 6 µg SAM-S-TCE					
	Group 9: 3 µg SAM-S-TCE					
	Group 10: 6 µg SAM-S-TCE					
	Group 11: 10 µg SAM-S-TCE					
	Group 13: 5 x 10^{10} vp ChAd-S-TCE					
	Group 14: 1 x 10^{11} vp ChAd-S-TCE					
	Group 15: 5 x 10^{11} vp ChAd-S-TCE					
	All Participants					
Day 8	…					
Day 8, Change from Baseline	…					
Day 29 (pre-dose 2 for Groups 1 and 3A)	…					
Day 29, Change from Baseline						
Day 36 (8 days post-dose 2 for Groups 3A and 4)						
Day 36, Change from Baseline						
Day 85 (pre-dose 2 for Groups 3B and 4)						
Day 85, Change from Baseline						
Day 92 (8 days post-dose 2 for Groups 3B and 4)						
Day 92, Change from Baseline						
Note: N = Number of participants in safety population						

Implementation Note:

The vaccination arms receiving one dose will be shown at Days 1 and 8 only. Groups 1 and 3A will be shown at Days 1, 8, 29, and 36. Groups 3B and 4 will be shown at Days 1, 8, 85, and 92).

Tables with similar format:

Table 330: Laboratory Summary Statistics by Parameter, Time Point, and Vaccination Arm – Hemoglobin

Table 331: Laboratory Summary Statistics by Parameter, Time Point, and Vaccination Arm – Platelets

14.3.6 Displays of Vital Signs

Table 332: Vital Signs by Assessment, Maximum Severity, Time Point, and Vaccination Arm – Any Assessment

Time Point	Vaccination Arm	N	None		Mild		Moderate		Severe		Missing	
			n	%	n	%	n	%	n	%	n	%
Baseline	Group 1: 5 x 10^{10} vp ChAd/ 30 µg SAM-S	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Group 3A: 30 µg SAM-S/ 30 µg SAM-S											
	Group 3B: 30 µg SAM-S/ 3 µg SAM-S											
	Group 4: 10 µg SAM-S-TCE/ 3 µg SAM-S-TCE											
	Group 5: 3 µg SAM-S-TCE											
	Group 6: 6 µg SAM-S-TCE											
	Group 9: 3 µg SAM-S-TCE											
	Group 10: 6 µg SAM-S-TCE											
	Group 11: 10 µg SAM-S-TCE											
	Group 13: 5 x 10^{10} vp ChAd-S-TCE											
	Group 14: 1 x 10^{11} vp ChAd-S-TCE											
	Group 15: 5 x 10^{11} vp ChAd-S-TCE											
	All Participants											
Day 2												
Day 8	…											
Day 15												
Day 29	…											
Day 36	…											
Day 43	…											
Day 57	…											
Day 85												

Time Point	Vaccination Arm	N	None		Mild		Moderate		Severe		Missing	
			n	%	n	%	n	%	n	%	n	%
Day 86												
Day 92												
Day 99												
Day 113												
Day 169												
Day 181												
Day 209												
Day 265												
Day 366												
Day 394	…											
Day 450												
Max Severity Post Baseline	…											
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.												

Implementation Note:

The vaccination arms shown at each time point will vary. Vaccination arms will be shown at each time point where vital signs were assessed.

Tables with similar format:

Table 333: Vital Signs by Assessment, Maximum Severity, Time Point, and Vaccination Arm – Temperature

Table 334: Vital Signs by Assessment, Maximum Severity, Time Point, and Vaccination Arm – Diastolic Blood Pressure

Table 335: Vital Signs by Assessment, Maximum Severity, Time Point, and Vaccination Arm – Systolic Blood Pressure

Table 336: Vital Signs by Assessment, Maximum Severity, Time Point, and Vaccination Arm – Pulse

14.4 Summary of Concomitant Medications

Table 337: Number and Percentage of Participants with Prior and Concurrent Medications by WHODrug Classification and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A

WHODrug Code Level 1, Anatomic Group	WHODrug Code Level 2, Therapeutic Subgroup	Group 1: 5 x 10^{10} vp ChAd/ 30 µg SAM-S (N=X)		Group 3A: 30 µg SAM-S/ 30 µg SAM-S (N=X)		All Participants (N=X)	
		n	%	n	%	n	%
Any Level 1 Codes	Any Level 2 Codes	x	xx	x	xx	x	xx
[ATC Level 1 - 1]	Any [ATC 1 – 1]						
	[ATC 2 - 1]						
	[ATC 2 - 2]						
	[ATC 2 - 3]						
[ATC Level 1 – 2]	[ATC 2 - 1]						
	[ATC 2 - 2]						
	[ATC 2 - 3]						

Tables with similar format:

Table 338: Number and Percentage of Participants with Prior and Concurrent Medications by WHODrug Classification and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4

Table 339: Number and Percentage of Participants with Prior and Concurrent Medications by WHODrug Classification and Vaccination Arm – COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts

Table 340: Number and Percentage of Participants with Prior and Concurrent Medications by WHODrug Classification and Vaccination Arm – COVID-19 mRNA Vaccinated, >60 years of age, SAM-S-TCE Boosts

Table 341: Number and Percentage of Participants with Prior and Concurrent Medications by WHODrug Classification and Vaccination Arm – COVID-19 mRNA Vaccinated, >60 years of age, ChAd-S-TCE Boosts

APPENDIX 2. FIGURE MOCK-UPS

LIST OF FIGURES

10.1 Disposition of Participants

Figure 1: CONSORT Flow Diagram – Stage 1

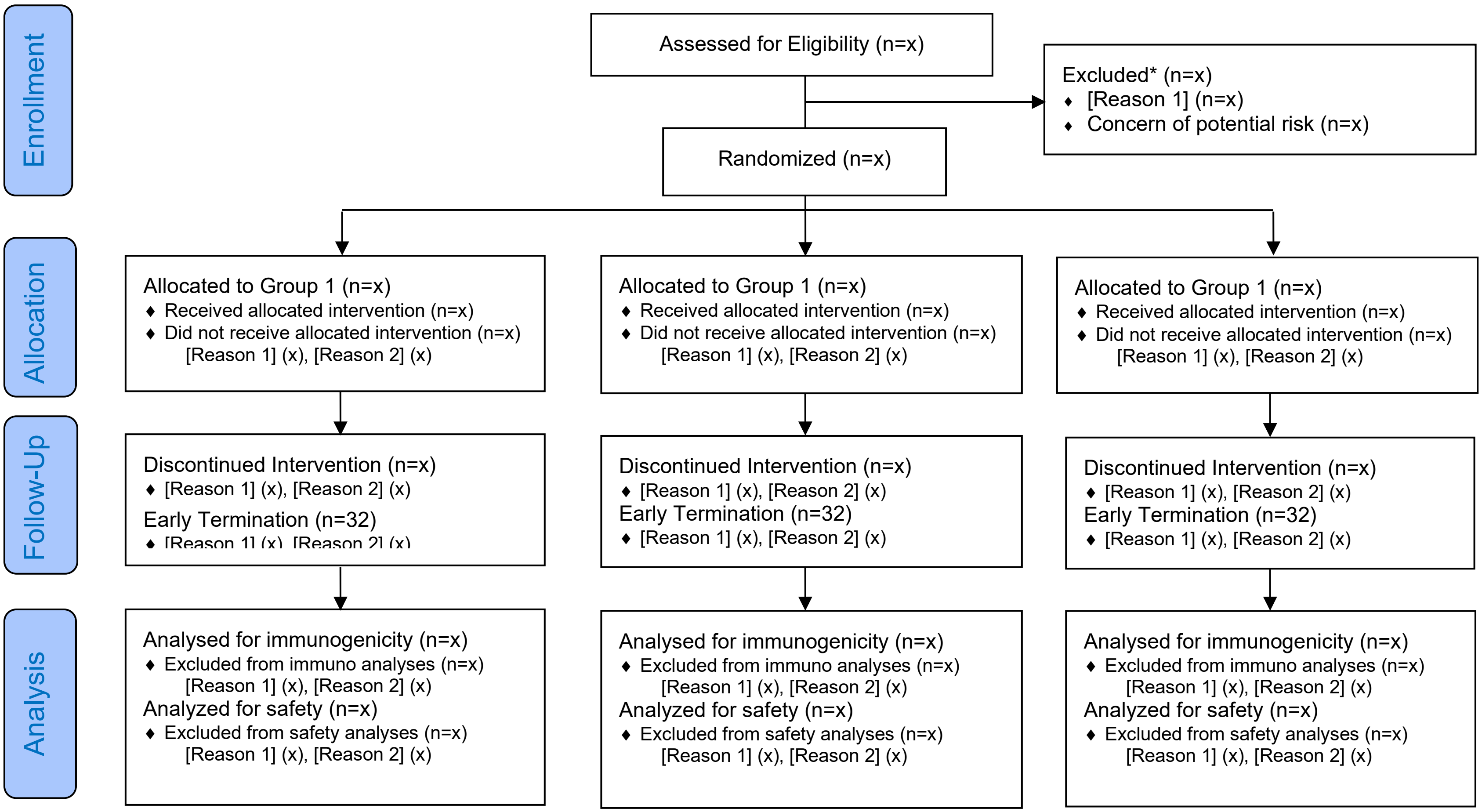
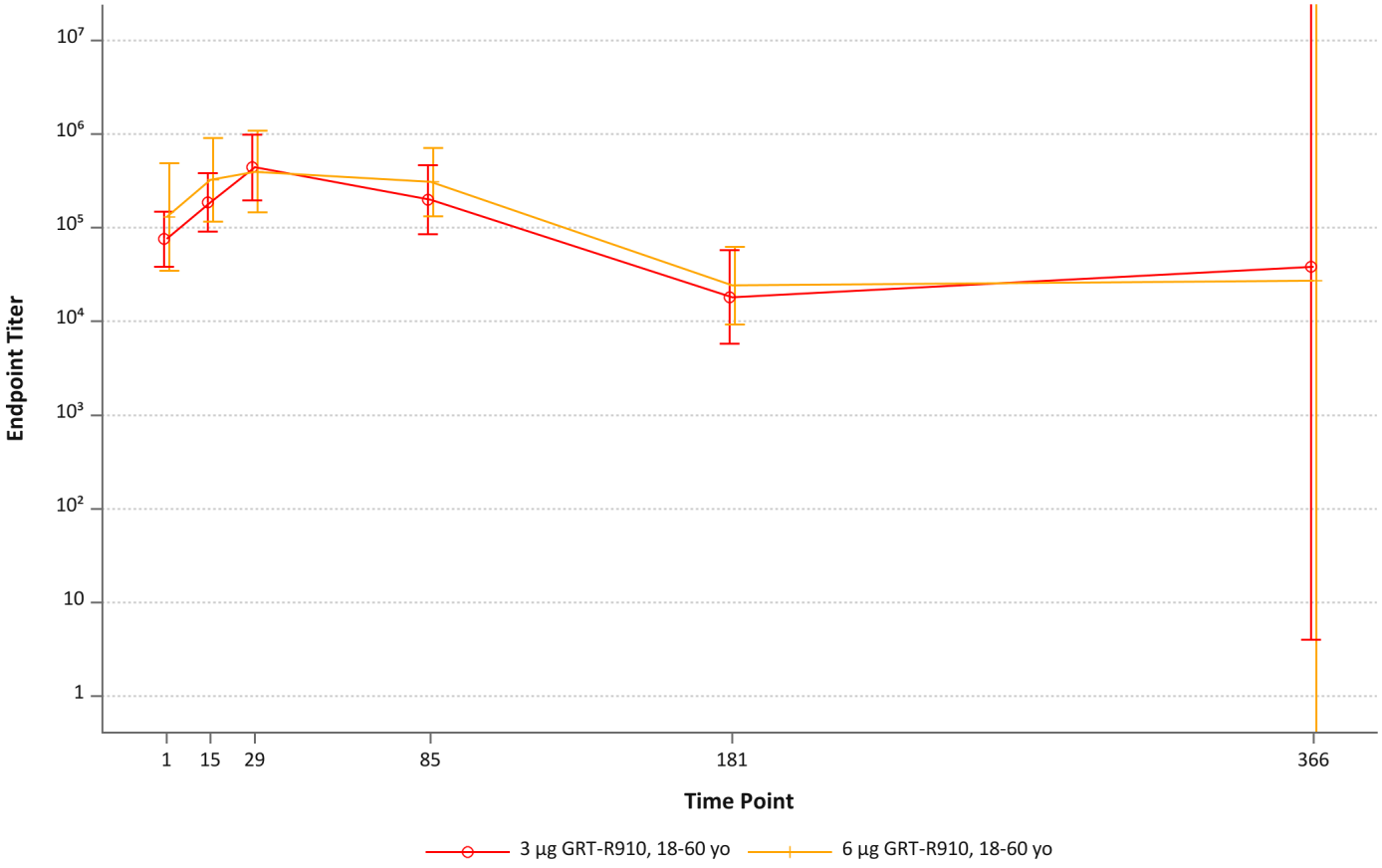


Figure with similar format:

Figure 2: CONSORT Flow Diagram – Stage 2

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

Figure 3: Mean and 95% CIs of ELISA IgG Antibody Against SARS-CoV-2 S-2P by Time Point and Vaccination Arm - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A, mITT Population



Implementation Notes:

The y-axis will be Endpoint Titer for the ELISA figures and ID_{50} or ID_{80} the pseudovirus neutralization and focus reduction test figures. The group labels will match the tables.

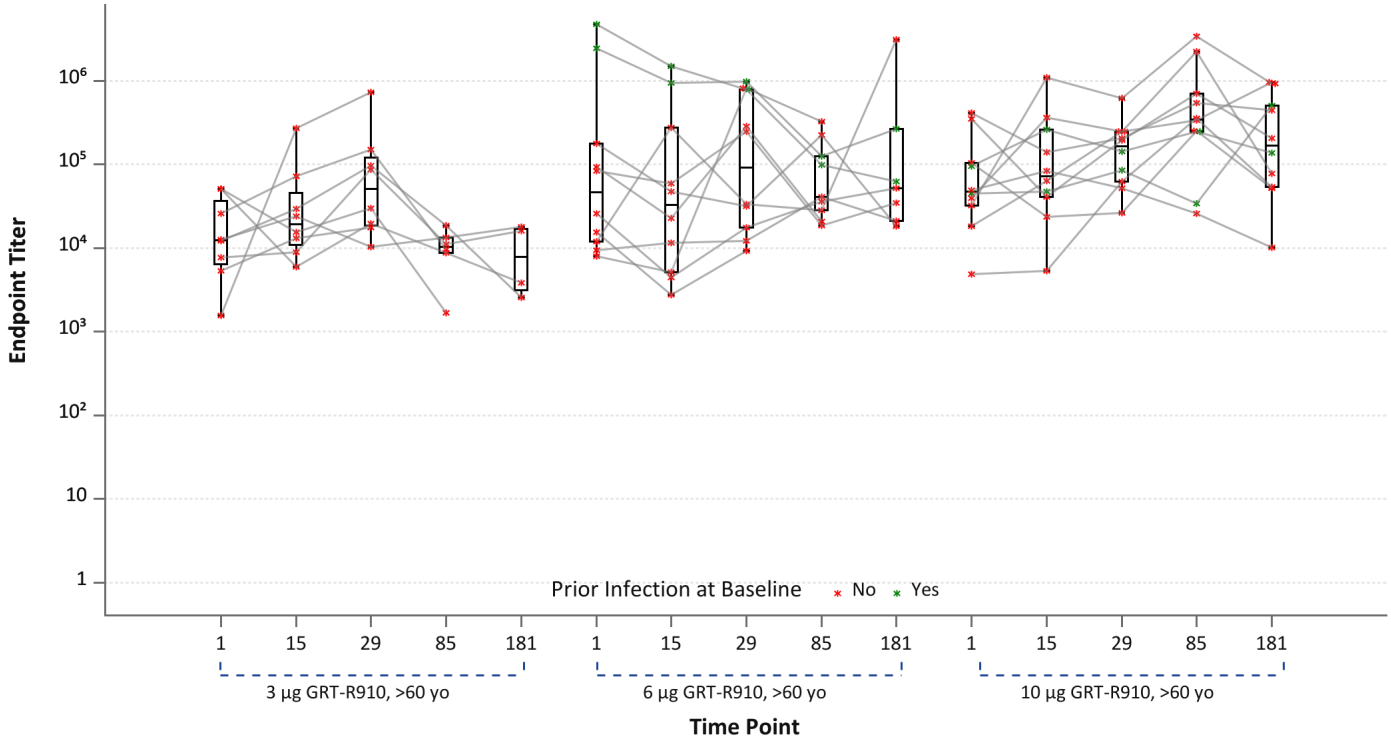
Figures with similar format:

Figure 4: Mean and 95% CIs of ELISA IgG Antibody Against SARS-CoV-2 S-2P by Time Point and Vaccination Arm - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A, Per Protocol Population

Figure 5: Mean and 95% CIs of ELISA IgG Antibody Against SARS-CoV-2 S-2P by Time Point and Vaccination Arm - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4, mITT Population

Figure 6: Mean and 95% CIs of ELISA IgG Antibody Against SARS-CoV-2 S-2P by Time Point and Vaccination Arm - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4, Per Protocol Population

Figure 143: Distribution of ELISA IgG Antibody Against SARS-CoV-2 S-2P by Time Point and Vaccination Arm - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A, mITT Population



Implementation Notes:

The y-axis label will be Endpoint Titer for the ELISA figures and ID_{50} or ID_{80} for the pseudovirus neutralization and focus reduction test figures. The group labels will match the tables. Participants with a prior infection at baseline will be marked by color.

Figures with similar format:

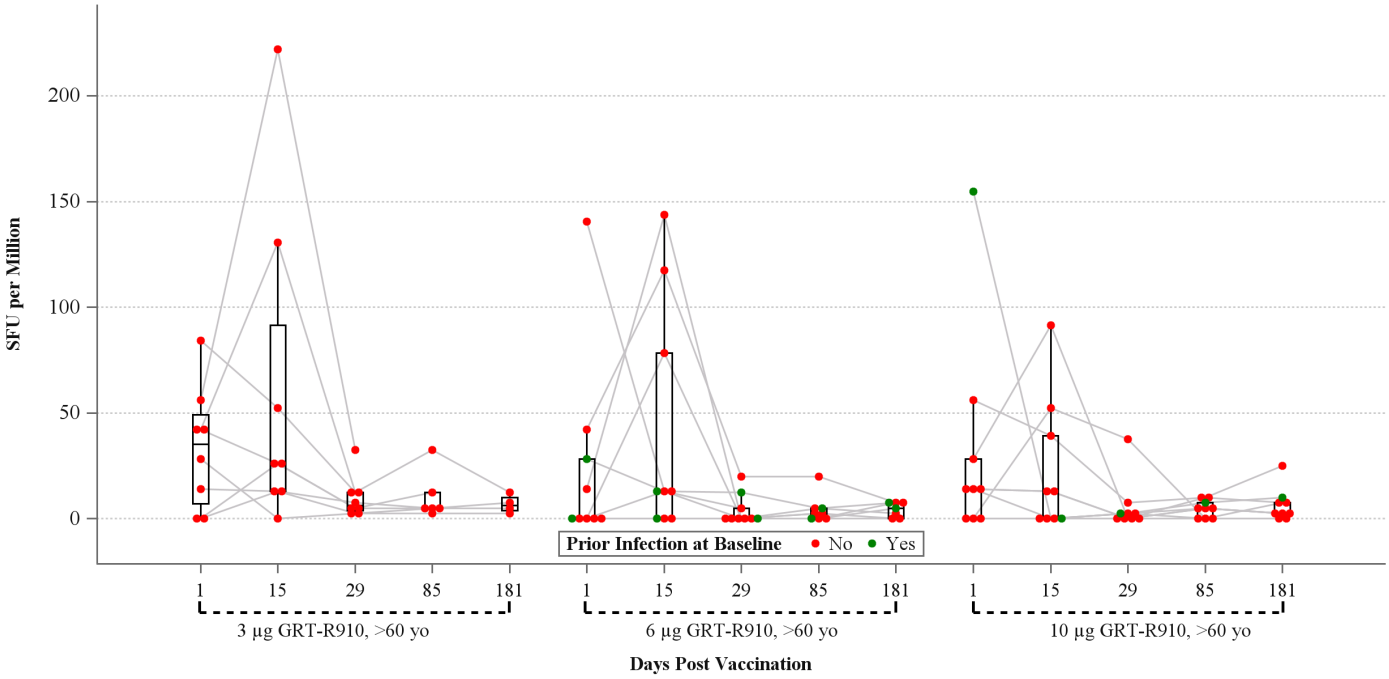
Figure 144: Distribution of ELISA IgG Antibody Against SARS-CoV-2 S-2P by Time Point and Vaccination Arm - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A, Per Protocol Population

Figure 145: Distribution of ELISA IgG Antibody Against SARS-CoV-2 S-2P by Time Point and Vaccination Arm - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4, mITT Population

Figure 146: Distribution of ELISA IgG Antibody Against SARS-CoV-2 S-2P by Time Point and Vaccination Arm - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4, Per Protocol Population

Figure 147: Distribution of ELISA IgG Antibody Against SARS-CoV-2 S-2P by Time Point and Vaccination Arm - COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts, mITT Population

Figure 283: Distribution of T Cells Expressing IFNγ as measured by the ELISpot Assay in Spot Forming Units (SFU) per Million by Time Point and Vaccination Arm, 15mer OLPs Spanning Membrane Frame - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A, mITT Population



Implementation Note:

Figure will include a horizontal dashed line for the LLOD.

Figures with similar format:

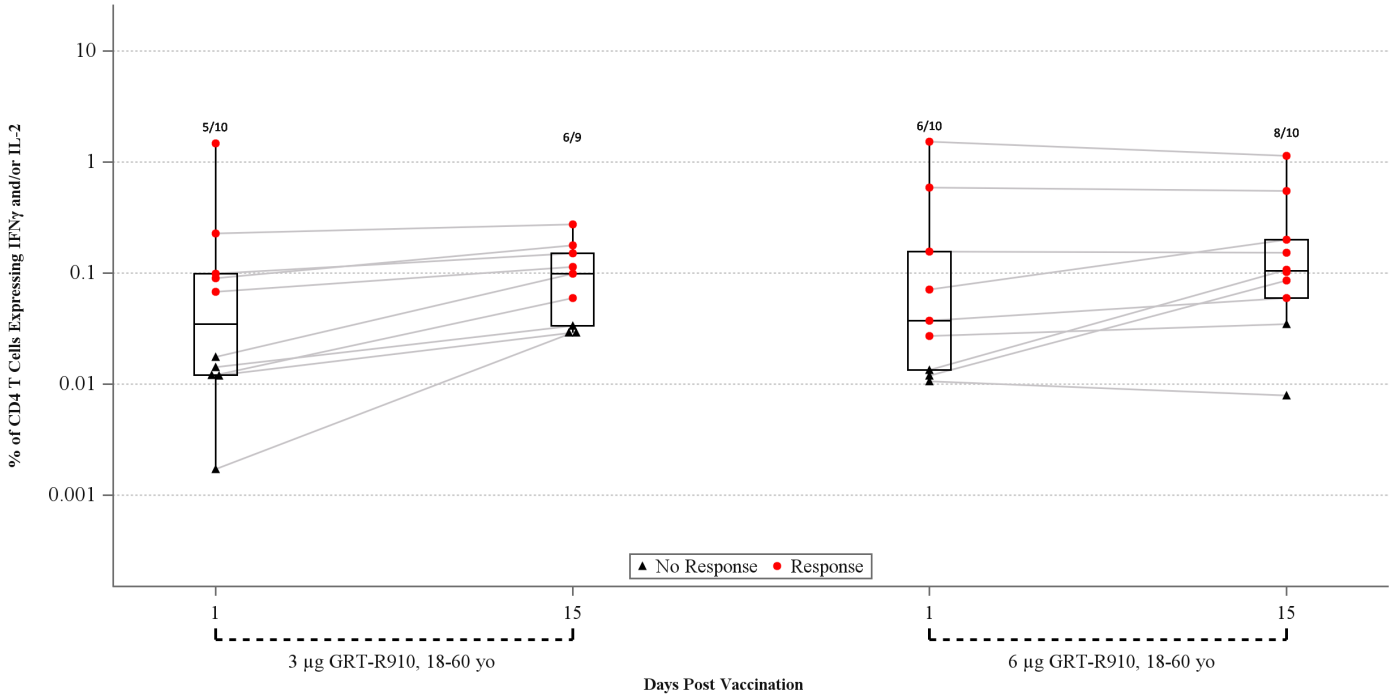
Figure 284: Distribution of T Cells Expressing IFNγ as measured by the ELISpot Assay in Spot Forming Units (SFU) per Million by Time Point and Vaccination Arm, 15mer OLPs Spanning Membrane Frame - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A, Per Protocol Population

Figure 285: Distribution of T Cells Expressing IFNγ as measured by the ELISpot Assay in Spot Forming Units (SFU) per Million by Time Point and Vaccination Arm, 15mer OLPs Spanning Membrane Frame - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4, mITT Population

Figure 286: Distribution of T Cells Expressing IFNγ as measured by the ELISpot Assay in Spot Forming Units (SFU) per Million by Time Point and Vaccination Arm, 15mer OLPs Spanning Membrane Frame - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4, Per Protocol Population

Figure 287: Distribution of T Cells Expressing IFNγ as measured by the ELISpot Assay in Spot Forming Units (SFU) per Million by Time Point and Vaccination Arm, 15mer OLPs Spanning Membrane Frame - COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts, mITT Population

Figure 393: Distribution of CD4 T Cells Expressing IFNγ and/or IL-2 by Time Point and Vaccination Arm, Any COV2 S - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A, mITT Population



Implementation Note:

Use color to represent responder status (No Response/Response) and symbol to represent prior infection (No/Yes).

Figures with similar format:

Figure 394: Distribution of CD4 T Cells Expressing IFNγ and/or IL-2 by Time Point and Vaccination Arm, Any COV2 S - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A, Per Protocol Population

Figure 395: Distribution of CD4 T Cells Expressing IFNγ and/or IL-2 by Time Point and Vaccination Arm, Any COV2 S - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4, mITT Population

Figure 396: Distribution of CD4 T Cells Expressing IFNγ and/or IL-2 by Time Point and Vaccination Arm, Any COV2 S - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4, Per Protocol Population

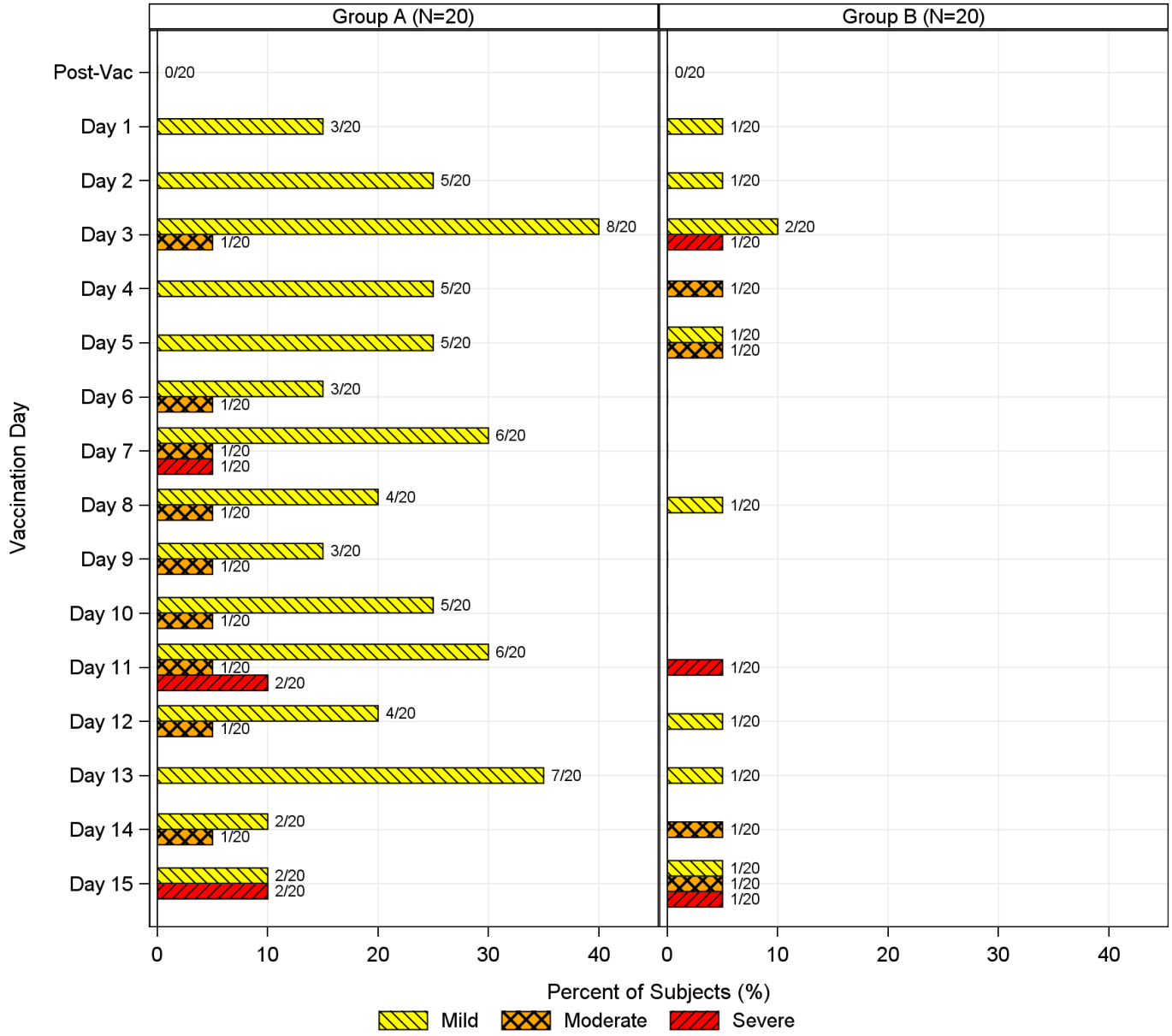
Figure 397: Distribution of CD4 T Cells Expressing IFNγ and/or IL-2 by Time Point and Vaccination Arm, Any COV2 S - COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts, mITT Population

Figure 398: Distribution of CD4 T Cells Expressing IFNγ and/or IL-2 by Time Point and Vaccination Arm, Any COV2 S - COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts, Per Protocol Population

Figure 542: Distribution of CD8 T Cells Expressing IFNγ and/or IL-2 by Time Point and Vaccination Arm, G-ORFa - COVID-19 mRNA Vaccinated, >60 years of age, ChAd-S-TCE Boosts, Per Protocol Population

14.3.1.1 Solicited Adverse Events

Figure 543: Maximum Severity of Solicited Systemic Symptoms per Participant by Day Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A - Dose 1



Figures with similar format:

Figure 544: Maximum Severity of Solicited Systemic Symptoms per Participant by Day Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A - Dose 2

Figure 545: Maximum Severity of Solicited Systemic Symptoms per Participant by Day Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A – Any Dose

Figure 546: Maximum Severity of Solicited Systemic Symptoms per Participant by Day Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4 - Dose 1

Figure 547: Maximum Severity of Solicited Systemic Symptoms per Participant by Day Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4 - Dose 2

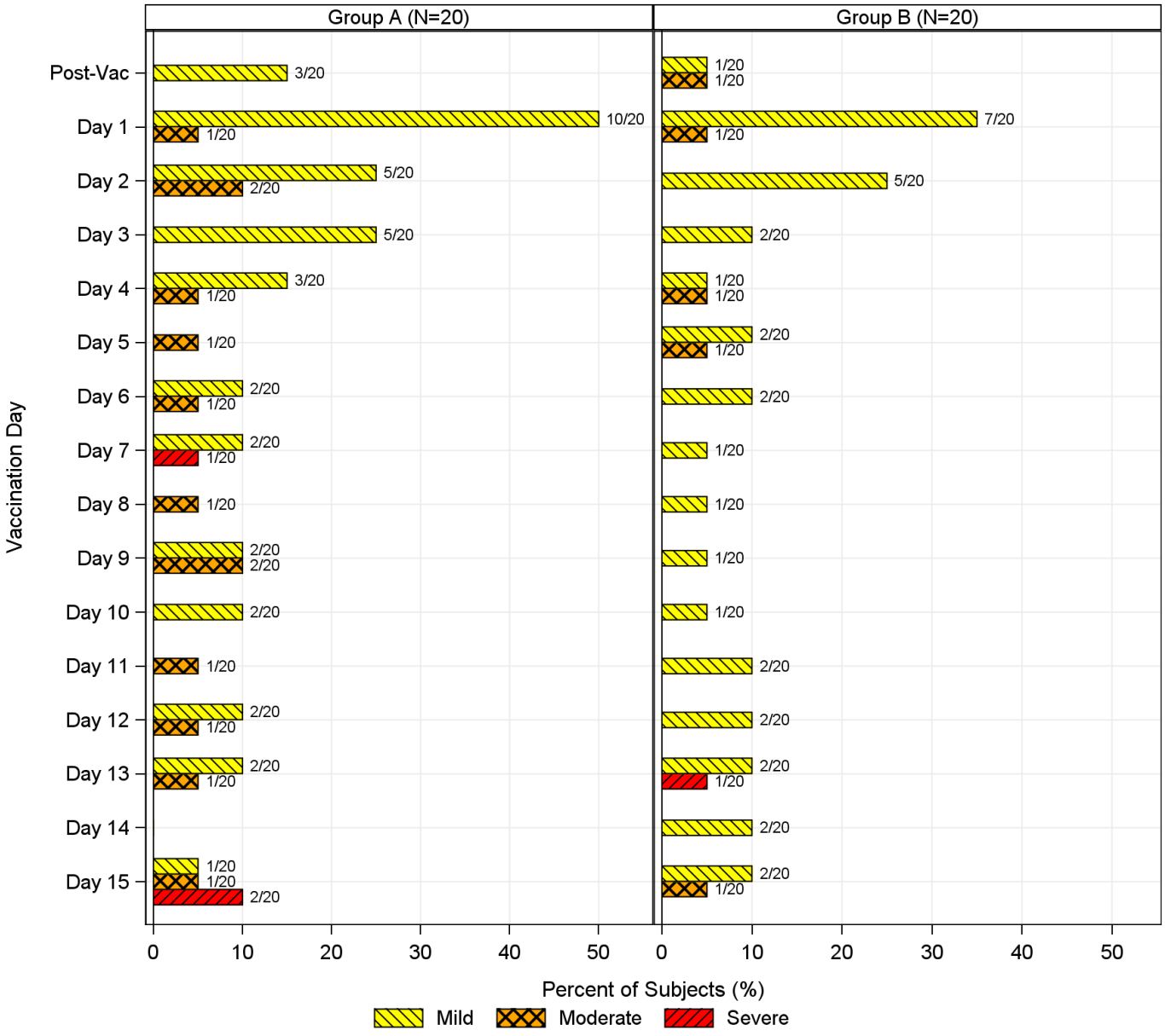
Figure 548: Maximum Severity of Solicited Systemic Symptoms per Participant by Day Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4 – Any Dose

Figure 549: Maximum Severity of Solicited Systemic Symptoms per Participant by Day Post Vaccination and Vaccination Arm – COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts

Figure 550: Maximum Severity of Solicited Systemic Symptoms per Participant by Day Post Vaccination and Vaccination Arm – COVID-19 mRNA Vaccinated, >60 years of age, SAM-S-TCE Boosts

Figure 551: Maximum Severity of Solicited Systemic Symptoms per Participant by Day Post Vaccination and Vaccination Arm – COVID-19 mRNA Vaccinated, >60 years of age, ChAd-S-TCE Boosts

Figure 552: Maximum Severity of Solicited Local Symptoms per Participant by Day Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A - Dose 1



Figures with similar format:

Figure 553: Maximum Severity of Solicited Local Symptoms per Participant by Day Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A - Dose 2

Figure 554: Maximum Severity of Solicited Local Symptoms per Participant by Day Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A – Any Dose

Figure 555: Maximum Severity of Solicited Local Symptoms per Participant by Day Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4 - Dose 1

Figure 556: Maximum Severity of Solicited Local Symptoms per Participant by Day Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4 - Dose 2

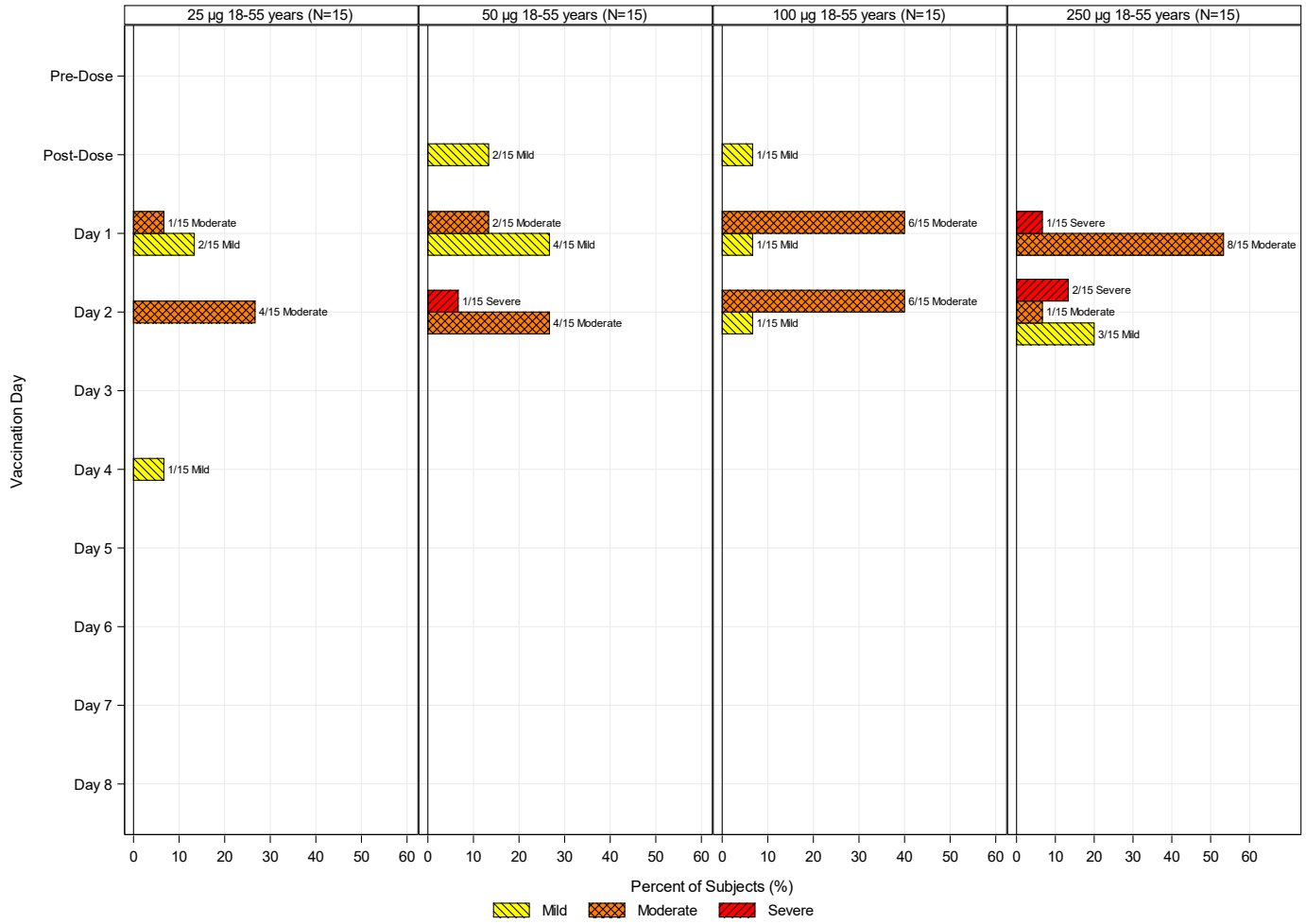
Figure 557: Maximum Severity of Solicited Local Symptoms per Participant by Day Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4 – Any Dose

Figure 558: Maximum Severity of Solicited Local Symptoms per Participant by Day Post Vaccination and Vaccination Arm – COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts

Figure 559: Maximum Severity of Solicited Local Symptoms per Participant by Day Post Vaccination and Vaccination Arm – COVID-19 mRNA Vaccinated, >60 years of age, SAM-S-TCE Boosts

Figure 560: Maximum Severity of Solicited Local Symptoms per Participant by Day Post Vaccination and Vaccination Arm – COVID-19 mRNA Vaccinated, >60 years of age, ChAd-S-TCE Boosts

Figure 561: Onset of Solicited Systemic Symptoms by Days Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A – Dose 1



Implementation Notes:

Have a panel for each vaccination arm in the figure.

Figures with similar format:

Figure 562: Onset of Solicited Systemic Symptoms by Days Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A – Dose 2

Figure 563: Onset of Solicited Systemic Symptoms by Days Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A – Any Dose

Figure 564: Onset of Solicited Systemic Symptoms by Days Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4 – Dose 1

Figure 565: Onset of Solicited Systemic Symptoms by Days Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4 – Dose 2

Figure 566: Onset of Solicited Systemic Symptoms by Days Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4 – Any Dose

Figure 567: Onset of Solicited Systemic Symptoms by Days Post Vaccination and Vaccination Arm – COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts

Figure 568: Onset of Solicited Systemic Symptoms by Days Post Vaccination and Vaccination Arm – COVID-19 mRNA Vaccinated, >60 years of age, SAM-S-TCE Boosts

Figure 569: Onset of Solicited Systemic Symptoms by Days Post Vaccination and Vaccination Arm – COVID-19 mRNA Vaccinated, >60 years of age, ChAd-S-TCE Boosts

Figure 570: Onset of Solicited Local Symptoms by Days Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A – Dose 1

Figure 571: Onset of Solicited Local Symptoms by Days Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A – Dose 2

Figure 572: Onset of Solicited Local Symptoms by Days Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A – Any Dose

Figure 573: Onset of Solicited Local Symptoms by Days Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4 – Dose 1

Figure 574: Onset of Solicited Local Symptoms by Days Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4 – Dose 2

Figure 575: Onset of Solicited Local Symptoms by Days Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4 – Any Dose

Figure 576: Onset of Solicited Local Symptoms by Days Post Vaccination and Vaccination Arm – COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts

Figure 577: Onset of Solicited Local Symptoms by Days Post Vaccination and Vaccination Arm – COVID-19 mRNA Vaccinated, >60 years of age, SAM-S-TCE Boosts

Figure 578: Onset of Solicited Local Symptoms by Days Post Vaccination and Vaccination Arm – COVID-19 mRNA Vaccinated, >60 years of age, ChAd-S-TCE Boosts

Figure 579: Solicited Symptoms by Days Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A - Arthralgia

Figures with similar format:

Figure 580: Solicited Symptoms by Days Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A - Diarrhea

Figure 581: Solicited Symptoms by Days Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A - Erythema

Figure 582: Solicited Symptoms by Days Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A - Erythema (mm)

Figure 583: Solicited Symptoms by Days Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A - Fatigue

Figure 584: Solicited Symptoms by Days Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A - Fever

Figure 585: Solicited Symptoms by Days Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A - Feverishness

Figure 586: Solicited Symptoms by Days Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A - Headache

Figure 587: Solicited Symptoms by Days Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A - Induration

Figure 588: Solicited Symptoms by Days Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A - Induration (mm)

Figure 589: Solicited Symptoms by Days Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A - Malaise

Figure 590: Solicited Symptoms by Days Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A - Myalgia

Figure 591: Solicited Symptoms by Days Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A - Nausea

Figure 592: Solicited Symptoms by Days Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A - Pain

Figure 593: Solicited Symptoms by Days Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A - Tenderness

Figure 594: Solicited Symptoms by Days Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4 - Arthralgia

Figure 595: Solicited Symptoms by Days Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4 - Diarrhea

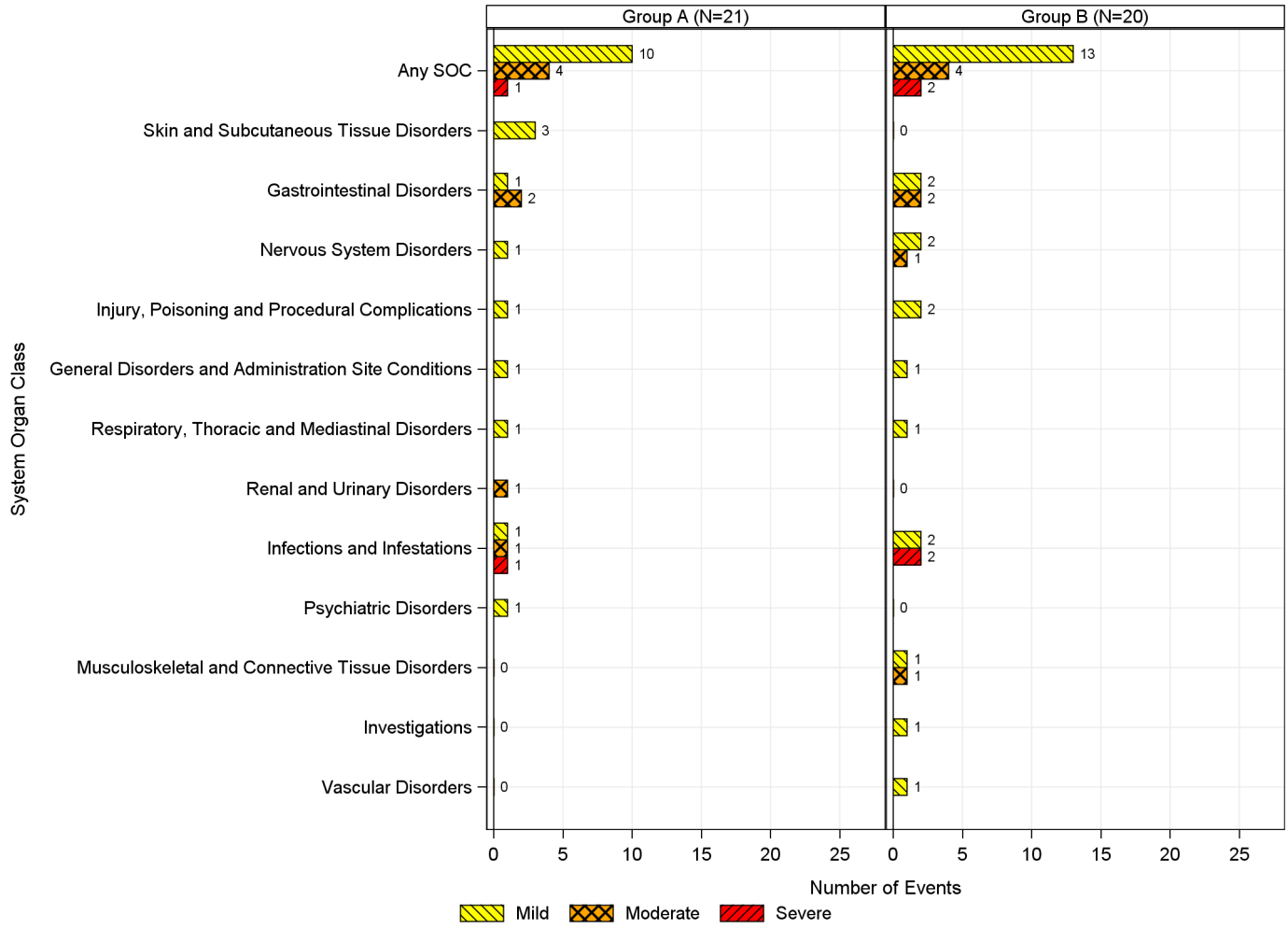
Figure 596: Solicited Symptoms by Days Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4 - Erythema

Figure 597: Solicited Symptoms by Days Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4 - Erythema (mm)

Figure 598: Solicited Symptoms by Days Post Vaccination and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4 - Fatigue

14.3.1.2 Unsolicited Adverse Events

Figure 654: Frequency of Adverse Events by MedDRA System Organ Class and Severity - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A



Implementation Notes:

There will be a panel for each vaccination arm.

Figures with similar format:

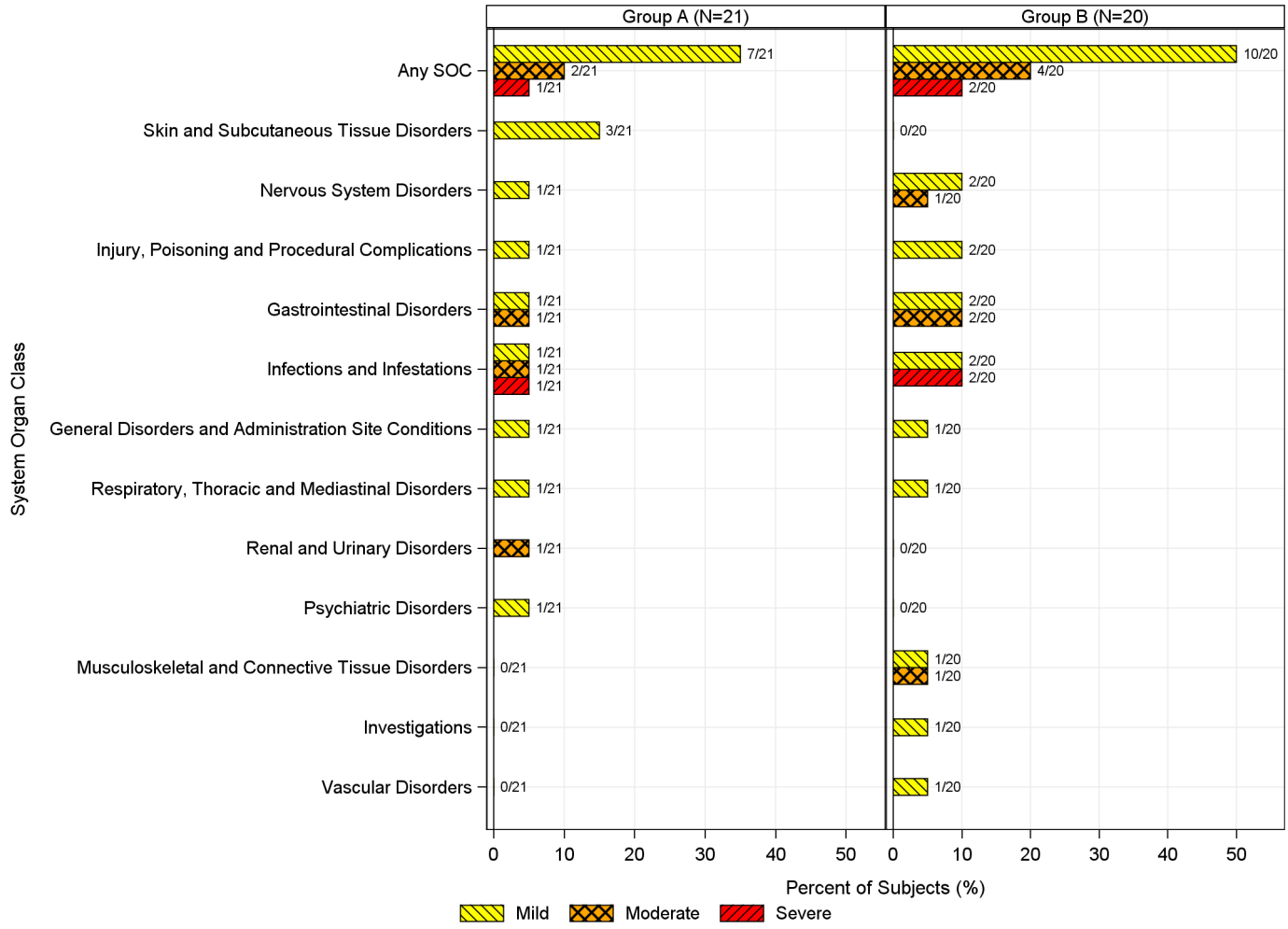
Figure 655: Frequency of Adverse Events by MedDRA System Organ Class and Severity - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4

Figure 656: Frequency of Adverse Events by MedDRA System Organ Class and Severity - COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts

Figure 657: Frequency of Adverse Events by MedDRA System Organ Class and Severity - COVID-19 mRNA Vaccinated, >60 years of age, SAM-S-TCE Boosts

Figure 658: Frequency of Adverse Events by MedDRA System Organ Class and Severity - COVID-19 mRNA Vaccinated, >60 years of age, ChAd-S-TCE Boosts

Figure 659: Incidence of Adverse Events by MedDRA System Organ Class and Maximum Severity - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A



Implementation Notes:

There will be a panel for each vaccination arm.

Figures with similar format:

Figure 660: Incidence of Adverse Events by MedDRA System Organ Class and Maximum Severity - COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4

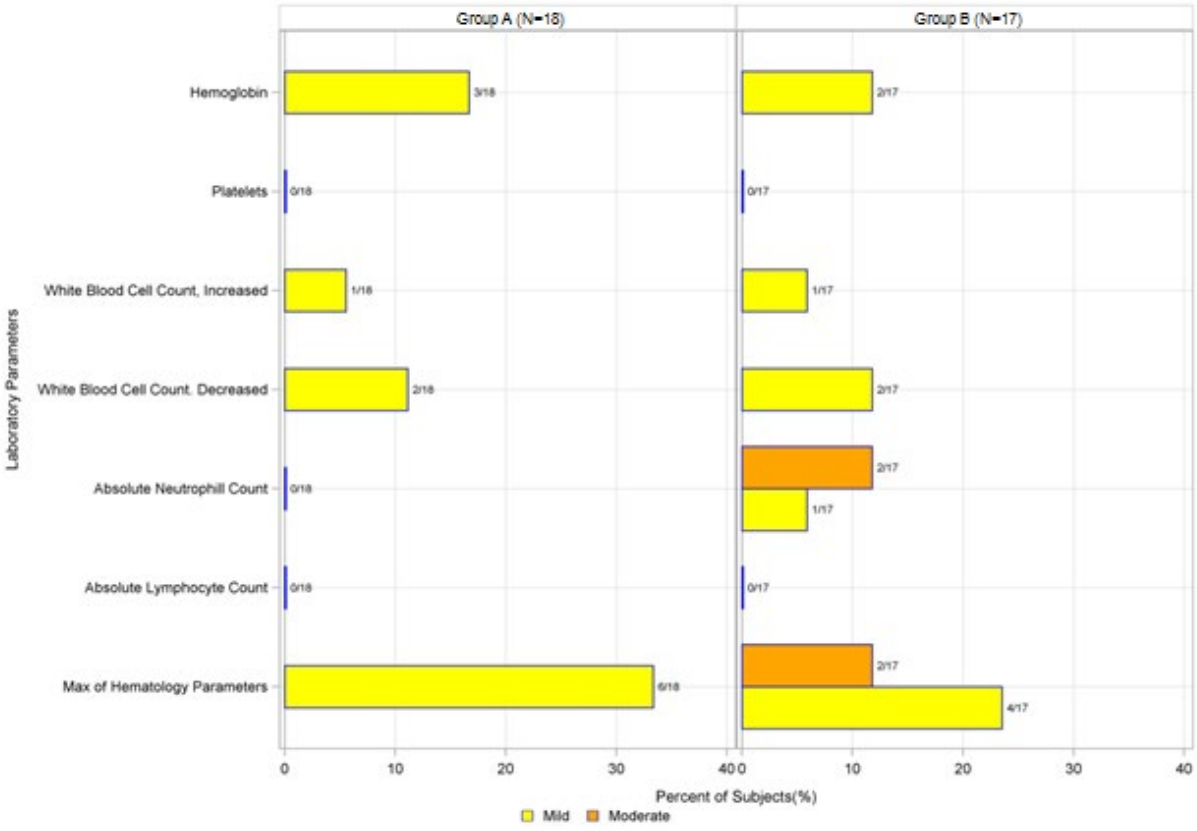
Figure 661: Incidence of Adverse Events by MedDRA System Organ Class and Maximum Severity - COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts

Figure 662: Incidence of Adverse Events by MedDRA System Organ Class and Maximum Severity - COVID-19 mRNA Vaccinated, >60 years of age, SAM-S-TCE Boosts

Figure 663: Incidence of Adverse Events by MedDRA System Organ Class and Maximum Severity - COVID-19 mRNA Vaccinated, >60 years of age, ChAd-S-TCE Boosts

14.3.5 Displays of Laboratory Results

Figure 664: Clinical Laboratory Results by Maximum Severity Post Baseline and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 1 and 3A



Implementation Note:

The figure will include all laboratory parameters assessed for the protocol after product administration. Screening labs will not be included. The figure will include all scheduled and non-scheduled post-vaccination assessments.

Figures with similar format:

Figure 665: Clinical Laboratory Results by Maximum Severity Post Baseline and Vaccination Arm – COVID-19 Vaccination Naïve, 18-60 years of age, Groups 3B and 4

Figure 666: Clinical Laboratory Results by Maximum Severity Post Baseline and Vaccination Arm – COVID-19 mRNA Vaccinated, 18-60 years of age, SAM-S-TCE Boosts

Figure 667: Clinical Laboratory Results by Maximum Severity Post Baseline and Vaccination Arm – COVID-19 mRNA Vaccinated, >60 years of age, SAM-S-TCE Boosts

Figure 668: Clinical Laboratory Results by Maximum Severity Post Baseline and Vaccination Arm – COVID-19 mRNA Vaccinated, >60 years of age, ChAd-S-TCE Boosts

APPENDIX 3. LISTINGS MOCK-UPS

LIST OF 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: Early Terminations or Discontinued Participants

Vaccination Arm	Participant ID	Category	Reason for Early Termination or Treatment Discontinuation	Study Day

Implementation Note:

Category will be either “Early Termination” or “Treatment Discontinuation.” In the “Reason” column, concatenate any “specify” fields, including AE number and DV number. In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Vaccination Arm, Participant ID, alphabetically by Category (in the case a participant both terminates early and discontinues treatment).

16.2.2 Protocol Deviations

Listing 3: 16.2.2.1: Participant-Specific Protocol Deviations

Vaccination Arm	Participant ID	DV Number	Deviation	Deviation Category	Study Day	Reason for Deviation	Deviation Resulted in AE?	Deviation Resulted in Participant Termination?	Deviation Affected Product Stability?	Deviation Resolution	Comments

Implementation Note:

In the "Deviation" column, concatenate any and all "specify" fields (including visit number, etc.). If "Reason for Deviation" is "Other," concatenate "specify" field, separate by a colon, e.g., "Other: Participant refusal." In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Vaccination Arm, Participant ID, DV Number.

Listing 4: 16.2.2.2: Non-Participant-Specific Protocol Deviations

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

Implementation Note:

In the "Deviation" column, concatenate any and all "specify" fields (including visit number, etc.). If "Reason for Deviation" is "Other," concatenate "specify" field, separate by a colon, e.g., "Other: Participant refusal." Sort order: Site, Start Date.

16.2.3 Participants Excluded from the Efficacy Analysis

Listing 5: 16.2.3: Participants Excluded from Analysis Populations

Vaccination Arm	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.

Implementation Note:

This data in this listing should be congruent with the "Analysis Populations by Vaccination Arm" table. The reasons included here should match the SAP text that describes who will be excluded from analyses. In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification.]
Sort order: Vaccination Arm, Participant ID.

16.2.4 Demographic Data

Listing 6: 16.2.4.1: Demographic Data

Vaccination Arm	Participant ID	Sex	Age at Enrollment (years)	Ethnicity	Race

Implementation Note:

If a participant is multi-racial, in "Race" column, note "Multiple: (list races, separated by a comma)." In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Vaccination Arm, Participant ID.

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

Vaccination Arm	Participant ID	MH Number	Medical History Term	Condition Start Day	Condition End Day	MedDRA System Organ Class	MedDRA Preferred Term

Implementation Note:

"Condition Start Day" and "Condition End Day" are relative to enrollment (which is Day 1, day before enrollment is Day -1). Rather than use exact study days, categorize as follows:

- 5 years prior to enrollment
- 1-5 years prior to enrollment
- 1-12 months prior to enrollment
- Within 1 month of enrollment
- During study
- If ongoing, display "Ongoing" in the "Condition End Day" column
- Within 1 month of enrollment
- During study

If ongoing, display "Ongoing" in the "Condition End Day" column

In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Vaccination Arm, Participant ID, MH Number.

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

Not applicable.

16.2.6 Individual Immunogenicity Response Data

Listing 8: 16.2.6: Individual Immunogenicity Response Data

Vaccination Arm	Participant ID	Planned Time Point	Actual Study Day	Assay	Units	Results

Listing should be sorted by Vaccination Arm, Participant ID, Planned Time Point.

16.2.7 Adverse Events

Listing 9: 16.2.7.1: Solicited Events – Systemic Symptoms

Vaccination Arm	Participant ID	Dose Number	Post Dose Day	Assessment[a]	Symptom	Severity	Attributed to Alternate Etiology?[b]	Alternate Etiology
				MA				
				Clinic				

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

Implementation Note:

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

Listing 10: 16.2.7.2: Solicited Events – Local Symptoms

Vaccination Arm	Participant ID	Dose Number	Post Dose Day	Assessment[a]	Symptom	Severity
				MA		
				Clinic		

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

Implementation Note:

This listing is not color-coded. To indicate severity for quantitative symptoms (e.g., temperature, measurements), include the grade in parentheses after the number, e.g., 100.7 (Mild). We are not indicating the "side" or arm assessed. If the arm assessed was wrong (not the arm that received treatment), then note this error in a footnote to the listing. This listing includes baseline assessments in addition to post-treatment assessments. In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Participant ID, Dose Number, Post Dose Day, Symptom.

Listing 11: 16.2.7.3: Unsolicited Adverse Events

Adverse Event	Associated with Dose No.	No. of Days Post Associated Dose (Duration)	Severity	SAE?	Relationship to Study Vaccination	In Not Related, Alternative Etiology	Action Taken with Study Vaccination	Participant Discontinued Due to AE	Outcome	MedDRA System Organ Class	MedDRA Preferred Term
Vaccination Arm: , Participant ID: , AE Number:											
Comments:											
Vaccination Arm: , Participant ID: , AE Number:											
Comments:											
Note: For additional details about SAEs, see Table 307.											

Implementation Note:

If the event is ongoing (no stop date), indicate "ongoing" in the "Duration" column. In the "If Not Related, Alternate Etiology" column, merge the 2 data fields for collecting alternate etiology, separate by a colon. This listing includes all unsolicited adverse events. If there are no comments for an event, populate 'Comments' row with 'None'. Add columns for MedDRA HLT or LLT depending on halting criteria or other study needs. In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Vaccination Arm, Participant ID, Associated with Dose No., No. of Days Post Associated Dose. If the table will be multi-page, move the footnote/explanation to the footer so that it repeats for each page of the table.

16.2.8 Individual Laboratory Measurements

Listing 12: 16.2.8.1: Clinical Laboratory Results – Chemistry

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

Implementation Note:

These listings (for hematology, chemistry, and urinalysis) include all laboratory results, scheduled and unscheduled. Severity should be included in parentheses after the result for abnormal results, e.g., 16.2 (Mild). Sort order: Vaccination Arm, Participant ID, and Planned Time Point.

Listing 13: 16.2.8.2: Clinical Laboratory Results – Hematology

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

16.2.9 Vital Signs and Physical Exam Findings

Listing 14: 16.2.9.1: Vital Signs

Vaccination Arm	Participant ID	Planned Time Point	Actual Study Day	Temperature (°C)	Systolic Blood Pressure (mmHg)	Diastolic Blood Pressure (mmHg)	Heart Rate (beats/min)	Respiratory Rate (breaths/min)	Weight (kg)	Height (cm)

Implementation Note:

This listing includes all vital sign assessments, scheduled and unscheduled. These listings are not color-coded, but the severity should be included in parentheses after the result for abnormal assessments, e.g., 100.7 (Mild). In the CSR, Participant ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Vaccination Arm, Participant ID, Planned Time Point.

Listing 15: 16.2.9.2: Physical Exam Findings

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

Implementation Note:

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

16.2.10 Concomitant Medications

Listing 16: 16.2.10: Concomitant Medications

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

Implementation Note:

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

- 5 years prior to enrollment
- 1-5 years prior to enrollment
- 1-12 months prior to enrollment

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

16.2.11 Pregnancy Reports

Listing 17: 16.2.11.1: Pregnancy Reports – Maternal Information

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

Listing 18: 16.2.11.2: Pregnancy Reports – Gravida and Para

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

Implementation Note:

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

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?	Illnesses/ Hospitalizations within 1 Month of Birth?
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)	Fetal Distress During Labor and Delivery?	Delivery Method	Gestational Age at Still Birth	Size for Gestational Age	Cord pH	Congenital Anomalies?	Autopsy Performed?	If Autopsy, Etiology for Still Birth Identified?

Listing 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