CLINICAL RESEARCH IN INFECTIOUS DISEASES

STATISTICAL ANALYSIS PLAN

for

DMID Protocol: 17-0093

Study Title:

A Phase 1, Randomized, Parallel-Group, Double-Blind Trial of AV7909 (Liquid) and Thermostable AV7909 (Lyophilized) in Healthy Adult Volunteers

NCT04660201

Version 1.0

DATE: 04 May 2023

RESTRICTED

STUDY TITLE

Protocol Number Code:	**DMID Protocol: 17-0093**
Development Phase:	Phase I
Products:	1. AV7909 liquid formulation vaccine manufactured by Emergent BioSystems • Licensed Anthrax Vaccine Adsorbed (AVA, BioThrax) • CPG 7909 adjuvant manufactured by Avecia Nitto Denko 2. Thermostable AV7909 lyophilized formulation vaccine manufactured by Emergent BioSystems • Licensed Anthrax Vaccine Adsorbed (AVA, BioThrax) • CPG 7909 adjuvant manufactured by Avecia Nitto Denko • Vaccine diluent manufactured by Fisher BioServices
Form/Route:	Intramuscular
Indication Studied:	Anthrax
Sponsor:	Division of Microbiology and Infectious Diseases National Institute of Allergy and Infectious Diseases National Institutes of Health
Clinical Trial Initiation Date:	25 May 2022
Clinical Trial Completion Date:	Expected September 2023
Date of the Analysis Plan:	04 May 2023
Version Number:	1.0

This study was performed in compliance with Good Clinical Practice.

TABLE OF CONTENTS

Table of Contents *(continued)*

Table of Contents *(continued)*

LIST OF ABBREVIATIONS

AE	Adverse Event/Adverse Experience
AESIs	Adverse Events of Special Interest
ALT	Alanine Aminotransferase
AVA	Anthrax Vaccine Adsorbed
AV7909	Anthrax Vaccine with CPG7909 Adjuvant
β hCG	Beta- human Chorionic Gonadotropin (Pregnancy Test)
BMI	Body Mass Index
BP	Blood Pressure
BUN	Blood Urea Nitrogen
CFR	Code of Federal Regulations
CI	Confidence Interval
CMS	Clinical Materials Services
COI	Conflict of Interest
CPG 7909	a CPG oligodeoxynucleotide adjuvant
CpG55.2	a CPG oligodeoxynucleotide adjuvant
Cr	Creatinine
CRP	C-Reactive Protein
CROMS	Clinical Research Operations and Management Support
CSR	Clinical Study Report
D	Day(s)
DNA	Deoxyribonucleic Acid
DCF	Data Collection Form
DMID	Division of Microbiology and Infectious Diseases, NIAID, NIH
ECG	Electrocardiogram
eCRF	Electronic Case Report Form
eClinical	Electronic Data Capture System
eMemory Aid	Electronic Memory Aid
ELISA	Enzyme Linked ImmunoSorbent Assay
FDA	Food and Drug Administration
FWA	Federal-Wide Assurance
GCP	Good Clinical Practice

List of Abbreviations *(continued)*

GMT	Geometric Mean Titer
HBsAg	Hepatitis B surface Antigen
HCV	Hepatitis C Virus
HEENT	Physical Exam of the Head, Eyes, Ears, Nose, and Throat
Hgb	Hemoglobin
HIPAA	Health Insurance Portability and Accountability Act
HIV	Human Immunodeficiency Virus
HLGT	High Level Group Term
HRPO	Human Research Protections Office
IATA	International Air Transport Association
ICF	Informed Consent Form
ICH	International Council for Harmonisation
IgG	Immunoglobulin G
IM	Intramuscular(ly)
IND	Investigational New Drug
IRB	Institutional Review Board
ISM	Independent Safety Monitor
IU/L	International Unit(s) per Liter
LLOQ	Lower Limit of Quantitation
MAAE	Medically-Attended Adverse Event
MedDRA®	Medical Dictionary for Regulatory Activities
mg/dL	Milligrams per Deciliter
mITT	Modified Intent-to-Treat
mL	Milliliter(s)
mm^3	Cubic Millimeter(s)
MOP	Manual of Procedures
N	Number of Subjects
NIAID	National Institute of Allergy and Infectious Diseases, NIH, DHHS
NIH	National Institutes of Health
OAC	Office of Accountability and Compliance
ODNs	Synthetic oligodeoxynucleotides
OER	Office of Extramural Research

List of Abbreviations *(continued)*

OHRP	Office for Human Research Protections
PHI	Personal (Protected) Health Information
PA	Protective Antigen
PI	Principal Investigator
PII	Personally Identifiable Information
PIMMCs	Potentially Immune-Mediated Medical Conditions
PP	Per Protocol
QA	Quality Assurance
QC	Quality Control
RF	Rheumatoid Factor
SAE	Serious Adverse Event/Serious Adverse Experience
SAP	Statistical Analysis Plan
SDCC	Statistical and Data Coordinating Center
SIRVA	Shoulder Injury Related to Vaccine Administration
SMC	Safety Monitoring Committee
SOP	Standard Operating Procedure
TNA	Toxin Neutralization Assay
ULN	Upper Limit of Normal
UMB	University of Maryland, Baltimore
US	United States
V	Visit(s)
VTEU	Vaccine and Treatment Evaluation Unit
WHO	World Health Organization

1. PREFACE

The Statistical Analysis Plan (SAP) for "A Phase 1, Randomized, Parallel-Group, Double-Blind Trial of AV7909 (Liquid) and Thermostable AV7909 (Lyophilized) in Healthy Adult Volunteers" (DMID Protocol 17-0093) describes and expands upon the statistical information presented in the protocol.

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

This document contains four sections: (1) a review of the study design, (2) general statistical considerations, (3) comprehensive statistical analysis methods for efficacy and safety outcomes, and (4) a list of proposed tables and figures. Within the table, figure, and listing 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

The anthrax vaccine that is currently licensed in the US, AVA, has been shown to be safe and immunogenic in people and has been shown to lead to antibody responses that, in non-human primate models of lethal anthrax spore challenge, are protective, even in the absence of antibiotics.[1] However, the vaccine was first given subcutaneously, leading to significant local reactogenicity, and it requires 3 priming doses and an onerous schedule for recipients to remain immune. An improved vaccine that leads to faster immune responses and requires fewer doses, while remaining safe and well tolerated, would be welcomed.

Due to the large number of doses required to generate a primary immune response in humans that leads to putative protective levels, as evidenced by animal challenge model protection, various approaches have been taken to improve anthrax vaccines. One approach that has proven successful to date is the addition of the TLR9 agonist adjuvant CPG 7909 to the currently licensed vaccine. This new vaccine, named AV7909, is being developed by Emergent BioSolutions as a vaccine with an indication for postexposure prophylaxis (PEP) that is intended to decrease the risk of anthrax disease after exposure. AV7909 has been shown to be safe and has improved immunogenicity when compared to AVA.[2, 3, 4] Early studies have shown that the addition of CPG 7909 to AVA has allowed for intramuscular injection, a priming series of only 2 doses, and resulted in more rapid induction of putatively protective antibody responses. AV7909 has been studied in animals and humans with a safety record similar to AVA itself. This vaccine, once studied in increasing numbers of persons, may prove superior enough to AVA to allow it to replace AVA as the standard of care. However, the current formulation is liquid and therefore prone to a shorter shelf life and stricter temperature storage requirements. Since anthrax vaccine sufficient for a response to an intentional act of bioterror is stored in the Strategic National Stockpile, a thermostable (lyophilized) formulation of the AV7909 adjuvanted anthrax vaccine would offer many advantages to a liquid formulation.

2.1. Purpose of the Analyses

The proposed trial will assess, in healthy adults, the safety, reactogenicity, and immunogenicity of the thermostable lyophilized formulation of AV7909 compared to the liquid formation of AV7909.

3. STUDY OBJECTIVES AND ENDPOINTS

3.1. Study Objectives

3.1.1. Primary

Safety:

- To assess the safety of lyophilized and liquid formulations of AV7909.

Tolerability:

- To assess the tolerability of lyophilized and liquid formulations of AV7909.

3.1.2. Secondary

Immunogenicity:

- To obtain initial estimate of comparative immunogenicity of liquid and lyophilized formulations of AV7909.

3.1.3. Exploratory

None

3.2. Endpoints

3.2.1. Primary

Safety:

- Occurrence of all SAEs through approximately 12 months following receipt of the second study vaccination (approximately Day 380).
- Occurrence of abnormal clinical safety laboratory AEs at approximately Day 29.
- Occurrence of all protocol specified AESIs (i.e., PIMMCs) and MAAEs, from the time of the first study vaccination through approximately 12 months following the second vaccination (approximately Day 380).
- Occurrence of unsolicited non-serious adverse events from the time of the first study vaccination through approximately Day 64.

Tolerability:

- Occurrence of solicited injection site and systemic reactogenicity events in the week after each study vaccination (Days 1 through 8 and Days 15 through 22, inclusive).

3.2.2. Secondary

Immunogenicity:

- Geometric mean titer and 95% confidence intervals of antibodies assayed by toxin neutralization assay (ED50 and NF50) and anti-PA IgG by ELISA in each study group before vaccination and on approximately Days 8, 15, 22, 29, 64, 195, and 380.
- Proportion and 95% confidence intervals of participants in each study group with seroconversion for antibodies detected by TNA and ELISA (defined as a ≥4-fold increase over baseline levels, or a ≥4-fold increase over the lower limit of quantification [LLOQ] if the baseline value is < LLOQ) on approximately Days 8, 15, 22, 29, 64, 195, and 380.
- Proportion and 95% confidence intervals of participants in each study group with putative seroprotection (defined as NF50 ≥ 0.56) before vaccination and on approximately Days 8, 15, 22, 29, 64, 195, and 380.

3.2.3. Exploratory

None.

3.3. Study Definitions and Derived Variables

"Baseline" value of any safety or efficacy parameter refers to the last value collected prior to receipt of first study vaccination.

For individual subjects, fold rise will be calculated as the ratio of: $\frac{post-vaccination\ value}{pre-vaccination\ value}$, where pre-vaccination value is the result obtained at Day 1 prior to the first study vaccination.

For calculations of geometric mean and fold rise of assay results, individual results below the LLOQ will be imputed as ½ × LLOQ. The LLOQ for each assay was defined by the central laboratory as follows: TNA ED_{50}: 33; TNA NF_{50}: 0.064; anti-PA IgG: 9.27 µg/mL.

For subjects with baseline assay result ≥ LLOQ, seroconversion is defined as at least a 4-fold increase over baseline value. For subjects with baseline assay result < LLOQ, seroconversion is defined as achieving a post-baseline result of at least 4 × LLOQ; this ensures that subjects with undetectable baseline antibody levels have achieved at least a 4-fold increase over baseline, regardless of the baseline result reported.

Putative seroprotection is defined as $NF_{50} \geq 0.56$.

4. INVESTIGATIONAL PLAN

4.1. Overall Study Design and Plan

DMID Protocol 17-0093 is a phase I randomized, parallel-group, double-blind controlled interventional trial in which the safety, tolerability, and immunogenicity of 2 formulations of adjuvanted anthrax vaccine (AV7909), lyophilized and liquid, both manufactured by Emergent BioSolutions, will be assessed and compared. AV7909 is an investigational vaccine that combines the currently licensed Anthrax Vaccine Adsorbed (AVA, BioThrax) with the adjuvant CPG 7909, an oligonucleotide.

Forty healthy young adults, 18 to 45 years old, inclusive, who meet all eligibility criteria, will be randomly allocated to one of two study groups in a 1:1 ratio: 20 will receive AV7909 as the thermostable lyophilized product and 20 will receive AV7909 as the liquid product. Stratification by age category and by sex will assure that near equal numbers of younger (18-30 years) and older (31-45 years) males and females will be assigned to each vaccine. The vaccines will be given intramuscularly in a 2-dose schedule, 2 weeks apart.

Safety will be assessed by evaluation of non-serious unsolicited Adverse Events, Serious Adverse Events (SAEs), Medically Attended Adverse Events (MAAEs), Adverse Events of Special Interest (AESIs) [the AESIs collected in this study are Potentially Immune-Mediated Medical Conditions (PIMMCs)], and by laboratory evaluations. SAEs, MAAEs, and AESIs will be collected from the time of study vaccination through approximately Day 380. Non-serious unsolicited AEs will be collected from Day 1 to Day 64, inclusive. Clinical laboratory evaluations for eligibility will be the following: specific hematology parameters, chemistry parameters, specific urine tests for drugs of abuse, and hemoglobin A1C. Also, an electrocardiogram will be performed at screening and reviewed by an investigator and cardiologist. The cardiologist will determine if any findings on the electrocardiogram are significant and thereby exclusionary. At approximately Day 29, laboratory tests for hematology and chemistries will be repeated.

Reactogenicity will be measured by the occurrence of solicited injection site and systemic reactions in the week after each study vaccination (Days 1 through 8 and target of Days 15 through 22, inclusive). The window for dose 2 includes Days 15 to 18. For participants who are vaccinated beyond Day 15, the study schedule will adjust so that a full week of reactogenicity data are collected, regardless. Any of these events that persist on Day 8 or Day 22 (or the final day of the second reactogenicity period) will be followed until resolution.

Immunogenicity testing will include performing serological assays to assess for toxin neutralizing antibodies (reported as ED50 and NF50), the gold standard assay for assessing response and protection following anthrax vaccines, prior to vaccination and on approximately Days 8, 15, 22, 29, 64, 195, and 380. Should the second dose of vaccine be given after Day 15 (the acceptable window is Days 15 to 18, inclusive) the remainder of the study schedule days shift accordingly, to maintain the intervals in the schedule. In addition, anti-PA IgG antibodies will be measured by ELISA from the serum of participants, on those same days.

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

This study follows a randomized, parallel-group, double-blind control design. All subjects receive two doses of either liquid formulation of AV7909 or lyophilized formulation of AV7909, administered intramuscularly at Days 1 and 15.

4.3. Selection of Study Population

The study population for this clinical trial is 40 males and non-pregnant females, 18 to 45 years of age, inclusive, who are in good health and meet all eligibility criteria. The target population reflects the community at large at the participating VTEU site, the University of Maryland, Baltimore (UMB).

4.4. Treatments

4.4.1. Treatments Administered

Liquid and lyophilized formulations of AV7909, manufactured by Emergent BioSolutions, will be administered intramuscularly in a 2-dose schedule, 2 weeks apart. AV7909 is an investigational vaccine that combines the currently licensed Anthrax Vaccine Adsorbed (AVA, BioThrax) with the adjuvant CPG 7909, an oligonucleotide.

4.4.2. Identity of Investigational Product(s)

See the study protocol for details of study product formulation.

4.4.3. Method of Assigning Subjects to Study Arms (Randomization)

Enrollment and randomization will be performed through the enrollment module in the electronic data capture system, maintained by the SDCC.

Eligible subjects will be randomized and assigned in a 1:1 ratio to liquid AV7909 or lyophilized AV7909, with stratification by age category (18-30 years old and 31-45 years old) and by sex. The randomization is based on a variable blocked scheme to provide an approximately balanced allocation to the study arms within each age/sex stratum.

4.4.4. Selection of Doses in the Study

Due to the large number of doses required to generate a primary immune response in humans that leads to putative protective levels, as evidenced by animal challenge model protection, various approaches have been taken to improve anthrax vaccines. One approach that has proven successful to date is the addition of the TLR9 agonist adjuvant CPG 7909 to the currently licensed vaccine, AVA. Early studies have shown that the addition of CPG 7909 to AVA has allowed for intramuscular injection, a priming series of only 2 doses, and resulted in more rapid induction of putatively protective antibody responses. AV7909 has been studied in animals and humans with a safety record similar to AVA itself. This vaccine, once studied in increasing numbers of persons, may prove superior enough to AVA to allow it to replace AVA as the standard of care. However, the current formulation is liquid and therefore prone to a shorter shelf life and stricter temperature storage requirements. Since anthrax vaccine sufficient for a response to an intentional act of bioterror is stored in the Strategic National Stockpile, a thermostable (lyophilized) formulation of the AV7909 adjuvanted anthrax vaccine would offer many advantages to a liquid formulation.

4.4.5. Selection and Timing of Dose for Each Subject

Each subject will be randomly allocated to one of two study groups in a 1:1 ratio: 20 will receive two doses of AV7909 as the thermostable liquid product and 20 will receive two doses of AV7909 as the lyophilized product. Subjects will receive the first study vaccination on the day of randomization, and the second study vaccination approximately 2 weeks later, on Day 15 (with protocol-defined window of Days 15 to 18).

4.4.6. Blinding

This is a double-blinded clinical trial; subjects, site investigators, and study personnel performing any study-related assessments following study vaccine administration are blinded to vaccine received. Laboratory personnel performing immunological assays will receive serum blinded to subject ID number, specimen visit number, and allocation group.

The randomization scheme was generated by the SDCC and provided to unblinded study personnel (i.e., research pharmacists performing study vaccination preparations and unblinded study vaccine administrators) at the participating VTEU site.

The Safety Monitoring Committee (SMC) may receive data in aggregate and presented by treatment group. The SMC may also be provided with expected and observed rates of the expected AEs in an unblinded fashion and may request the treatment assignment be unblinded for an individual participant if required for safety assessment. The SMC will review grouped and unblinded data in the closed session only.

4.4.7. Prior and Concomitant Therapy

Administration of any medications, therapies, or vaccines taken in the 60 days prior to signing the ICF through approximately Day 64 will be solicited from the subject during screening, enrollment, and follow-up. Concomitant medications (new medications or changes to previously reported medications) that are reported after Day 64 will only be recorded when they are taken in relation to a MAAE, AESI (PIMMC), or SAE. Prescription and over-the-counter drugs will be included as well as herbals, vitamins, and supplements. Use of a new medication should prompt evaluation for the occurrence of any AE, MAAE, AESI (PIMMC), or SAE.

Medications that might interfere with the evaluation of the investigational product should not be used during the trial-reporting period (approximately 12 months after the second study vaccination, approximately Day 380) 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 5.1.2). In addition, the site PI or appropriate sub-investigator may identify other medications, herbals, vitamins, or supplements that should not be used due to a risk to participant safety or assessment of reactogenicity and immunogenicity.

4.4.8. Treatment Compliance

All subjects were to receive two doses of study product administered in the clinic.

4.5. Immunogenicity and Safety Variables

See Table 1 for schedule of study procedures.

4.5.1. Immunogenicity Variables

Serum for toxin neutralization assay (TNA) will be collected at Days 1, 8, 15, 22, 29, 64, 195, and 380. The TNA assay measures the functional ability of antisera containing anti-PA antibodies to specifically protect cells against *B. anthracis* lethal toxin cytotoxicity {Stinson et al, 2005; Li et al., 2008}. The TNA assay results will be reported as the reciprocal titer of a serum sample dilution that results in 50% neutralization of lethal toxin cytotoxicity, which is referred to as 50% effective dilution (ED_{50}). To standardize assay results, the results are divided by the ED_{50} of a serum reference standard, AVR801, and the resulting ratio is reported as a 50% neutralization factor (NF_{50}). Individual ED_{50} and NF_{50} results will be reported by the central laboratory, Battelle.

Serum for anti-PA IgG ELISA will be collected at Days 1, 8, 15, 22, 29, 64, 195, and 380. Individual anti-PA IgG concentrations (µg/mL) will be reported by Battelle.

4.5.2. Safety Variables

Safety will be assessed by the frequency and severity of the following:

1. SAEs occurring from the time of the first study vaccination through approximately 12 months after the second study vaccination (approximately Day 380).
2. Solicited reactogenicity events occurring from the time of each study vaccination (Day 1) through Day 8 after each study vaccination (or until resolved):
    a) Injection site reactions including pruritus, ecchymosis, erythema, edema/induration, pain, and tenderness.
    b) Systemic reactions including fever, feverishness, fatigue, malaise, myalgia, arthralgia, headache, and nausea.
3. Clinical safety laboratory AEs occurring from the time of the first study vaccination through approximately Day 29. Laboratory parameters include blood urea nitrogen (BUN), serum creatinine, alkaline phosphatase, alanine aminotransferase (ALT), total bilirubin, hemoglobin, hemoglobin decrease from baseline, white blood cell (WBC) count, absolute eosinophil count, absolute neutrophil count, and platelets. Additional laboratory parameters were measured under Protocol Version 3.0, including random glucose, aspartate aminotransferase (AST), urine protein, and urine glucose, but collection of these parameters was no longer required after the finalization of Protocol Version 4.0.
4. Non-serious unsolicited AEs occurring from the time of the first study vaccination through approximately Day 64.
5. AESIs (PIMMCs) and MAAEs occurring from the time of the first study vaccination through approximately Day 380.

Grading scales for injection site and systemic solicited reactions, vital signs, and clinical laboratory parameters are provided in Table 6, Table 7, Table 8, Table 9, Table 10, Table 11 and Table 12

5. SAMPLE SIZE CONSIDERATIONS

This study is planned to enroll a total of 40 subjects, with 20 subjects in each study arm. This phase I study is not designed to test a formal null hypothesis. Rather, it is intended to obtain sufficient data to obtain meaningful estimates of the immune response induced by either vaccine formulation and to uncover any safety issues that occur at a sufficiently high rate that they might be observed in a study of this size. As such, the type one error rate, alpha = 0.05, is not adjusted for multiple comparisons. While this study is not designed to test any specific null hypothesis, the following tables illustrate the precision and power that is available for select estimates and comparisons of interest.

Table 2 indicates the probability of observing one or more safety events, such as solicited injection site or systemic reactogenicity events or an unsolicited AE of a particular type, for a single treatment arm (N=20), and for all enrolled subjects (N=40).

Binomial confidence intervals (CI) are widest (have the least precision) when the response rate is 50%. Table 3 is presented to indicate the worst-case scenario for precision of observed exact (Clopper-Pearson) binomial confidence intervals.

For each of the primary immunogenicity objectives, a power analysis is provided below for testing the following hypotheses with the planned sample size, where p_c = probability of response in comparator arm; where p_e = probability of response in experimental arm.

Test for difference in proportion responders:

H_0: $p_c - p_e = 0$; No difference in response probabilities

H_1: $p_c - p_e \neq 0$; difference in response probabilities

Table 4 illustrates the minimum detectable differences in the probability of responding (e.g., attaining seroconversion or $NF_{50} \geq 0.56$ [seroprotection]) between participants who receive AV7909 as the lyophilized formulation or liquid formulation using a two-sided likelihood ratio test with 80% power and alpha = 0.05. It is assumed that up to 10% of subjects (N=2) will be excluded from the per-protocol analysis in each group. Seroconversion rates of 10% to 60% are considered.

6. GENERAL STATISTICAL CONSIDERATIONS

6.1. General Principles

Unless otherwise specified, all continuous variables will be summarized using the following descriptive statistics: n (non-missing sample size), mean, standard deviation, median, maximum and minimum. For post-baseline visits, fold rise from baseline will be calculated. Unless otherwise specified, confidence intervals for means (arithmetic or geometric) will be calculated using Student's t distribution with confidence level α=0.05 (95% confidence). The frequency and percentages (based on the non-missing sample size) of observed levels will be reported for all categorical measures. Unless otherwise specified, exact binomial confidence intervals for percentages will be calculated using Clopper-Pearson methodology. In general, all data will be listed, sorted by study arm and subject, and when appropriate by visit number within subject. All summary tables will be structured with a column for each study arm in the following order:

- Liquid AV7909
- Lyophilized AV7909

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

6.2. Timing of Analyses

The final CSR will be completed after the last participant's last visit is completed, the final clinical database including all long-term safety follow-up data is cleaned, monitored, and locked, and all primary and secondary immunogenicity data are available. There are no planned exploratory immunogenicity endpoints. If any are added via protocol amendment, then the additional exploratory immunogenicity endpoint data not available at the time of CSR preparation may be included in an addendum to the CSR.

Additional statistical reports may be generated as deemed necessary and appropriate by DMID. Safety and immunogenicity summary reports may be generated for the SMC.

After the final CSR is complete, and upon request and DMID approval, the SDCC will provide the participating VTEU site with a summary of results by treatment arm and/or participant treatment assignment. In this regard, the participating VTEU site requesting such information to share with participants must do so in accordance with IRB requirements.

6.3. Analysis Populations

6.3.1. Safety Population

The safety population includes all participants who received the first dose of study vaccine. For analyses using the safety population, participants will be grouped based on study vaccinations received.

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

The modified intent-to-treat (mITT) population includes all randomized participants who received the first dose of study vaccine and contributed at least one post-first study vaccination venous blood sample for immunogenicity testing for which valid results were reported. For analyses using the mITT population, participants will be grouped based on randomized treatment arm.

6.3.3. Per Protocol Population

The per protocol (PP) population includes all participants in the mITT population with the following exclusions:

- Data from all available visits for participants found to be ineligible at baseline.
- Data from all visits for participants that did not contribute venous blood samples for immunogenicity testing.
- Data from all visits subsequent to major protocol deviations, such as:
    - Second vaccination not received
    - Second vaccination received out of window
    - Receipt of immunosuppressive therapy (e.g., corticosteroids) within 30 days before or after each study vaccination.
    - Receipt of non-study licensed live vaccine within 30 days before or after each study vaccination.
    - Receipt of non-study licensed inactivated vaccine within 14 days before or after each study vaccination.
- Data from any visit that occurs substantially out of window.

For analyses using the PP population, participants will be grouped based on study vaccinations received.

6.4. Covariates and Subgroups

TNA ED_{50} and NF_{50} and anti-PA IgG antibody responses will be summarized and stratified by sex and age category (18-30 years, 31-45 years). These analyses are considered exploratory as the study was not powered for subgroup analyses.

6.5. Missing Data

All attempts will be made to collect all data per protocol. As missing data are expected to be minimal, no imputation will be performed for missing values. Any data point that appears to be erroneous or inexplicable based on clinical judgment will be investigated. Immunogenicity results identified as invalid will be indicated as such in the report and may be excluded from analyses.

The group “Missing Data Matters” has been funded by both the FDA and PCORI to develop a suite of free, open source SAS and R software tools that will allow users to conduct global sensitivity analyses of their studies. Per their website, “Global sensitivity analysis is like "stress testing" in reliability engineering, where a product is systematically subjected to increasingly exaggerated forces (i.e., assumptions) in order to determine its breaking point (i.e., non-significant result). If the breaking point occurs at forces that are judged to be extreme, then the results are judged to be robust; otherwise, the results are judged to be fragile” While the software is not yet publicly available, the underlying statistical methodology has been publicly presented. A non-ignorable missing data model is fit to monotone missing data which has the ignorable model as a special case when the sensitivity parameter alpha is set to zero. By varying alpha over a range of values and re-estimating the treatment effect, the data analyst can determine the robustness of results to the MAR assumption.]

6.6. Interim Analyses and Data Monitoring

No interim analyses are planned.

6.6.1. Interim Safety Review

An interim safety review may include enrollment and demographic information, medical history, concomitant medications, physical assessments, clinical laboratory values, dosing compliance, and solicited and unsolicited AE/SAEs. Additional data may be requested by the SMC, and interim statistical reports may be generated as deemed necessary and appropriate by DMID. The SMC may receive data in aggregate and presented by treatment arm, including expected and observed rates of the expected AEs. The SMC will review grouped data in the closed session only. The SMC will meet and review this data at scheduled time points or ad hoc as needed during this trial as defined in the SMC charter. As an outcome of each review/meeting, the

SMC will make a recommendation as to the advisability of proceeding with study vaccinations (as applicable), and to continue, modify, or terminate this trial.

6.7. Multicenter Studies

This study is conducted at a single clinical site.

6.8. Multiple Comparisons/Multiplicity

This study was designed to obtain preliminary estimates of safety and immune response to two doses of AV7909 administered as either the thermostable lyophilized product or as the liquid product. The study was not designed to test any specific null hypothesis, and as such no adjustment for multiple comparisons will be performed.

7. STUDY SUBJECTS

7.1. Disposition of Subjects

Table 17 will present a summary of the reasons that subjects were screened but not enrolled.

The composition of analysis populations, including reasons for subject exclusion, by treatment arm, is presented in Table 14.

The disposition of subjects in the study will be tabulated by study arm (Table 13). This table shows the total number of subjects who were screened, enrolled, received each study vaccination, completed all safety and immunogenicity blood draws, completed study follow-up, and completed the study per protocol.

A flowchart showing the disposition of study subjects, adapted from the Consort Statement[5], will be included (Figure 2). This figure will present the number of subjects screened, enrolled, lost to follow-up, and analyzed by treatment arm.

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

7.2. Protocol Deviations

A summary of subject-specific protocol deviations will be presented by the reason for the deviation, the deviation category, and study arm for all enrolled subjects (Table 5). Major deviations will be reviewed for possible subject exclusion from the per protocol population. See Section 6.3.3 for per protocol exclusion definitions. All subject-specific protocol deviations and non-subject specific protocol deviations will be included in Appendix 3 as data listings (Listing 3 and Listing 4, respectively).

8. EFFICACY EVALUATION

Summaries and analysis of immunogenicity data will be presented for the mITT and PP populations. Immune responses in terms of TNA ED_{50} and NF_{50}, and anti-PA IgG by ELISA will be summarized by study arm at each time point. Descriptive summary statistics by study arm will be provided for all assays and time points, including number of subjects with non-missing results, GMT (geometric mean titer) for TNA results or GMC (geometric mean concentration) for IgG ELISA results, GMFR (geometric mean fold rise from baseline), and percentage of subjects achieving seroconversion (see Section 3.3). Additionally, the percentage of subjects in each study arm achieving putative seroprotection (see Section 3.3) will be assessed at each time point. GMT/GMC and GMFR results will be presented with corresponding 95% confidence intervals (CIs) based on Student's t-distribution. Exact binomial 95% CIs calculated using the Clopper-Pearson method (SAS Proc Freq with a binomial option) will be presented for proportional endpoints. No exploratory immunologic outcomes are anticipated.

Individual TNA ED_{50}, TNA NF_{50}, and anti-PA IgG assay results will be provided in Listing 9.

8.1. Primary Efficacy Analysis

This protocol does not define any primary immunogenicity objectives or outcome measures.

8.2. Secondary Efficacy Analyses

TNA ED_{50}, TNA NF_{50}, and anti-PA IgG assay results will be presented for both the mITT and PP populations, providing a comparison of the sensitivity of immunogenicity results to subject adherence to protocol-defined conditions. The secondary immunogenicity endpoints of GMT/GMC, percentage of subjects achieving seroconversion, and percentage of subjects achieving putative seroprotection will be summarized as described above. These descriptive summaries are presented in Table 21, Table 22, Table 25, Table 26, Table 29 and Table 30.

Reverse cumulative distribution (RCD) curves will be presented for each assay (TNA ED_{50}, TNA NF_{50}, and anti-PA IgG), generated with separate panels for each visit and separate curves within each panel for each study arm. RCD curves are presented in Figure 3, Figure 4, Figure 5, Figure 6, Figure 7 and Figure 8.

Figures depicting the GMT (TNA ED_{50} and TNA NF_{50}) or GMC (anti-PA IgG) for each assay over time will be presented by study arm in Figure 9, Figure 10, Figure 11, Figure 12, Figure 13 and Figure 14. Exploratory Efficacy Analyses

This protocol does not define any exploratory immunogenicity objectives or outcome measures. However, as enrollment for this study was stratified by sex and age category, secondary immunogenicity endpoint summaries will be stratified by sex and age category as exploratory analyses. TNA ED_{50} and NF_{50} and anti-PA IgG antibody responses will be summarized, stratified by sex and age category (18-30 years, 31-45 years), in Table 23, Table 24, Table 27, Table 28, Table 31 and Table 32.

9. SAFETY EVALUATION

All summaries and analysis of safety data will be presented for the safety population. Safety summaries will be presented overall and grouped by study arm.

Listings will be sorted by study arm, subject ID, parameter (if applicable), and visit.

Continuous variables will be summarized using the following descriptive statistics: n (non-missing sample size), mean, standard deviation, median, maximum, and minimum. All categorical measures will be summarized by the frequency and percentages of observed levels will be reported for all categorical measures. The denominator for the percentages may be based on the number of non-missing observations for an assessment or based on the number of subjects in a population. This will be described for each table.

9.1. Demographic and Other Baseline Characteristics

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

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

9.1.1. Prior and Concurrent Medical Conditions

All current illnesses and past or pre-existing medical conditions will be coded using Medical Dictionary for Regulatory Activities (MedDRA®) version 25.1 or higher.

Summaries of subjects' prior and concurrent medical conditions will be presented by study arm (Table 20).

Individual subject listings will be presented for all reported medical history including prior and concurrent medical conditions (Listing 7).

9.1.2. Prior and Concomitant Medications

Prior and concomitant medications will be coded to the Anatomical Therapeutic Chemical (ATC) classification system as defined by the WHO Drug Dictionary. Summaries of medications that were started prior to dosing and continuing at the time of dosing will be presented by ATC levels 1 and 2 and study arm for subjects in the safety population (Table 86).

Individual subject listings will be presented for all concomitant medications (Listing 18).

9.2. Measurements of Treatment Compliance

All subjects are to receive 2 study vaccinations administered in the clinic. The number of subjects receiving study vaccination by week will be presented by study arm in Table 15 and Table 16 and as part of the subject disposition table (Table 13). Listing 1 presents subjects who received investigational product with randomized study arm and study product received for each study vaccination. Listing 8 presents subjects who missed doses of study vaccine or received study vaccine out of window.

9.3. Adverse Events

A summary of all adverse events is provided in Table 33. A summary of those events that occurred in ≥5% of subjects in any study group is provided in Table 34.

9.3.1. Solicited Events and Symptoms

Systemic solicited adverse events were collected pre-vaccination, and systemic and local solicited adverse events were collected 30 minutes post-vaccination and then daily for 7 days after each vaccination and graded on a scale of 0 (absent), 1 (mild), 2 (moderate) and 3 (severe). Systemic events include fever, feverishness, fatigue, malaise, myalgia, arthralgia, headache, and nausea, with grading scales as defined in Table 8; the quantitative grading scale for fever is included in Table 9. Injection site events include pain, tenderness, pruritus, ecchymosis, erythema/redness, and edema/induration with grading scales as defined in Table 6. Ecchymosis, erythema/redness, and edema/induration are measured by both functional and measurement grading scales as defined in Table 7.

The number and percentage of subjects reporting at least one solicited adverse event will be summarized for each solicited adverse event, any systemic symptom, any local symptom, and any symptoms. Corresponding 95% CIs will be calculated using Clopper-Pearson methodology from a binomial distribution (SAS Proc Freq with a binomial option). Solicited events occurring post first vaccination will be presented in Table 35, post second vaccination in Table 36, and post any vaccination in Table 37. Summaries of solicited events following any vaccination will be stratified by sex in Table 38 and stratified by age category in Table 39.

For each systemic and local event, any systemic event, any local event, and any solicited event, the maximum severity over 7 days after each vaccination will be summarized for the safety population. The number and percentage of subjects reporting each event will be summarized by the maximum severity and study arm, separately for each vaccination and over all vaccinations (Table 40, Table 41 and Table 42).

The number of subjects reporting a solicited adverse event will be summarized for each day post vaccination for each vaccination and for all vaccinations combined both in tabular form (Table 43, Table 44, Table 45 and Table 46) and graphically in bar charts (Figure 15 and Figure 16). A comparison of the event rate for each study arm between vaccination 1 and vaccination 2 will be presented in Table 47.

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

9.3.2. Unsolicited Adverse Events

When calculating the incidence of unsolicited AEs (i.e., on a per subject basis), each subject will only be counted once at the highest severity and/or relationship, and any repetitions of AEs within a subject will be ignored; the denominator will be the total number of subjects in the safety population. All AEs reported will be included in the summaries and analyses.

The number and percentage of subjects reporting at least one unsolicited AE will be summarized by MedDRA system organ class and preferred term. Denominators for percentages are the number of subjects who received the study vaccination. A 95% CI will be presented for the percentage of subjects reporting any unsolicited AE (serious or non-serious) for each MedDRA system organ class and preferred term.

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

- Subject incidence and total frequency of adverse events over time with 95% CI (Table 48).

- Incidence of AEs by severity and relationship to study product (Table 49 and Table 50).
- Subject listing of non-serious adverse events of moderate or greater severity (Table 52).
- Bar charts displaying total frequency and incidence of AEs by severity, MedDRA system organ class, and study arm (Figure 17 and Figure 18).
- Bar charts displaying total frequency and incidence of AEs by relationship to study product, MedDRA system organ class, and study arm (Figure 19 and Figure 20).

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

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

- Deaths and serious adverse events (Table 51).
- Other significant adverse events, including AESIs/PIMMCs and MAAEs (Table 53).

9.5. Pregnancies

For any subjects in the safety population who became pregnant during the study, every attempt will be made to follow these subjects to completion of pregnancy to document the outcome, including information regarding any complications with pregnancy and/or delivery.

Listing 19, Listing 20, Listing 21, Listing 22 and Listing 23 will present any study pregnancies and their outcomes.

9.6. Clinical Laboratory Evaluations

Clinical safety laboratory parameters will be collected from each subject prior to the first study vaccination (baseline) and approximately 2 weeks after the second study vaccination (Day 29). Laboratory parameters include blood urea nitrogen (BUN), serum creatinine, alkaline phosphatase, alanine aminotransferase (ALT), total bilirubin, hemoglobin, hemoglobin decrease from baseline, white blood cell (WBC) count, absolute eosinophil count, absolute neutrophil count, and platelets. Additional laboratory parameters were measured under Protocol Version 3.0, including random glucose, aspartate aminotransferase (AST), urine protein, and urine glucose, but collection of these parameters was no longer required after the finalization of Protocol Version 4.0; all available results for these clinical labs are reported, but fewer reported results are expected for these discontinued laboratory measures. The grading scale for clinical laboratory evaluations used under Protocol Version 4.0 is presented in Table 11. The grading scale for additional laboratory parameters measured under Protocol Version 3.0 and below (random glucose, AST, urine protein, and urine glucose) is presented in Table 12.

The distribution of laboratory results by severity, study day, and study arm will be presented in Table 57 through Table 64 for chemistry parameters, Table 67 through Table 73 for hematology parameters, and Table 76 through Table 78 for urinalysis parameters. Summaries of abnormal laboratory results related to study product will be presented by severity, study day, and study arm (chemistry: Table 65; hematology: Table 74; urinalysis: Table 79). Descriptive statistics including mean, standard deviation, median, minimum, maximum, and change from baseline will be summarized for each parameter (chemistry: Table 66;

hematology: Table 75; urinalysis: Table 80). Boxplots illustrating the change from baseline for each laboratory parameter will be presented in Figure 21 through Figure 35.

A complete listing of individual clinical laboratory results will be presented in Listing 12, Listing 13, and Listing 14 for chemistry, hematology, and urinalysis, respectively, sorted by study arm, subject ID, parameter, and visit number. Listings of abnormal chemistry, hematology, and urinalysis results will be presented in Table 54, Table 55 and Table 56, respectively.

9.7. Vital Signs and Physical Evaluations

Vital signs including oral temperature, systolic blood pressure, diastolic blood pressure, and pulse will be assessed prior to each study vaccination (Day 1 and approximately Day 15). The grading scale for oral temperature is presented in Table 9, and the grading scales for blood pressure and pulse are presented Table 10. Summaries of vital signs by maximum severity will be tabulated by visit and study arm (Table 81, Table 82, Table 83, Table 84 and Table 85). A listing of vital signs will be presented (Listing 16).

Targeted physical examinations will be performed, if indicated, based on a subject's medical history. A listing of physical exam findings will be presented (Listing 17).

9.8. Concomitant Medications

Concomitant medications will be collected for the 60 days prior to signing the ICF through approximately Day 64 or early termination, whichever occurs first. Concomitant medications will be coded to the Anatomical Therapeutic Classification using the WHO Drug Dictionary. The use of prior and concomitant medications taken during the study will be recorded on the CRFs. A by-subject listing of concomitant medication use will be presented (Listing 18). The use of concomitant medications during the study will be summarized by ATC1, ATC2 code, and study arm for the safety population (Table 86).

9.9. Other Safety Measures

Not applicable.

10. PHARMACOKINETICS

Not applicable.

11. IMMUNOGENICITY

See Section 8.

12. OTHER ANALYSES

Not applicable.

13. REPORTING CONVENTIONS

P-values ≥0.001 and ≤0.999 will be reported to 3 decimal places; p-values less than 0.001 will be reported as "< 0.001"; p-values greater than 0.999 will be reported as "> 0.999". The mean, median, standard deviation, and any other statistics (other than minimum and maximum) will be reported to one decimal place greater than the original data. Minimum and maximum will be reported to the same number of decimal places as the original data. Proportions will be reported to two decimal places; values <0.01 will be presented as "< 0.01". Percentages will be reported to the nearest whole number; non-zero values < 1% will be presented as "< 1"; values greater than 99% but less than 100% will be presented as "> 99". Estimated parameters that are not on the same scale as raw observations (e.g. regression coefficients) will be reported to 3 significant figures.

14. TECHNICAL DETAILS

SAS version 9.4 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

The clinical safety laboratory parameters outlined in Protocol Version 3.0 and below included random glucose, aspartate aminotransferase (AST), urine protein, and urine glucose. At screening, high levels of these laboratory parameters were being collected, resulting in the screen failure of many healthy potential study participants. These laboratory parameters were deemed unnecessary for determining the overall health and eligibility of participants. Random glucose, AST, urine protein, and urine glucose were removed from Protocol Version 4.0 and no longer required for collection from subjects after this protocol amendment. All available clinical laboratory results are reported, but fewer reported results are expected for these discontinued laboratory measures.

16. REFERENCES

1. Fellows PF, Linscott MK, Ivins BE, et al. Efficacy of a human anthrax vaccine in guinea pigs, rabbits, and rhesus macaques against challenge by Bacillus anthracis isolates of diverse geographical origin. Vaccine 2001;19:3241-7.
2. Hopkins RJ, Daczkowski NF, Kaptur PE, et al. Randomized, double-blind, placebo- controlled, safety and immunogenicity study of 4 formulations of Anthrax Vaccine Adsorbed plus CPG 7909 (AV7909) in healthy adult volunteers. Vaccine 2013;31:3051-8.
3. Minang JT, Inglefield JR, Harris AM, et al. Enhanced early innate and T cell-mediated responses in subjects immunized with Anthrax Vaccine Adsorbed Plus CPG 7909 (AV7909). Vaccine 2014;32:6847-54.
4. Rynkiewicz D, Rathkopf M, Sim I, et al. Marked enhancement of the immune response to BioThrax(R) (Anthrax Vaccine Adsorbed) by the TLR9 agonist CPG 7909 in healthy volunteers. Vaccine 2011;29:6313-20
5. Drummond R. CONSORT Revised: Improving the Reporting of Randomized Clinical Trials. JAMA. 2001; 285(15):2006-2007.

17. LISTING OF TABLES, FIGURES, AND LISTINGS

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

APPENDICES

APPENDIX 1. TABLE MOCK-UPS

LIST OF TABLES

9.1 Overall Study Design and Plan Description

9.5.1 Efficacy/Immunogenicity and Safety Measurements Assessed and Flow Chart

Table 1: Schedule of Study Procedures

Study Visit (V)	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**Early Termination**
Study Day#	**pre**	**1**	**8**	**15#**	**22#**	**29#**	**64#**	**195#**	**380#**	
Window Open	**-28**	**1**	**8**	**15**	**22**	**27**	**60**	**188**	**373**	
Window Close	**-2**	**1**	**11**	**18**	**25**	**31**	**68**	**202**	**387**	
Study Week	**pre**	**1**	**1**	**2**	**3**	**4**	**9**	**28**	**54**	
Activity/Procedure										
Inform prospective participant about study details[1]	X									
Obtain informed consent, HIPAA authorization, enroll[2]	X									
Obtain, record, update demographics, medical history, concomitant medications[3]	X	X	X	X	X	X	X	X	X	X
Perform physical examination[4]	X	X	X	X	X	X	X	X	X	X
Collect blood/urine for eligibility or post-vaccination safety[5]	X					X				X
Perform pregnancy test[6]	X	X		X						
Perform 12-lead electrocardiogram[7]	X									
Review eligibility criteria or criteria for subsequent vacination[8]	X	X		X						
Perform randomization[9]		X								
Vaccinate[10]		X		X						
Perform post-vaccination reactogenicity assessment, instruct on eMemory Aid, & provide study related materials[11]		X		X						
Counsel on avoidance of pregnancy[12]	X	X	X	X	X	X	X			
Review memory aid (solicited AEs/reactogenicity) & confirm data[13]			X		X					
Examine study vaccination site[14]			X		X					X
Collect blood - Toxin Neutralization Assay (TNA) and anti-PA IgG by ELISA[15]		X	X	X	X	X	X	X	X	X
Collect blood - to be stored for use if PIMMC occurs[16]	X									
Perform assessment[17] of non-serious unsolicited AEs		X	X	X	X	X	X			X
Perform SAE, MAAE, and AESI assessment[18]		X	X	X	X	X	X	X	X	X

Note that all visits after Visit 3 (target Day 15, second vaccination) are based on the day that Visit 3 occurs. If it occurs on Day 15, all subsequent visits and windows are as written in Appendix A. If it occurs after Day 15, subsequent visit days will be adjusted to maintain the intervals. For example, if Visit 3 occurs on Day 16, then the remaining target Days are 23, 30, 65, 196, and 381. The number of days in the accompanying acceptable windows for each visit will remain the same. The Days for each visit, as written in the Table above and described throughout the protocol and elsewhere, reflect the schedule if Visit 3 occurs on Day 15.

1. Prior to screening, participants may be given information about the study design and purpose, eligibility criteria, procedures, and other approved details by telephone or otherwise. At the screening visit, prospective participants will be provided detailed information about the trial, will be asked to review the informed consent document, will have all their questions answered, and will be evaluated for their ability to provide informed consent.

2. Participants will provide written informed consent, including optional secondary use provisions, HIPAA authorization, acknowledgment of the Notice of Privacy Practices, and other study research related documents. Upon completion of the initial informed consent process, they will be enrolled and will begin screening.

3. In a private space, trained study team members will collect demographics, medical history, and concomitant medications. At screening and the Day 1 visit, these activities will be performed for the purposes of determining eligibility and baseline health status. On subsequent visits, updates to the medical history and medications will be collected and recorded to evaluate for AEs. Concomitant medications will be recorded routinely through Day 64. After Day 64, only concomitant medications (new and updates to previously reported ones) that are taken in relation to MAAEs, SAEs, and AESIs (PIMMCs) will be recorded.

4. At screening, a more detailed physical examination will be performed to determine eligibility and any baseline findings. This exam includes a height and weight for the determination of Body Mass Index (BMI). At Day 1 and at subsequent visits, a physical examination will only be performed if the participant reports a symptom warranting an exam. The screening exam will be "detailed"; the subsequent exams, when needed, will be "targeted". The screening exam, Day 1, Day 15, and ET visits will also include vital signs (blood pressure, heart rate, oral temperature). Vital signs may be repeated at the discretion of the clinician, up to 3 times.

5. Blood and urine will be collected at screening to determine eligibility. Blood will be collected at Day 29 to determine laboratory safety. Tests performed are found in the protocol.

6. A serum pregnancy test (β hCG) will be sent with the screening laboratory specimens and a point-of-care urine pregnancy test will be performed on Days 1 and 15, with results determined to be negative before randomization and vaccination. Should Visit 3 (second vaccination) occur after Day 15, the pregnancy test will be performed on the day of the visit, with results determined to be negative before vaccination.

7. A routine 12-lead electrocardiogram will be performed at screening. It will be read by the automated ECG machine, reviewed by the investigator, and officially read by a cardiologist. Participants with clinically significant abnormalities will be excluded. Adjustments may be made while the ECG is being performed, but once it is complete, no repeat ECGs will be performed unless the reviewing cardiologist requires a repeat study for clarification. No repeat ECGs will be performed after vaccination.

8. Prior to randomization and enrollment, the PI or his/her delegate will review all eligibility criteria and record his/her determination. Prior to the second dose on Day 15 (or as late as Day 18), the PI or his/her delegate will review all criteria for subsequent dosing and record his/her determination.

9. Upon determination of eligibility, the pharmacy will be notified to proceed with randomization and preparation of the vaccine either as the liquid formulation or lyophilized formulation.

10. A pre-administration reactogenicity assessments will be performed immediately prior to study vaccination to establish baseline. The participant will be vaccinated intramuscularly, in the deltoid of the arm chosen by the participant, by an unblinded study team member
11. In the 30 minutes after vaccination, the participant will be evaluated for immediate reactogenicity and will be instructed on the use of the electronic memory aid to record solicited adverse events (reactogenicity) on Days 1 through 8 and Days 15 through 22, inclusive. Should Visit 3 (second vaccination) occur after Day 15, the reactogenicity period will be adjusted to collect a full 7 days of data. Any other study-related materials available for the participant, such as study contact information, ruler, and thermometer, will be provided.

12. Women of childbearing potential will be counseled to avoid pregnancy until 60 days after the second (final) vaccination, i.e., Day 75 if Visit 3 occurs on Day 15.

13. In the 7 days following vaccination (Days 1 through 8, inclusively and Days 15 through 22, inclusively; or adjusted, as described above, should second vaccination occur after Day 15), during which the participants will be directly entering their reactogenicity profiles through a secure web portal, the study team will be reviewing the entries, answering questions, and contacting the participant if they have failed to enter data. On Days 8 and 22 (or 7 days after the second vaccination, if the second vaccination occurs after Day 15), when the post-vaccination diaries will have been completed, the study team will confirm all entries. At these visits, the participant will also be asked about unsolicited AEs. If solicited AEs persist in Day 8 or Day 22 (beyond the seventh day after second vaccination), they will be followed to resolution.

14. The site of the vaccination will be examined and findings recorded on the appropriate CRF.

15. The toxin neutralization assay is the gold standard immunologic assay for protection against anthrax. It is performed on serum. ELISA will also be performed, to measure the concentration of anti-PA IgG. On vaccination days (Visits 1 and 3), these will be collected prior to vaccination.

16. Blood will be collected for storage in case the participant develops signs and/or symptoms of a PIMMC.

17. Information on unsolicited AEs that are not serious will be collected from the time of the first study vaccination to the Day 64 visit (or the Day as determined in an adjusted schedule, should the second vaccination, Visit 3, occur after Day 15).

18. Information on SAEs, MAAEs, and AESIs will be collected from the time of the first study vaccination to the Day 380 visit (which may be adjusted, should the second vaccination, Visit 3, occur after Day 15). The only AESIs for this study are potentially immune mediated diseases (PIMMCs). If an AESI is reported, the participant will be asked to have an evaluation performed.

9.7.1 Sample Size

Table 2: Power (%) to Detect Safety Events

Event Frequency	Single Treatment Arm N=20	All Enrolled Subjects N=40
10% Very Common	87	98
1% Common	18	33
0.1% Uncommon	1	3
0.01% Rare	<0.1	<0.1

Table 3: Precision of Binomial Confidence Intervals

N	95% CI
20	27-73
40	34-66

Table 4: Minimum Detectable Difference in the Probability of Response with 80% Power

Assumed Proportion of Responders in Comparator Group A	80% Power (N = 18)	
	Minimal Detectable Difference	Probability of Response in Experimental Group B
0.10	0.39	0.49
0.20	0.43	0.63
0.30	0.43	0.73
0.40	0.42	0.82
0.50	0.39	0.89
0.60	0.35	0.95

10.2 Protocol Deviations

Table 5: Distribution of Protocol Deviations by Category, Type, and Study Arm

Category	Deviation Type	Liquid AV7909 (N=X)		Lyophilized AV7909 (N=X)		All Subjects (N=X)	
		No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.
Eligibility/enrollment	Any type	x	x	x	x	x	x
	Did not meet inclusion criterion	x	x	x	x	x	x
	Met exclusion criterion	x	x	x	x	x	x
	ICF not signed prior to study procedures	x	x	x	x	x	x
	Other	x	x	x	x	x	x
Treatment administration schedule	Any type	x	x	x	x	x	x
	Out of window visit	x	x	x	x	x	x
	Missed visit/visit not conducted	x	x	x	x	x	x
	Missed treatment administration	x	x	x	x	x	x
	Delayed treatment administration	x	x	x	x	x	x
	Other	x	x	x	x	x	x
Follow-up visit schedule	Any type	x	x	x	x	x	x
	Out of window visit	x	x	x	x	x	x
	Missed visit/visit not conducted	x	x	x	x	x	x
	Other	x	x	x	x	x	x
Protocol procedure/assessment	Any type	x	x	x	x	x	x
	Incorrect version of ICF signed	x	x	x	x	x	x
	Blood not collected	x	x	x	x	x	x
	Urine not collected	x	x	x	x	x	x
	Stool not collected	x	x	x	x	x	x
	Other specimen not collected	x	x	x	x	x	x
	Too few aliquots obtained	x	x	x	x	x	x
	Specimen result not obtained	x	x	x	x	x	x
	Required procedure not conducted	x	x	x	x	x	x
	Required procedure done incorrectly	x	x	x	x	x	x
	Study product temperature excursion	x	x	x	x	x	x
	Specimen temperature excursion	x	x	x	x	x	x

Table 5: Distribution of Protocol Deviations by Category, Type, and Study Arm *(continued)*

Category	Deviation Type	Liquid AV7909 (N=X)		Lyophilized AV7909 (N=X)		All Subjects (N=X)	
		No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.
	Other	x	x	x	x	x	x
Treatment administration	Any type	x	x	x	x	x	x
	Required procedure done incorrectly	x	x	x	x	x	x
	Study product temperature excursion	x	x	x	x	x	x
	Other	x	x	x	x	x	x
Blinding policy/procedure	Any type	x	x	x	x	x	x
	Treatment unblinded	x	x	x	x	x	x
	Other	x	x	x	x	x	x
Note: N = Number of enrolled subjects.							

12.2.2 Displays of Adverse Events

Table 6: Injection Site Reactogenicity Grading Scale

Injection Site Reaction	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)
Pain - experienced without touching the injection site (spontaneous discomfort)	Subject is aware of pain, but it does not interfere with daily activity, and if pain medication is used, it is Over the Counter (OTC) and used for less than 24 hours	Subject is aware of pain; there is interference with daily activity or OTC pain medication is used for more than 24 hours	Subject is aware of pain, and it prevents daily activity or pain requires prescription medication
Tenderness-experienced with touching the injection site	Subject is aware of pain, but it does not interfere with daily activity, and if pain medication is used, it is Over the Counter (OTC) and used for less than 24 hours	Subject is aware of pain; there is interference with daily activity or OTC pain medication is used for more than 24 hours	Subject is aware of pain, and it prevents daily activity or pain requires prescription medication
Pruritus	Does not interfere with daily activity	Interferes with daily activity	Prevents daily activity or requires prescription medication
Ecchymosis (Bruising)*	Does not interfere with daily activity	Interferes with daily activity	Prevents daily activity
Erythema (Redness)*	Does not interfere with daily activity	Interferes with daily activity	Prevents daily activity
Edema (Swelling)/Induration (Hardness)*	Does not interfere with daily activity	Interferes with daily activity	Prevents daily activity
* Will also be measured in mm but size will not be used as halting criteria.			

Table 7: Injection Site Reactogenicity Measurements

Injection Site Reaction	Small	Medium	Large
Ecchymosis (Bruising)*	< 20 mm	20 mm - 50 mm	> 50 mm
Erythema (Redness)*	< 20 mm	20 mm - 50 mm	> 50 mm
Edema (Swelling)/Induration (Hardness)*	< 20 mm	20 mm - 50 mm	> 50 mm
* Will not be used as halting criteria.			

Table 8: Subjective Systemic Reactogenicity Grading

Systemic (Subjective)	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)
Feverishness	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity
Fatigue	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity
Malaise	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity
Myalgia*	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity
Arthralgia*	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity
Headache	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity or headache requires prescription medication.
Nausea	No interference with daily activity	Some interference with daily activity	Significant interference, prevents daily activity or nausea requires prescription medication.
* Not at injection site.			

Table 9: Quantitative Systemic (Oral Temperature) Reactogenicity Grading

Systemic (Subjective)	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)
Fever[#]* - oral[†]	38.0°C - 38.4°C 100.4°F - 101.1°F	38.5°C - 38.9°C 101.2°F - 102.0°F	> 38.9°C > 102.0°F

[#] Oral temperature assessed on Day 1 prior to the first study vaccination will be considered as baseline.
[*] A fever can be considered not related to the study product if an alternative etiology can be documented.
[†] Participants must not eat or drink anything hot or cold, or smoke within 10 minutes prior to taking oral temperature.

Table 10: Pulse and BP Adverse Event Grading

Physiologic Parameter[#]	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)
Bradycardia - beats per minute	45 - 50	40 - 44	< 40
Tachycardia - beats per minute	101 - 130	131 - 155	> 155
Hypotension (systolic) mmHg	80 - 84	75 - 79	< 75
Hypotension (diastolic) mmHg	50 - 54	45 - 49	< 45
Hypertension (systolic) mmHg	141 - 155	156 - 160	> 160
Hypertension (diastolic) mmHg	91 - 100	101 - 110	> 110

[#] Pulse and BP assessed on Day 1 prior to the first study vaccination will be considered as baseline.

12.4.1 Individual Laboratory Measurements and Abnormal Laboratory Values

Table 11: Clinical Safety Laboratory Adverse Event Grading Scale (Protocol Version 4.0)

Panel and Analyte[a]	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)
Serum Chemistry			
Blood Urea Nitrogen (mg/dL)	23-26	27-31	>31
Creatinine (mg/dL) female	1.3-1.7	1.8-2.0	>2.0
Creatinine (mg/dL) male	1.4-1.7	1.8-2.0	>2.0
Alkaline phosphatase (U/L) female	147-196	197-294	>294
Alkaline phosphatase (U/L) male	192-256	257-384	>384
ALT(U/L)	68-113	114-225	>225
Total Bilirubin when accompanied by any grade ALT (mg/dL)	1.3-1.6	1.7-2.0	>2.0
Total Bilirubin when not accompanied by any grade ALT (mg/dL)	1.3-2.0	2.1-2.6	>2.6
Hematology			
Hemoglobin, female (g/dL)	10.0-10.9	9.0-9.9	<9.0
Hemoglobin decrease from baseline value, female (g/dL)	1.0-1.5	1.6-2.0	>2.0
Hemoglobin, male (g/dL)	11.5-12.4	10.5-11.4	<10.5
Hemoglobin decrease from baseline value, male (g/dL)	1.0-1.5	1.6-2.0	>2. 0
WBC (leukocytosis) (cell/mm^3)	12,001-15,000	15,001-20,000	>20,000
WBC (leukopenia) (cell/mm^3)	2,500-2999	1,500-2,499	<1,500
Eosinophils (absolute eosinophilia) (cell/mm^3)	1201-1500	1,501-5,000	>5,000
Neutrophil (neutropenia) (cell/mm^3)	1001-1200	751-1,000	<751
Platelets (thrombocytopenia)(cell/mm^3)	100,000-126,000	50,000-99,999	<50,000

ALT = alanine aminotransferase; WBC = white blood cell.
[a] Laboratory normal reference ranges have been taken into consideration for the toxicity grading scale. If the laboratory provides a value that has additional significant digits beyond what is provided in the table, digits of 0-4 will be rounded down and digits of 5-9 will be rounded up, for purposes of delineating a grade.

Table 12: Clinical Safety Laboratory Adverse Event Grading Scale (Additional Laboratory Parameters from Protocol Version 3.0 and below)

Panel and Analyte[a]	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)
Serum Chemistry			
Glucose - random (mg/dL)	110-125	126-200	>200
AST (U/L) female	45-75	76-150	>150
AST (U/L) male	60-100	101-200	>200
Urine			
Protein	1+	2+	3+
Glucose	Trace	1+	2+

AST = aspartate aminotransferase.
[a] Laboratory normal reference ranges have been taken into consideration for the toxicity grading scale. If the laboratory provides a value that has additional significant digits beyond what is provided in the table, digits of 0-4 will be rounded down and digits of 5-9 will be rounded up, for purposes of delineating a grade.

14.1 Description of Study Subjects

14.1.1 Disposition of Subjects

Table 13: Subject Disposition by Study Arm - All Enrolled Subjects

Subject Disposition	Liquid AV7909 (N=X)		Lyophilized AV7909 (N=X)		All Subjects (N=X)	
	n	%	n	%	n	%
Screened	--	--	--	--	x	--
Enrolled/Randomized	x	100	x	100	x	100
Received Study Vaccination 1	x	xx	x	xx	x	xx
Received Study Vaccination 2	x	xx	x	xx	x	xx
Received All Scheduled Vaccinations [a]	x	xx	x	xx	x	xx
Completed All Safety Blood Draws	x	xx	x	xx	x	xx
Completed All Immunogenicity Blood Draws	x	xx	x	xx	x	xx
Completed Follow-up (Study Day 380)[a]	x	xx	x	xx	x	xx
Completed All Visits Per Protocol [b]	x	xx	x	xx	x	xx

Note: N = Number of enrolled subjects.
[a] Refer to Listing 16.2.1 for reasons subjects discontinued or terminated early.
[b] Refer to Listing 16.2.3 for reasons subjects are excluded from the analysis populations .

Table 14: Analysis Populations by Study Arm - All Enrolled Subjects

Analysis Population	Reason Subjects Excluded	Liquid AV7909 (N=X)		Lyophilized AV7909 (N=X)		All Subjects (N=X)	
		n	%	n	%	%	n
Safety Population	Any Reason	x	xx	x	xx	x	xx
	Study Vaccination 1 Not Received	x	xx	x	xx	x	xx
Modified Intent-to-Treat Population	Any Reason	x	xx	x	xx	x	xx
	Study Vaccination 1 Not Received						
	No Post-Vaccination Immunogenicity Results						
Per Protocol Population	Any Reason						
	Study Vaccination 1 Not Received						
	No Post-Vaccination Immunogenicity Results						
	Found to be Ineligible at Baseline						
Note: N = Number of enrolled subjects.							

Table 15: Dates of First Vaccination by Study Arm - All Vaccinated Subjects

[Implementation Note: Each row should represent one week, starting with the first date of Dose 1 administration in the study.]

Dates of Dosing	Liquid AV7909 (N=X)	Lyophilized AV7909 (N=X)	All Subjects (N=X)
Total (Entire period of enrollment)	x	x	x
DDMMMYYYY - DDMMMYYYY	x	x	x
DDMMMYYYY - DDMMMYYYY	x	x	x
DDMMMYYYY - DDMMMYYYY	x	x	x
DDMMMYYYY - DDMMMYYYY	x	x	x
Note: N = Number of subjects who received the first study vaccination.			

Table with similar format:

Table 16: Dates of Second Vaccination by Study Arm - All Vaccinated Subjects

[Implementation Note: Each row should represent one week, starting with the first date of Dose 2 administration in the study.]

Table 17: Ineligibility Summary of Screen Failures

Category	Criterion	n[a]	%[b]
All Subjects	Total number of subjects who failed any eligibility criterion or were eligible but not enrolled	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
Eligible but not enrolled	Any other reason		
	Time commitment		
	Concern of potential risks		
	Number of procedures/blood draws		
	Unable to contact subject		
	Other		

[a] More than one criterion may be marked per subject.
[b] Denominator for percentages is the total number of screen failures and those eligible but not enrolled.

14.1.2 Demographic Data by Study Group

Table 18: Summary of Categorical Demographic and Baseline Characteristics by Study Arm - All Enrolled Subjects

Variable	Characteristic	Liquid AV7909 (N=X)		Lyophilized AV7909 (N=X)		All Subjects (N=X)	
		n	%	n	%	n	%
Sex	Male	x	xx	x	xx	x	xx
	Female						
Age Category	18-30 years old	x	xx	x	xx	x	xx
	31-45 years old						
Ethnicity	Not Hispanic or Latino	x	xx	x	xx	x	xx
	Hispanic or Latino						
	Not Reported						
	Unknown						
Race	American Indian or Alaska Native	x	xx	x	xx	x	xx
	Asian						
	Native Hawaiian or Other Pacific Islander						
	Black or African American						
	White						
	Multi-Racial						
	Unknown						

Note: N = Number of enrolled subjects.

Table 19: Summary of Continuous Demographic and Baseline Characteristics by Study Arm - All Enrolled Subjects

Variable	Statistic	Liquid AV7909 (N=X)	Lyophilized AV7909 (N=X)	All Subjects (N=X)
Age (years)	Mean	xx.x	xx.x	xx.x
	Standard Deviation	xx.x	xx.x	xx.x
	Median	xx.x	xx.x	xx.x
	Minimum	xx	xx	xx
	Maximum	xx	xx	xx
Height (cm)	Mean	xx.x	xx.x	xx.x
	Standard Deviation	xx.x	xx.x	xx.x
	Median	xx.x	xx.x	xx.x
	Minimum	xx	xx	xx
	Maximum	xx	xx	xx
Weight (kg)	Mean	xx.x	xx.x	xx.x
	Standard Deviation	xx.x	xx.x	xx.x
	Median	xx.x	xx.x	xx.x
	Minimum	xx	xx	xx
	Maximum	xx	xx	xx
BMI (kg/m^2)	Mean	xx.x	xx.x	xx.x
	Standard Deviation	xx.x	xx.x	xx.x
	Median	xx.x	xx.x	xx.x
	Minimum	xx	xx	xx
	Maximum	xx	xx	xx
Note: N = Number of enrolled subjects.				

14.1.3 Prior and Concurrent Medical Conditions

Table 20: Summary of Subjects with Pre-Existing Medical Conditions by MedDRA System Organ Class and Study Arm - Safety Population

MedDRA System Organ Class	Liquid AV7909 (N=X)		Lyophilized AV7909 (N=X)		All Subjects (N=X)	
	n	%	n	%	n	%
Any SOC	x	xx	x	xx	x	xx
[SOC 1]						
[SOC 2]						
[SOC 3]						
[SOC 4]						

Notes: N = Number of subjects in the safety population; n = Number of subjects reporting medical history within the specified SOC.
A subject is counted only once per SOC.

14.2 Efficacy/Immunogenicity Data

Table 21: Summaries of TNA ED_{50} by Study Day and Study Arm - Modified Intent-to-Treat Population

Study Day	Statistic	Liquid AV7909 (N=X)	Lyophilized AV7909 (N=X)
Baseline (Pre-Vaccination 1)	n	x	x
	GMT (95% CI)[a]	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
Day 8	n	x	x
	GMT (95% CI)[a]	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
	GMFR (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Seroconversion - % (95% CI)[b]	xx (xx, xx)	xx (xx, xx)
Day 15 (Pre-Vaccination 2)	n	x	x
	GMT (95% CI)[a]	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
	GMFR (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Seroconversion - % (95% CI)[b]	xx (xx, xx)	xx (xx, xx)
Day 22	n		
	GMT (95% CI)[a]		
	GMFR (95% CI)		
	Seroconversion - % (95% CI)[b]		
Day 29	n		
	GMT (95% CI)[a]		
	GMFR (95% CI)		
	Seroconversion - % (95% CI)[b]		
Day 64	n		
	GMT (95% CI)[a]		
	GMFR (95% CI)		
	Seroconversion - % (95% CI)[b]		
Day 195	n		
	GMT (95% CI)[a]		
	GMFR (95% CI)		
	Seroconversion - % (95% CI)[b]		
Day 380	n		
	GMT (95% CI)[a]		

Table 21: Summaries of TNA ED_{50} by Study Day and Study Arm - Modified Intent-to-Treat Population *(continued)*

Study Day	Statistic	Liquid AV7909 (N=X)	Lyophilized AV7909 (N=X)
	GMFR (95% CI)		
	Seroconversion - % (95% CI)[b]		

Notes: N = Number of subjects in the Modified Intent-to-Treat Population; n = Number of subjects with results reported; GMT = Geometric Mean Titer; GMFR = Geometric Mean Fold Rise (relative to baseline).
Seroconversion is defined as at least a 4-fold increase over baseline result, or at least a 4-fold increase over the lower limit of quantification (LLOQ = 33) if baseline result is below LLOQ.
[a] Confidence interval calculated based on Student's t-distribution.
[b] Exact binomial confidence interval calculated using Clopper-Pearson methodology.

Table with similar format:

Table 22: Summaries of TNA ED_{50} by Study Day and Study Arm - Per Protocol Population

Table 23: Summaries of TNA ED_{50} by Study Day, Study Arm, and Sex - Per Protocol Population

Study Day	Statistic	Liquid AV7909 (N=X)	Lyophilized AV7909 (N=X)
Female			
Baseline (Pre-Vaccination 1)	n	x	x
	GMT (95% CI)[a]	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
Day 8	n	x	x
	GMT (95% CI)[a]	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
	GMFR (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Seroconversion - % (95% CI)[b]	xx (xx, xx)	xx (xx, xx)
Day 15 (Pre-Vaccination 2)	n	x	x
	GMT (95% CI)[a]	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
	GMFR (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Seroconversion - % (95% CI)[b]	xx (xx, xx)	xx (xx, xx)
Day 22			
Day 29			
Day 64			
Day 195			
Day 380			

Table 23: Summaries of TNA ED_{50} by Study Day, Study Arm, and Sex - Per Protocol Population *(continued)*

Study Day	Statistic	Liquid AV7909 (N=X)	Lyophilized AV7909 (N=X)
Male			
Baseline (Pre-Vaccination 1)	n	x	x
	GMT (95% CI)[a]	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
Day 8	n	x	x
	GMT (95% CI)[a]	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
	GMFR (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Seroconversion - % (95% CI)[b]	xx (xx, xx)	xx (xx, xx)
Day 15 (Pre-Vaccination 2)	n	x	x
	GMT (95% CI)[a]	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
	GMFR (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Seroconversion - % (95% CI)[b]	xx (xx, xx)	xx (xx, xx)
Day 22			
Day 29			
Day 64			
Day 195			
Day 380			

Notes: N = Number of subjects in the Per Protocol Population; n = Number of subjects with results reported; GMT = Geometric Mean Titer; GMFR = Geometric Mean Fold Rise (relative to baseline).
Seroconversion is defined as at least a 4-fold increase over baseline result, or at least a 4-fold increase over the lower limit of quantification (LLOQ = 33) if baseline result is below LLOQ.
[a] Confidence interval calculated based on Student's t-distribution.
[b] Exact binomial confidence interval calculated using Clopper-Pearson methodology.

Table with similar format:

Table 24: Summaries of TNA ED_{50} by Study Day, Study Arm, and Age Category - Per Protocol Population

[Implementation Note: Replace “Female” and “Male” with “Age 18-30 years” and “Age 31-45 years”.]

Table 25: Summaries of TNA NF_{50} by Study Day and Study Arm - Modified Intent-to-Treat Population

Study Day	Statistic	Liquid AV7909 (N=X)	Lyophilized AV7909 (N=X)
Baseline (Pre-Vaccination 1)	n	x	x
	GMT (95% CI)[a]	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
	Putative Seroprotection - % (95% CI)[b]	xx (xx, xx)	xx (xx, xx)
Day 8	n	x	x
	GMT (95% CI)[a]	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
	GMFR (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Seroconversion - % (95% CI)[b]	xx (xx, xx)	xx (xx, xx)
	Putative Seroprotection - % (95% CI)[b]	xx (xx, xx)	xx (xx, xx)
Day 15 (Pre-Vaccination 2)	n	x	x
	GMT (95% CI)[a]	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
	GMFR (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Seroconversion - % (95% CI)[b]	xx (xx, xx)	xx (xx, xx)
	Putative Seroprotection - % (95% CI)[b]	xx (xx, xx)	xx (xx, xx)
Day 22	n		
	GMT (95% CI)[a]		
	GMFR (95% CI)		
	Seroconversion - % (95% CI)[b]		
	Putative Seroprotection - % (95% CI)[b]		
Day 29	n		
	GMT (95% CI)[a]		
	GMFR (95% CI)		
	Seroconversion - % (95% CI)[b]		
	Putative Seroprotection - % (95% CI)[b]		
Day 64	n		
	GMT (95% CI)[a]		
	GMFR (95% CI)		
	Seroconversion - % (95% CI)[b]		
	Putative Seroprotection - % (95% CI)[b]		
Day 195	n		
	GMT (95% CI)[a]		

Table 25: Summaries of TNA NF_{50} by Study Day and Study Arm - Modified Intent-to-Treat Population *(continued)*

Study Day	Statistic	Liquid AV7909 (N=X)	Lyophilized AV7909 (N=X)
	GMFR (95% CI)		
	Seroconversion - % (95% CI)[b]		
	Putative Seroprotection - % (95% CI)[b]		
Day 380	n		
	GMT (95% CI)[a]		
	GMFR (95% CI)		
	Seroconversion - % (95% CI)[b]		
	Putative Seroprotection - % (95% CI)[b]		

Notes: N = Number of subjects in the Modified Intent-to-Treat Population; n = Number of subjects with results reported; GMT = Geometric Mean Titer; GMFR = Geometric Mean Fold Rise (relative to baseline).
Seroconversion is defined as at least a 4-fold increase over baseline result, or at least a 4-fold increase over the lower limit of quantification (LLOQ = 0.064) if baseline result is below LLOQ.
Putative seroprotection is defined as $NF_{50} \geq 0.56$.
[a] Confidence interval calculated based on Student's t-distribution.
[b] Exact binomial confidence interval calculated using Clopper-Pearson methodology.

Table with similar format:

Table 26: Summaries of TNA NF_{50} by Study Day and Study Arm - Per Protocol Population

Table 27: Summaries of TNA NF_{50} by Study Day, Study Arm, and Sex - Per Protocol Population

Study Day	Statistic	Liquid AV7909 (N=X)	Lyophilized AV7909 (N=X)
Female			
Baseline (Pre-Vaccination 1)	n	x	x
	GMT (95% CI)[a]	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
	Putative Seroprotection - % (95% CI)[b]	xx (xx, xx)	xx (xx, xx)
Day 8	n	x	x
	GMT (95% CI)[a]	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
	GMFR (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Seroconversion - % (95% CI)[b]	xx (xx, xx)	xx (xx, xx)
	Putative Seroprotection - % (95% CI)[b]	xx (xx, xx)	xx (xx, xx)
Day 15 (Pre-Vaccination 2)	n	x	x
	GMT (95% CI)[a]	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
	GMFR (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Seroconversion - % (95% CI)[b]	xx (xx, xx)	xx (xx, xx)
	Putative Seroprotection - % (95% CI)[b]	xx (xx, xx)	xx (xx, xx)
Day 22			
Day 29			
Day 64			
Day 195			

Table 27: Summaries of TNA NF_{50} by Study Day, Study Arm, and Sex - Per Protocol Population *(continued)*

Study Day	Statistic	Liquid AV7909 (N=X)	Lyophilized AV7909 (N=X)
Day 380			
Male			
Baseline (Pre-Vaccination 1)	n	x	x
	GMT (95% CI)[a]	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
	Putative Seroprotection - % (95% CI)[b]	xx (xx, xx)	xx (xx, xx)
Day 8	n	x	x
	GMT (95% CI)[a]	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
	GMFR (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Seroconversion - % (95% CI)[b]	xx (xx, xx)	xx (xx, xx)
	Putative Seroprotection - % (95% CI)[b]	xx (xx, xx)	xx (xx, xx)
Day 15 (Pre-Vaccination 2)	n	x	x
	GMT (95% CI)[a]	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
	GMFR (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Seroconversion - % (95% CI)[b]	xx (xx, xx)	xx (xx, xx)
	Putative Seroprotection - % (95% CI)[b]	xx (xx, xx)	xx (xx, xx)
Day 22			
Day 29			

Table 27: Summaries of TNA NF_{50} by Study Day, Study Arm, and Sex - Per Protocol Population *(continued)*

Study Day	Statistic	Liquid AV7909 (N=X)	Lyophilized AV7909 (N=X)
Day 64			
Day 195			
Day 380			

Notes: N = Number of subjects in the Per Protocol Population; n = Number of subjects with results reported; GMT = Geometric Mean Titer; GMFR = Geometric Mean Fold Rise (relative to baseline).
Seroconversion is defined as at least a 4-fold increase over baseline result, or at least a 4-fold increase over the lower limit of quantification (LLOQ = 0.064) if baseline result is below LLOQ.
Putative seroprotection is defined as $NF_{50} \geq 0.56$.
[a] Confidence interval calculated based on Student's t-distribution.
[b] Exact binomial confidence interval calculated using Clopper-Pearson methodology.

Table with similar format:

Table 28: Summaries of TNA NF_{50} by Study Day, Study Arm, and Age Category - Per Protocol Population

[Implementation Note: Replace "Female" and "Male" with "Age 18-30 years" and "Age 31-45 years".]

Table 29: Summaries of anti-PA IgG by Study Day and Study Arm - Modified Intent-to-Treat Population

Study Day	Statistic	Liquid AV7909 (N=X)	Lyophilized AV7909 (N=X)
Baseline (Pre-Vaccination 1)	n	x	x
	GMC - µg/mL (95% CI)[a]	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
Day 8	n	x	x
	GMC - µg/mL (95% CI)[a]	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
	GMFR (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Seroconversion - % (95% CI)[b]	xx (xx, xx)	xx (xx, xx)
Day 15 (Pre-Vaccination 2)	n	x	x
	GMC - µg/mL (95% CI)[a]	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
	GMFR (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Seroconversion - % (95% CI)[b]	xx (xx, xx)	xx (xx, xx)
Day 22	n		
	GMC - µg/mL (95% CI)[a]		
	GMFR (95% CI)		
	Seroconversion - % (95% CI)[b]		
Day 29	n		
	GMC - µg/mL (95% CI)[a]		
	GMFR (95% CI)		
	Seroconversion - % (95% CI)[b]		
Day 64	n		
	GMC - µg/mL (95% CI)[a]		
	GMFR (95% CI)		
	Seroconversion - % (95% CI)[b]		
Day 195	n		
	GMC - µg/mL (95% CI)[a]		
	GMFR (95% CI)		
	Seroconversion - % (95% CI)[b]		
Day 380	n		
	GMC - µg/mL (95% CI)[a]		
	GMFR (95% CI)		
	Seroconversion - % (95% CI)[b]		

Table 29: Summaries of anti-PA IgG by Study Day and Study Arm - Modified Intent-to-Treat Population *(continued)*

Study Day	Statistic	Liquid AV7909 (N=X)	Lyophilized AV7909 (N=X)
Notes: N = Number of subjects in the Modified Intent-to-Treat Population; n = Number of subjects with results reported; GMC = Geometric Mean Concentration (µg/mL); GMFR = Geometric Mean Fold Rise (relative to baseline). Seroconversion is defined as at least a 4-fold increase over baseline result, or at least a 4-fold increase over the lower limit of quantification (LLOQ = 9.27 µg/mL) if baseline result is below LLOQ. [a] Confidence interval calculated based on Student's t-distribution. [b] Exact binomial confidence interval calculated using Clopper-Pearson methodology.			

Table with similar format:

Table 30: Summaries of anti-PA IgG by Study Day and Study Arm - Per Protocol Population

Table 31: Summaries of anti-PA IgG by Study Day, Study Arm, and Sex - Per Protocol Population

Study Day	Statistic	Liquid AV7909 (N=X)	Lyophilized AV7909 (N=X)
Female			
Baseline (Pre-Vaccination 1)	n	x	x
	GMC - µg/mL (95% CI)[a]	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
Day 8	n	x	x
	GMC - µg/mL (95% CI)[a]	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
	GMFR (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Seroconversion - % (95% CI)[b]	xx (xx, xx)	xx (xx, xx)
Day 15 (Pre-Vaccination 2)	n	x	x
	GMC - µg/mL (95% CI)[a]	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
	GMFR (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Seroconversion - % (95% CI)[b]	xx (xx, xx)	xx (xx, xx)
Day 22			
Day 29			
Day 64			
Day 195			
Day 380			

Table 31: Summaries of anti-PA IgG by Study Day, Study Arm, and Sex - Per Protocol Population *(continued)*

Study Day	Statistic	Liquid AV7909 (N=X)	Lyophilized AV7909 (N=X)
Male			
Baseline (Pre-Vaccination 1)	n	x	x
	GMC - µg/mL (95% CI)[a]	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
Day 8	n	x	x
	GMC - µg/mL (95% CI)[a]	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
	GMFR (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Seroconversion - % (95% CI)[b]	xx (xx, xx)	xx (xx, xx)
Day 15 (Pre-Vaccination 2)	n	x	x
	GMC - µg/mL (95% CI)[a]	xx.x (xx.x, xx.x)	xx.x (xx.x, xx.x)
	GMFR (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Seroconversion - % (95% CI)[b]	xx (xx, xx)	xx (xx, xx)
Day 22			
Day 29			
Day 64			
Day 195			
Day 380			

Table 31: Summaries of anti-PA IgG by Study Day, Study Arm, and Sex - Per Protocol Population *(continued)*

Study Day	Statistic	Liquid AV7909 (N=X)	Lyophilized AV7909 (N=X)

Notes: N = Number of subjects in the Per Protocol Population; n = Number of subjects with results reported; GMC = Geometric Mean Concentration (µg/mL); GMFR = Geometric Mean Fold Rise (relative to baseline).
Seroconversion is defined as at least a 4-fold increase over baseline result, or at least a 4-fold increase over the lower limit of quantification (LLOQ = 9.27 µg/mL) if baseline result is below LLOQ.
[a] Confidence interval calculated based on Student's t-distribution.
[b] Exact binomial confidence interval calculated using Clopper-Pearson methodology.

Table with similar format:

Table 32: Summaries of anti-PA IgG by Study Day, Study Arm, and Age Category - Per Protocol Population

[Implementation Note: Replace "Female" and "Male" with "Age 18-30 years" and "Age 31-45 years".]

14.3 Safety Data

14.3.1 Displays of Adverse Events

Table 33: Overall Summary of Adverse Events - Safety Population

		Liquid AV7909 (N=X)		Lyophilized AV7909 (N=X)		All Subjects (N=X)	
Event Category[a]	**Subcategory[a]**	**n**	**%**	**n**	**%**	**n**	**%**
At least one local solicited adverse event	Any Severity	x	x	x	x	x	x
	Mild (Grade 1)						
	Moderate (Grade 2)						
	Severe (Grade 3)						
At least one systemic solicited adverse event	Any Severity						
	Mild (Grade 1)						
	Moderate (Grade 2)						
	Severe (Grade 3)						
At least one unsolicited adverse event	--						
At least one related unsolicited adverse event	Any Severity						
	Mild (Grade 1)						
	Moderate (Grade 2)						
	Severe (Grade 3)						
At least one severe (Grade 3) unsolicited adverse event	Any Relationship						
	Related						
	Not Related						
At least one serious adverse event[b]	--						
At least one related, serious adverse event[b]	--						
At least one adverse event leading to early termination[c]	--						
At least one medically attended adverse event	--						

Table 33: Overall Summary of Adverse Events - Safety Population *(continued)*

		Liquid AV7909 (N=X)		Lyophilized AV7909 (N=X)		All Subjects (N=X)	
Event Category[a]	**Subcategory[a]**	**n**	**%**	**n**	**%**	**n**	**%**
At least one adverse event of special interest[d]	--						

Notes: N = Number of subjects in the safety population.
[a] Subjects are counted once for each category regardless of the number of events.
[b] A listing of Serious Adverse Events is included in Section 14.3.2.
[c] As reported on the Adverse Event eCRF.
[d] The adverse events of special interest (AESIs) collected in this study are potentially immune-mediated medical conditions (PIMMCs).

Table 34: Adverse Events Occurring in 5% of Subjects in Any Study Arm by MedDRA System Organ Class and Preferred Term, and Study Arm - Safety Population

		Liquid AV7909 (N=X)			Lyophilized AV7909 (N=X)			All Subjects (N=X)		
MedDRA System Organ Class	**Preferred Term**	**n**	**%**	**Events**	**n**	**%**	**Events**	**n**	**%**	**Events**
Serious Adverse Events										
All	All	x	x	x	x	x	x	x	x	x
[SOC 1]	[PT 1]	x	x	x	x	x	x	x	x	x
	[PT 2]	x	x	x	x	x	x	x	x	x
[SOC 2]	[PT 1]	x	x	x	x	x	x	x	x	x
	[PT 2]	x	x	x	x	x	x	x	x	x
Other (Non-Serious) Adverse Events										
All	All	x	x	x	x	x	x	x	x	x
[SOC 1]	[PT 1]	x	x	x	x	x	x	x	x	x
	[PT 2]	x	x	x	x	x	x	x	x	x
[SOC 2]	[PT 1]	x	x	x	x	x	x	x	x	x
	[PT 2]	x	x	x	x	x	x	x	x	x
[SOC 3]	[PT 1]	x	x	x	x	x	x	x	x	x
	[PT 2]	x	x	x	x	x	x	x	x	x

Notes: N = Number of subjects in the safety population (number of subjects at risk); n = Number of subjects reporting event; Events = Total frequency of events reported.

14.3.1.1 Solicited Adverse Events

Table 35: Number and Percentage of Subjects Experiencing Solicited Events Post First Vaccination with 95% Confidence Intervals by Symptom and Study Arm - Safety Population

	Liquid AV7909 (N=X)		Lyophilized AV7909 (N=X)		All Subjects (N=X)	
Symptom	**n**	**% (95% CI)[a]**	**n**	**% (95% CI)[a]**	**n**	**% (95% CI)[a]**
All Symptoms						
Any Symptom	x	x (x.x, x.x)	x	x (x.x, x.x)	x	x (x.x, x.x)
Systemic Symptoms						
Any Systemic Symptom	x	x (x.x, x.x)	x	x (x.x, x.x)	x	x (x.x, x.x)
Fever	x	x (x.x, x.x)	x	x (x.x, x.x)	x	x (x.x, x.x)
Feverishness	x	x (x.x, x.x)	x	x (x.x, x.x)	x	x (x.x, x.x)
Fatigue						
Malaise						
Myalgia						
Arthralgia						
Headache						
Nausea						
Injection Site Symptoms						
Any Injection Site Symptom	x	x (x.x, x.x)	x	x (x.x, x.x)	x	x (x.x, x.x)
Pain	x	x (x.x, x.x)	x	x (x.x, x.x)	x	x (x.x, x.x)
Tenderness	x	x (x.x, x.x)	x	x (x.x, x.x)	x	x (x.x, x.x)
Pruritus						
Ecchymosis						
Ecchymosis (measurement)						
Erythema						

Table 35: Number and Percentage of Subjects Experiencing Solicited Events Post First Vaccination with 95% Confidence Intervals by Symptom and Study Arm - Safety Population *(continued)*

	Liquid AV7909 (N=X)		Lyophilized AV7909 (N=X)		All Subjects (N=X)	
Symptom	**n**	**% (95% CI)[a]**	**n**	**% (95% CI)[a]**	**n**	**% (95% CI)[a]**
Erythema (measurement)						
Edema/Induration						
Edema/Induration (measurement)						

Notes: N = Number of subjects in the safety population who received the first study vaccination; n = Number of subjects with reported event.
[a] Exact binomial confidence interval calculated using Clopper-Pearson methodology.

Tables with similar format:

Table 36: Number and Percentage of Subjects Experiencing Solicited Events Post Second Vaccination with 95% Confidence Intervals by Symptom and Study Arm - Safety Population

[Implementation Note: Update N footnote to "…who received the second study vaccination"]

Table 37: Number and Percentage of Subjects Experiencing Solicited Events Post Any Vaccination with 95% Confidence Intervals by Symptom and Study Arm - Safety Population

[Implementation Note: Update N footnote to "…who received any study vaccination"]

Table 38: Number and Percentage of Subjects Experiencing Solicited Events Post Any Vaccination by Symptom, Study Arm, and Sex - Safety Population

	Liquid AV7909 (N=X)				Lyophilized AV7909 (N=X)				All Subjects (N=X)			
	Female		Male		Female		Male		Female		Male	
Symptom	n	%	n	%	n	%	n	%	n	%	n	%
All Symptoms												
Any Symptom	x	x	x	x	x	x	x	x	x	x	x	x
Systemic Symptoms												
Any Systemic Symptom	x	x	x	x	x	x	x	x	x	x	x	x
Fever	x	x	x	x	x	x	x	x	x	x	x	x
Feverishness	x	x	x	x	x	x	x	x	x	x	x	x
Fatigue												
Malaise												
Myalgia												
Arthralgia												
Headache												
Nausea												
Injection Site Symptoms												
Any Injection Site Symptom	x	x	x	x	x	x	x	x	x	x	x	x
Pain	x	x	x	x	x	x	x	x	x	x	x	x
Tenderness	x	x	x	x	x	x	x	x	x	x	x	x
Pruritus												
Ecchymosis												
Ecchymosis (measurement)												
Erythema												
Erythema (measurement)												

Table 38: Number and Percentage of Subjects Experiencing Solicited Events Post Any Vaccination by Symptom, Study Arm, and Sex - Safety Population *(continued)*

	Liquid AV7909 (N=X)				Lyophilized AV7909 (N=X)				All Subjects (N=X)			
	Female		Male		Female		Male		Female		Male	
Symptom	n	%	n	%	n	%	n	%	n	%	n	%
Edema/Induration												
Edema/Induration (measurement)												

Notes: N = Number of subjects in the safety population who received the first study vaccination; n = Number of subjects with reported event.
[a] Exact binomial confidence interval calculated using Clopper-Pearson methodology.

Tables with similar format:

Table 39: Number and Percentage of Subjects Experiencing Solicited Events Post Any Vaccination by Symptom, Study Arm, and Age Category - Safety Population

[Implementation Note: Replace “Female” and “Male” with “Age 18-30” and “Age 31-45”.]

Table 40: Number and Percentage of Subjects Experiencing Solicited Events Post First Vaccination by Symptom, Maximum Severity and Study Arm - Safety Population

		Liquid AV7909 (N=X)		Lyophilized AV7909 (N=X)		All Subjects (N=X)	
Symptom	**Severity**	**n**	**% (95% CI)[a]**	**n**	**% (95% CI)[a]**	**n**	**% (95% CI)[a]**
All Symptoms							
Any Symptom	None	x	x (x.x, x.x)	x	x (x.x, x.x)	x	x (x.x, x.x)
	Mild						
	Moderate						
	Severe						
Systemic Symptoms							
Any Systemic Symptom	None	x	x (x.x, x.x)	x	x (x.x, x.x)	x	x (x.x, x.x)
	Mild						
	Moderate						
	Severe						
Fever	None	x	x (x.x, x.x)	x	x (x.x, x.x)	x	x (x.x, x.x)
	Mild						
	Moderate						
	Severe						
Feverishness	None	x	x (x.x, x.x)	x	x (x.x, x.x)	x	x (x.x, x.x)
	Mild						
	Moderate						
	Severe						
Fatigue	None	x	x (x.x, x.x)	x	x (x.x, x.x)	x	x (x.x, x.x)
	Mild						
	Moderate						
	Severe						
Malaise	None	x	x (x.x, x.x)	x	x (x.x, x.x)	x	x (x.x, x.x)
	Mild						

Table 40: Number and Percentage of Subjects Experiencing Solicited Events Post First Vaccination by Symptom, Maximum Severity and Study Arm – Safety Population *(continued)*

		Liquid AV7909 (N=X)		Lyophilized AV7909 (N=X)		All Subjects (N=X)	
Symptom	**Severity**	**n**	**% (95% CI)[a]**	**n**	**% (95% CI)[a]**	**n**	**% (95% CI)[a]**
	Moderate						
	Severe						
Myalgia	None	x	x (x.x, x.x)	x	x (x.x, x.x)	x	x (x.x, x.x)
	Mild						
	Moderate						
	Severe						
Arthralgia	None	x	x (x.x, x.x)	x	x (x.x, x.x)	x	x (x.x, x.x)
	Mild						
	Moderate						
	Severe						
Headache	None	x	x (x.x, x.x)	x	x (x.x, x.x)	x	x (x.x, x.x)
	Mild						
	Moderate						
	Severe						
Nausea	None	x	x (x.x, x.x)	x	x (x.x, x.x)	x	x (x.x, x.x)
	Mild						
	Moderate						
	Severe						
Injection Site Symptoms							
Any Injection Site Symptom	None	x	x (x.x, x.x)	x	x (x.x, x.x)	x	x (x.x, x.x)
	Mild						
	Moderate						
	Severe						
Pain	None	x	x (x.x, x.x)	x	x (x.x, x.x)	x	x (x.x, x.x)

Table 40: Number and Percentage of Subjects Experiencing Solicited Events Post First Vaccination by Symptom, Maximum Severity and Study Arm – Safety Population *(continued)*

		Liquid AV7909 (N=X)		Lyophilized AV7909 (N=X)		All Subjects (N=X)	
Symptom	**Severity**	**n**	**% (95% CI)[a]**	**n**	**% (95% CI)[a]**	**n**	**% (95% CI)[a]**
	Mild						
	Moderate						
	Severe						
Tenderness	None	x	x (x.x, x.x)	x	x (x.x, x.x)	x	x (x.x, x.x)
	Mild						
	Moderate						
	Severe						
Pruritus	None	x	x (x.x, x.x)	x	x (x.x, x.x)	x	x (x.x, x.x)
	Mild						
	Moderate						
	Severe						
Ecchymosis	None	x	x (x.x, x.x)	x	x (x.x, x.x)	x	x (x.x, x.x)
	Mild						
	Moderate						
	Severe						
Ecchymosis (measurement)	None	x	x (x.x, x.x)	x	x (x.x, x.x)	x	x (x.x, x.x)
	Mild						
	Moderate						
	Severe						
Erythema	None	x	x (x.x, x.x)	x	x (x.x, x.x)	x	x (x.x, x.x)
	Mild						
	Moderate						
	Severe						
Erythema (measurement)	None	x	x (x.x, x.x)	x	x (x.x, x.x)	x	x (x.x, x.x)

Table 40: Number and Percentage of Subjects Experiencing Solicited Events Post First Vaccination by Symptom, Maximum Severity and Study Arm – Safety Population *(continued)*

		Liquid AV7909 (N=X)		Lyophilized AV7909 (N=X)		All Subjects (N=X)	
Symptom	**Severity**	**n**	**% (95% CI)[a]**	**n**	**% (95% CI)[a]**	**n**	**% (95% CI)[a]**
	Mild						
	Moderate						
	Severe						
Edema/Induration	None	x	x (x.x, x.x)	x	x (x.x, x.x)	x	x (x.x, x.x)
	Mild						
	Moderate						
	Severe						
Edema/Induration (measurement)	None	x	x (x.x, x.x)	x	x (x.x, x.x)	x	x (x.x, x.x)
	Mild						
	Moderate						
	Severe						

Notes: N = Number of subjects in the safety population who received the first study vaccination; n = Number of subjects with reported event.
[a] Exact binomial confidence interval calculated using Clopper-Pearson methodology.

Tables with similar format:

Table 41: Number and Percentage of Subjects Experiencing Solicited Events Post Second Vaccination by Symptom, Maximum Severity, and Study Arm - Safety Population

[Implementation Note: Update N footnote to "…who received the second study vaccination"]

Table 42: Number and Percentage of Subjects Experiencing Solicited Events Post Any Vaccination by Symptom, Maximum Severity, and Study Arm - Safety Population

[Implementation Note: Update N footnote to "…who received any study vaccination"]

Table 43: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity, and Day Post First Vaccination - Liquid AV7909, Safety Population

Symptom	Severity	Pre-Dose		Post-Dose		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8+	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
All Symptoms																					
Any Symptom	None																				
	Mild																				
	Moderate																				
	Severe																				
Systemic Symptoms																					
Any Systemic Symptoms	None																				
	Mild																				
	Moderate																				
	Severe																				
Fever	None	N/A	N/A	N/A	N/A																
	Mild	N/A	N/A	N/A	N/A																
	Moderate	N/A	N/A	N/A	N/A																
	Severe	N/A	N/A	N/A	N/A																
Feverishness	None																				
	Mild																				
	Moderate																				
	Severe																				
Fatigue	None																				
	Mild																				
	Moderate																				
	Severe																				

Table 43: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity, and Day Post First Vaccination - Liquid AV7909, Safety Population *(continued)*

Symptom	Severity	Pre-Dose		Post-Dose		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8+	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Malaise	None																				
	Mild																				
	Moderate																				
	Severe																				
Myalgia	None																				
	Mild																				
	Moderate																				
	Severe																				
Arthralgia	None																				
	Mild																				
	Moderate																				
	Severe																				
Headache	None																				
	Mild																				
	Moderate																				
	Severe																				
Nausea	None																				
	Mild																				
	Moderate																				
	Severe																				
Injection Site Symptoms																					
Any Injection Site Symptom	None																				

Table 43: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity, and Day Post First Vaccination - Liquid AV7909, Safety Population *(continued)*

Symptom	Severity	Pre-Dose		Post-Dose		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8+	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Mild																				
	Moderate																				
	Severe																				
Pain	None																				
	Mild																				
	Moderate																				
	Severe																				
Tenderness	None																				
	Mild																				
	Moderate																				
	Severe																				
Pruritus	None																				
	Mild																				
	Moderate																				
	Severe																				
Ecchymosis	None																				
	Mild																				
	Moderate																				
	Severe																				
Ecchymosis (measurement)	None																				
	Mild																				
	Moderate																				

Table 43: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity, and Day Post First Vaccination - Liquid AV7909, Safety Population *(continued)*

Symptom	Severity	Pre-Dose		Post-Dose		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8+	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Severe																				
Erythema	None																				
	Mild																				
	Moderate																				
	Severe																				
Erythema (measurement)	None																				
	Mild																				
	Moderate																				
	Severe																				
Induration/Swelling	None																				
	Mild																				
	Moderate																				
	Severe																				
Induration/Swelling (measurement)	None																				
	Mild																				
	Moderate																				
	Severe																				

Notes: N = Number of subjects in the safety population who received the first study vaccination; n = Number of subjects with reported event.
Symptoms were solicited in clinic immediately before and after dosing ("Pre-Dose" and"Post-Dose" columns) and via Memory Aid over the following 8 days. The "Day 1" column refers to events reported on Day 1 via Memory Aid.
Severity is the maximum severity reported post dosing for each subject for each day.

Tables with similar format:

Table 44: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity, and Day Post First Vaccination - Lyophilized AV7909, Safety Population

Table 45: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity, and Day Post Second Vaccination - Liquid AV7909, Safety Population

[Implementation Note: Update N footnote to "…who received the second study vaccination"]

Table 46: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity, and Day Post Second Vaccination - Lyophilized AV7909, Safety Population

[Implementation Note: Update N footnote to "…who received the second study vaccination"]

Table 47: Number and Percentage of Subjects Experiencing Solicited Events for Dose 1 Compared with Dose 2 by Study Arm - Safety Population

Study Arm		Dose 2 - No Symptoms n (%)	Dose 2 - Mild or Greater Symptoms n (%)	Dose 2 - Total n (%)
Systemic Symptoms				
Liquid AV7909 (N=X)	Dose 1 - No Symptoms	x (%)	x (%)	x (%)
	Dose 1 - Mild or Greater Symptoms	x (%)	x (%)	x (%)
	Dose 1 - Total	x (%)	x (%)	x (100%)
Lyophilized AV7909 (N=X)	Dose 1 - No Symptoms	x (%)	x (%)	x (%)
	Dose 1 - Mild or Greater Symptoms	x (%)	x (%)	x (%)
	Dose 1 - Total	x (%)	x (%)	x (100%)
Injection Site Symptoms				
Liquid AV7909 (N=X)	Dose 1 - No Symptoms	x (%)	x (%)	x (%)
	Dose 1 - Mild or Greater Symptoms	x (%)	x (%)	x (%)
	Dose 1 - Total	x (%)	x (%)	x (100%)
Lyophilized AV7909 (N=X)	Dose 1 - No Symptoms	x (%)	x (%)	x (%)
	Dose 1 - Mild or Greater Symptoms	x (%)	x (%)	x (%)
	Dose 1 - Total	x (%)	x (%)	x (100%)

Notes: N = Number of subjects in the safety population; n = Number of subjects with reported event.
Denominators for percentages are the number of subjects in the safety population who received the first and second dose of study vaccination.

14.3.1.2 Unsolicited Adverse Events

Table 48: Number and Percentage of Subjects Experiencing Unsolicited Adverse Events with 95% Confidence Intervals by MedDRA System Organ Class and Preferred Term, and Study Arm - Safety Population

		Liquid AV7909 (N=X)			Lyophilized AV7909 (N=X)			All Subjects (N=X)		
MedDRA System Organ Class	**MedDRA Preferred Term**	**n**	**% (95% CI)[a]**	**Events**	**n**	**% (95% CI)[a]**	**Events**	**n**	**% (95% CI)[a]**	**Events**
Any SOC	Any PT	x	xx (xx.x, xx.x)	x	x	xx (xx.x, xx.x)	x	x	xx (xx.x, xx.x)	x
[SOC 1]	Any PT	x	xx (xx.x, xx.x)	x	x	xx (xx.x, xx.x)	x	x	xx (xx.x, xx.x)	x
	[PT 1]	x	xx (xx.x, xx.x)	x	x	xx (xx.x, xx.x)	x	x	xx (xx.x, xx.x)	x
	[PT 2]									
[SOC 2]	Any PT									
	[PT 1]									
	[PT 2]									

Notes: N = Number of subjects in the safety population; n = Number of subjects with reported event; Events = Total frequency of events reported.
[a] Exact binomial confidence interval calculated using Clopper-Pearson methodology.

Table 49: Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Maximum Severity, Relationship, and Study Arm - Safety Population

			Liquid AV7909 (N = X)						Lyophilized AV7909 (N = X)						All Subjects (N = X)					
			Related		Not Related		Total		Related		Not Related		Total		Related		Not Related		Total	
MedDRA System Organ Class	MedDRA Preferred Term	Severity	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Any SOC	Any PT	Any Severity	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Moderate	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Severe	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
[SOC 1]	[PT 1]	Any Severity	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Mild	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
		Moderate																		
		Severe																		
	[PT 2]	Any Severity																		
		Mild																		
		Moderate																		
		Severe																		

Notes: N = Number of subjects in the safety population; n = Number of subjects with reported event.
For severity, a subject is counted only once per preferred term and is summarized according to their highest severity.
For relationship, a subject is counted only once per preferred term and is summarized according to their closest relationship.

Table 50: Number and Percentage of Subjects Experiencing Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Severity, and Relationship - Safety Population

				Severity						Relationship to Treatment			
		Any Incidence		Mild		Moderate		Severe		Not Related		Related	
MedDRA System Organ Class	MedDRA Preferred Term	n	%	n	%	n	%	n	%	n	%	n	%
Liquid AV7909 (N=X)													
Any SOC	Any PT	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
[SOC 1]	Any PT	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	[PT 1]	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	[PT 2]												
[SOC 2]	Any PT												
	[PT 1]												
	[PT 2]												
Lyophilized AV7909 (N=X)													
Any SOC	Any PT	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
[SOC 1]	Any PT	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	[PT 1]	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	[PT 2]												
[SOC 2]	Any PT												
	[PT 1]												
	[PT 2]												

Notes: N = Number of subjects in the safety population; n = Number of subjects with reported event.
A subject is counted only once per PT and is summarized according to their highest severity and closest relationship.

14.3.2 Listing of Deaths, Other Serious and Significant Adverse Events

Table 51: Listing of Serious Adverse Events - Safety Population

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

Table 52: Listing of Non-Serious, Unsolicited, Moderate or Severe Adverse Events - Safety Population

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	Subject Discontinued Due to AE?	Outcome	MedDRA System Organ Class	MedDRA Preferred Term
Subject ID: , Study Arm: , AE Number:										
Comments:										
Subject ID: , Study Arm: , AE Number:										
Comments:										

Table 53: Listing of Other Significant Adverse Events - Safety Population

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

14.3.3 Narratives of Deaths, Other Serious and Significant Adverse Events

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

14.3.4 Abnormal Laboratory Value Listings (by Subject)

Table 54: Listing of Abnormal Laboratory Results - Chemistry, Safety Population

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

Table 55: Listing of Abnormal Laboratory Results - Hematology, Safety Population

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

Table 56: Listing of Abnormal Laboratory Results - Urinalysis, Safety Population

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

14.3.5 Displays of Laboratory Results

14.3.5.1 Chemistry Results

[General Implementation Note: Red text is included as a placeholder; this text should NOT be included in the following tables unless instructed in the individual table's corresponding implementation note.]

Table 57: Laboratory Results by Parameter, Maximum Severity, Study Day, and Study Arm - Any Chemistry Parameter, Safety Population

[Implementation Note:
1) Include "Day 64[a] " rows.
2) Include footnote, "AST and random glucose collection were no longer required following the finalization of protocol version 4.0."
3) Include footnote, "[a] Safety laboratories are not scheduled for collection at Day 64, but any results collected at this visit are reported."]

			None		Mild / Grade 1		Moderate / Grade 2		Severe / Grade 3	
Study Day	**Study Arm**	**N**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Baseline (Pre-Vaccination)	Liquid AV7909	x	x	xx	x	xx	x	xx	x	xx
	Lyophilized AV7909									
Day 29	Liquid AV7909									
	Lyophilized AV7909									
Day 64[a]	Liquid AV7909									
	Lyophilized AV7909									
Max Severity Post Baseline	Liquid AV7909									
	Lyophilized AV7909									

Notes: N = Number of subjects in the safety population with available data at the corresponding time point; N is the denominator for percentages.
The "Max Severity Post Baseline" rows indicate the maximum severity experienced by each subject at any time point post baseline, including unscheduled assessments. If a subject has only ungraded results post baseline, their maximum severity is considered "None".
[LAB NAME] collection was no longer required following the finalization of protocol version 4.0.
[a] Safety laboratories are not scheduled for collection at Day 64, but any results collected at this visit are reported.

Tables with similar format:

Table 58: Laboratory Results by Parameter, Maximum Severity, Study Day, and Study Arm - Alkaline Phosphatase (ALP), Safety Population

Table 59: Laboratory Results by Parameter, Maximum Severity, Study Day, and Study Arm - Alanine Transaminase (ALT), Safety Population

Table 60: Laboratory Results by Parameter, Maximum Severity, Study Day, and Study Arm - Aspartate Aminotransferase (AST), Safety Population

[Implementation Note: Include footnote, "AST collection was no longer required following the finalization of protocol version 4.0."]

Table 61: Laboratory Results by Parameter, Maximum Severity, Study Day, and Study Arm - Total Bilirubin, Safety Population

Table 62: Laboratory Results by Parameter, Maximum Severity, Study Day, and Study Arm -Blood Urea Nitrogen (BUN), Safety Population

Table 63: Laboratory Results by Parameter, Maximum Severity, Study Day, and Study Arm - Creatinine, Safety Population

Table 64: Laboratory Results by Parameter, Maximum Severity, Study Day, and Study Arm - Random Glucose, Safety Population

[Implementation Notes:
1) Include "Day 64[a]" rows.
2) Include footnote, "Random glucose collection was no longer required following the finalization of protocol version 4.0."
3) Include footnote, "[a] Safety laboratories are not scheduled for collection at Day 64, but any results collected at this visit are reported."]

Table 65: Abnormal Chemistry Results Related to Study Treatment by Parameter, Maximum Severity, Study Day, and Study Arm - Safety Population

[Implementation Note: If there are any subjects with related abnormal lab results at Day 64, include Day 64 rows where applicable, and add the footnote, "Safety laboratories are not scheduled for collection at Day 64, but any results collected at this visit are reported."]

				Mild / Grade 1		Moderate / Grade 2		Severe / Grade 3	
Laboratory Parameter	**Study Day**	**Study Arm**	**N**	**n**	**%**	**n**	**%**	**n**	**%**
Any Chemistry Parameter	Day 29	Liquid AV7909	x	x	xx	x	xx	x	xx
		Lyophilized AV7909							
	Max Severity Post Baseline	Liquid AV7909							
		Lyophilized AV7909							
Alkaline Phosphatase	Day 29	Liquid AV7909							
		Lyophilized AV7909							
	Max Severity Post Baseline	Liquid AV7909							
		Lyophilized AV7909							
Alanine Transaminase	Day 29	Liquid AV7909							
		Lyophilized AV7909							
	Max Severity Post Baseline	Liquid AV7909							
		Lyophilized AV7909							
Aspartate Aminotransferase	Day 29	Liquid AV7909							
		Lyophilized AV7909							
	Max Severity Post Baseline	Liquid AV7909							
		Lyophilized AV7909							
Total Bilirubin	Day 29	Liquid AV7909							
		Lyophilized AV7909							
	Max Severity Post Baseline	Liquid AV7909							
		Lyophilized AV7909							
Blood Urea Nitrogen	Day 29	Liquid AV7909							

Table 65: Abnormal Chemistry Results Related to Study Treatment by Parameter, Maximum Severity, Study Day, and Study Arm - Safety Population *(continued)*

				Mild / Grade 1		Moderate / Grade 2		Severe / Grade 3	
Laboratory Parameter	**Study Day**	**Study Arm**	**N**	**n**	**%**	**n**	**%**	**n**	**%**
		Lyophilized AV7909							
	Max Severity Post Baseline	Liquid AV7909							
		Lyophilized AV7909							
Creatinine	Day 29	Liquid AV7909							
		Lyophilized AV7909							
	Max Severity Post Baseline	Liquid AV7909							
		Lyophilized AV7909							
Random Glucose	Day 29	Liquid AV7909							
		Lyophilized AV7909							
	Max Severity Post Baseline	Liquid AV7909							
		Lyophilized AV7909							

Notes: N = Number of subjects in the safety population with available data at the corresponding time point; N is the denominator for percentages.
The "Max Severity Post Baseline" rows indicate the maximum severity experienced by each subject at any time point post baseline, including unscheduled assessments. If a subject has only ungraded results post baseline, their maximum severity is considered "None".
AST and random glucose collection were no longer required following the finalization of protocol version 4.0.

Table 66: Chemistry Summary Statistics by Parameter, Study Day, and Study Arm - Safety Population

Laboratory Parameter (Units)	Study Day	Study Arm	N	Mean	Standard Deviation	Median	Min, Max
Alkaline Phosphatase (U/L)	Baseline	Liquid AV7909					
		Lyophilized AV7909					
	Day 29	Liquid AV7909					
		Lyophilized AV7909					
	Day 29 Change from Baseline	Liquid AV7909					
		Lyophilized AV7909					
Alanine Transaminase (U/L)	Baseline	Liquid AV7909					
		Lyophilized AV7909					
	Day 29	Liquid AV7909					
		Lyophilized AV7909					
	Day 29 Change from Baseline	Liquid AV7909					
		Lyophilized AV7909					
Aspartate Aminotransferase (U/L)	Baseline	Liquid AV7909					
		Lyophilized AV7909					
	Day 29	Liquid AV7909					
		Lyophilized AV7909					
	Day 29 Change from Baseline	Liquid AV7909					
		Lyophilized AV7909					
Total Bilirubin (mg/dL)	Baseline	Liquid AV7909					
		Lyophilized AV7909					
	Day 29	Liquid AV7909					
		Lyophilized AV7909					
	Day 29 Change from Baseline	Liquid AV7909					
		Lyophilized AV7909					
Blood Urea Nitrogen (mg/dL)	Baseline	Liquid AV7909					

Table 66: Chemistry Summary Statistics by Parameter, Study Day, and Study Arm - Safety Population *(continued)*

Laboratory Parameter (Units)	Study Day	Study Arm	N	Mean	Standard Deviation	Median	Min, Max
		Lyophilized AV7909					
	Day 29	Liquid AV7909					
		Lyophilized AV7909					
	Day 29 Change from Baseline	Liquid AV7909					
		Lyophilized AV7909					
Creatinine (mg/dL)	Baseline	Liquid AV7909					
		Lyophilized AV7909					
	Day 29	Liquid AV7909					
		Lyophilized AV7909					
	Day 29 Change from Baseline	Liquid AV7909					
		Lyophilized AV7909					
Random Glucose (mg/dL)	Baseline	Liquid AV7909					
		Lyophilized AV7909					
	Day 29	Liquid AV7909					
		Lyophilized AV7909					
	Day 29 Change from Baseline	Liquid AV7909					
		Lyophilized AV7909					

Notes: N = Number of subjects in the safety population with available data at the corresponding timepoint.
AST and random glucose collection were no longer required following the finalization of protocol version 4.0.

14.3.5.2 Hematology Results

[General Implementation Note: Red text is included as a placeholder; this text should NOT be included in the following tables unless instructed in the individual table's corresponding implementation note.]

Table 67: Laboratory Results by Parameter, Maximum Severity, Study Day, and Study Arm - Any Hematology Parameter, Safety Population

[Implementation Notes:
1) Include "Day 64[a] " rows.
2) Include footnote, "[a] Safety laboratories are not scheduled for collection at Day 64, but any results collected at this visit are reported."]

			None		Mild / Grade 1		Moderate / Grade 2		Severe / Grade 3	
Study Day	**Study Arm**	**N**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Baseline (Pre-Vaccination)	Liquid AV7909	x	x	xx	x	xx	x	xx	x	xx
	Lyophilized AV7909									
Day 29	Liquid AV7909									
	Lyophilized AV7909									
Day 64[a]	Liquid AV7909									
	Lyophilized AV7909									
Max Severity Post Baseline	Liquid AV7909									
	Lyophilized AV7909									

Notes: N = Number of subjects in the safety population with available data at the corresponding time point; N is the denominator for percentages.
The "Max Severity Post Baseline" rows indicate the maximum severity experienced by each subject at any time point post baseline, including unscheduled assessments. If a subject has only ungraded results post baseline, their maximum severity is considered "None".
[a] Safety laboratories are not scheduled for collection at Day 64, but any results collected at this visit are reported.

Tables with similar format:

Table 68: Laboratory Results by Parameter, Maximum Severity, Study Day, and Study Arm - Hemoglobin, Safety Population

[Implementation Notes:
1) Include "Day 64[a] " rows.
2) Include footnote, "[a] Safety laboratories are not scheduled for collection at Day 64, but any results collected at this visit are reported."]

Table 69: Laboratory Results by Parameter, Maximum Severity, Study Day, and Study Arm - Hemoglobin Decrease from Baseline, Safety Population

[Implementation Notes:
1) Include "Day 64[a] " rows.
2) Include footnote, "[a] Safety laboratories are not scheduled for collection at Day 64, but any results collected at this visit are reported."]

Table 70: Laboratory Results by Parameter, Maximum Severity, Study Day, and Study Arm - Platelets, Safety Population

Table 71: Laboratory Results by Parameter, Maximum Severity, Study Day, and Study Arm - Absolute Eosinophil Count, Safety Population

Table 72: Laboratory Results by Parameter, Maximum Severity, Study Day, and Study Arm - Absolute Neutrophil Count, Safety Population

Table 73: Laboratory Results by Parameter, Maximum Severity, Study Day, and Study Arm - White Blood Cells, Safety Population

			None		Mild / Grade 1				Moderate / Grade 2				Severe / Grade 3			
					Low		High		Low		High		Low		High	
Study Day	**Study Arm**	**N**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Baseline (Pre-Vaccination)	Liquid AV7909	x	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Lyophilized AV7909															
Day 29	Liquid AV7909															
	Lyophilized AV7909															
Day 64[a]	Liquid AV7909															
	Lyophilized AV7909															
Max Severity Post Baseline	Liquid AV7909															
	Lyophilized AV7909															

Notes: N = Number of subjects in the safety population with available data at the corresponding time point; N is the denominator for percentages.
The "Max Severity Post Baseline" rows indicate the maximum severity experienced by each subject at any time point post baseline, including unscheduled assessments. If a subject has only ungraded results post baseline, their maximum severity is considered "None".
[a] Safety laboratories are not scheduled for collection at Day 64, but any results collected at this visit are reported.

Table 74: Abnormal Hematology Results Related to Study Treatment by Parameter, Maximum Severity, Study Day, and Study Arm - Safety Population

[Implementation Note: If there are any subjects with related abnormal lab results at Day 64, include Day 64 rows where applicable, and add the footnote, "Safety laboratories are not scheduled for collection at Day 64, but any results collected at this visit are reported."]

				Mild / Grade 1		Moderate / Grade 2		Severe / Grade 3	
Laboratory Parameter	**Study Day**	**Study Arm**	**N**	**n**	**%**	**n**	**%**	**n**	**%**
Any Hematology Parameter	Day 29	Liquid AV7909	x	x	xx	x	xx	x	xx
		Lyophilized AV7909							
	Max Severity Post Baseline	Liquid AV7909							
		Lyophilized AV7909							
Hemoglobin	Day 29	Liquid AV7909							
		Lyophilized AV7909							
	Max Severity Post Baseline	Liquid AV7909							
		Lyophilized AV7909							
Hemoglobin Decrease from Baseline	Day 29	Liquid AV7909							
		Lyophilized AV7909							
	Max Severity Post Baseline	Liquid AV7909							
		Lyophilized AV7909							
Platelets	Day 29	Liquid AV7909							
		Lyophilized AV7909							
	Max Severity Post Baseline	Liquid AV7909							
		Lyophilized AV7909							
White Blood Cells - High (Leukocytosis)	Day 29	Liquid AV7909							
		Lyophilized AV7909							
	Max Severity Post Baseline	Liquid AV7909							
		Lyophilized AV7909							

Table 74: Abnormal Hematology Results Related to Study Treatment by Parameter, Maximum Severity, Study Day, and Study Arm - Safety Population *(continued)*

				Mild / Grade 1		Moderate / Grade 2		Severe / Grade 3	
Laboratory Parameter	**Study Day**	**Study Arm**	**N**	**n**	**%**	**n**	**%**	**n**	**%**
White Blood Cells - Low (Leukopenia)	Day 29	Liquid AV7909							
		Lyophilized AV7909							
	Max Severity Post Baseline	Liquid AV7909							
		Lyophilized AV7909							
Absolute Eosinphil Count	Day 29	Liquid AV7909							
		Lyophilized AV7909							
	Max Severity Post Baseline	Liquid AV7909							
		Lyophilized AV7909							
Absolute Neutrophil Count	Day 29	Liquid AV7909							
		Lyophilized AV7909							
	Max Severity Post Baseline	Liquid AV7909							
		Lyophilized AV7909							

Notes: N = Number of subjects in the safety population with available data at the corresponding time point; N is the denominator for percentages.
The "Max Severity Post Baseline" rows indicate the maximum severity experienced by each subject at any time point post baseline, including unscheduled assessments. If a subject has only ungraded results post baseline, their maximum severity is considered "None".

Table 75: Hematology Summary Statistics by Parameter, Study Day, and Study Arm - Safety Population

Laboratory Parameter (Units)	Study Day	Study Arm	N	Mean	Standard Deviation	Median	Min, Max
Hemoglobin (g/dL)	Baseline	Liquid AV7909					
		Lyophilized AV7909					
	Day 29	Liquid AV7909					
		Lyophilized AV7909					
	Day 29 Change from Baseline	Liquid AV7909					
		Lyophilized AV7909					
Hemoglobin Decrease from Baseline (g/dL)	Baseline	Liquid AV7909					
		Lyophilized AV7909					
	Day 29	Liquid AV7909					
		Lyophilized AV7909					
	Day 29 Change from Baseline	Liquid AV7909					
		Lyophilized AV7909					
Platelets (cells/mm^3)	Baseline	Liquid AV7909					
		Lyophilized AV7909					
	Day 29	Liquid AV7909					
		Lyophilized AV7909					
	Day 29 Change from Baseline	Liquid AV7909					
		Lyophilized AV7909					
White Blood Cells (cells/mm^3)	Baseline	Liquid AV7909					
		Lyophilized AV7909					
	Day 29	Liquid AV7909					
		Lyophilized AV7909					
	Day 29 Change from Baseline	Liquid AV7909					
		Lyophilized AV7909					
	Baseline	Liquid AV7909					

Table 75: Hematology Summary Statistics by Parameter, Study Day, and Study Arm - Safety Population *(continued)*

Laboratory Parameter (Units)	Study Day	Study Arm	N	Mean	Standard Deviation	Median	Min, Max
Absolute Eosinphil Count (cells/mm^3)		Lyophilized AV7909					
	Day 29	Liquid AV7909					
		Lyophilized AV7909					
	Day 29 Change from Baseline	Liquid AV7909					
		Lyophilized AV7909					
Absolute Neutrophil Count (cells/mm^3)	Baseline	Liquid AV7909					
		Lyophilized AV7909					
	Day 29	Liquid AV7909					
		Lyophilized AV7909					
	Day 29 Change from Baseline	Liquid AV7909					
		Lyophilized AV7909					
Notes: N = Number of enrolled subjects in the safety population with available data at the corresponding timepoint.							

14.3.5.3 Urinalysis Results

[General Implementation Note: Red text is included as a placeholder; this text should NOT be included in the following tables unless instructed in the individual table's corresponding implementation note.]

Table 76: Laboratory Results by Parameter, Maximum Severity, Study Day, and Study Arm - Any Urinalysis Parameter, Safety Population

[Implementation Note:
1) Include "Day 64[a] " rows.
2) Include footnote, "Urine protein and urine glucose collection were no longer required following the finalization of protocol version 4.0."
3) Include footnote, "[a] Safety laboratories are not scheduled for collection at Day 64, but any results collected at this visit are reported."]

			None		Mild / Grade 1		Moderate / Grade 2		Severe / Grade 3	
Study Day	**Study Arm**	**N**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Baseline (Pre-Vaccination)	Liquid AV7909	x	x	xx	x	xx	x	xx	x	xx
	Lyophilized AV7909									
Day 29	Liquid AV7909									
	Lyophilized AV7909									
Day 64[a]	Liquid AV7909									
	Lyophilized AV7909									
Max Severity Post Baseline	Liquid AV7909									
	Lyophilized AV7909									

Notes: N = Number of subjects in the safety population with available data at the corresponding time point; N is the denominator for percentages.
The "Max Severity Post Baseline" rows indicate the maximum severity experienced by each subject at any time point post baseline, including unscheduled assessments. If a subject has only ungraded results post baseline, their maximum severity is considered "None".
[LAB NAME] collection was no longer required following the finalization of protocol version 4.0.
[a] Safety laboratories are not scheduled for collection at Day 64, but any results collected at this visit are reported.

Tables with similar format:

Table 77: Laboratory Results by Parameter, Maximum Severity, Study Day, and Study Arm - Urine Protein, Safety Population

[Implementation Notes:
1) Include "Day 64[a] " rows.
2) Include footnote, "Urine protein collection was no longer required following the finalization of protocol version 4.0."
3) Include footnote, "[a] Safety laboratories are not scheduled for collection at Day 64, but any results collected at this visit are reported."]

Table 78: Laboratory Results by Parameter, Maximum Severity, Study Day, and Study Arm - Urine Glucose, Safety Population

[Implementation Notes:
1) Include "Day 64[a] " rows.
2) Include footnote, "Urine glucose collection was no longer required following the finalization of protocol version 4.0."
3) Include footnote, "[a] Safety laboratories are not scheduled for collection at Day 64, but any results collected at this visit are reported."]

Table 79: Abnormal Urinalysis Results Related to Study Treatment by Parameter, Maximum Severity, Study Day, and Study Arm - Safety Population

[Implementation Note: If there are any subjects with related abnormal lab results at Day 64, include Day 64 rows where applicable, and add the footnote, "Safety laboratories are not scheduled for collection at Day 64, but any results collected at this visit are reported."]

				Mild / Grade 1		Moderate / Grade 2		Severe / Grade 3	
Laboratory Parameter	**Study Day**	**Study Arm**	**N**	**n**	**%**	**n**	**%**	**n**	**%**
Any Urinalysis Parameter	Day 29	Liquid AV7909	x	x	xx	x	xx	x	xx
		Lyophilized AV7909							
	Max Severity Post Baseline	Liquid AV7909							
		Lyophilized AV7909							
Urine Protein	Day 29	Liquid AV7909							
		Lyophilized AV7909							
	Max Severity Post Baseline	Liquid AV7909							
		Lyophilized AV7909							
Urine Glucose	Day 29	Liquid AV7909							
		Lyophilized AV7909							
	Max Severity Post Baseline	Liquid AV7909							
		Lyophilized AV7909							

Notes: N = Number of subjects in the safety population with available data at the corresponding time point; N is the denominator for percentages.
The "Max Severity Post Baseline" rows indicate the maximum severity experienced by each subject at any time point post baseline, including unscheduled assessments. If a subject has only ungraded results post baseline, their maximum severity is considered "None".

Table 80: Urinalysis Summary Statistics by Parameter, Study Day, and Study Arm - Safety Population

Laboratory Parameter (Units)	Study Day	Study Arm	N	Mean	Standard Deviation	Median	Min, Max
Urine Protein	Baseline	Liquid AV7909					
		Lyophilized AV7909					
	Day 29	Liquid AV7909					
		Lyophilized AV7909					
	Day 29 Change from Baseline	Liquid AV7909					
		Lyophilized AV7909					
Urine Glucose	Baseline	Liquid AV7909					
		Lyophilized AV7909					
	Day 29	Liquid AV7909					
		Lyophilized AV7909					
	Day 29 Change from Baseline	Liquid AV7909					
		Lyophilized AV7909					

Notes: N = Number of enrolled subjects in the safety population with available data at the corresponding timepoint.
Urine protein and urine glucose collection were no longer required following the finalization of protocol version 4.0.

14.3.6 Displays of Vital Signs

Table 81: Vital Signs by Assessment, Maximum Severity, Study Day, and Study Arm - Any Assessment, Safety Population

Study Day	Study Arm	N	None		Mild		Moderate		Severe	
			n	%	n	%	n	%	n	%
Baseline	Liquid AV7909	x	x	xx	x	xx	x	xx	x	xx
	Lyophilized AV7909									
Day 15	Liquid AV7909									
	Lyophilized AV7909									
Max Severity Post Baseline	Liquid AV7909									
	Lyophilized AV7909									

Notes: N = Number of subjects in the safety population with available data at the corresponding time point; N is the denominator for percentages.
The "Max Severity Post Baseline" rows indicate the maximum severity experienced by each subject at any time point post baseline, including unscheduled assessments. If a subject has only ungraded results post baseline, their maximum severity is considered "None".

Table with similar format:

Table 82: Vital Signs by Assessment, Maximum Severity, Study Day, and Study Arm - Oral Temperature, Safety Population

[Implementation Note: Report only temperatures recorded on the vital signs form.]

Table 83: Vital Signs by Assessment, Maximum Severity, Study Day, and Study Arm - Systolic Blood Pressure, Safety Population

Study Day	Study Arm	N	None		Mild (Low)		Mild (High)		Moderate (Low)		Moderate (High)		Severe (Low)		Severe (High)	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%
Baseline	Liquid AV7909	x	x	xx	x							xx	x	xx	x	xx
	Lyophilized AV7909															
Day 15	Liquid AV7909															
	Lyophilized AV7909															
Max Severity Post Baseline	Liquid AV7909															
	Lyophilized AV7909															

Notes: N = Number of subjects in the safety population with available data at the corresponding time point; N is the denominator for percentages.
The "Max Severity Post Baseline" rows indicate the maximum severity experienced by each subject at any time point post baseline, including unscheduled assessments. If a subject has only ungraded results post baseline, their maximum severity is considered "None".

Tables with similar format:

Table 84: Vital Signs by Assessment, Maximum Severity, Study Day, and Study Arm - Diastolic Blood Pressure, Safety Population

Table 85: Vital Signs by Assessment, Maximum Severity, Study Day, and Study Arm - Pulse, Safety Population

14.4 Summary of Concomitant Medications

Table 86: Number and Percentage of Subjects with Prior and Concurrent Medications by WHO Drug Classification and Study Arm - Safety Population

WHO Drug Code Level 1, Anatomic Group	WHO Drug Code Level 2, Therapeutic Subgroup	Liquid AV7909 (N=X)		Lyophilized AV7909 (N=X)		All Subjects (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]						

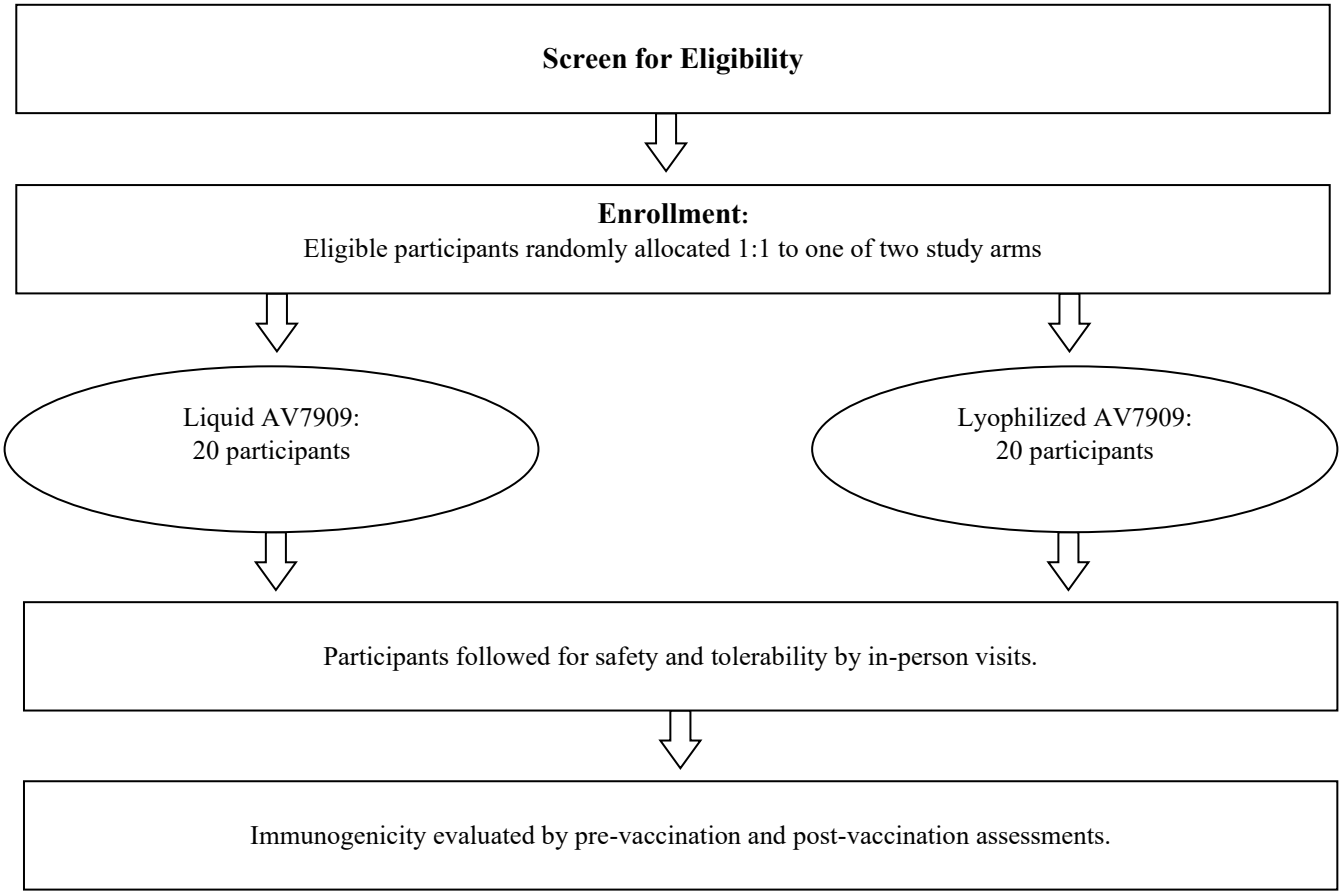
N = Number of subjects in the safety population; n = Number of subjects reporting taking at least one medication in the specific WHO Drug Class.

APPENDIX 2. FIGURE MOCK-UPS

[General Implementation Notes: In all figures, study arms should be displayed in the following order: Liquid AV7909, Lyophilized AV7909. In plots separated by study arm, the Liquid AV7909 arm should be colored blue, and the Lyophilized AV7909 arm should be colored red.]

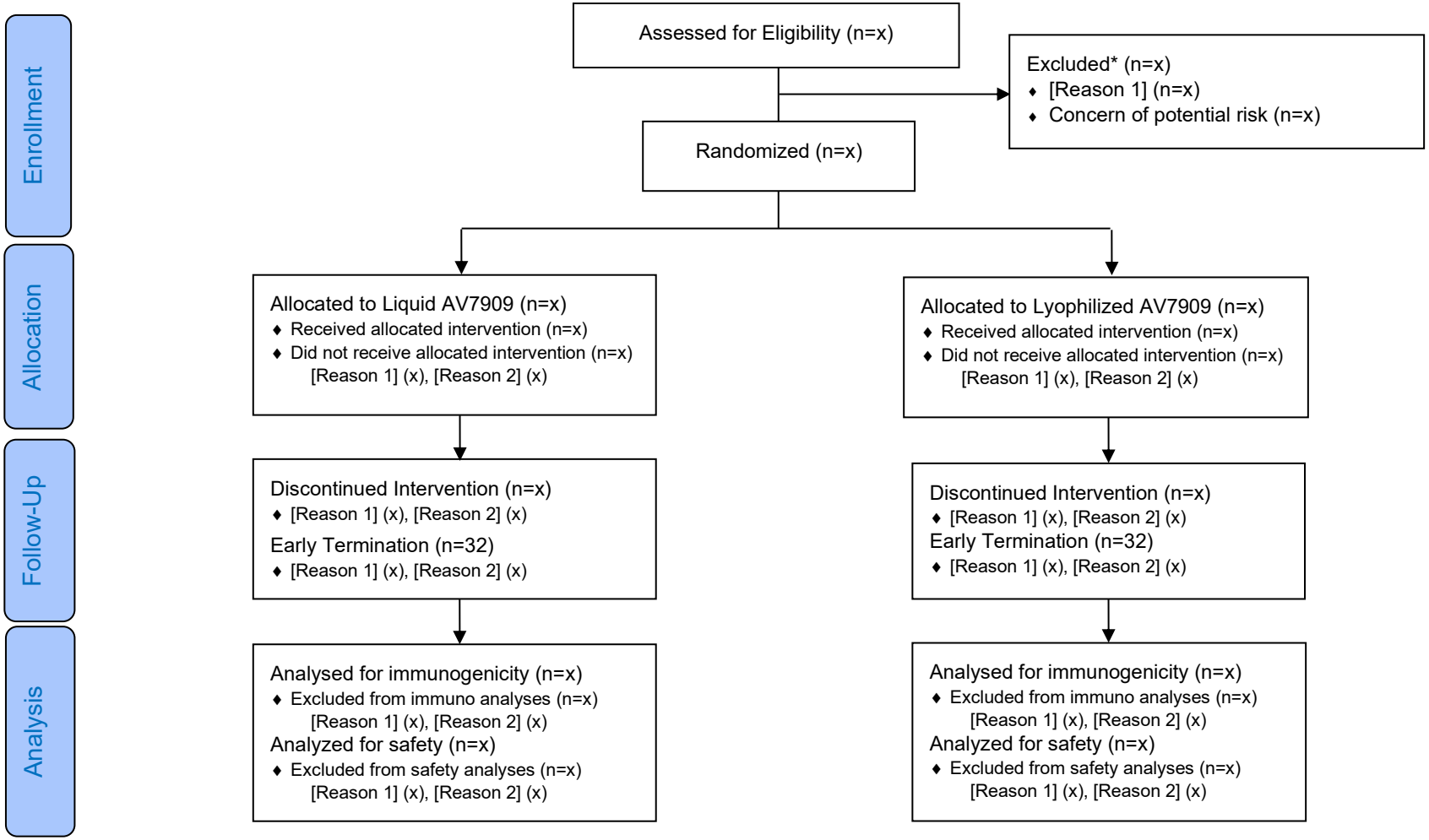
LIST OF FIGURES

Figure 1: Schematic of Study Design



10.1 Disposition of Subjects

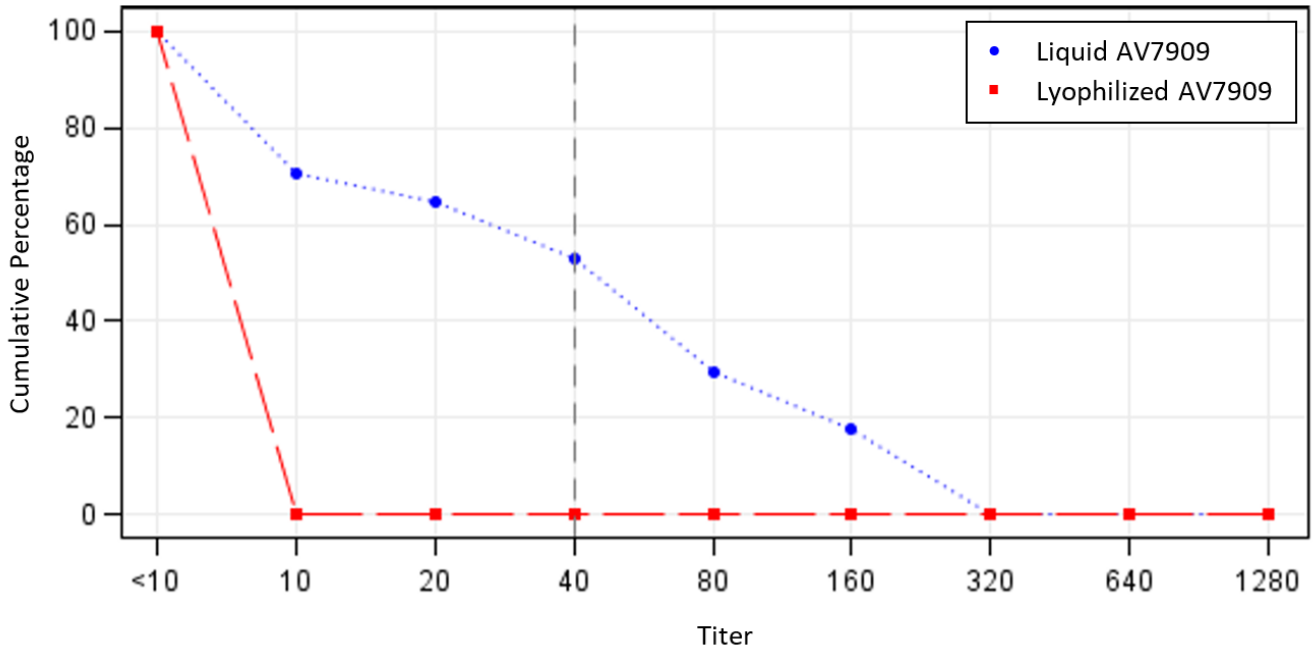
Figure 2: CONSORT Flow Diagram



14.2.2 Immunogenicity Response Figures by Measure, Vaccination, and Study Day

Figure 3: Reverse Cumulative Distribution of TNA ED_{50} by Study Day and Study Arm - Modified Intent-to-Treat Population

[Implementation Note: A generic sample figure is shown below. The RCD curves should be presented in a single figure with eight separate panels for timepoint (Days 1, 8, 15, 22, 29, 64, 195, and 380). Visit labels should be included in the panel headers. Within each panel, individual curves should be used for each study arm (two curves). Each study arm should have a separate color and marker shape.]



Figures with similar format:

Figure 4: Reverse Cumulative Distribution of TNA ED_{50} by Study Day and Study Arm - Per Protocol Population

Figure 5: Reverse Cumulative Distribution of TNA NF_{50} by Study Day and Study Arm - Modified Intent-to-Treat Population

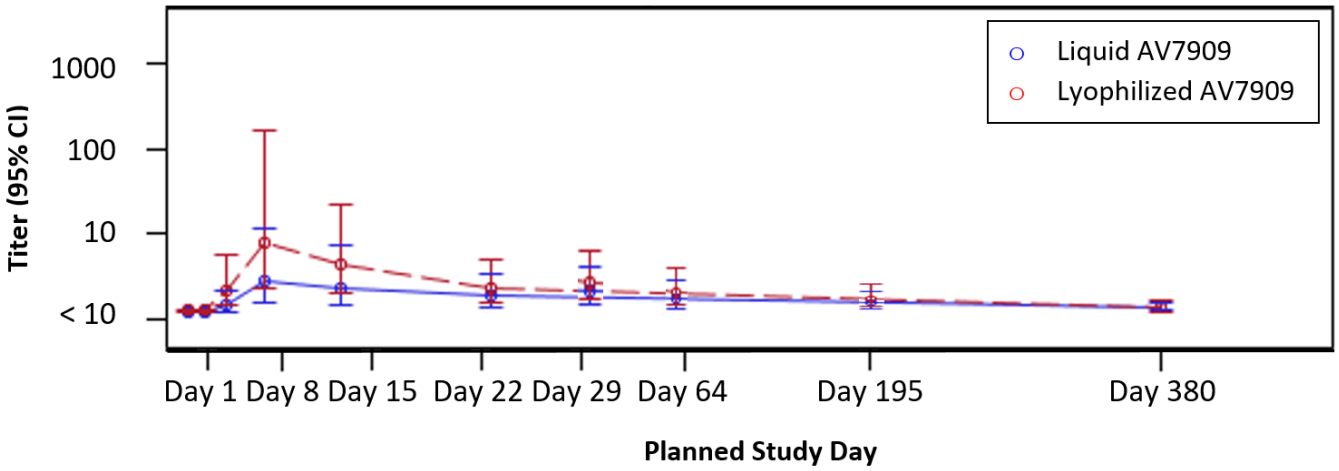
Figure 6: Reverse Cumulative Distribution of TNA NF_{50} by Study Day and Study Arm - Per Protocol Population

Figure 7: Reverse Cumulative Distribution of anti-PA IgG by Study Day and Study Arm - Modified Intent-to-Treat Population

Figure 8: Reverse Cumulative Distribution of anti-PA IgG by Study Day and Study Arm - Per Protocol Population

Figure 9: Geometric Mean Titers of TNA ED_{50} by Study Day and Study Arm - Modified Intent-to-Treat Population

[Implementation Note: A generic sample figure is shown below. Planned Study Day (Days 1, 8, 15, 22, 29, 64, 195, and 380) is plotted along the x-axis, with visit labels as tick labels. Geometric mean titer/concentration is plotted on the y-axis; the y-axis scale will be determined based on the distribution of the data distributed. Geometric mean titer /concentration should be plotted at each visit with upper and lower error bars for the 95% CI for each study arm with different marker shapes/colors for each study arm. Each study arm should have a separate color and marker shape.]



Figures with similar format:

Figure 10: Geometric Mean Titers of TNA ED_{50} by Study Day and Study Arm - Per Protocol Population

Figure 11: Geometric Mean Titers of TNA NF_{50} by Study Day and Study Arm - Modified Intent-to-Treat Population

Figure 12: Geometric Mean Titers of TNA NF_{50} by Study Day and Study Arm - Per Protocol Population

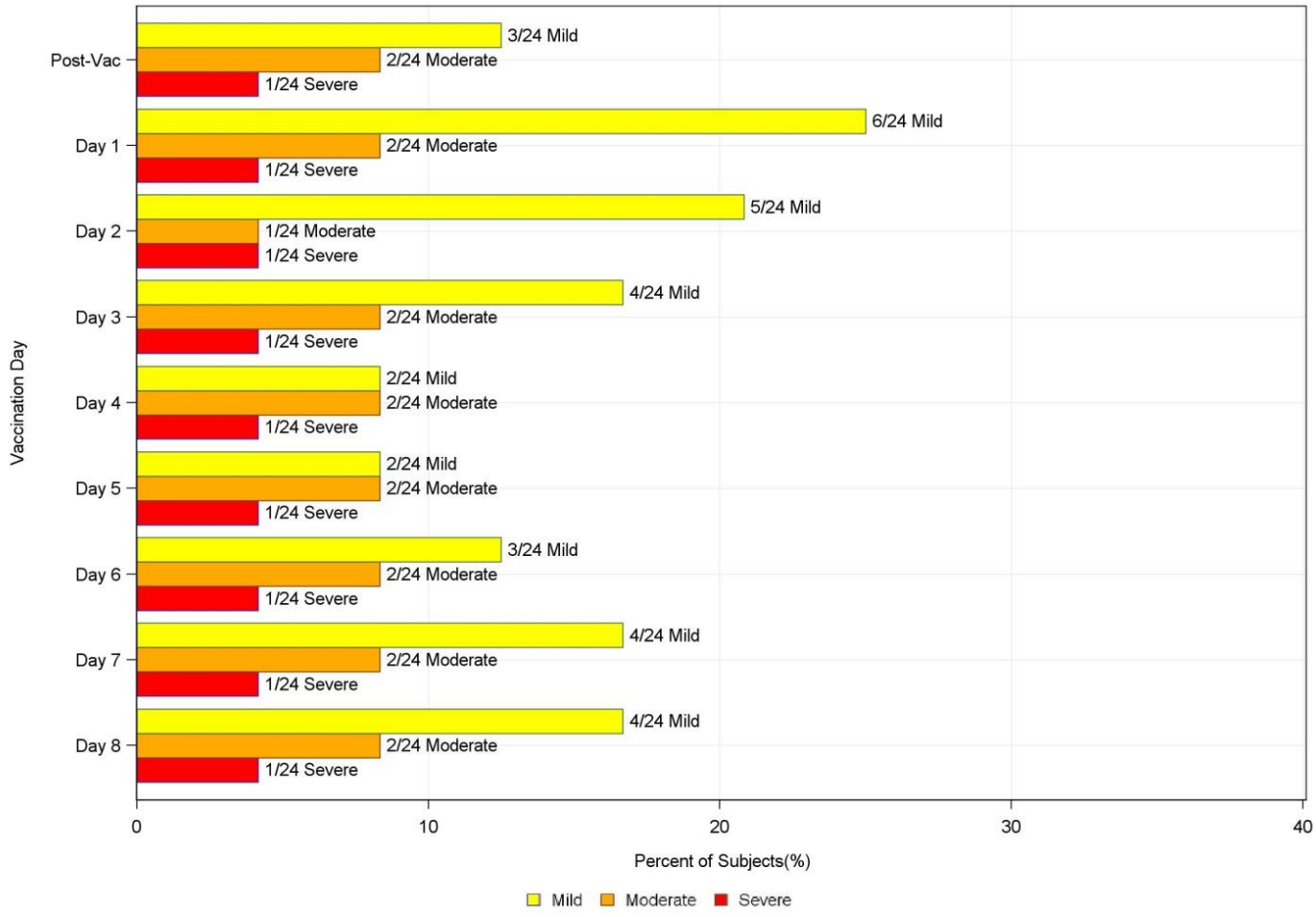
Figure 13: Geometric Mean Concentrations of anti-PA IgG by Study Day and Study Arm - Modified Intent-to-Treat Population

Figure 14: Geometric Mean Concentrations of anti-PA IgG by Study Day and Study Arm - Per Protocol Population

14.3.1.1 Solicited Adverse Events

Figure 15: Maximum Severity of Solicited Systemic Symptoms per Subject by Day Post Treatment - Safety Population

[Implementation Note: A generic sample figure is shown below. A horizontal bar chart should be presented in 1 image file with separate panels for each study arm (2 panels). Axes should be labeled as follows: y-axis label: Study Day, x-axis label: Percentage of Subjects (%). The study arms should be indicated in the panel headers including "(N=X)", where N = the number of subjects in the safety population who received the first study vaccination. Subjects are counted at most once at the maximum severity across all systemic events reported for the specified time point.]



Note: "Post-Vac" refers to symptoms solicited in clinic immediately after dosing. "Day 1" refers to events reported on Day 1 via Memory Aid.

Figure with similar format:

Figure 16: Maximum Severity of Solicited Injection Site Symptoms per Subject by Day Post Treatment - Safety Population

14.3.1.2 Unsolicited Adverse Events

Figure 17: Frequency of Related Adverse Events by MedDRA System Organ Class and Severity - Safety Population

[Implementation Note: A generic sample figure is shown below. This figure includes all unsolicited events across all doses. A horizontal bar chart should be presented in separate panels for each study arm (2 columns). Axes should be labeled as follows: y-axis label: System Organ Class, x-axis label: Number of Events. The study arm should be indicated in the panel headers including "(N=X)", where N = the number of subjects in the in the safety population. The y-axis should present all SOCs reported by at least 1 subject and an "All Events" category. Y-axis should be sorted with "All Events" first, then in decreasing order of total frequency.]

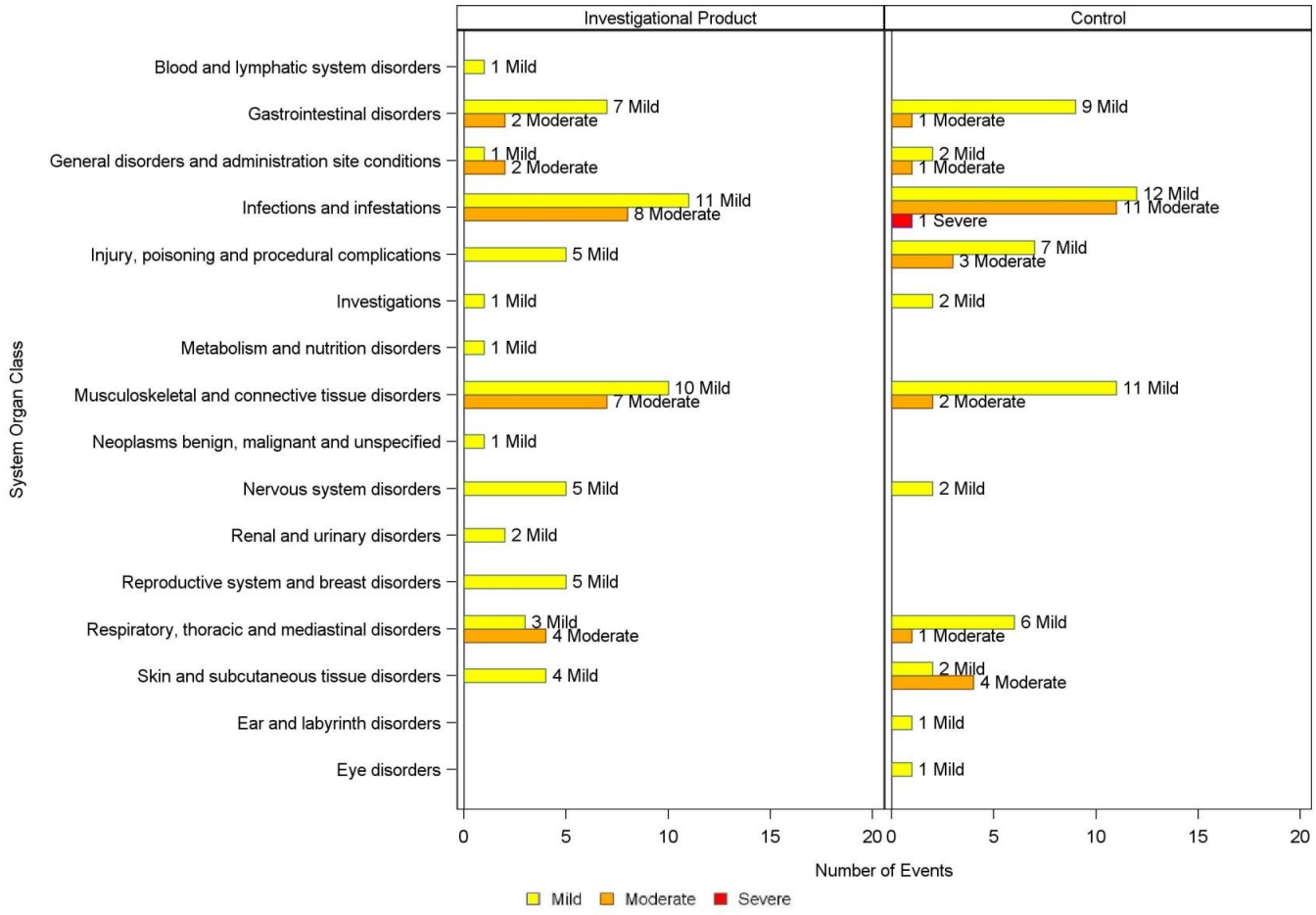


Figure 18: Incidence of Related Adverse Events by MedDRA® System Organ Class and Maximum Severity - Safety Population

[Implementation Note: A generic sample figure is shown below. This figure includes all unsolicited events across all doses. A horizontal bar chart should be presented in 1 image file with separate panels for each study arm (2 columns). Axes should be labeled as follows: y-axis label: System Organ Class, x-axis label: Percentage of Subjects (%). The treatment groups should be indicated in the panel headers including "(N=X)", where N = the number of subjects in the in the safety population. Subjects are counted at most once at the maximum severity across for any events in the applicable SOC. The y-axis should present all SOCs reported by at least 1 subject and an "All Events" category. Y-axis should be sorted with "All Events" first, then in decreasing order of total incidence.]

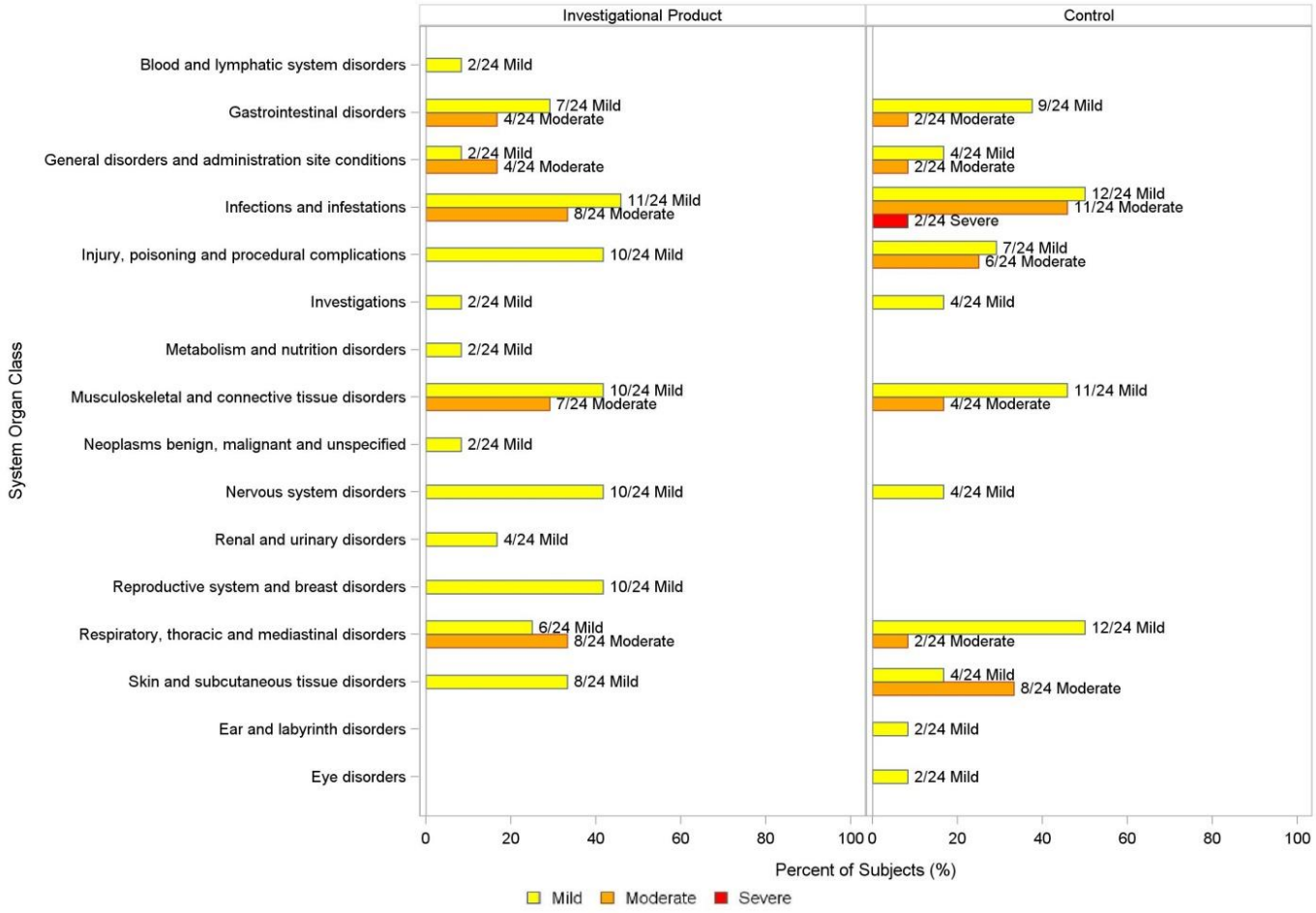


Figure 19: Frequency of Unsolicited Adverse Events by MedDRA® System Organ Class and Relationship to Treatment - Safety Population

[Implementation Note: A generic sample figure is shown below. This figure includes all unsolicited events across all doses. A horizontal bar chart should be presented in 1 image file with separate panels for each study arm (2 columns (study arms) x 1 row). Axes should be labeled as follows: y-axis label: System Organ Class, x-axis label: Number of Events. The treatment groups should be indicated in the panel headers including "(N=X)", where N = the number of subjects in the in the safety population. The y-axis should present all SOCs reported by at least 1 subject and an "All Events" category. Y-axis should be sorted with "All Events" first, then in decreasing order of total frequency.]

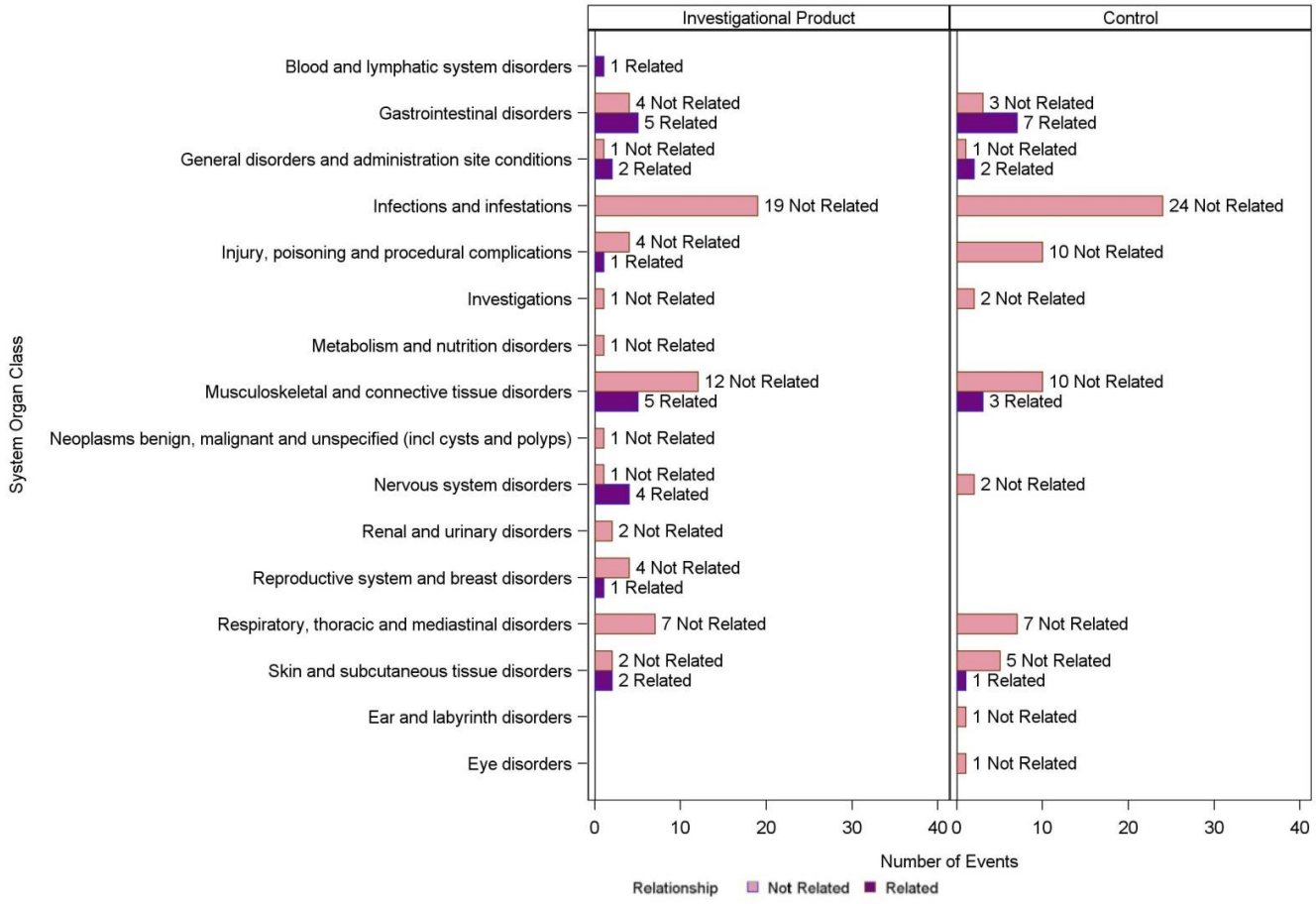
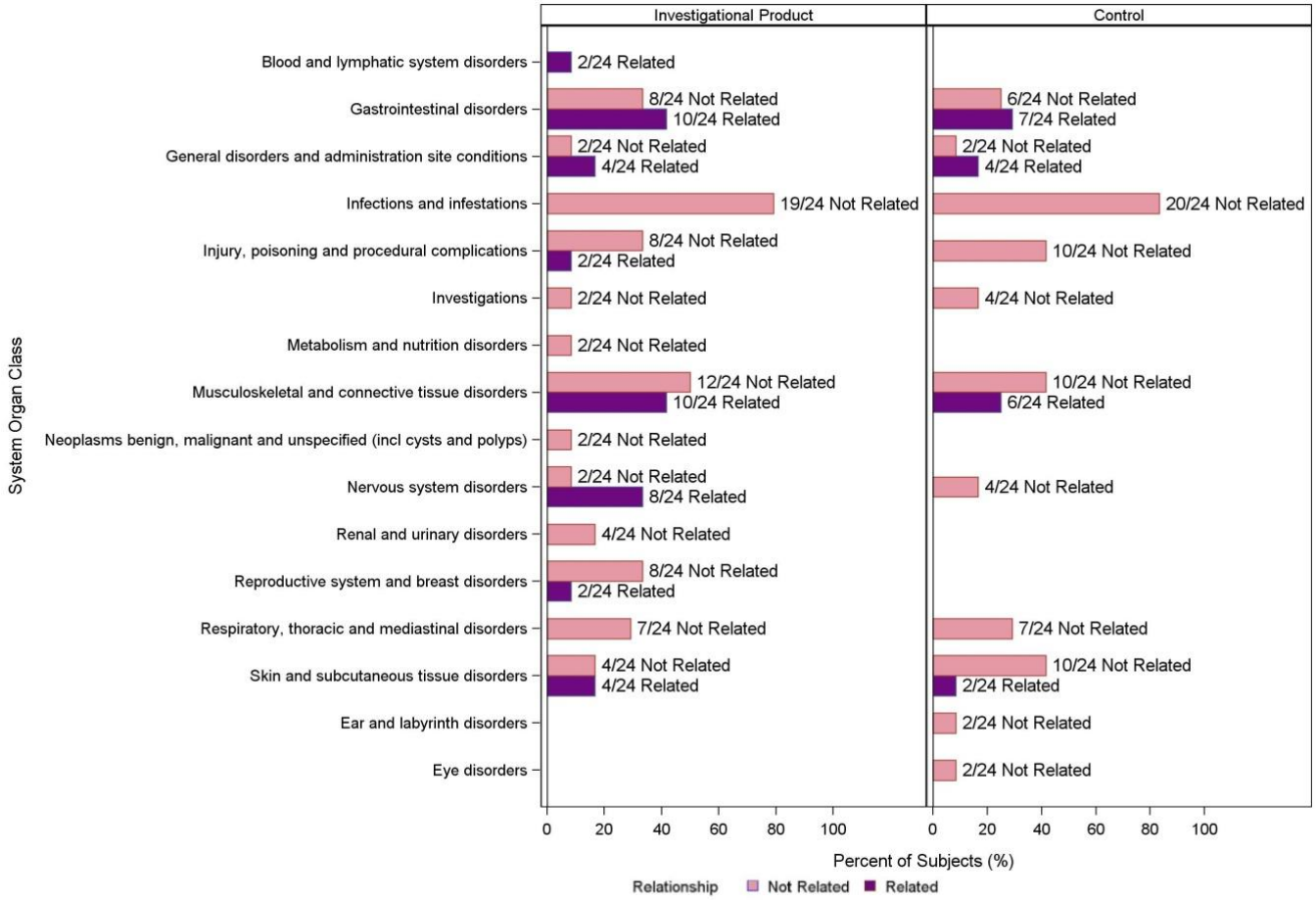


Figure 20: Incidence of Unsolicited Adverse Events by MedDRA® System Organ Class and Relationship to Treatment - Safety Population

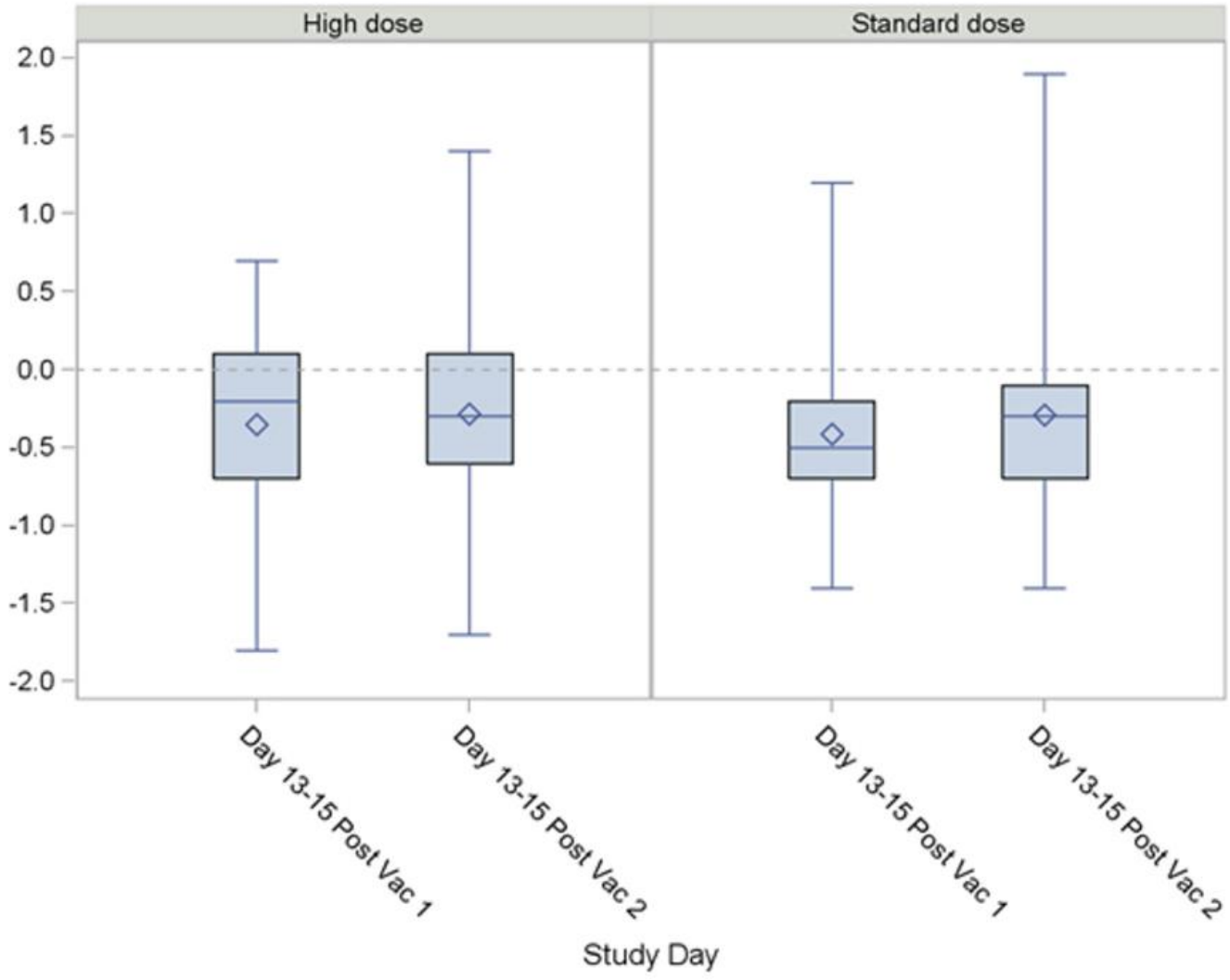
[Implementation Note: A Generic figure is shown below. This figure includes all unsolicited events across all doses. A horizontal bar chart should be presented in a 1 image file with separate panels for each study arm (2 columns). Axes should be labeled as follows: y-axis label: System Organ Class, x-axis label: Percentage of Subjects (%). The treatment groups should be indicated in the panel headers including "(N=X)", where N = the number of subjects in the in the safety population. Subjects are counted at most once at the maximum relationship (related > not-related) across for any events in the applicable SOC. The y-axis should present all SOCs reported by at least 1 subject and an "All Events" category. Y-axis should be sorted with "All Events" first, then in decreasing order of total incidence.]



14.3.5 Displays of Laboratory Results

Figure 21: Laboratory Results at Day 29: Mean Change from Baseline by Laboratory Parameter and Study Arm - Alkaline Phosphatase

[Implementation Note: A generic sample figure is shown below. Change from baseline will be displayed for each study arm at Day 29. One image file should be generated with separate panels for each study arm (2 columns). Y-axis should be labeled "[Parameter] Change from Baseline ([units]) and x-axis will be labeled 'Study Day'. Repeat for all clinical laboratory parameters.]



Figures with similar format:

Figure 22: Laboratory Results at Day 29: Mean Change from Baseline by Laboratory Parameter and Study Arm - Alanine Aminotransferase

Figure 23: Laboratory Results at Day 29: Mean Change from Baseline by Laboratory Parameter and Study Arm - Aspartate Aminotransferase

Figure 24: Laboratory Results at Day 29: Mean Change from Baseline by Laboratory Parameter and Study Arm - Total Bilirubin

Figure 25: Laboratory Results at Day 29: Mean Change from Baseline by Laboratory Parameter and Study Arm - Blood Urea Nitrogen (BUN)

Figure 26: Laboratory Results at Day 29: Mean Change from Baseline by Laboratory Parameter and Study Arm - Creatinine

Figure 27: Laboratory Results at Day 29: Mean Change from Baseline by Laboratory Parameter and Study Arm - Random Glucose

Figure 28: Laboratory Results at Day 29: Mean Change from Baseline by Laboratory Parameter and Study Arm - Hemoglobin

Figure 29: Laboratory Results at Day 29: Mean Change from Baseline by Laboratory Parameter and Study Arm - Hemoglobin Decrease from Baseline

Figure 30: Laboratory Results at Day 29: Mean Change from Baseline by Laboratory Parameter and Study Arm - Platelets

Figure 31: Laboratory Results at Day 29: Mean Change from Baseline by Laboratory Parameter and Study Arm - White Blood Cells

Figure 32: Laboratory Results at Day 29: Mean Change from Baseline by Laboratory Parameter and Study Arm - Absolute Eosinophil Count

Figure 33: Laboratory Results at Day 29: Mean Change from Baseline by Laboratory Parameter and Study Arm - Absolute Neutrophil Count

Figure 34: Laboratory Results at Day 29: Mean Change from Baseline by Laboratory Parameter and Study Arm - Urine Protein

Figure 35: Laboratory Results at Day 29: Mean Change from Baseline by Laboratory Parameter and Study Arm - Urine Glucose

APPENDIX 3. LISTING MOCK-UPS

LISTINGS

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

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

16.2 Database Listings by Subject

16.2.1 Discontinued Subjects

Listing 2: 16.2.1: Early Terminations or Discontinued Subjects

[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, Subject ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Study Arm, Subject ID, alphabetically by Category (in the case a subject both terminates early and discontinues treatment).]

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

16.2.2 Protocol Deviations

Listing 3: 16.2.2.1: Subject-Specific Protocol Deviations

[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: Subject refusal." In the CSR, Subject ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Study Arm, Subject ID, DV Number.]

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

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

[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: Subject refusal." Sort by Start Date.]

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

16.2.3 Subjects Excluded from the Efficacy Analysis

Listing 5: 16.2.3: Subjects Excluded from Analysis Populations

[Implementation Note: In the CSR, Subject ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Study Arm, Subject ID.]

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

16.2.4 Demographic Data

Listing 6: 16.2.4.1: Demographic Data

[Implementation Note: If a subject is multi-racial, in "Race" column, note "Multiple: (list races, separated by a comma)." In the CSR, Subject ID should be USUBJID (not PATID) for purposes of de-identification.] Sort order: Study Arm, Subject ID.]

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

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

[Implementation Note: "Condition Start Day" and "Condition End Day" are relative to enrollment (which is Day 1, day before enrollment is Day -1). In the CSR, Subject ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Study Arm, Subject ID, MH Number.]

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

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

Listing 8: 16.2.5: Treatment Compliance

[Implementation Note: If dose was missed, enter "N/A" in "Dose Out of Window?" and "Actual Day of Dosing" columns.]

Study Arm	Subject ID	Dose No.	Dose Missed?	Dose Out of Window?	Planned Day of Dosing (Window)	Actual Day of Dosing
		1/2	Yes/No	Yes/No	Day XX (Days XX to XX)	Day X

16.2.6 Individual Immunogenicity Response Data

Listing 9: 16.2.6.1: Individual Immunogenicity Response Data

Study Arm	Subject ID	Planned Study Day	Actual Study Day	TNA ED_{50} (titer)	TNA NF_{50} (titer)	Anti-PA IgG (µg/mL)

16.2.7 Adverse Events

Listing 10: 16.2.7.1: Solicited Events - Systemic Symptoms

[Implementation Note: To indicate severity for quantitative symptoms (e.g., temperature, measurements), include the grade in parentheses after the number, e.g., 100.7 (Mild). Oral temperature reported on vital signs forms will not be included in this listing. This listing includes baseline assessments in addition to post-treatment assessments. In the CSR, Subject ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Study Arm, Subject ID, Dose Number, Post Dose Day, Symptom.]

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

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

Listing 11: 16.2.7.2: Solicited Events - Local Symptoms

[Implementation Note: 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, Subject ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Study Arm, Subject ID, Dose Number, Post Dose Day, Symptom.]

Study Arm	Subject ID	Dose Number	Post Dose Day	Assessment[a]	Symptom	Severity
				MA		
				Clinic		

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

Listing 12: 16.2.7.3: Unsolicited Adverse Events

[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'. In the CSR, Subject ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Study Arm, Subject ID, Associated with Dose No., No. of Days Post Associated Dose.]

Adverse Event	Associated with Dose No.	No. of Days Post Associated Dose (Duration)	Severity	SAE?	Relationship to Study Treatment	In Not Related, Alternative Etiology	Action Taken with Study Treatment	Subject Discontinued Due to AE	Outcome	MedDRA System Organ Class	MedDRA Preferred Term
Study Arm: , Subject ID: , AE Number:											
Comments:											
Study Arm: , Subject ID: , AE Number:											
Comments:											
Note: For additional details about SAEs, see Section 14.3.2.											

16.2.8 Individual Laboratory Measurements

Listing 13: 16.2.8.1: Clinical Laboratory Results - Chemistry

[Implementation Note: This listing includes all laboratory results, scheduled and unscheduled. The severity should be included in parentheses after the result for abnormal results, e.g., 16.2 (Mild). In the CSR, Subject ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Study Arm, Subject ID, and Planned Study Day.]

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

Listing 14: 16.2.8.2: Clinical Laboratory Results - Hematology

[Implementation Note: This listing includes all laboratory results, scheduled and unscheduled. The severity should be included in parentheses after the result for abnormal results, e.g., 16.2 (Mild). In the CSR, Subject ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Study Arm, Subject ID, and Planned Study Day.]

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

Listing 15: 16.2.8.3: Clinical Laboratory Results - Urinalysis

[Implementation Note: This listing includes all laboratory results, scheduled and unscheduled. The severity should be included in parentheses after the result for abnormal results, e.g., 16.2 (Mild). In the CSR, Subject ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Study Arm, Subject ID, and Planned Study Day.]

Study Arm	Subject ID	Planned Study Day	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 16: 16.2.9.1: Vital Signs

[Implementation Note: This listing includes all vital sign assessments, scheduled and unscheduled. Oral temperature reported on solicited event forms will not be included in this listing. 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).]

Study Arm	Subject ID	Planned Study Day	Actual Study Day	Temperature (°C)	Systolic Blood Pressure (mmHg)	Diastolic Blood Pressure (mmHg)	Heart Rate (beats/min)	Respiratory Rate (breaths per min)

Listing 17: 16.2.9.2: Physical Exam Findings

[Implementation Note: This listing includes all physical exam findings, scheduled and unscheduled. If a subject 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, Subject ID should be USUBJID (not PATID) for purposes of de-identification.] Sort order: Study Arm, Subject ID, Planned Time Point.]

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

16.2.10 Concomitant Medications

Listing 18: 16.2.10: Concomitant Medications

[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 year 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, Subject ID should be USUBJID (not PATID) for purposes of de-identification. Sort order: Study Arm, Subject ID, and CM Number.]

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

16.2.11 Pregnancy Reports

[Implementation Note: Only include the "Pregnancy Number" column if a subject 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.]

Listing 19: 16.2.11.1: Pregnancy Reports - Maternal Information

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

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

Listing 20: 16.2.11.2: Pregnancy Reports - Gravida and Para

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

Note: Gravida includes the current pregnancy, para events do not.
[a] Preterm Birth
[b] Term Birth

Listing 21: 16.2.11.3: Pregnancy Reports - Live Birth Outcomes

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

Note: Congenital Anomalies are included in the Adverse Event listing.

Listing 22: 16.2.11.4: Pregnancy Reports - Still Birth Outcomes

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

Listing 23: 16.2.11.5: Pregnancy Reports - Spontaneous, Elective, or Therapeutic Abortion Outcomes

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

APPENDIX 4. NCA TEMPLATE

See separate document, if applicable.