CLINICAL RESEARCH IN INFECTIOUS DISEASES

STATISTICAL ANALYSIS PLAN
for
DMID Protocol: 18-0018
Study Title:
A Phase 1, Open-Label, Dose-Escalation Trial to Evaluate the Safety, Reactogenicity, and Immunogenicity of the Sm-p80 + GLA-SE (SchistoShield®) Vaccine in Healthy Adults

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DATE: 01 FEB 2024

RESTRICTED

STUDY TITLE:

A Phase 1, Open-Label, Dose-Escalation Trial to Evaluate the Safety, Reactogenicity, and Immunogenicity of the Sm-p80 + GLA-SE (SchistoShield®) Vaccine in Healthy Adults

Protocol Number Code:	**DMID Protocol: 18-0018**
Development Phase:	Phase 1
Products:	Sm-p80 + GLA-SE (SchistoShield®) Vaccine
Form/Route:	Intramuscular injections
Indication Studied:	Intestinal schistosomiasis
Sponsor:	Division of Microbiology and Infectious Diseases National Institute of Allergy and Infectious Diseases National Institutes of Health
Clinical Trial Initiation Date:	28 February 2022
Clinical Trial Completion Date:	Ongoing
Date of the Analysis Plan:	01 FEB 2024
Version Number:	Version 4.0

This study was performed in compliance with Good Clinical Practice.

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LIST OF ABBREVIATIONS

ADCC	Antibody-Dependent Cellular Cytotoxicity
AE	Adverse Event
ALT	Alanine Aminotransferase
ATC	Anatomical Therapeutic Classification
BP	Blood Pressure
BMI	Body Mass Index
CI	Confidence Interval
CRF	Case Report Form
CSR	Clinical Study Report
DMID	Division of Microbiology and Infectious Diseases, NIAID, NIH
eCRF	Electronic Case Report Form
ELISA	Enzyme-linked Immunosorbent Assay
FDA	Food and Drug Administration
GLA-SE	Glucopyranosyl Lipid Adjuvant Stable oil-in-water Emulsion
GMFR	Geometric Mean Fold Rise
GMT	Geometric Mean Titers
HCV	Hepatitis C Virus
ICH	International Conference on Harmonisation
ICS	Intracellular Cytokine Staining
IM	Intramuscular
LLOQ	Lower Limit of Quantification
MAAE	Medically Attended Adverse Events
MedDRA	Medical Dictionary for Regulatory Activities
mITT	Modified Intention to Treat
MOP	Manual of Procedures
N	Number (refers to number of subjects)
NIH	National Institutes of Health
NOCMC	New Onset Chronic Medical Condition
PBMC	Peripheral Blood Mononuclear Cell
PI	Principal Investigator
PIMMC	Potentially Immune-Mediated Medical Condition
PP	Per Protocol

List of Abbreviations *(continued)*

PT	Preferred Term
RCD	Reverse Cumulative Distribution
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SDCC	Statistical and Data Coordinating Center
SMC	Safety Monitoring Committee
Sm-p80	*S. mansoni* Caplain Protein with a mass of approximately 80 kDa
SOC	System Organ Class
ULN	Upper Limit of Normal
ULOQ	Upper Limit of Quantification
WBC	White Blood Cell
WFI	Water-For-Injection
WHO	World Health Organization

1. PREFACE

The Statistical Analysis Plan (SAP) for "A Phase 1, Open-Label, Dose-Escalation Trial to Evaluate the Safety, Reactogenicity, and Immunogenicity of Sm-p80 + GLA-SE (SchistoShield®) Vaccine in Healthy Adults" (DMID Protocol 18-0018) 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 Harmonization 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 (Appendix 1, Appendix 2, and Appendix 3, respectively), 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

In preclinical and safety studies, Sm-p80-based vaccines provided comprehensive coverage against different stages of the parasite's life cycle, including its eggs, schistosomula, and adult worms. Sm-p80 is unique in that it has demonstrated desirable outcomes of Sm-p80 vaccination including: 1) prophylactic efficacy against *S. mansoni* (intestinal/hepatic schistosomiasis); [9] 2) reduction in egg-induced tissue/organ pathology; [9] 3) ost-exposure therapeutic efficacy by elimination of established adult worms in chronic disease[11] 4) cross species-protection against *S. haematobium* (urinary schistosomiasis) [12] and *S. japonicum* (Asiatic/oriental disease); [13] 5) long lived immunity as Sm-p80 specific IgG titers are present in mice for up to 60 weeks and 5-8 years in baboons; [14] and 6) maternal transfer of Sm-p80-specific antibodies in baboons. [14] Sm-p80-specific IgE has not been detected in high-risk or infected populations from Africa and South America, thus reducing the possibility of hypersensitivity following vaccination with the Sm-p80 vaccine in humans. The protective immune response to *Schistosoma* is thought to be antibody mediated with cell-mediated help to skew the antibody isotypes to IgG1 and IgG3.

The 5 µg dose of GLA-Se to be used in this trial is comfortably in the mid-range of tested doses of the adjuvant and has been shown to be safe and well tolerated in hundreds of human subjects. As reported in the GLA-SE Investigator Brochure (v5, March 2016) many preclinical and nonclinical studies in mice, guinea pigs, rats, rabbits, and non-human primates have demonstrated the immunostimulatory properties of GLA-SE with no significant safety signals. GLA-SE has also been evaluated in numerous completed and ongoing clinical trials. These trials have investigated GLA-SE formulated with antigens, including recombinant antigens, developed for vaccines against a wide variety of diseases, including leishmaniasis, [15] tuberculosis, [16, 17] influenza, [18, 19] schistosomiasis, [20] and malaria. These clinical trials have evaluated GLA-SE at 0.5, 1, 2, 2.5, 5, 10, or 20 µg dose levels. In these studies, over 1100 subjects have received at least one study injection containing GLA-SE. Safety data have not revealed any significant safety issues at any dose level tested. Reactions to vaccines varied from study to study, but were generally mild, resolved quickly, and typical of vaccinations by the IM route.

In the GLP-toxicity study of SchistoShield®, there were no findings definitively attributed to systemic toxicity of Sm-p80 with or without GLA-SE. This study indicated that the SchistoShield® vaccine is safe and well tolerated in rabbits when administered IM for up to four injections at the highest proposed human dose of Sm-p80 antigen given with GLA-SE. No significant local or systemic toxicity was found. A general safety assessment of SchistoShield® vaccine in baboons also indicated that the vaccine is safe and well tolerated for up to the highest dose of 250 µg of Sm-p80 and 50 µg of GLA-SE, further supporting the observation from the GLP-toxicity study in rabbits. Based on the N+1 rule, the GLP-toxicity study in rabbits supports the use of SchistoShield® vaccine in the first-in-human clinical trial for up to three injections at the high dose of 100 µg Sm-p80.

The promising results of the preclinical evaluations and the urgent need for an effective schistosomiasis vaccine support advancement of the SchistoShield® vaccine candidate to an initial Phase 1 human trial in healthy volunteers in the United States.

2.1. Purpose of the Analyses

The purpose of this trial is to determine the safety, reactogenicity, and immunogenicity in 45 healthy adult subjects of the candidate investigational schistosomiasis vaccine: Sm-p80 (10 µg, 30 µg, and 100 µg) adjuvanted with 5 µg of GLA-SE adjuvant. The analyses will also assess the necessity of the adjuvant by comparison of the previous doses to 100 µg Sm-p80 only (Table 1). Subjects will receive three IM injections

of 0.5 mL of the designated study product formulation, on Days 1, 29, and 57 (28 days apart) or on a delayed booster dose schedule on Days 1, 29, and 180.

The protocol for DMID 18-0018 calls for a planned interim analysis on safety data and immunogenicity assays, including total IgG Enzyme-linked Immunosorbent Assay (ELISA), at the discretion of the study team prior to completion of follow-up of all subjects.

3. STUDY OBJECTIVES AND ENDPOINTS

3.1. Study Objectives

3.1.1. Primary

- To assess the safety and reactogenicity following receipt of three doses of the following
  - Group A: 100 µg Sm-p80 (unadjuvanted)
  - Group B: 10 µg Sm-p80 + 5 µg GLA-SE
  - Group C: 30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)
  - Group D: 30 µg Sm-p80 + 5 µg GLA-SE
  - Group E: 100 µg Sm-p80 + 5 µg GLA-SE

  with Groups A, B, D, and E administered intramuscularly on Days 1, 29, and 57 and Group C administered on Days 1, 29, and 180.

3.1.2. Secondary

- To assess anti-Sm-p80 IgG antibody responses from samples collected at specified time points.

3.1.3. Exploratory

- To assess innate and adaptive immune signatures from samples collected at specified time points.

3.2. Study Endpoints or Outcome Measures

3.2.1. Primary

- Occurrence of study vaccine-related SAEs from the time of the first study vaccination through approximately 12 months after the last study vaccination
- Occurrence of solicited injection site and systemic reactogenicity events from the time of each study vaccination through 7 days after each study vaccination
- Occurrence of clinical safety laboratory AEs form the time of each study vaccination through approximately 28 days after each study vaccination
- Occurrence of all unsolicited AEs, regardless of the assessment of seriousness or relatedness, from the time of each study vaccination through 28 days after each study vaccination
- Occurrence of SAEs, MAAEs, NOCMCs, and PIMMCs from the time of the first study vaccination through approximately 12 months after the last study vaccination

3.2.2. Secondary

- For Sm-p80 IgG antibodies, number of subjects achieving seroconversion, defined as fourfold rise from baseline, at approximately 28 days after the first, second, and third study vaccinations
- Geometric mean titers of serum Sm-p80 IgG antibodies from samples collected at 7 and 28 days after each vaccination, and at 124 days after the last vaccination

3.2.3. Exploratory

- Identification and characterization of gene expression changes as measured using RNA-seq analysis from whole blood relative to last vaccination
  - Days 8 and 29 vs. Day 1, and Day 36 vs. Day 29 for all study groups
  - Day 57 vs. Day 29, Day 64 vs. Day 57 for Groups A, B, D, and E
  - Day 187 vs. Day 180 for Group C
- Identification and characterization of gene expression changes as measured using RNA-seq relative to last vaccination that correlate with peak Sm-p80 IgG antibody levels
  - Days 8 and 29 vs. Day 1, and Day 36 vs. Day 29 for all study groups
  - Day 57 vs. Day 29, Day 64 vs. Day 57 for Groups A, B, D, and E
  - Day 187 vs. Day 180 for Group C

3.3. Study Definitions and Derived Variables

Seroconversion is defined as a fourfold rise from baseline.

Clinical laboratory evaluations, vital signs, reactogenicity, and immunogenicity will be assessed on the day of, prior to the first study product injection (Day 1) to establish baseline. If a single ELISA result is below the lower limit of quantification (LLOQ) or above the upper limit of quantification (ULOQ) then the result will be imputed as LLOQ or ULOQ, respectively. If both ELISA results are below LLOQ, then the value will be imputed as ½*LLOQ. If both ELISA results are above ULOQ, then ULOQ will be reported.

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

4. INVESTIGATIONAL PLAN

4.1. Overall Study Design and Plan

This is a Phase 1, open label, dose-escalation clinical trial to evaluate the safety, reactogenicity, and immunogenicity of Sm-p80 + GLA-SE candidate schistosomiasis vaccine (SchistoShield®) in healthy adults 18 through 55 years of age. The Sm-p80 antigen is a recombinant protein produced in *E. coli* and GLA-SE is an immunological adjuvant.

Five treatment groups, each including nine subjects, will receive three intramuscular (IM) injections of 0.5 mL of designated study product on either Days 1, 29, and 57 or on Days 1, 29, and 180. Group A (unadjuvanted comparator) will receive 100 µg Sm-p80 alone on Days 1, 29, and 57; Group B (low dose standard schedule) will receive 10 µg Sm-p80 + 5 µg GLA-SE on Days 1, 29, and 57; Group C (mid dose delayed booster) will receive 30 µg Sm-p80 + 5 µg GLA-SE on Days 1, 29, and 180; Group D (mid dose standard schedule) will receive 30 µg Sm-p80 + 5 µg GLA-SE on Days 1, 29, and 57; Group E (high dose standard schedule) will receive 100 µg Sm-p80 + 5 µg GLA-SE on Days 1, 29, and 57. Dose escalation will proceed as described in the Protocol Summary (protocol v2.0).

Reactogenicity will be measured by the occurrence of solicited injection site and systemic reactions form the time of each study product injection through seven days after each study product injection. Unsolicited AEs of all severities, and concomitant medications, will be collected form the time of each study product injection through the next 28 days. During period of follow-up outside of the 28-day post-vaccination interval, only SAEs, medically attended adverse events (MAAEs), new onset chronic medical conditions (NOCMCs), and potentially immune-mediated medical conditions (PIMMCs) will be collected. Clinical laboratory evaluations for safety will be performed on venous blood collected prior to, and approximately seven days after, each study vaccination.

Immunogenicity testing will include measuring titers of total IgG against the Sm-p80 protein by ELISA. Gene expression will be evaluated using RNA Seq analysis from whole blood.

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

4.3. Selection of Study Population

The study population of 45 subjects will be enrolled from a population of healthy, *Schistosoma*-naïve subjects ages 18 through 55 years at a single study site in Seattle, Washington.

Subject Inclusion and Exclusion Criteria must be assessed by a study clinician licensed to make medical diagnoses and listed on the Form FDA 1572 as the site PI or sub-investigator. No exemptions are granted on Subject Inclusion/Exclusion Criteria in DMID-sponsored studies. Questions about eligibility will be directed toward the DMID Medical Officer.

Subject Inclusion Criteria

Subjects must meet all the following inclusion criteria to be eligible for enrollment in this study

1. Male or non-pregnant female 18 through 55 years of age, inclusive, at the time of consent
2. Able and willing to participate for the duration of the study and able to understand and comply with planned study procedures
3. Able and willing to provide written (not proxy) informed consent

4. Is in good health, as judged by the investigator, and determined by medical history and physical examination*

   *Existing medical diagnoses or conditions (except those in the Subject Exclusion Criteria) must be deemed as stable. A stable medical condition is defined as no change in prescription medication, dose, or frequency of medication in the last three months (90 days) and health outcomes of the specific disease are considered to be within acceptable limits in the last size months (180 days). Any change due to change of health care provider, insurance company, or that is done for financial reasons, as long as in the same class of medication, will nor be considered a violation of this inclusion criterion. Any change in prescription medication due to **improvement** of a disease outcome, as determined by the site PI or appropriate sub-investigator, will not be considered a violation of this inclusion criterion. Subjects may be on chronic or as needed (prn) medications if, in the opinion of the site PI or appropriate sub-investigator, they pose no additional risk to the subject safety or assessment of solicited events and immunogenicity.

   Topical, nasal, and inhaled medications (with the exception of some uses of corticosteroids as outlined in the Subject Exclusion Criteria), vitamins, and contraceptives are permitted.

5. Women of childbearing potential* must have a negative serum pregnancy test at screening and a negative urine pregnancy test within 24 hours prior to each study product injection

   *Not sterilized via bilateral tubal ligation, bilateral oophorectomy, or hysterectomy, or, if menopausal, still menstruating or < 1 year of the last menses.

6. Women of childbearing potential must have used an acceptable form of contraception* in the 30 days prior to their first study product injection

   *Acceptable single forms of contraception include abstinence from sexual activity that could lead to pregnancy, monogamous relationship with vasectomized partner who has been vasectomized for six months or more prior to enrollment, successful Essure® placement (permanent, non-surgical, non-hormonal sterilization), intrauterine devices, and hormonal methods, including the birth control patch, shot (Depo-Provera), pills, the vaginal ring (NuvaRing), and the contraceptive implant (Nexplanon). Acceptable barrier methods include diaphragm or cervical cap with spermicide and the contraceptive sponge.

7. Women of childbearing potential must agree to continue use of an acceptable form of contraception through 30 days after their last study product injection

8. Weight ≥ 50 kg and body mass index (BMI) < 35.0 kg/m^2

9. Vital signs (oral temperature, pulse, and blood pressure) are within normal protocol-defined ranges*

   *The normal protocol-defined ranges for vital signs include (a) oral temperature less than 38°C (100.4°F), (b) pulse no greater than 100 bpm, (c) systolic blood pressure 85 to 150 mmHg, inclusive, and (d) diastolic BP ≤ 100 mmHg.

10. Screening clinical lab values are all within normal protocol-defined reference ranges*

    *The normal protocol-defined ranges for laboratory tests include (a) ALT of < 47 IU/L, (b) creatinine less than or equal to the laboratory upper limit of normal, (c) WBC ≥ $3.80x10^3$/UL and ≤ $13.00x10^3$/UL, (d) hemoglobin 11.5 g/dL or greater for females or 12.6 g/dL or greater for males, (e) platelets between $131x10^3$/UL and $415x10^3$/UL, inclusive.

Subject Exclusion Criteria

Subjects must not meet any of the exclusion criteria at baseline to be eligible for enrollment in this study.

1. Has had known schistosomiasis infection or has traveled to an endemic area for schistosomiasis infection and, during that travel, was potentially exposed to a Schistosoma species
2. Has been treated for schistosomiasis
3. Has previous exposure to schistosome vaccines or experimental products containing GLA-SE
4. Female subjects who are breastfeeding a child, or who plan to breastfeed a child from the first study product injection through 30 days after the last study product injection
5. Asthma, other than mild, well-controlled asthma*

   *Cold or exercise-induced asthma controlled with inhaled medications other than inhaled corticosteroids is permissible. Subjects should be excluded if they require daily bronchodilator use or have had an asthma exacerbation requiring oral/parental steroid use or have used theophylline or inhaled corticosteroids in the past year.
6. Known atherosclerotic cardiovascular disease or history of myocardial infarction, pericarditis, or myocarditis
7. Diabetes mellitus
8. History of psychiatric condition that may make study compliance difficult, such as schizophrenia, or poorly controlled bipolar disorder*

   *Includes persons with psychoses or history of suicide attempt or gesture in the 3 years before study entry or an ongoing risk for suicide.
9. Chronic or active neurologic condition (including seizures* and migraine headaches**)

   *Seizure within the past 5 years.

   **Four or more migraine headaches in the past 12 months that interfered with normal daily activity or any migraine headache in the past 5 years that required emergency or inpatient medical care.
10. Autoimmune disease*

    *Autoimmune hypothyroidism with or without replacement therapy, and vitiligo or mild eczema or psoriasis not requiring chronic therapy, are permissible
11. Known or suspected congenital or acquired immunodeficiency including anatomic or functional asplenia* or immunosuppression as a result of underlying illness or treatment

    *Any splenectomy is exclusionary
12. Use of alcohol or drugs that, in the opinion of the investigator, may interfere with ability to comply with the protocol or increase risk to subject's health during the study period

    *Subjects with a history of malignancy may be included if treated by surgical excision, or by chemotherapy or radiation therapy and has been observed for a period that in the investigator's estimation provides a reasonable assurance of sustained cure (not less than 36 months). Cervical neoplasia under surveillance and non-melanoma skin cancer are not exclusionary.
13. Active neoplastic disease*

*Subjects with a history of malignancy may be included if treated by surgical excision, or by chemotherapy or radiation therapy and has been observed for a period that in the investigator's estimation provides a reasonable assurance of sustained cure (not less than 36 months). Cervical neoplasia under surveillance and non-melanoma skin cancer are not exclusionary.

14. Chronic topical or systemic corticosteroid use*

    *Corticosteroid nasal sprays for allergic rhinitis are permissible. Persons using a topical corticosteroid for a limited duration for mild uncomplicated dermatitis such as poison ivy or contact dermatitis prior to enrollment may be enrolled the day after their therapy is completed. Oral or parenteral (intravenous, IM, subcutaneous) corticosteroids given for non-chronic conditions not expected to recur are permissible if, within the year prior to enrollment, the longest course of therapy was no more than 14 days and no oral or parenteral corticosteroids were given within 30 days prior to enrollment. Intraarticular, bursal, tendon, or epidural injections of corticosteroids are permissible if the most recent injection was at least 30 days prior to enrollment. Topical or systemic corticosteroid use for study related AEs is not exclusionary.

15. Known contraindication to repeated phlebotomy*

    *Such as minimal venous access or recent history of anemia

16. Receipt or planned receipt of inactivated vaccine or allergy desensitization injection within 14 days before or after a study product injection

17. Receipt or planned receipt of live attenuated vaccine 28 days before or after a study product injection

18. Receipt of blood products or immunoglobulin within six months prior to, or donation of unit of blood within two months prior to, the first study product injection.

19. Receipt of any experimental agent* within 30 days prior to screening or planned receipt prior to the last study visit**

    *Vaccine, drug, biologic, device, blood product, or medication.

    **Receipt of experimental COVID-19 related products are not necessarily exclusionary and will be evaluated on a case-by-case basis.

20. Plan to undergo surgery (elective or otherwise) within six months after study enrollment

21. Plans to enroll in another interventional clinical trial* at any time during the study period

    *Includes trials evaluating interventions such as a drug, biologic, or device.

22. Positive confirmatory test for HIV infection

23. Positive serologic test for hepatitis B surface antigen (HBsAg)

24. Positive confirmatory test for hepatitis C virus (HCV) infection

25. Acute febrile illness (oral temperature ≥ 38°C) or other acute illness within three days prior to study product injection*

    *Note for afebrile, acute illness only: If a subject is afebrile, his/her acute illness is nearly resolved with only minor residual symptoms remaining, and, in the opinion of the site PI or appropriate sub-investigator, the residual symptoms will not interfere with the ability ro assess

safety parameters as required by the protocol, the subject may receive study product injection without further approval form the DMID Medical Officer.

26. Not willing to avoid donating blood during the study
27. Has any condition that would, in the opinion of the site investigator, place the subject at an unacceptable risk of injury or render the subject unable to meet the requirements of the protocol

4.4. Treatments

4.4.1. Treatments Administered

Each dose of study vaccine will be administered as a single 0.5-mL IM injection in the deltoid muscle of the participant's arm. Participants will be observed in the clinic for a minimum of 30 minutes following the study product injection. After 30 minutes, the injections site will be examined and the participant will be questioned about the presence of any localized or generalized reactogenicity symptoms. Any spontaneous AEs that occur will be assessed.

See the protocol-specific MOP for detailed information on the administration of the study product for each group. Treatment for each study group is summarized in Table 1.

4.4.2. Identity of Investigational Product(s)

The vaccine product is a two-component system comprised of Sm-p80 antigen and GLA-SE adjuvant.

Sm-p80 for injection

Sm-p80 is a recombinant protein produced in *E. coli* bacteria. The protein antigen is the largesubunit of the *S. mansoni* calcium-activated neutral protease, calpain. The Sm-p80 protein is formulated and lyophilized to yield the vaccine antigen, Sm-p80 for Injection. The final 758 amino acid protein antigen has a predicted mass of approximately 87kDa.

GLA-SE Adjuvant

GLA-SE is a synthetic Monophosphoryl Lipid A-like molecule which is a Toll-like receptor 4 agonist formulated in a SE to produce GLA-SE.

Sm-p80 + GLA-SE

Sm-p80 + GLA-SE contains the antigen and adjuvant. After reconstitution of the antigen with water-for-injection (WFI) and mixing with the liquid adjuvant, it is ready for administration tothe study participant.

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

This is a non-randomized trial. Approximately 9 subjects will be assigned to each treatment arm.

4.4.4. Selection of Doses in the Study

Subjects receive 100 µg Sm-p80 alone or 10 µg, 30 µg, or 100 µg Sm-p80 with 5 µg GLA-SE.

The adjuvant dose of 5 µg of GLA-SE is selected for this trial as this dose is in the mid-range of doses evaluated in the 1100 previous subjects, has been shown to increase antibody levels and cellular immune responses, and has been evaluated in multiple clinical trials, including administering three vaccinations, demonstrating an acceptable safety profile. The preclinical studies of SchistoShield® do not inform the

selection of antigen dose for this study, as non-human primates require much higher doses of antigen and adjuvant than humans due to the tolerizing effects of their environment. In other vaccine trials in humans, GLA-SE adjuvant administered with antigen doses suggest that lower antigen doses are best to elicit T cell responses while the higher doses tend to elicit better humoral responses. Since it appears that the primary mechanism of action of SchistoShield® is mediated by humoral responses, this study will evaluate a range of Sm-p80 doses from 10 to 100 µg.

4.4.5. Selection and Timing of Dose for Each Subject

Subjects were evenly distributed between treatment arms. Each subject receives three doses of the study product on Days 1, 29, and 57 or Days 1, 29, and 180. Each dose of study vaccine will be administered as a single 0.5-mL IM injection in the deltoid muscle of the participant's arm. Detailed descriptions of study agent preparation and administration are found in the study MOP.

4.4.6. Blinding

This is an open-label clinical trial.

Subjects, investigators, study personnel performing any study-related assessments following study vaccine administration are not blinded to study treatment. Laboratory personnel performing immunologic assays will receive samples blinded to subject ID number and sample visit number.

4.4.7. Prior and Concomitant Therapy

Administration of any medications, therapies, or vaccines will be recorded on the appropriate eCRF. Concomitant medications will include all current medications and medications taken in the 60 days prior to the first vaccination and those taken from the time of vaccination through approximately 28 days after each vaccination, as described in Section 3.1. Medications reportedin the electronic case report form (eCRF) are limited to those taken within 30 days prior to the first study product injection and those taken in the 28-day post-vaccination interval. Prescriptionand over-the-counter drugs will be included as well as herbals, vitamins, and supplements. In addition, receipt of non-study vaccines will be solicited from the time of each vaccination through approximately 28 days after each vaccination and reported in the eCRF. Use of a new medication should prompt evaluation for the occurrence of any MAAE, including a NOCMC.

Medications that might interfere with the evaluation of the investigational product(s) should not be used during the trial-reporting period (approximately 12 months after the last study vaccination) unless clinically indicated as part of the subject's health care. Medications in this category include the prohibited medications per the Subject Exclusion Criteria (see Section 4.3). In addition, the site PI or appropriate sub-investigator may identify other medications thatshould not be used due to a risk to subject safety or assessment of reactogenicity and immunogenicity.

4.4.8. Treatment Compliance

All subjects receive a total of three doses of study product delivered intramuscularly in the clinic by a qualified study personnel member according to subject treatment assignment.

4.5. Efficacy (Immunogenicity) and Safety Variables

As this is a Phase 1 clinical trial in healthy adult subjects, there is no assessment of drug efficacy. For a detailed schedule of activities, refer to Table 2 and Table 3. Refer to Section 3 for a list of primary and secondary objectives.

In general, multiple observations within a specific visit period will be accepted. In case of multiple observations within a specific window, the assessment value that is closest to the scheduled visit window will be used in the analyses for the post-baseline records. If observations have the same distance to the scheduled assessment, the latest one will be used. All recorded data will be listed.

4.5.1. Safety Variables

Serious adverse events (SAEs) will be assessed from the time of the first study product injection through the end of the follow-up which is approximately 12 months after the last study product injection.

Solicited adverse events (AEs) will document reactogenicity events occurring from the time of each study product injection through 7 days after each study product injection. Injection site reactions of interest include pruritus, erythema, induration/swelling, pain, and tenderness. Systemic reactions of interest include fever, chills, fatigue malaise, myalgia, arthralgia, headache, nausea, and vomiting.

Unsolicited AEs will document non-serious AEs occurring from the time of each study product injection through 28 days after the study product injection.

Clinical safety laboratory AEs will be collected on the day of and prior to each study product injection, approximately 7 days after each study product injection, and approximately 28 days after each study product injection (which may also serve as the clinical safety laboratory samples for the second and/or third study product injection). Parameters to be evaluated include white blood cells (WBC), hemoglobin, platelets, alanine aminotransferase (ALT), and creatinine.

MAAEs, NOCMCs, and PIMMCs will be assessed from the time of the first study product injection through the end of the follow-up period, which is approximately 12 months after the last study product injection.

All solicited and unsolicited AEs and laboratory values are graded on a scale of 0 (absent), 1 (mild), 2 (moderate), and 3 (severe) according to toxicity grading scales (Table 6, Table 7).

4.5.2. Immunogenicity Variables

Assessment of antibody responses are measured by total IgG production to Sm-p80 protein using ELISA. RNA-Seq data will be pre-processed by removing adaptors and low-quality reads, trimming low quality ends, and mapping sequences to the latest human reference genome using splice-aware alignment software such as *HISAT2* for transcriptomic exploratory analysis.

Samples for immunogenicity assays are collected prior to each vaccination on the day of vaccination, at 7 and 28 days after each vaccination, and at 124 days after the last vaccination. The 28-day post-vaccination sample will also serve as the day of vaccination sample for a subsequent vaccination given at a 28-day interval.

Additional details on RNA-Seq analysis will be described in a separate SAP, and the analyses will be presented in a CSR Addendum.

5. SAMPLE SIZE CONSIDERATIONS

This Phase 1 study is not designed for confirmatory testing but rather to detect AEs related to the study product. If an AE has a 20% chance of occurring after receiving one of the product formulations being tested, then there is an 87% probability that the event would be observed in one or more of the 9 subjects in that treatment group in this study. If the event has a 20% chance or higher of occurring in any of the product formulations being tested, then there is at > 99% probability that the event would be observed in one or more of the 45 subjects in any treatment group in the study. The Table 4 shows analogous probabilities for events with other frequencies.

6. GENERAL STATISTICAL CONSIDERATIONS

6.1. General Principles

All continuous variables will be summarized using the following descriptive statistics: n (non-missing sample size), mean, standard deviation, median, maximum, and minimum. The frequency and percentages (based on the non-missing sample size) of observed levels will be reported for all categorical measures. In general, all data will be listed, sorted by treatment and subject, and when appropriate by visit number within subject. All summary tables will be structured with a column for each treatment in the order (Group A, Group B, Group C, Group D, Group E) and will be annotated with the total population size relevant to that table/treatment, including any missing observations. If the table including all treatment groups in one table results in the table being too wide, separate tables will be made for each treatment group.

6.2. Timing of Analyses

Two interim analyses of safety and immunogenicity data will be conducted prior to completion of follow-up of all subjects: 1.) after the Day 85 visit for Groups A and B and 2.) after the Day 208 visit for Group C or the Day 85 visit for Group D, whichever occurs last. The data will be cleaned but not locked. The following TFLs will be included in these interim analyses:

Tables:

- Table 8: Subject Disposition by Treatment Group
- Table 9: Analysis Population by Treatment Group
- Table 12: Summary of Categorical Demographic and Baseline Characteristics by Treatment Group, All Enrolled Subjects
- Table 13: Summary of Continuous Demographic and Baseline Characteristics by Treatment Group, All Enrolled Subjects
- All immunogenicity tables listed in Section 11 (Table 15, Table 16, Table 17)
- Table 18 : Overall Summary of Adverse Events
- Table 19: Adverse Events Occurring in 5% of Subjects in Any Treatment MedDRA System Organ Class and Preferred Term, and Treatment Group - Safety Population
- Table 20: Number and Percentage of Subjects Experiencing Solicited Events with 95% Confidence Intervals by Symptom and Treatment Group - Post Dose 1
- Table 21: Number and Percentage of Subjects Experiencing Solicited Events with 95% Confidence Intervals by Symptom and Treatment Group - Post Dose 2
- Table 22: Number and Percentage of Subjects Experiencing Solicited Events with 95% Confidence Intervals by Symptom and Treatment Group - Post Dose 3
- Table 23: Number and Percentage of Subjects Experiencing Solicited Events with 95% Confidence Intervals by Symptom and Treatment Group - Post Any Dose
- Table 48: Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Maximum Severity, Relationship, and Treatment Group
- Table 54: Listing of Serious Adverse Events

- Table 55: Listing of Non-Serious, Unsolicited, Moderate or Severe Adverse Events
- Table 56: Listing of Other Significant Adverse Events
- Table 57: Listing of Abnormal Laboratory Results - Chemistry
- Table 58: Listing of Abnormal Laboratory Results - Hematology
- Table 59: Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group - Any Chemistry Parameter
- Table 60: Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group - Creatinine
- Table 61: Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group - Alanine Aminotransferase
- Table 67 : Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group - Any Hematology Parameter
- Table 68: Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group - White Blood Cells
- Table 69: Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group - Hemoglobin
- Table 70: Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group - Platelets

Figures:

- All immunogenicity figures listed in Section 11 (Figure 2, Figure 3, Figure 4)
- Figure 8: Number and Percentage of Subjects Experiencing Solicited Systemic Events by Event, Maximum Severity, and Treatment Group - Post Dose 1
- Figure 9: Number and Percentage of Subjects Experiencing Solicited Systemic Events by Event, Maximum Severity, and Treatment Group - Post Dose 2
- Figure 10: Number and Percentage of Subjects Experiencing Solicited Systemic Events by Event, Maximum Severity, and Treatment Group - Post Dose 3
- Figure 11: Number and Percentage of Subjects Experiencing Solicited Systemic Events by Event, Maximum Severity, and Treatment Group - Post Any Dose
- Figure 15 : Number and Percentage of Subjects Experiencing Solicited Injection Site Events by Event, Maximum Severity, and Treatment Group - Post Dose 1
- Figure 16 : Number and Percentage of Subjects Experiencing Solicited Injection Site Events by Event, Maximum Severity, and Treatment Group - Post Dose 2
- Figure 17: Number and Percentage of Subjects Experiencing Solicited Injection Site Events by Event, Maximum Severity, and Treatment Group - Post Dose 3
- Figure 18: Number and Percentage of Subjects Experiencing Solicited Injection Site Events by Event, Maximum Severity, and Treatment Group - Post Any Dose
- Figure 19: Frequency of Related Adverse Events by MedDRA System Organ Class and Severity

Listings:

- Listing 9: Individual Immunogenicity Response Data

The SMC will review safety at least annually. A final SMC review meeting will occur 6 to 8 months after clinical database lock. Additional interim analyses of safety and immunogenicity data may be conducted at the discretion of the SMC prior to completion of follow-up of all subjects. The final analysis will be performed after all outcome data from all subjects through the final study visit have been monitored and locked.

6.3. Analysis Populations

Summaries and analysis for safety data will be presented for the Safety Population. Summaries and analysis of immunogenicity data will be presented for the modified intention-to-treat population. If there are major protocol deviations, a per-protocol (PP) analysis may also be performed. Immunogenicity data from any visit that occurs substantially out of window will be reviewed by the Principal Investigator, DMID Scientific Lead, and/or DMID Medical Officer for decisions regarding inclusion or exclusion of the data. A tabular listing of all subjects, visits, and observations excluded from the analysis will be provided in the CSR (Listing 5).

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

The modified intention-to-treat (mITT) immunogenicity population includes all subjects who received at least one dose of study vaccine and contributed both pre- and at least one post-study vaccination venous blood sample for immunogenicity testing for which valid results were reported. For analyses using the mITT immunogenicity population, subjects will be grouped based on treatment assignments: 100 µg Sm-p80 (unadjuvanted), 10 µg Sm-p80 + 5 µg GLA-SE, 30 µg Sm-p80 + 5 µg GLA-SE (delayed booster), 30 µg Sm-p80 + 5 µg GLA-SE, 100 µg Sm-p80 + 5 µg GLA-SE.

6.3.2. Per Protocol Population

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

- Data from all available visits for subjects found to be ineligible.
- Data from all visits subsequent to protocol deviations such as:
  - Second or third study vaccine not received,
  - Second or third vaccine received out of window,
  - Receipt of non-study licensed live vaccine within 30 days prior to or 28 days after each study vaccination,
  - Receipt of non-study licensed inactivated vaccine within 14 days prior to or 28 days after each study vaccination,
  - Receipt of immunosuppressive therapy (e.g., systemic corticosteroids) or cytotoxic drugs within 30 days prior to or 28 days after each study vaccine.
- Data from any visit that occurs substantially out of window.

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

All subject visits identified for exclusion from the PP population will be reviewed by the Principal Investigator, DMID Scientific Lead, and/or DMID Medical Officer.

6.3.3. Safety Population

The safety population will include all subjects who received at least one dose of the study product and will be summarized according to treatment received.

6.4. Covariates and Subgroups

The protocol does not define any formal subgroup analyses, and the study is not adequately powered to perform subgroup analyses. No analysis for this study has planned covariate adjustment.

6.5. Missing Data

Analyses for this Phase 1 study will be descriptive and are exploratory rather than confirmatory in nature. 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.

6.6. Interim Analyses and Data Monitoring

Interim analyses will be used to terminate this trial in the event that unanticipated safety events deemed to be of sufficient concern require such action by the sponsor. These assessments will not be made on the basis of testing a formal statistical hypothesis; therefore, p-value adjustment will not be made to any analyses. A SMC will be convened by DMID to review study progress and participant, clinical, safety, reactogenicity and immunogenicity data as described in Protocol v3.0 Section 8.7.

To guide protocol development of future studies of the candidate vaccine, interim analyses of safety data and immunogenicity assays, including the total IgG ELISA assay, will be performed as data is available for Groups A and B and again when data is available for Groups C and D prior to the completion of follow-up of all subjects. The interim immunogenicity analyses report(s) will include between-Group comparisons of those who received different Sm-p80 study product formulations and different schedules. The information from the reports may be used in abstracts and scientific presentations and reports.

6.6.1. Interim Safety Review

An interim safety review may include enrollment and demographic information, medical history, concomitant medications, physical assessments, 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. 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. Additionally, this trial will be monitored to determine if any of the halting rules described in Protocol v3.0 Section 8.6 are met.

6.6.2. Interim Immunogenicity or Efficacy Review

Interim immunogenicity analyses of, for example, total IgG ELISA responses will be performed for each Study Group, as the data is available for each study group. Depending on the timing of data availability, a report may cover one or more Study Groups. Immunogenicity reports will be provided by the SDCC to the DMID Scientific Lead and CPM, the IDCRC LOU representative(s), the study PI and investigators, and the SMC. Reports will include data summarized by Study Group. The data will be cleaned but not locked. These

reports along with interim safety results may be presented in publications, or public forums and used by the product developers for internal decision-making.

6.7. Multicenter Studies

Not applicable.

6.8. Multiple Comparisons/Multiplicity

This study is not designed to test any specific null hypothesis, and as such no adjustments for multiple testing are planned.

7. STUDY SUBJECTS

7.1. Disposition of Subjects

Table 11 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 9.

The disposition of subjects in the study will be tabulated by treatment group (Table 8). The table shows the total number of subjects screened, enrolled, received first dose, received second dose, received third dose, discontinued dosing or terminated from study follow-up, and the number completing the study. The number of subjects in each cohort who received study product by month will be summarized in Table 10.

A flowchart showing the disposition of study subjects, adapted from the Consort Statement will be included (Figure 1). 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 treatment group for all subjects (Table 5). Deviations that are considered major deviations that will be reviewed for possible subject exclusion from the per protocol population include: ineligibility and product deviations. 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

Not applicable. No efficacy evaluations will be performed for the main study objectives.

9. SAFETY EVALUATION

All safety analyses will be presented using the safety population. Subjects will be grouped for summary statistics using treatment group. An additional "All Subjects" group will be included to summarize across groups for solicited and unsolicited AE exhibits.

Any medical condition that is present at the time that the subject is screened will be considered baseline and not reported as an AE, unless it worsens in severity or increases in frequency during the study.

9.1. Demographic and Other Baseline Characteristics

Summaries of age, sex, ethnicity, race, height, weight and BMI will be presented by treatment group and overall (Table 12 and Table 13). 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. Numeric variables will be summarized by mean and standard deviation; categorical variables will be tabulated.

Individual subject listings (Appendix 3) will be presented for all demographics (Listing 6); pre-existing medical conditions (Listing 7); vital signs and oral temperature (Listing 15); and concomitant medications (Listing 17).

9.1.1. Prior and Concurrent Medical Conditions

All current illnesses and past pre-existing medical conditions will be Medical Dictionary for Regulatory Activities® (MedDRA) coded using MedDRA dictionary version 25.0 or higher.

Summaries of subjects' pre-existing medical conditions will be presented by treatment group (Table 14).

9.1.2. Prior and Concomitant Medications

Summaries of medications that were started prior to dosing and continuing at the time of dosing will be presented by World Health Organization (WHO) Drug Terms 2 and 3 and treatment group (Table 83).

9.2. Measurements of Treatment Compliance

Any subject receiving any number of doses of study product will be tabulated in Listing 8. The number of subjects who enrolled but were not vaccinated, the number who received any study product, and the number who received all scheduled treatments will be presented by treatment group as part of the subject disposition table (Table 8). Table 10 will present the time and number of subjects who received first dose by treatment arm.

9.3. Adverse Events

When calculating the incidence of adverse events (i.e., on a per subject basis), each subject will only be counted once and any repetitions of adverse events within a subject will be ignored; the denominator will be the total population size. All adverse events reported will be included in the summaries and analyses. An overall summary of adverse events is presented in Table 18 along with adverse events occurring in the Safety Population (Table 19). A summary of the proportion of subjects with solicited and unsolicited AEs by treatment group with be presented in Table 24.

9.3.1. Solicited Events and Symptoms

Systemic solicited adverse events were collected pre-vaccination, and systemic and injection site 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, chills, fatigue, malaise, myalgia, arthralgia, headache, nausea, and vomiting. Injection site events include: pruritus, erythema, induration/swelling, pain, and tenderness.

The proportion of subjects reporting at least one solicited adverse event will be summarized for each solicited adverse event, any systemic symptom, any injection site symptom, and any symptoms. The 95% CI calculated using Wilson score methodology from binomial distribution without continuity correction (Table 20, Table 21, Table 22, Table 23).

For each systemic and injection site event, any systemic event, any injection site event, and any solicited event, the maximum severity over 7 days after each vaccination will be summarized for the Safety population. The number and percentage of subjects reporting each event will be summarized by the maximum severity and treatment group, separately for each vaccination and over all vaccinations. For each event the denominator is the number of subjects with non-missing data for the specific event (Table 25, Table 26, Table 27, Table 28; and Figure 8, Figure 9, Figure 10, Figure 11, Figure 15, Figure 16, Figure 17, Figure 18) .

The number of subjects reporting a solicited adverse event will be summarized for each day post vaccination for each vaccination and for all vaccinations combined both in a summary table beginning Table 29 and continuing through Table 43, and graphically in a bar chart (Figure 5, Figure 6, Figure 7 , Figure 12, Figure 13, Figure 14). A comparison of the event rate for each treatment group between vaccination 1 and vaccination 2 and vaccination 1 and vaccination 3 will be presented (Table 44).

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

9.3.2. Unsolicited Adverse Events

The proportion of subjects reporting at least one unsolicited adverse event will be summarized by MedDRA system organ class and preferred term for each vaccination and over all vaccinations. Denominators for percentages are the number of subjects who received the vaccination being summarized. The 95% CI will be calculated using Wilson score methodology from binomial distribution without continuity correction.

Adverse events by subject will be presented in Listing 12.

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

- Subject incidence and total frequency of adverse events by treatment group and dose with 95% CI (Table 45, Table 46, Table 47);
- Summary of severity and relationship to study product (Table 48);
- Subject incidence and total frequency of related adverse events over time (Table 49, Table 50, Table 51, Table 52, Table 53);
- Subject listing of non-serious adverse events of moderate or greater severity (Table 55);
- Listing of other significant adverse events (Table 56);
- Bar chart of non-serious related adverse events by severity and MedDRA system organ class (Figure 19);

- Bar chart of non-serious related adverse events by severity (Figure 20);

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

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

- Deaths and Serious Adverse Events (Table 54);
- Adverse Events of Special Interest;
- New Onset Chronic Medical Conditions.

9.5. Pregnancies

For any subjects in the Safety population who became pregnant during the study, every attempt was made to follow these subjects to completion of pregnancy to document the outcome, including information regarding any complications with pregnancy and/or delivery. A listing of pregnancies and outcomes will be presented (Listing 18, Listing 19, Listing 20, Listing 21, Listing 22) if a pregnancy occurs post dosing.

9.6. Clinical Laboratory Evaluations

The distribution of laboratory results by severity, time point, and treatment group will be presented in Table 59, Table 60 and Table 61 for chemistry parameters and Table 67, Table 68, Table 69 and Table 70 for hematology parameters. Descriptive statistics including mean, standard deviation, median, minimum, and maximum values by time point, for each laboratory parameter, will be summarized in Table 65, Table 66, Table 75, Table 76 and Table 77. Changes in laboratory values will be presented in Figure 21, Figure 22, Figure 23, Figure 24 and Figure 25.

Subject visits with related laboratory results will be presented in Table 62, Table 63 and Table 64 for chemistry parameters and Table 71, Table 72, Table 73, and Table 74 for hematology parameters. A list of abnormal results will be presented in Table 57 and Table 58.

Listing 13 and Listing 14 will provide a complete listing of individual clinical laboratory results with applicable reference ranges.

9.7. Vital Signs and Physical Evaluations

Vital sign measurements included oral temperature, pulse, and blood pressure. Vital signs were assessed at screening visit, at vaccination visits, and at clinic visits scheduled within 7 days after vaccination. At other visits, vital signs were assessed if clinically indicated. Vital signs will be tabulated by visit and treatment group (Table 78, Table 79, Table 80, Table 81, Table 82 and Listing 15).

Physical Examinations performed at screening visit. At subsequent clinic visits, a targeted physical examination may be performed, if indicated based on the subject's interim medical history, by a study clinician licensed to make medical diagnoses. Targeted physical examinations also include an assessment for signs suggestive of MAAE/NOCMC/PIMMC. A full listing of abnormal physical exam findings by subject is presented in Listing 16.

9.8. Concomitant Medications

Concomitant medications will be coded to the Anatomical Therapeutic Classification (ATC) using the WHO Drug Dictionary. The use of prior and concomitant medications taken during the study will be recorded on the CRFs. A by-subject listing of concomitant medication use will be presented. The use of concomitant medications during the study will be summarized by ATC1, ATC2 code and treatment group for the Safety population (Table 83).

9.9. Other Safety Measures

Not applicable.

10. PHARMACOKINETICS

Not applicable.

11. IMMUNOGENICITY

11.1. Secondary Immunogenicity Analysis

11.1.1. ELISA (anti Sm-p80 Total IgG)

Antibody responses, measured by total IgG production to the recombinant Sm-p80 protein using ELISA will be presented at baseline (Day 1) and by study day (Days 8, 29, 36, 57 for all treatment groups; additionally Days 64, 85, 181 for Groups A, B, D, and E, and Days 180, 187, 208, 304 for Group C) using descriptive statistics in Table 15 (mITT immunogenicity population). For post-baseline timepoints, geometric mean fold rise (GMFR) and the proportion of subjects with at least a 4-fold rise will be presented with 95% confidence intervals for mITT population in Table 16 (mITT immunogenicity population). The ELISA seroresponse (at least 4-fold rise) rates at 28-days post vaccination will be compared between Group A vaccine group and each treatment group using Fisher's Exact Test (Table 17). Confidence intervals for proportions are calculated using Wilson Score methodology without continuity correction. Confidence intervals calculated for GMT and GMFR follow a t-distribution.

Antibody responses will be adjusted for baseline. Reverse cumulative distributions (RCD) curves will be presented with separate panels for each timepoint for mITT population in Figure 2. Graphs of Geometric Mean Anti-Sm-p80 ELISA responses over time will be presented in Figure 3. Individual time trends for each Anti-Sm-p80 ELISA will be presented in Figure 4.

Results of individual total IgG immunogenicity responses, scheduled and unscheduled, will be presented in Listing 9.

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

14. TECHNICAL DETAILS

All tables, figures, and listings will be generated using SAS version 9.4 or above or R version 3.4.2 or above.

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

Version 2.0 of Statistical Analysis Plan incorporates the following updates:

- Section 11.2 added for exploratory immunogenicity analysis. Details of ELISA IgG subclasses were moved from Section 11.1 to Section 11.2. Section 11.1 only includes ELISA total IgG information. The exploratory immunogenicity analysis will be included in a CSR addendum, after the completion of the interim CSR.
- Tables and figures pertaining to ELISA IgG subclasses were removed from Section 6.2.

Version 3.0 of Statistical Analysis Plan incorporates the following updates:

- Removal of text related to ELISA IgG subclasses including Section 11.2 exploratory immunogenicity analysis. These exploratory analyses will no longer be performed.
- Tables and figures pertaining to ELISA IgG subclasses were removed from Appendix 1 and Appendix 2. Listings that included ELISA IgG subclasses were revised in Appendix 3.

Version 4.0 of Statistical Analysis Plan incorporates the following updates:

- Removal of exploratory endpoints with the exception of RNA-Seq in Section 3.1.3 and Section 3.2.3.
- Removal of text related to exploratory endpoints with the exception of RNA-Seq in Section 4.1 and Section 4.5.2.
- Clarifications added to Section 9.1, Section 9.3.2 and Section 9.6.

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APPENDICES

APPENDIX 1. TABLE MOCK-UPS

LIST OF TABLES

9.1 Overall Study Design and Plan Description

Table 1: Study Design

Study Group	N	Study Product	Administration Schedule
A	9	100 µg Sm-p80 (unadjuvanted)	Day 1, 29, 57
B	9	10 µg Sm-p80 + 5 µg GLA-SE	Day 1, 29, 57
C	9	30 µg Sm-p80 + 5 µg GLA-SE	Day 1, 29, 180 (delayed booster)
D	9	30 µg Sm-p80 + 5 µg GLA-SE	Day 1, 29, 57
E	9	100 µg Sm-p80 + 5 µg GLA-SE	Day 1, 29, 57

9.5.1 Efficacy/Immunogenicity and Safety Measurements Assessed and Flow Chart

Table 2: Schedule of Events and Study Procedures, Study Groups A, B, D, and E

		Study Product Injection and Follow Up Visits												
Study day		1	2	4	8	29	32	36	57	60	64	85	181	422
Days after most recent vaccination		0	1	3	7	28	3	7	28	3	7	28	124	365
Visit Window (± number of days)		0	0	1	1	3	1	1	3	1	1	3	14	14
Study visit		01	02P	03	04	05	06	07	08	09	10	11	12	13P
Clinical Evaluations and Procedures	Tube													
Assessment of eligibility		X												
Assessment of individual halting criteria						X			X					
Review medical history and con meds[3]		X	X	X	X	X	X	X	X	X	X	X	X	X
Vital signs (blood pressure, pulse, and oral temperature[5])		X		X	X	X	X	X	X	X	X	X[4]	X[4]	
Enrollment		X												
Study Product Injection[1]		**I-1**				**I-2**			**I-3**					
Targeted physical exam		{X}		{X}	{X}	{X}	{X}	{X}	{X}	{X}	{X}	{X}	{X}	
Pre-administration reactogenicity assessment		X				X			X					
Evaluate study product injection site		X		X	X	X	X	X	X	X	X			

Table 2: Schedule of Events and Study Procedures, Study Groups A, B, D, and E *(Continued)*

		Study Product Injection and Follow Up Visits												
Study day		1	2	4	8	29	32	36	57	60	64	85	181	422
Days after most recent vaccination		0	1	3	7	28	3	7	28	3	7	28	124	365
Visit Window (± number of days)		0	0	1	1	3	1	1	3	1	1	3	14	14
Study visit		01	02P	03	04	05	06	07	08	09	10	11	12	13P
Clinical Evaluations and Procedures	Tube													
Provide and explain use of memory aid and thermometer		X				X			X					
Review memory aid			X	X	X		X	X		X	X			
Collection of solicited AEs		X	X	X	X	X	X	X	X	X	X			
Collection of unsolicited AEs and SAEs[3]		X	X	X	X	X	X	X	X	X	X	X	X	X
Pregnancy test (urine)[2]		X				X			X					
WBC, hemoglobin, platelets (mL)	EDTA	3			3	3		3	3		3	3		
Creatinine, ALT[6]	SST	10			10	10		10	10		10	10		
Serum collection for antibody assays and secondary research (mL)	SST	8.5			8.5	8.5		8.5	8.5		8.5	8.5	8.5	
PBMC isolation for secondary research (mL)	NaHep/ACD[7]	60			60	60		60	60		60	34	60	
Whole blood collection for gene expression assays	PAXGene	2.5			2.5	2.5		2.5	2.5		2.5			

Table 2: Schedule of Events and Study Procedures, Study Groups A, B, D, and E *(Continued)*

		Study Product Injection and Follow Up Visits												
Study day		1	2	4	8	29	32	36	57	60	64	85	181	422
Days after most recent vaccination		0	1	3	7	28	3	7	28	3	7	28	124	365
Visit Window (± number of days)		0	0	1	1	3	1	1	3	1	1	3	14	14
Study visit		01	02P	03	04	05	06	07	08	09	10	11	12	13P
Clinical Evaluations and Procedures	Tube													
Total volume per visit (mL)		84			84	84		84	84		84	55.5	68.5	
Cumulative volume (prior 56 days)		113.5			197.5	281.5		365.5	420		420	391.5	68.5	

{ } required at this visit only if clinically indicated
P = phone assessment
[1]0.5 mL of the designated study product will be injected IM in the deltoid muscle. Prior to the injection, a pre-administration reactogenicity assessment will be performed to establish baseline. After the injection, subjects will be observed for 30 minutes. The injection site will be evaluated and vital signs obtained during that period and before the subject leaves the clinic. Subjects will be provided with a Memory Aid and thermometer for recording daily maximum oral temperature, solicited injection site and systemic reactions, unsolicited AEs, and concomitant medications, beginning on the evening of the day of study product injection and continuing daily for the next seven days. Subjects will be encouraged to take their temperature around the same time each day and also if they feel feverish. Subjects will be instructed on how to use the memory aid and how to rate any AEs. Subjects will also be instructed to notify the study center if they develop any severe reactions and/or fever ≥ 38°C (100.4°F).
[2]For women of childbearing potential. Must be confirmed as negative prior to injection of study product. The visit will also include review of contraceptive/menstrual history and pregnancy avoidance counseling.
[3]After Study Visit 11 (or Study Day 85 if Study Visit 11 is not attended), through the end of study follow-up (Day 422), only SAEs, MAAEs, NOCMCs, and PIMMCs will be collected. Other unsolicited AEs and concomitant medications will not be collected.
[4]Vital signs will be assessed only if clinically indicated.
[5]Subjects must not eat or drink anything hot or cold, or smoke within 10 minutes prior to taking oral temperature.
[6]Blood collection volumes shown are the maximum that may potentially be drawn from the participant at each visit based on collection tube availability.
[7]ACD collection tubes can be used to collect blood that will be processed for PBMC if appropriate NaHep tubes are unavailable.

Table 3: Schedule of Events and Study Procedures, Study Group C

		Study Product Injection and Follow Up Visits													
Study day		1	2	4	8	29	32	36	57	180	183	187	208	304	545
Days after most recent vaccination		0	1	3	7	28	3	7	28	151	3	7	28	124	365
Visit Window (± number of days)		0	0	1	1	3	1	1	3	7	1	1	3	14	14
Study visit		01	02P	03	04	05	06	07	08	09	10	11	12	13	14P
Clinical Evaluations and Procedures	Tube														
Assessment of eligibility		X													
Assessment of individual halting criteria						X				X					
Review medical history and con meds[3]		X	X	X	X	X	X	X	X	X	X	X	X	X	X
Vital signs (blood pressure, pulse, and oral temperature[5])		X		X	X	X	X	X	X	X	X	X	X[4]	X[4]	
Enrollment		X													
Study Product Injection[1]		**I-1**				**I-2**				**I-3**					
Targeted physical exam		{X}		{X}	{X}	{X}	{X}	{X}	{X}	{X}	{X}	{X}	{X}	{X}	
Pre-administration reactogenicity assessment		X				X				X					
Evaluate study product injection site		X		X	X	X	X	X		X	X	X			
Provide and explain use of memory aid and thermometer		X				X				X					
Review memory aid			X	X	X		X	X			X	X			
Collection of solicited AEs		X	X	X	X	X	X	X		X	X	X			
Collection of unsolicited AEs and SAEs[3]		X	X	X	X	X	X	X	X[3]	X	X	X	X	X	X
Pregnancy test (urine)[2]		X				X				X					
WBC, hemoglobin, platelets (mL)	EDTA	3			3	3		3	3	3		3	3		
Creatinine, ALT[6]	SST	10			10	10		10	10	10		10	10		
Serum collection for antibody assays and secondary research (mL)	SST	8.5			8.5	8.5		8.5	8.5	8.5		8.5	8.5	8.5	
PBMC isolation for secondary research (mL)	NaHep/ACD[7]	60			60	60		60	60	60		60	34	60	

Table 3: Schedule of Events and Study Procedures, Study Group C *(Continued)*

		Study Product Injection and Follow Up Visits													
Study day		1	2	4	8	29	32	36	57	180	183	187	208	304	545
Days after most recent vaccination		0	1	3	7	28	3	7	28	151	3	7	28	124	365
Visit Window (± number of days)		0	0	1	1	3	1	1	3	7	1	1	3	14	14
Study visit		01	02P	03	04	05	06	07	08	09	10	11	12	13	14P
Clinical Evaluations and Procedures	Tube														
Whole blood collection for gene expression assays	PAXGene	2.5			2.5	2.5		2.5		2.5		2.5			
Total volume per visit (mL)		84			84	84		84	84	84		84	55.5	68.5	
Cumulative volume (prior 56 days)		113.5			197.5	281.5		365.5	420	84		168	223.5	68.5	

{ } required at this visit only if clinically indicated
P = phone assessment
[1]0.5 mL of the designated study product will be injected IM in the deltoid muscle. Prior to the injection, a pre-administration reactogenicity assessment will be performed to establish baseline. After the injection, subjects will be observed for 30 minutes. The injection site will be evaluated and vital signs obtained during that period and before the subject leaves the clinic. Subjects will be provided with a Memory Aid and thermometer for recording daily maximum oral temperature, solicited injection site and systemic reactions, unsolicited AEs, and concomitant medications, beginning on the evening of the day of study product injection and continuing daily for the next seven days. Subjects will be encouraged to take their temperature around the same time each day and also if they feel feverish. Subjects will be instructed on how to use the memory aid and how to rate any AEs. Subjects will also be instructed to notify the study center if they develop any severe reactions and/or fever ≥ 38°C (100.4°F).
[2]For women of childbearing potential. Must be confirmed as negative prior to injection of study product. The visit will also include review of contraceptive/menstrual history and pregnancy avoidance counseling.
[3]After Study Visit 8 (or Study Day 57 if Study Visit 8 is not attended), through the time of the third study vaccination at Study Visit 09, only SAEs, MAAEs, NOCMCs, and PIMMCs will be collected. Other unsolicited AEs and concomitant medications will not be collected during this period. Collection of unsolicited AEs and concomitant medications will then resume at the time of the third vaccination and continue through Study Visit 12 (or Study Day 208 if Study Visit 12 is not attended), after which only SAEs, MAAEs, NOCMCs, and PIMMCs will be collected.
[4]Vital signs will be assessed only if clinically indicated.
[5]Subjects must not eat or drink anything hot or cold, or smoke within 10 minutes prior to taking oral temperature.
[6]Blood collection volumes shown are the maximum that may potentially be drawn from the participant at each visit based on collection tube availability.
[7]ACD collection tubes can be used to collect blood that will be processed for PBMC if appropriate NaHep tubes are unavailable.

9.7.1 Sample Size

Table 4: Sample Size/Probability Estimates

Probability of event after receiving studyproduct	Probability of observing event among 9 subjects	Probability of observing event among 45 subjects
0.01	0.086	0.364
0.05	0.370	0.901
0.10	0.613	0.991
0.15	0.768	0.999
0.20	0.866	>0.99
0.25	0.925	>0.99

10.2 Protocol Deviations

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

[Implementation Note: Only deviation types with at least one deviation observed in any treatment group will be shown. If none observed, that deviation type will not be shown.]

Category	Deviation Type	Group A: 100 µg Sm-p80 (unadjuvanted) (N=X)		Group B: 10 µg Sm-p80 + 5 µg GLA-SE (N=X)		Group C: 30 µg Sm-p80 + 5 µg GLA-SE (delayed booster) (N=X)		Group D: 30 µg Sm-p80 + 5 µg GLA-SE (N=X)		Group E: 100 µg Sm-p80 + 5 µg GLA-SE (N=X)		All Subjects (N=X)	
		No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.
Eligibility/enrollment	Any type												
	Did not meet inclusion criterion	x	x	x	x	x	x	x	x	x	x	x	x
	Met exclusion criterion												
	ICF not signed prior to study procedures												
	Other												
Treatment administration schedule	Any type												
	Out of window visit												
	Missed visit/visit not conducted												
	Missed treatment administration												
	Delayed treatment administration												
	Other												
Follow-up visit schedule	Any type												

Table 5: Distribution of Protocol Deviations by Category, Type, and Treatment Group *(Continued)*

Category	Deviation Type	Group A: 100 µg Sm-p80 (unadjuvanted) (N=X)		Group B: 10 µg Sm-p80 + 5 µg GLA-SE (N=X)		Group C: 30 µg Sm-p80 + 5 µg GLA-SE (delayed booster) (N=X)		Group D: 30 µg Sm-p80 + 5 µg GLA-SE (N=X)		Group E: 100 µg Sm-p80 + 5 µg GLA-SE (N=X)		All Subjects (N=X)	
		No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.
	Out of window visit												
	Missed visit/visit not conducted												
	Other												
Protocol procedure/assessment	Any type												
	Incorrect version of ICF signed												
	Blood not collected												
	Urine not collected												
	Stool not collected												
	Other specimen not collected												
	Too few aliquots obtained												
	Specimen result not obtained												
	Required procedure not conducted												
	Required procedure done incorrectly												
	Study product temperature excursion												

Table 5: Distribution of Protocol Deviations by Category, Type, and Treatment Group *(Continued)*

Category	Deviation Type	Group A: 100 µg Sm-p80 (unadjuvanted) (N=X)		Group B: 10 µg Sm-p80 + 5 µg GLA-SE (N=X)		Group C: 30 µg Sm-p80 + 5 µg GLA-SE (delayed booster) (N=X)		Group D: 30 µg Sm-p80 + 5 µg GLA-SE (N=X)		Group E: 100 µg Sm-p80 + 5 µg GLA-SE (N=X)		All Subjects (N=X)	
		No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.	No. of Subj.	No. of Dev.
	Specimen temperature excursion												
	Other												
Treatment administration	Any type												
	Required procedure done incorrectly												
	Study product temperature excursion												
	Other												
Note: N = Number of subjects enrolled to the specific treatment group.													

12.2.2 Displays of Adverse Events

Table 6: Solicited Adverse Event Grading Scale

Pulse and Blood Pressure

	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)
Physiologic Parameter			
Tachycardia - beats per minute	101 – 115	116 – 130	> 130
Hypotension (systolic) mm Hg[1]	85 – 89	80 – 84	< 80
Hypertension (systolic) mm Hg[2]	141 – 150	151 – 155	> 155
Hypertension (diastolic) mm Hg[3]	96 – 100	101 – 105	>105

The inclusion criteria for systolic blood pressure includes values from 85 through 150, inclusive and for diastolic blood pressure includes values ≤ 100.

[1]Subjects with baseline (prior to first vaccination) Grade 1 values of 85-89 mm Hg are defined with a hypotension (systolic) AE only due to post-vaccination values ≤ 84 mm Hg and the AE isDefined as Grade 1 based on values of 80 through 84 and Grade 2 based on values less than 80.

[2]Subjects with baseline (prior to first vaccination) Grade 1 values of 141-150 mm Hg are definedwith a hypertension (systolic) AE only due to post-vaccination values over 150 mm Hg and the AE is Defined as Grade 1 based on values of 151 through 155 mm Hg and Grade 2 based on values over 155.

[3]Subjects with baseline (prior to first vaccination) Grade 1 values of 96-100 mm Hg are defined with a hypertension (diastolic) AE only due to post-vaccination values ≥ 101 mm Hg and the AEis Defined as Grade 1 based on values of 101 through 105 mm Hg and Grade 2 based on values over 105.

Table 6: Solicited Adverse Event Grading Scale *(Continued)*

Clinical Adverse Events

	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)
Cardiovascular			
Arrhythmia		Asymptomatic, transient signs, no Rx required	Recurrent/persistent; symptomatic Rx required
Hemorrhage, Blood Loss	Estimated blood loss ≤ 100 mL	Estimated blood loss > 100 mL, no transfusion required	Transfusionrequired
Respiratory			
Cough	Transient- notreatment	Persistent cough;	Interferes withdaily activities
Bronchospasm, Acute	Transient; no treatment; 71% – 80% FEV1 of peak flow	Requires treatment; normalizes with bronchodilator; FEV1 60% – 70% (of peak flow)	No normalizationwith bronchodilator; FEV1 < 60% of peak flow
Dyspnea	Does not interfere with usual and social activities	Interferes with usual and social activities, no treatment	Prevents daily and usual social activityor requires treatment
Gastrointestinal			
Vomiting	No interference with activity or 1 - 2 episodes/24hours	Some interference with activity or > 2 episodes/24hours	Prevents daily activity or requiresIV hydration
Diarrhea	2 - 3 loose or watery stools or < 400 gms/24 hours	4 - 5 loose or watery stools or 400 - 800 gms/24hours	6 or more loose or watery stools or > 800gms/24 hours orrequires IV hydration
Systemic Reactions			
Allergic Reaction	Pruritus without rash	Localized urticaria	Generalized urticaria; angioedema or anaphylaxis
All Other conditions			
Illness or clinical adverse event (as defined according to applicable regulations)	No interference with activity	Some interference with activity not requiring medical intervention	Prevents daily activity and requires medical intervention

12.4.1 Individual Laboratory Measurements and Abnormal Laboratory Values

Table 7: Laboratory Adverse Event Grading Scale

	Mild (Grade 1)	Moderate (Grade 2)	Severe (Grade 3)
Hematology			
WBC 10^3/UL (Decrease)	2.50 – 3.50	1.50 – 2.49	< 1.50
WBC 10^3/UL (Increase)	13.01 – 15.00	15.01 – 20.00	> 20.00
HgB g/dL (Decrease) (Female)	11.0 – 11.49	9.5 – 10.9	< 9.5
HgB g/dL (Decrease) (Male)	12.0 – 12.5	10.0 – 11.9	< 10.0
Platelets 10^3/UL (Decrease)	120 – 130	100 – 119	< 100
Platelets 10^3/UL (Increase)	416 – 550	551– 750	> 750
Chemistry			
ALT IU/L (Increase)	47 – 105	106 – 175	> 175
Creatinine mg/dL (Increase)	> ULN – 1.7	1.8 – 2.0	> 2.0
ULN = upper limit of normal range			

14.1 Description of Study Subjects

14.1.1 Disposition of Subjects

Table 8: Subject Disposition by Treatment Group

[Implementation Note: Percentages are calculated using the denominators displayed in the header. Listings should be referenced by title for clarity.]

Subject Disposition	Group A: 100 µg Sm-p80 (unadjuvanted) (N=X)		Group B: 10 µg Sm-p80 + 5 µg GLA-SE (N=X)		Group C: 30 µg Sm-p80 + 5 µg GLA-SE (delayed booster) (N=X)		Group D: 30 µg Sm-p80 + 5 µg GLA-SE (N=X)		Group E: 10 µg Sm-p80 + 5 µg GLA-SE (N=X)		All Subjects (N=X)	
	n	%	n	%	n	%	n	%	n	%	n	%
Screened	--	--	--	--	--	--	--	--	--	--	x	--
Enrolled/Randomized	x	100	x	100	x	100	x	100	x	100	x	100
Received One Scheduled Treatment	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Received Two Scheduled Treatments	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Received All Scheduled Treatments [a]	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Completed All Safety Blood Draws Groups A, B, D, E [Days 1, 8, 29, 36, 57, 64, 85] Group C [Days 1, 8, 29, 36, 57, 180, 187, 208]												
Completed All Immunogenicity Blood Draws for Antibody Assays Groups A, B, D, E [Days 1, 8, 29, 36, 57, 64, 85, 181] Group C [Days 1, 8, 29, 36, 57, 180, 187, 208, 304]												
Completed Follow-up [a] Groups A, B, D, E (Study Day 422) Group C (Study Day 545)												
Completed Per Protocol [b]												

Note: N = Number of subjects enrolled to the specified treatment group.
[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 9: Analysis Populations by Treatment Group

Analysis Populations	Reason Subjects Excluded	Group A: 100 µg Sm-p80 (unadjuvanted) (N=X)		Group B: 10 µg Sm-p80 + 5 µg GLA-SE (N=X)		Group C: 30 µg Sm-p80 + 5 µg GLA-SE (delayed booster) (N=X)		Group D: 30 µg Sm-p80 + 5 µg GLA-SE (N=X)		Group E: 100 µg Sm-p80 + 5 µg GLA-SE (N=X)		All Subjects (N=X)	
		n	%	n	%	n	%	n	%	n	%	%	n
Safety Population	Any Reason	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Did not receive study product												
	[Reason 2]												
mITT Immunogenicity Population	Any Reason												
	Did not have post-baseline immunogenicity assay												
	[Reason 2]												
Per Protocol Population	Any Reason												
	Did not have post-baseline immunogenicity assay												
	Found to be ineligible at baseline after the enrollment												
	[Reason 3]												

Note: N = Number of subjects enrolled to the specified treatment group. Subjects may be counted for more than one reason but will only be counted up to one time for "Any Reason" per population.

Table 10: Dates of First Treatment by Treatment Group

Dates of Dosing	Group A: 100 µg Sm-p80 (unadjuvanted) (N=X)	Group B: 10 µg Sm-p80 + 5 µg GLA-SE (N=X)	Group C: 30 µg Sm-p80 + 5 µg GLA-SE (delayed booster) (N=X)	Group D: 30 µg Sm-p80 + 5 µg GLA-SE (N=X)	Group E: 10 µg Sm-p80 + 5 µg GLA-SE (N=X)	All Subjects (N=X)
Total (Entire period of enrollment)						
DDMMMYYYY-DDMMMYYYY [categorize based on length of enrollment period]	x	x	x	x	x	x
Note: N = Number of subjects enrolled to the specified treatment group.						

Table 11: Ineligibility Summary of Screen Failures

[Implementation Note: Inclusion and exclusion criteria are listed in **Section 4.3**.]

Inclusion/Exclusion Category	Inclusion/Exclusion Criterion	n[a]	%[b]
Inclusion and Exclusion	Number of subjects failing any eligibility criterion	x	100
Inclusion	Any inclusion criterion	x	xx
	[inclusion criterion 1]	x	xx
	[inclusion criterion 2]	x	xx
	[inclusion criterion 3]	x	xx
Exclusion	Any exclusion criterion	x	xx
	[exclusion criterion 1]	x	xx
	[exclusion criterion 2]	x	xx
	[exclusion criterion 3]	x	xx
Eligible but not enrolled	[Reason 1]	x	xx
	[Reason 2]	x	xx

[a] More than one criterion may be marked per subject.
[b] Denominator for percentages is the total number of screen failures.

14.1.2 Demographic Data by Study Group

Table 12: Summary of Categorical Demographic and Baseline Characteristics by Treatment Group, All Enrolled Subjects

Variable	Characteristic	Group A: 100 µg Sm-p80 (unadjuvanted) (N=X)		Group B: 10 µg Sm-p80 + 5 µg GLA-SE (N=X)		Group C: 30 µg Sm-p80 + 5 µg GLA-SE (delayed booster) (N=X)		Group D: 30 µg Sm-p80 + 5 µg GLA-SE (N=X)		Group E: 100 µg Sm-p80 + 5 µg GLA-SE (N=X)		All Subjects (N=X)	
		n	%	n	%	n	%	n	%	n	%	n	%
Sex	Male	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Female												
Ethnicity	Not Hispanic or Latino	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Hispanic or Latino												
	Not Reported												
	Unknown												
Race	American Indian or Alaska Native	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Asian												
	Native Hawaiian or Other Pacific Islander												
	Black or African American												
	White												
	Multi-Racial												
	Unknown												

Note: N = Number of subjects in the Safety Population.

Table 13: Summary of Continuous Demographic and Baseline Characteristics by Treatment Group

Variable	Statistic	Group A: 100 µg Sm-p80 (unadjuvanted) (N=X)	Group B: 10 µg Sm-p80 + 5 µg GLA-SE (N=X)	Group C: 30 µg Sm-p80 + 5 µg GLA-SE (delayed booster) (N=X)	Group D: 30 µg Sm-p80 + 5 µg GLA-SE (N=X)	Group E: 100 µg Sm-p80 + 5 µg GLA-SE (N=X)	All Subjects (N=X)
Age (years)	Mean	xx	xx	xx	xx	xx	xx
	Standard Deviation	xx	xx	xx	xx	xx	xx
	Median	x	x	x	x	x	x
	Minimum	x	x	x	x	x	x
	Maximum	x	x	x	x	x	x
Height (cm)	Mean						
	Standard Deviation						
	Median						
	Minimum						
	Maximum						
Weight (kg)	Mean						
	Standard Deviation						
	Median						
	Minimum						
	Maximum						
BMI (kg/m^2)	Mean						
	Standard Deviation						
	Median						
	Minimum						
	Maximum						
Note: N = Number of subjects in the Safety Population.							

14.1.3 Prior and Concurrent Medical Conditions

Table 14: Summary of Subjects with Pre-Existing Medical Conditions by MedDRA System Organ Class and Treatment Group

MedDRA System Organ Class	Group A: 100 µg Sm-p80 (unadjuvanted) (N=X)		Group B: 10 µg Sm-p80 + 5 µg GLA-SE (N=X)		Group C: 30 µg Sm-p80 + 5 µg GLA-SE (delayed booster) (N=X)		Group D: 30 µg Sm-p80 + 5 µg GLA-SE (N=X)		Group E: 100 µg Sm-p80 + 5 µg GLA-SE (N=X)		All Subjects (N=X)	
	n	%	n	%	n	%	n	%	n	%	n	%
Any SOC	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
[SOC 1]												
[SOC 2]												
[SOC 3]												

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

14.2 Immunogenicity Data

Table 15: Anti-Sm-p80 ELISA Total IgG Geometric Mean Titers (GMT) Results with 95% Confidence Intervals by Time Point and Treatment Group, mITT Immunogenicity Population

Time Point	Statistic	Group A: 100 µg Sm-p80 (unadjuvanted) (N=X)	Group B: 10 µg Sm-p80 + 5 µg GLA-SE (N=X)	Group C: 30 µg Sm-p80 + 5 µg GLA-SE (delayed booster) (N=X)	Group D: 30 µg Sm-p80 + 5 µg GLA-SE (N=X)	Group E: 100 µg Sm-p80 + 5 µg GLA-SE (N=X)
Study Day 1 (Pre-Dose 1) (Baseline)	n	x	x	x	x	x
	GMT (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Mean	x.x	x.x	x.x	x.x	x.x
	Std. Dev.	x.x	x.x	x.x	x.x	x.x
	Median	x.x	x.x	x.x	x.x	x.x
	(Minimum, Maximum)	(x.x, x.x)	(x.x, x.x)	(x.x, x.x)	(x.x, x.x)	(x.x, x.x)
Study Day 8 (7 Days Post Dose 1)	n					
	GMT (95% CI)					
	Mean					
	Std. Dev.					
	Median					
	(Minimum, Maximum)					
Study Day 29 (28 Days Post Dose 1; Pre-Dose 2)	n					
	GMT (95% CI)					
	Mean					

Table 15: Anti-Sm-p80 ELISA Total IgG Geometric Mean Titers (GMT) Results with 95% Confidence Intervals by Time Point and Treatment Group, mITT Immunogenicity Population *(Continued)*

Time Point	Statistic	Group A: 100 µg Sm-p80 (unadjuvanted) (N=X)	Group B: 10 µg Sm-p80 + 5 µg GLA-SE (N=X)	Group C: 30 µg Sm-p80 + 5 µg GLA-SE (delayed booster) (N=X)	Group D: 30 µg Sm-p80 + 5 µg GLA-SE (N=X)	Group E: 100 µg Sm-p80 + 5 µg GLA-SE (N=X)
	Std. Dev.					
	Median					
	(Minimum, Maximum)					
Study Day 36 (7 Days Post Dose 2)	n					
	GMT (95% CI)					
	Mean					
	Std. Dev.					
	Median					
	(Minimum, Maximum)					
Study Day 57 (Groups A, B, D, E: 28 Days Post Dose 2; Pre-Dose 3) (Group C: 28 Days Post Dose 2)	n					
	GMT (95% CI)					
	Mean					
	Std. Dev.					
	Median					
	(Minimum, Maximum)					
Study Day 64 (Groups A, B, D, E: 7 Days Post Dose 3)	n				N/A	

Table 15: Anti-Sm-p80 ELISA Total IgG Geometric Mean Titers (GMT) Results with 95% Confidence Intervals by Time Point and Treatment Group, mITT Immunogenicity Population *(Continued)*

Time Point	Statistic	Group A: 100 µg Sm-p80 (unadjuvanted) (N=X)	Group B: 10 µg Sm-p80 + 5 µg GLA-SE (N=X)	Group C: 30 µg Sm-p80 + 5 µg GLA-SE (delayed booster) (N=X)	Group D: 30 µg Sm-p80 + 5 µg GLA-SE (N=X)	Group E: 100 µg Sm-p80 + 5 µg GLA-SE (N=X)
	GMT (95% CI)			N/A		
	Mean			N/A		
	Std. Dev.			N/A		
	Median			N/A		
	(Minimum, Maximum)			N/A		
Study Day 85 (Groups A, B, D, E: 28 Days Post Dose 3)	n			N/A		
	GMT (95% CI)			N/A		
	Mean			N/A		
	Std. Dev.			N/A		
	Median			N/A		
	(Minimum, Maximum)			N/A		
Study Day 180 (Group C: Pre-Dose 3)	n	N/A	N/A		N/A	N/A
	GMT (95% CI)	N/A	N/A		N/A	N/A
	Mean	N/A	N/A		N/A	N/A
	Std. Dev.	N/A	N/A		N/A	N/A
	Median	N/A	N/A		N/A	N/A
	(Minimum, Maximum)	N/A	N/A		N/A	N/A

Table 15: Anti-Sm-p80 ELISA Total IgG Geometric Mean Titers (GMT) Results with 95% Confidence Intervals by Time Point and Treatment Group, mITT Immunogenicity Population *(Continued)*

Time Point	Statistic	Group A: 100 µg Sm-p80 (unadjuvanted) (N=X)	Group B: 10 µg Sm-p80 + 5 µg GLA-SE (N=X)	Group C: 30 µg Sm-p80 + 5 µg GLA-SE (delayed booster) (N=X)	Group D: 30 µg Sm-p80 + 5 µg GLA-SE (N=X)	Group E: 100 µg Sm-p80 + 5 µg GLA-SE (N=X)
Study Day 187 (Group C: 7 Days Post Dose 3)	n	N/A	N/A		N/A	N/A
	GMT (95% CI)	N/A	N/A		N/A	N/A
	Mean	N/A	N/A		N/A	N/A
	Std. Dev.	N/A	N/A		N/A	N/A
	Median	N/A	N/A		N/A	N/A
	(Minimum, Maximum)	N/A	N/A		N/A	N/A
Study Day 181 (Groups A, B, D, E: 124 Days Post Dose 3)	n			N/A		
	GMT (95% CI)			N/A		
	Mean			N/A		
	Std. Dev.			N/A		
	Median			N/A		
	(Minimum, Maximum)			N/A		
Study Day 208 (Group C: 28 Days Post Dose 3)	n	N/A	N/A		N/A	N/A
	GMT (95% CI)	N/A	N/A		N/A	N/A
	Mean	N/A	N/A		N/A	N/A

Table 15: Anti-Sm-p80 ELISA Total IgG Geometric Mean Titers (GMT) Results with 95% Confidence Intervals by Time Point and Treatment Group, mITT Immunogenicity Population *(Continued)*

Time Point	Statistic	Group A: 100 µg Sm-p80 (unadjuvanted) (N=X)	Group B: 10 µg Sm-p80 + 5 µg GLA-SE (N=X)	Group C: 30 µg Sm-p80 + 5 µg GLA-SE (delayed booster) (N=X)	Group D: 30 µg Sm-p80 + 5 µg GLA-SE (N=X)	Group E: 100 µg Sm-p80 + 5 µg GLA-SE (N=X)
	Std. Dev.	N/A	N/A		N/A	N/A
	Median	N/A	N/A		N/A	N/A
	(Minimum, Maximum)	N/A	N/A		N/A	N/A
Study Day 304 (Group C: 124 Days Post Dose 3)	n	N/A	N/A		N/A	N/A
	GMT (95% CI)	N/A	N/A		N/A	N/A
	Mean	N/A	N/A		N/A	N/A
	Std. Dev.	N/A	N/A		N/A	N/A
	Median	N/A	N/A		N/A	N/A
	(Minimum, Maximum)	N/A	N/A		N/A	N/A

Note: N = Number of subjects in the mITT Immunogenicity Population; n = Number of subjects with results at the given time point. GMT = Geometric mean titer.

Pseudo Code:

```
/*Geometric Mean Titers*/
data dsn2;
 set dsn1;
      log_aval = log(aval);
proc means data=dsn2 n mean clm noprint;
 by stdy trta;
 var log_aval;
 output out= gmt0(drop=_type_ _freq_)
            n= n
            mean= mean
            std= sd
            median= med
            max= max
            min= min
            lclm=lclm
            uclm=uclm;
data gmt;
 set gmt0;
      gmt = put(exp(mean),8.1);                                          /*geometric mean titer*/
      gmt_l = put(exp(lclm), 8.1);                                       /*lower bound*/
      gmt_u = put(exp(uclm), 8.1);                                       /*upper bound*/
      gmt_ci = strip(gmt)||' ('||strip(gmt_l)||', '||strip(gmt_u)||')'; /*GMT(95% CI)*/
      gmt_mm = '('||strip(min)||', '||strip(max)||')';                   /*(Min, Max)*/
run;
```

Table 16: Anti-Sm-p80 ELISA Total IgG Geometric Mean Fold Rise (GMFR) and Seroconversion Results by Time Point and Treatment Group, mITT Immunogenicity Population

Time Point	Statistic	Group A: 100 µg Sm-p80 (unadjuvanted) (N=X)	Group B: 10 µg Sm-p80 + 5 µg GLA-SE (N=X)	Group C: 30 µg Sm-p80 + 5 µg GLA-SE (delayed booster) (N=X)	Group D: 30 µg Sm-p80 + 5 µg GLA-SE (N=X)	Group E: 100 µg Sm-p80 + 5 µg GLA-SE (N=X)
Study Day 8 (7 Days Post Dose 1)	n	x	x	x	x	x
	GMFR[a] (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Number (%) of Responders[b]	x (xx)	x (xx)	x (xx)	x (xx)	x (xx)
	95% CI	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x
Study Day 29 (28 Days Post Dose 1; Pre-Dose 2)	n	x	x	x	x	x
	GMFR[a] (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Number (%) of Responders[b]	x (xx)	x (xx)	x (xx)	x (xx)	x (xx)
	95% CI	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x
Study Day 36 (7 Days Post Dose 2)	n	x	x	x	x	x
	GMFR[a] (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Number (%) of Responders[b]	x (xx)	x (xx)	x (xx)	x (xx)	x (xx)
	95% CI	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x
Study Day 57 (Groups A, B, D, E: 28 Days Post Dose 2; Pre-Dose 3) (Group C: 28 Days Post Dose 2)	n	x	x	x	x	x
	GMFR[a] (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)	x.x (x.x, x.x)
	Number (%) of Responders[b]	x (xx)	x (xx)	x (xx)	x (xx)	x (xx)
	95% CI	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x	x.x, x.x

Table 16: Anti-Sm-p80 ELISA Total IgG Geometric Mean Fold Rise (GMFR) and Seroconversion Results by Time Point and Treatment Group, mITT Immunogenicity Population *(Continued)*

Time Point	Statistic	Group A: 100 µg Sm-p80 (unadjuvanted) (N=X)	Group B: 10 µg Sm-p80 + 5 µg GLA-SE (N=X)	Group C: 30 µg Sm-p80 + 5 µg GLA-SE (delayed booster) (N=X)	Group D: 30 µg Sm-p80 + 5 µg GLA-SE (N=X)	Group E: 100 µg Sm-p80 + 5 µg GLA-SE (N=X)
Study Day 64 (Groups A, B, D, E: 7 Days Post Dose 3)	n	x	x	N/A	x	x
	GMFR[a] (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	N/A	x.x (x.x, x.x)	x.x (x.x, x.x)
	Number (%) of Responders[b]	x (xx)	x (xx)	N/A	x (xx)	x (xx)
	95% CI	x.x, x.x	x.x, x.x	N/A	x.x, x.x	x.x, x.x
Study Day 85 (Groups A, B, D, E: 28 Days Post Dose 3)	n	x	x	N/A	x	x
	GMFR[a] (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	N/A	x.x (x.x, x.x)	x.x (x.x, x.x)
	Number (%) of Responders[b]	x (xx)	x (xx)	N/A	x (xx)	x (xx)
	95% CI	x.x, x.x	x.x, x.x	N/A	x.x, x.x	x.x, x.x
Study Day 180 (Group C: Pre-Dose 3)	n	N/A	N/A	x	N/A	N/A
	GMFR[a] (95% CI)	N/A	N/A	x.x (x.x, x.x)	N/A	N/A
	Number (%) of Responders[b]	N/A	N/A	x (xx)	N/A	N/A
	95% CI	N/A	N/A	x.x, x.x	N/A	N/A
Study Day 187 (Group C: 7 Days Post Dose 3)	n	N/A	N/A	x	N/A	N/A
	GMFR[a] (95% CI)	N/A	N/A	x.x (x.x, x.x)	N/A	N/A
	Number (%) of Responders[b]	N/A	N/A	x (xx)	N/A	N/A
	95% CI	N/A	N/A	x.x, x.x	N/A	N/A
Study Day 181 (Groups A, B, D, E: 124 Days Post Dose 3)	n	x	x	N/A	x	x

Table 16: Anti-Sm-p80 ELISA Total IgG Geometric Mean Fold Rise (GMFR) and Seroconversion Results by Time Point and Treatment Group, mITT Immunogenicity Population *(Continued)*

Time Point	Statistic	Group A: 100 µg Sm-p80 (unadjuvanted) (N=X)	Group B: 10 µg Sm-p80 + 5 µg GLA-SE (N=X)	Group C: 30 µg Sm-p80 + 5 µg GLA-SE (delayed booster) (N=X)	Group D: 30 µg Sm-p80 + 5 µg GLA-SE (N=X)	Group E: 100 µg Sm-p80 + 5 µg GLA-SE (N=X)
	GMFR[a] (95% CI)	x.x (x.x, x.x)	x.x (x.x, x.x)	N/A	x.x (x.x, x.x)	x.x (x.x, x.x)
	Number (%) of Responders[b]	x (xx)	x (xx)	N/A	x (xx)	x (xx)
	95% CI	x.x, x.x	x.x, x.x	N/A	x.x, x.x	x.x, x.x
Study Day 208 (Group C: 28 Days Post Dose 3)	n	N/A	N/A	x	N/A	N/A
	GMFR[a] (95% CI)	N/A	N/A	x.x (x.x, x.x)	N/A	N/A
	Number (%) of Responders[b]	N/A	N/A	x (xx)	N/A	N/A
	95% CI	N/A	N/A	x.x, x.x	N/A	N/A
Study Day 304 (Group C: 124 Days Post Dose 3)	n	N/A	N/A	x	N/A	N/A
	GMFR[a] (95% CI)	N/A	N/A	x.x (x.x, x.x)	N/A	N/A
	Number (%) of Responders[b]	N/A	N/A	x (xx)	N/A	N/A
	95% CI	N/A	N/A	x.x, x.x	N/A	N/A

Note: N = Number of subjects in the mITT Immunogenicity Population; n = Number of subjects with results at the given timepoint.
[a] GMFR represents the geometric mean fold rise in antibody compared to pre-dose 1.
[b] Number of responders represents the percentage of subjects with at least a 4-Fold Rise in antibody compared to Day 1, pre-dose 1.

Pseudo Code:

```
/*Geometric Mean Fold Rise*/
data dsn2;
 set dsn1;
      log_fold = log(mchg);
proc means data= dsn2 n mean clm noprint;
 by stdy trta;
 var log_fold;
 output out= gmfr0(drop= _type_ _freq_)
            n= n2
            mean= mean
            lclm= lclm
            uclm= uclm;
data gmfr;
 set gmfr0;
      gmfr = put(exp(mean),8.1);                                        /*geometric mean fold rise*/
      gmfr_l = put(exp(lclm), 8.1);                                     /*lower bound*/
      gmfr_u = put(exp(uclm), 8.1);                                     /*upper bound*/
      gmfr_ci = strip(gmfr)||' ('||strip(gmfr_l)||', '||strip(gmfr_u)||')';   /*GMFR(95%CI)*/

run;

/*Seroresponders*/
proc freq data= dsn1 noprint;
  table stdy*trta / out= totcnt(keep= stdy trta count rename= count=totcnt);

proc freq data= dsn1 noprint;
  where crit1fl ^= '';  /*seroconversion flag = Y*/
  table stdy*trta / out= cnt(keep= stdy trta count);
```

Pseudo Code *(continued)*:

```
data cntp;
 merge cnt totcnt;
 by stdy trta;
      if count=. then count=0;
      scn = put(count/totcnt*100, 5.1);
data cntci;
 set cntp;
      sym = 1;          /*seroconversion*/
 output;
      sym = 0;          /*no seroconversion*/
      count = totcnt - count;
 output;
proc freq data= cntci;
 by stdy trta;
 tables sym / nocum norow binomial(cl= wilson);
 weight count;          /*zeros: for CI of zero*/
  *exact binomial;
 ods output binomial= binany (keep=stdy trta name1 nvalue1 where=(name1 in ('XL_BIN','XU_BIN')));

run;
```

Table 17: Comparison of Anti-Sm-p80 ELISA Total IgG Seroresponse Rates between Group A and Each Treatment Group 28-Days Post Dose – mITT Immunogenicity Population

Analysis Population	Dose	Statistic	Group A: 100 µg Sm-p80 (unadjuvanted) (N=X)	Group B: 10 µg Sm-p80 + 5 µg GLA-SE (N=X)	Group C: 30 µg Sm-p80 + 5 µg GLA-SE (delayed booster) (N=X)	Group D: 30 µg Sm-p80 + 5 µg GLA-SE (N=X)	Group E: 100 µg Sm-p80 + 5 µg GLA-SE (N=X)
mITT Immunogenicity Population	1	Fraction Responders, n[a]	x	x	x	x	x
		Responders, Rate	xx%	xx%	xx%	xx%	xx%
		95% CI[b]	x.xxx, x.xxx	x.xxx, x.xxx	x.xxx, x.xxx	x.xxx, x.xxx	x.xxx, x.xxx
		Difference in Proportion	--	x.xxx	x.xxx	x.xx	x.xxxx
		p-value[c]	--	0.xxxx	0.xxxx	0.xxxx	0.xxxx
	2	…					
	3	…					
Per Protocol Population	…	…					

[a] Responder is defined as subjects with at least a 4-fold rise in antibody compared to pre-dose 1.
[b] 95% confidence intervals are from the Wilson score method without continuity correction.
[c] P-values were calculated using Fisher's Exact Test.

14.3 Safety Data

14.3.1 Displays of Adverse Events

Table 18: Overall Summary of Adverse Events

	Group A: 100 µg Sm-p80 (unadjuvanted) (N = X)		Group B: 10 µg Sm-p80 + 5 µg GLA-SE (N = X)		Group C: 30 µg Sm-p80 + 5 µg GLA-SE (delayed booster) (N = X)		Group D: 30 µg Sm-p80 + 5 µg GLA-SE (N = X)		Group E: 100 µg Sm-p80 + 5 µg GLA-SE (N = X)		All Subjects (N = X)	
Subjects[a] with	n	%	n	%	n	%	n	%	n	%	n	%
At least one local solicited adverse event	x	x	x	x	x	x	x	x	x	x	x	x
At least one systemic solicited adverse event	x	x	x	x	x	x	x	x	x	x	x	x
At least one unsolicited adverse event	x	x	x	x	x	x	x	x	x	x	x	x
At least one related unsolicited adverse event	x	x	x	x	x	x	x	x	x	x	x	x
Mild (Grade 1)	x	x	x	x	x	x	x	x	x	x	x	x
Moderate (Grade 2)	x	x	x	x	x	x	x	x	x	x	x	x
Severe (Grade 3)	x	x	x	x	x	x	x	x	x	x	x	x
Not yet assessed												
At least one severe (Grade 3) unsolicited adverse event	x	x	x	x	x	x	x	x	x	x	x	x
Related	x	x	x	x	x	x	x	x	x	x	x	x
Unrelated	x	x	x	x	x	x	x	x	x	x	x	x
At least one serious adverse event[b]	x	x	x	x	x	x	x	x	x	x	x	x
At least one related, serious adverse event	x	x	x	x	x	x	x	x	x	x	x	x
At least one adverse event leading to early termination[c]	x	x	x	x	x	x	x	x	x	x	x	x
At least one medically attended adverse event	x	x	x	x	x	x	x	x	x	x	x	x

Table 18: Overall Summary of Adverse Events *(Continued)*

	Group A: 100 µg Sm-p80 (unadjuvanted) (N = X)		**Group B: 10 µg Sm-p80 + 5 µg GLA-SE (N = X)**		**Group C: 30 µg Sm-p80 + 5 µg GLA-SE (delayed booster) (N = X)**		**Group D: 30 µg Sm-p80 + 5 µg GLA-SE (N = X)**		**Group E: 100 µg Sm-p80 + 5 µg GLA-SE (N = X)**		**All Subjects (N = X)**	
Subjects[a] with	n	%	n	%	n	%	n	%	n	%	n	%
At least one new onset chronic medical condition	x	x	x	x	x	x	x	x	x	x	x	x
At least one potentially immune mediated medical condition	x	x	x	x	x	x	x	x	x	x	x	x

Note: 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 the Serious Adverse Event Listing.
[c] As reported on the Adverse Event eCRF.

Table 19: Adverse Events Occurring in 5% of Subjects in Any Treatment MedDRA System Organ Class and Preferred Term, and Treatment Group - Safety Population

Preferred Term	MedDRA System Organ Class	Group A: 100 µg Sm-p80 (unadjuvanted) (N=X)			Group B: 10 µg Sm-p80 + 5 µg GLA-SE (N=X)			Group C: 30 µg Sm-p80 + 5 µg GLA-SE (delayed booster) (N=X)			Group D: 30 µg Sm-p80 + 5 µg GLA-SE (N=X)			Group E: 100 µg Sm-p80 + 5 µg GLA-SE (N=X)			All Subjects (N=X)		
		n	%	Events	n	%	Events	n	%	Events	n	%	Events	n	%	Events	n	%	Events
Serious Adverse Events																			
All	All	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
PT1	SOC1	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Etc.	Etc.																		
Other (Non-serious) Adverse Events																			
All	All	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
PT1	SOC1	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Etc.	Etc.																		
Note: 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 20: Number and Percentage of Subjects Experiencing Solicited Events with 95% Confidence Intervals by Symptom and Treatment Group – Post Dose 1

[Implementation Note: Confidence intervals will be computed via the Wilson Score method.]

Symptom	Group A: 100 µg Sm-p80 (unadjuvanted) (N=X)			Group B: 10 µg Sm-p80 + 5 µg GLA-SE (N=X)			Group C: 30 µg Sm-p80 + 5 µg GLA-SE (delayed booster) (N=X)			Group D: 30 µg Sm-p80 + 5 µg GLA-SE (delayed booster) (N=X)			Group E: 100 µg Sm-p80 + 5 µg GLA-SE (N=X)		
	n	%	95% CI[a]	n	%	95% CI[a]	n	%	95% CI[a]	n	%	95% CI[a]	n	%	95% CI[a]
Any Symptom	x	xx	x.x, x.x	x	xx	x.x, x.x	x	xx	x.x, x.x	x	xx	x.x, x.x	x	xx	x.x, x.x
Any Systemic Symptom															
[Systemic Symptom 1]															
[Systemic Symptom 2]															
Any Injection Site Symptom															
[Injection Site Symptom 1]															
[Injection Site Symptom 2]															

Note: N = Number of subjects in the Safety Population who received the specified dose; n = number of subjects reporting the specified event.
[a]95% confidence intervals are from the Wilson score method without continuity correction.

Tables with similar format to Table 20:

Table 21: Number and Percentage of Subjects Experiencing Solicited Events with 95% Confidence Intervals by Symptom and Treatment Group – Post Dose 2

Table 22: Number and Percentage of Subjects Experiencing Solicited Events with 95% Confidence Intervals by Symptom and Treatment Group – Post Dose 3

Table 23: Number and Percentage of Subjects Experiencing Solicited Events with 95% Confidence Intervals by Symptom and Treatment Group – Post Any Dose

Table 24: Comparison of the Proportion of Subjects Experiencing Solicited Events by Treatment Group

[Implementation Note: Confidence intervals will be computed via the Wilson Score method.]

Symptom	Statistic	Group A: 100 µg Sm-p80 (unadjuvanted) (N=X)	Group B: 10 µg Sm-p80 + 5 µg GLA-SE (N=X)	Group C: 30 µg Sm-p80 + 5 µg GLA-SE (delayed booster) (N=X)	Group D: 30 µg Sm-p80 + 5 µg GLA-SE (N=X)	Group E: 100 µg Sm-p80 + 5 µg GLA-SE (N=X)
Any Symptom	Proportion	x.xx	x.xx	x.xx	x.xx	x.xx
	95% CI[a] (for proportion)	x.xx, x.xx	x.xx, x.xx	x.xx, x.xx	x.xx, x.xx	x.xx, x.xx
	Difference		x.xx	x.xx	x.xx	x.xx
	95% CI[a] (for difference)		x.xx, x.xx	x.xx, x.xx	x.xx, x.xx	x.xx, x.xx
Any Systemic Symptom	Proportion					
	95% CI[a] (for proportion)					
	Difference					
	95% CI[a] (for difference)					
[Systemic Symptom 1]	…					
Any Injection Site Symptom	…					
[Injection Site Symptom 1]	…					

Note: N = Number of subjects in the Safety Population who received at least one dose.
[a]95% confidence intervals are from the Wilson score method without continuity correction.

Table 25: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity, and Treatment Group – Post Dose 1

[Implementation Note: Rows for Mild, Moderate, and Severe will only be shown if there is at least one non-zero count in that row. Confidence intervals will be computed via the Wilson Score method.]

Symptom	Severity	Group A: 100 µg Sm-p80 (unadjuvanted) (N=X)			Group B: 10 µg Sm-p80 + 5 µg GLA-SE (N=X)			Group C: 30 µg Sm-p80 + 5 µg GLA-SE (delayed booster) (N=X)			Group D: 30 µg Sm-p80 + 5 µg GLA-SE (N=X)			Group E: 100 µg Sm-p80 + 5 µg GLA-SE (N=X)			All Subjects (N = X)		
		n	%	95% CI[a]	n	%	95% CI[a]	n	%	95% CI[a]	n	%	95% CI[a]	n	%	95% CI[a]	n	%	95% CI[a]
Any Symptom	None	x	xx	x.x, x.x	x	xx	x.x, x.x	x	xx	x.x, x.x	x	xx	x.x, x.x	x	xx	x.x, x.x	x	xx	x.x, x.x
	Mild																		
	Moderate																		
	Severe																		
Systemic Symptoms																			
Any Systemic Symptom	None	x	xx	x.x, x.x	x	xx	x.x, x.x	x	xx	x.x, x.x	x	xx	x.x, x.x	x	xx	x.x, x.x	x	xx	x.x, x.x
	Mild																		
	Moderate																		
	Severe																		
[Systemic Symptom 1]	None																		
	Mild																		
	Moderate																		
	Severe																		
[Systemic Symptom 2]	None																		

Table 25: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity and Treatment Group – Post Dose 1 *(Continued)*

Symptom	Severity	Group A: 100 µg Sm-p80 (unadjuvanted) (N=X)			Group B: 10 µg Sm-p80 + 5 µg GLA-SE (N=X)			Group C: 30 µg Sm-p80 + 5 µg GLA-SE (delayed booster) (N=X)			Group D: 30 µg Sm-p80 + 5 µg GLA-SE (N=X)			Group E: 100 µg Sm-p80 + 5 µg GLA-SE (N=X)			All Subjects (N = X)		
		n	%	95% CI[a]	n	%	95% CI[a]	n	%	95% CI[a]	n	%	95% CI[a]	n	%	95% CI[a]	n	%	95% CI[a]
	Mild																		
	Moderate																		
	Severe																		
Injection Site Symptoms																			
Any Injection Site Symptom	None	x	xx	x.x, x.x	x	xx	x.x, x.x	x	xx	x.x, x.x	x	xx	x.x, x.x	x	xx	x.x, x.x	x	xx	x.x, x.x
	Mild																		
	Moderate																		
	Severe																		
[Injection Site Symptom 1]	None																		
	Mild																		
	Moderate																		
	Severe																		
[Injection Site Symptom 2]	None																		
	Mild																		
	Moderate																		
	Severe																		

Table 25: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity and Treatment Group – Post Dose 1 *(Continued)*

Symptom	Severity	Group A: 100 µg Sm-p80 (unadjuvanted) (N=X)			Group B: 10 µg Sm-p80 + 5 µg GLA-SE (N=X)			Group C: 30 µg Sm-p80 + 5 µg GLA-SE (delayed booster) (N=X)			Group D: 30 µg Sm-p80 + 5 µg GLA-SE (N=X)			Group E: 100 µg Sm-p80 + 5 µg GLA-SE (N=X)			All Subjects (N = X)		
		n	%	95% CI[a]	n	%	95% CI[a]	n	%	95% CI[a]	n	%	95% CI[a]	n	%	95% CI[a]	n	%	95% CI[a]
Note: N = Number of subjects in the Safety Population who received the specified dose. Severity is the maximum severity reported over all solicited symptoms post dosing for each subject. [a]95% confidence intervals are from the Wilson score method without continuity correction.																			

Tables with similar format to Table 25:

Table 26: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity, and Treatment Group – Post Dose 2

Table 27: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity, and Treatment Group – Post Dose 3

Table 28: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Maximum Severity, and Treatment Group – Post Any Dose

Table 29: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity, and Day Post Dosing – Group A: 100 µg Sm-p80 (unadjuvanted), Post Dose 1

100 µg Sm-p80 (unadjuvanted), Post Dose 1 (N=X)																			
		Pre-Dose		Post-Dose		Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7+	
Symptom	Severity	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Any Symptom	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild																		
	Moderate																		
	Severe																		
	Not Reported																		
Systemic Symptoms																			
Any Systemic Symptom	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild																		
	Moderate																		
	Severe																		
	Not Reported																		
[Systemic Symptom 1]	None																		
	Mild																		
	Moderate																		
	Severe																		
	Not Reported																		
[Systemic Symptom 2]	None																		

Table 29: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity, and Day Post Dosing – Group A: 100 µg Sm-p80 (unadjuvanted), Post Dose 1 *(Continued)*

100 µg Sm-p80 (unadjuvanted), Post Dose 1 (N=X)																			
		Pre-Dose		**Post-Dose**		**Day 1**		**Day 2**		**Day 3**		**Day 4**		**Day 5**		**Day 6**		**Day 7+**	
Symptom	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
	Mild																		
	Moderate																		
	Severe																		
	Not Reported																		
Injection Site Symptoms																			
Any Injection Site Symptom	None	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Mild																		
	Moderate																		
	Severe																		
	Not Reported																		
[Injection Site Symptom 1]	None																		
	Mild																		
	Moderate																		
	Severe																		
	Not Reported																		
[Injection Site Symptom 2]	None																		
	Mild																		

Table 29: Number and Percentage of Subjects Experiencing Solicited Events by Symptom, Severity, and Day Post Dosing – Group A: 100 µg Sm-p80 (unadjuvanted), Post Dose 1 *(Continued)*

100 µg Sm-p80 (unadjuvanted), Post Dose 1 (N=X)																			
		Pre-Dose		**Post-Dose**		**Day 1**		**Day 2**		**Day 3**		**Day 4**		**Day 5**		**Day 6**		**Day 7+**	
Symptom	**Severity**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
	Moderate																		
	Severe																		
	Not Reported																		
Note: N = Number of subjects in the Safety Population who received the specified dose. Severity is the maximum severity reported post dosing for each subject for each day.																			

Tables with similar format to Table 29:

[Implementation Note: Replace header with appropriate treatment and dose.]

Table 44: Number and Percentage of Subjects Experiencing Solicited Events for Dose 1 Compared with Dose 2 and Dose 3 by Treatment Group

[Implementation Note: Add group name to treatment, e.g. "Group A: 100 µg Sm-p80 (unadjuvanted)".]

Treatment Group		Dose 2 – Subjects with No Symptoms	Dose 2 – Subjects with Moderate or Greater Symptoms	Dose 2 – Total Number of Subjects	Dose 3 – Subjects with No Symptoms	Dose 3 – Subjects with Moderate or Greater Symptoms	Dose 3 – Total Number of Subjects
Systemic Symptoms							
100 µg Sm-p80 (unadjuvanted)	Dose 1 Subject with No Symptoms	x (%)	x (%)	x (%)	x (%)	x (%)	x (%)
	Dose 1 Subjects with Moderate or Greater Symptoms	x (%)	x (%)	x (%)	x (%)	x (%)	x (%)
	Dose 1 Total Number of Subjects	x (%)	x (%)	x (100%)	x (%)	x (%)	x (100%)
10 µg Sm-p80 + 5 µg GLA-SE	Dose 1 Subject with No Symptoms						
	Dose 1 Subjects with Moderate or Greater Symptoms						
	Dose 1 Total Number of Subjects						
30 µg Sm-p80 + 5 µg GLA-SE	Dose 1 Subject with No Symptoms						
	Dose 1 Subjects with Moderate or Greater Symptoms						
	Dose 1 Total Number of Subjects						
30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)	Dose 1 Subject with No Symptoms						

Table 44: Number and Percentage of Subjects Experiencing Solicited Events for Dose 1 Compared with Dose 2 and Dose 3 by Treatment Group *(Continued)*

	Dose 1 Subjects with Moderate or Greater Symptoms						
	Dose 1 Total Number of Subjects						
100 µg Sm-p80 + 5 µg GLA-SE	Dose 1 Subject with No Symptoms						
	Dose 1 Subjects with Moderate or Greater Symptoms						
	Dose 1 Total Number of Subjects						
Local Symptoms							
100 µg Sm-p80 (unadjuvanted)	Dose 1 Subjects with No Symptoms	x (%)	x (%)	x (%)			
	Dose 1 Subjects with Moderate or Greater Symptoms	x (%)	x (%)	x (%)			
	Dose 1Total Number of Subjects	x (%)	x (%)	x (100%)			
10 µg Sm-p80 + 5 µg GLA-SE	Dose 1 Subject with No Symptoms						
	Dose 1 Subjects with Moderate or Greater Symptoms						
	Dose 1 Total Number of Subjects						
30 µg Sm-p80 + 5 µg GLA-SE	Dose 1 Subject with No Symptoms						

Table 44: Number and Percentage of Subjects Experiencing Solicited Events for Dose 1 Compared with Dose 2 and Dose 3 by Treatment Group *(Continued)*

	Dose 1 Subjects with Moderate or Greater Symptoms						
	Dose 1 Total Number of Subjects						
30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)	Dose 1 Subject with No Symptoms						
	Dose 1 Subjects with Moderate or Greater Symptoms						
	Dose 1 Total Number of Subjects						
100 µg Sm-p80 + 5 µg GLA-SE	Dose 1 Subject with No Symptoms						
	Dose 1 Subjects with Moderate or Greater Symptoms						
	Dose 1 Total Number of Subjects						
Note: Denominators for percentages are the number of subjects in the Safety Population who received both doses being compared.							

Pseudo Code:

```
/*Data Format*/
 ID      Dose1   Dose2   Dose3
 A           0       1       0
 B           1       1       1
 C           0       0       1
 D           1       1       0
Where 0 = No Symptoms and 1 = Moderate or Greater at the given dose

proc freq data= t56;
 tables Dose1*Dose2 / out= _dose12; /*counts for dose 1 vs. dose 2*/
 tables Dose1*Dose3 / out= _dose13; /*counts for dose 1 vs. dose 3*/
run;
```

14.3.1.2 Unsolicited Adverse Events

Table 45: Summary of Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, and Treatment Group – Post Dose 1

MedDRA System Organ Class/ Preferred Term	Group A: 100 µg Sm-p80 (unadjuvanted) (N=X)			Group B: 10 µg Sm-p80 + 5 µg GLA-SE (N=X)			Group C: 30 µg Sm-p80 + 5 µg GLA-SE (delayed booster) (N=X)			Group D: 30 µg Sm-p80 + 5 µg GLA-SE (N=X)			Group E: 100 µg Sm-p80 + 5 µg GLA-SE (N=X)			All Subjects (N=X)		
	n	%	95% CI[a]	n	%	95% CI[a]	n	%	95% CI[a]	n	%	95% CI[a]	n	%	95% CI[a]	n	%	95% CI[a]
Any SOC	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx	x	xx	xx, xx
[SOC 1]																		
[PT 1]																		
[PT 2]																		
[SOC 2]																		
[PT 1]																		
[PT 2]																		

Note: N = number of subjects in the Safety Population who received the specified dose. This table presents number and percentage of subjects. A subject is only counted once per PT/time point.
[a]95% confidence intervals are from the Wilson score method without continuity correction.

Tables with similar format to Table 45:

Table 46: Summary of Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, and Treatment Group – Post Dose 2

Table 47: Summary of Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, and Treatment Group – Post Dose 3

Table 48: Unsolicited Adverse Events by MedDRA System Organ Class and Preferred Term, Maximum Severity, Relationship, and Treatment Group

MedDRA System Organ Class	Preferred Term	Severity	Group A: 100 µg Sm-p80 (unadjuvanted) (N = X)				Group B: 10 µg Sm-p80 + 5 µg GLA-SE (N = X)				Group C: 30 µg Sm-p80 + 5 µg GLA-SE (delayed booster) (N = X)				Group D: 30 µg Sm-p80 + 5 µg GLA-SE (N = X)				Group E: 100 µg Sm-p80 + 5 µg GLA-SE (N = X)				All Subjects (N = X)			
			Related		Not Related		Related		Not Related		Related		Not Related		Not Related		Not Related		Related		Not Related		Related		Not Related					
			n	%	n	%	n	%	n	%	n	%	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	x	xx	x	xx	x	xx	x	xx
		Mild																										
		Moderate																										
		Severe																										
SOC 1	PT 1	Any Severity																										
		Mild																										
		Moderate																										
		Severe																										
	PT 2	Any Severity																										
		Mild																										
		Moderate																										
		Severe																										

Note: N = Number of subjects in the Safety Population.

Table 49: Related Unsolicited Adverse Events Within 28 Days Post Dosing by MedDRA System Organ Class and Preferred Term and Dose – Group A: 100 µg Sm-p80 (unadjuvanted) (N=X)

		Post Dose 1			Post Dose 2			Post Dose 3			Post Any Dose		
MedDRA System Organ Class	**MedDRA Preferred Term**	**n**	**%**	**Events**	**n**	**%**	**Events**	**n**	**%**	**Events**	**n**	**%**	**Events**
Any SOC	Any PT	x	xx	x	x	xx	x	x	xx	x	x	xx	x
[SOC 1]	Any PT												
	[PT 1]												
	[PT 2]												
[SOC 2]	Any PT												
	[PT 1]												
	[PT 2]												

Note: N = Number of subjects in the Safety Population. This table presents number and percentage of subjects. For each time point, a subject is only counted once per PT.

Tables with similar format to Table 49:

Table 50: Related Unsolicited Adverse Events Within 28 Days Post Dosing by MedDRA System Organ Class and Preferred Term, and Dose – Group B: 10 µg Sm-p80 + 5 µg GLA-SE (N=X)

Table 51: Related Unsolicited Adverse Events Within 28 Days Post Dosing by MedDRA System Organ Class and Preferred Term, and Dose – Group C: 30 µg Sm-p80 + 5 µg GLA-SE (delayed booster) (N=X)

Table 52: Related Unsolicited Adverse Events Within 28 Days Post Dosing by MedDRA System Organ Class and Preferred Term, and Dose – Group D: 30 µg Sm-p80 + 5 µg GLA-SE (N=X)

Table 53: Related Unsolicited Adverse Events Within 28 Days Post Dosing by MedDRA System Organ Class and Preferred Term, and Dose – Group E: 100 µg Sm-p80 + 5 µg GLA-SE (N=X)

14.3.2 Listing of Deaths, Other Serious and Significant Adverse Events

Table 54: Listing of Serious Adverse Events

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

Table 55: Listing of Non-Serious, Unsolicited, Moderate or Severe Adverse Events

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

Table 56: Listing of Other Significant Adverse Events

Adverse Event	Number of Doses Received at Time of Event	No. of Days Post Associated Dose	Duration of Event	Severity	MedDRA System Organ Class	MAAE?	PIMMC/AESI?	NOCMC?	Relationship	Outcome
Subject ID: , Treatment Group: , AE Number:										
	Comments:									
Subject ID: , Treatment Group: , AE Number:										
	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 57: Listing of Abnormal Laboratory Results - Chemistry

Subject ID	Treatment Group	Sex	Age (years)	Planned Time Point	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 58: Listing of Abnormal Laboratory Results - Hematology

Subject ID	Treatment Group	Sex	Age (years)	Planned Time Point	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

Table 59: Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Any Chemistry Parameter

[Implementation Note: Add group name to treatment, e.g. "Group A: 100 µg Sm-p80 (unadjuvanted)".]

Time Point	Treatment Group	N	None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Missing	
			n	%	n	%	n	%	n	%	n	%
Study Day 1 (Baseline)	100 µg Sm-p80 (unadjuvanted)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	10 µg Sm-p80 + 5 µg GLA-SE											
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)											
	30 µg Sm-p80 + 5 µg GLA-SE											
	100 µg Sm-p80 + 5 µg GLA-SE											
Study Day 8	100 µg Sm-p80 (unadjuvanted)											
	10 µg Sm-p80 + 5 µg GLA-SE											
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)											
	30 µg Sm-p80 + 5 µg GLA-SE											
	100 µg Sm-p80 + 5 µg GLA-SE											
Study Day 29	100 µg Sm-p80 (unadjuvanted)											
	10 µg Sm-p80 + 5 µg GLA-SE											
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)											
	30 µg Sm-p80 + 5 µg GLA-SE											
	100 µg Sm-p80 + 5 µg GLA-SE											
Study Day 36	100 µg Sm-p80 (unadjuvanted)											

Table 59: Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Any Chemistry Parameter *(Continued)*

Time Point	Treatment Group	N	None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Missing	
			n	%	n	%	n	%	n	%	n	%
	10 µg Sm-p80 + 5 µg GLA-SE											
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)											
	30 µg Sm-p80 + 5 µg GLA-SE											
	100 µg Sm-p80 + 5 µg GLA-SE											
Study Day 57	100 µg Sm-p80 (unadjuvanted)											
	10 µg Sm-p80 + 5 µg GLA-SE											
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)											
	30 µg Sm-p80 + 5 µg GLA-SE											
	100 µg Sm-p80 + 5 µg GLA-SE											
Study Day 64	100 µg Sm-p80 (unadjuvanted)											
	10 µg Sm-p80 + 5 µg GLA-SE											
	30 µg Sm-p80 + 5 µg GLA-SE											
	100 µg Sm-p80 + 5 µg GLA-SE											
Study Day 85	100 µg Sm-p80 (unadjuvanted)											
	10 µg Sm-p80 + 5 µg GLA-SE											
	30 µg Sm-p80 + 5 µg GLA-SE											
	100 µg Sm-p80 + 5 µg GLA-SE											
Study Day 180	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)											
Study Day 187	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)											

Table 59: Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Any Chemistry Parameter *(Continued)*

Time Point	Treatment Group	N	None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Missing	
			n	%	n	%	n	%	n	%	n	%
Study Day 208	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)											
Max Severity Post Baseline	100 µg Sm-p80 (unadjuvanted)											
	10 µg Sm-p80 + 5 µg GLA-SE											
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)											
	30 µg Sm-p80 + 5 µg GLA-SE											
	100 µg Sm-p80 + 5 µg GLA-SE											

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

Tables with similar format to Table 59:

Table 60: Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Creatinine

Table 61: Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group -- Alanine Aminotransferase

Table 62: Abnormal Laboratory Results Related to Study Treatment by Parameter, Maximum Severity, Time Point, and Treatment Group – Any Chemistry Parameter

[Implementation Note: Only scheduled time points at which at least one related abnormal lab result is observed in any treatment group will be shown. Add group name to treatment, e.g. "Group A: 100 µg Sm-p80 (unadjuvanted)".]

Time Point	Treatment Group	N	None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
			n	%	n	%	n	%	n	%
Study Day 1 (Baseline)	100 µg Sm-p80 (unadjuvanted)	x	x	x	x	x	x	x	x	x
	10 µg Sm-p80 + 5 µg GLA-SE									
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)									
	30 µg Sm-p80 + 5 µg GLA-SE									
	100 µg Sm-p80 + 5 µg GLA-SE									
Study Day 8	100 µg Sm-p80 (unadjuvanted)									
	10 µg Sm-p80 + 5 µg GLA-SE									
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)									
	30 µg Sm-p80 + 5 µg GLA-SE									
	100 µg Sm-p80 + 5 µg GLA-SE									
Study Day 29	100 µg Sm-p80 (unadjuvanted)									
	10 µg Sm-p80 + 5 µg GLA-SE									
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)									
	30 µg Sm-p80 + 5 µg GLA-SE									
	100 µg Sm-p80 + 5 µg GLA-SE									
Study Day 36	100 µg Sm-p80 (unadjuvanted)									
	10 µg Sm-p80 + 5 µg GLA-SE									
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)									
	30 µg Sm-p80 + 5 µg GLA-SE									
	100 µg Sm-p80 + 5 µg GLA-SE									

Table 62: Abnormal Laboratory Results Related to Study Treatment by Parameter, Maximum Severity, Time Point, and Treatment Group – Any Chemistry Parameter *(Continued)*

Time Point	Treatment Group	N	None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
			n	%	n	%	n	%	n	%
Study Day 57	100 µg Sm-p80 (unadjuvanted)									
	10 µg Sm-p80 + 5 µg GLA-SE									
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)									
	30 µg Sm-p80 + 5 µg GLA-SE									
	100 µg Sm-p80 + 5 µg GLA-SE									
Study Day 64	100 µg Sm-p80 (unadjuvanted)									
	10 µg Sm-p80 + 5 µg GLA-SE									
	30 µg Sm-p80 + 5 µg GLA-SE									
	100 µg Sm-p80 + 5 µg GLA-SE									
Study Day 85	100 µg Sm-p80 (unadjuvanted)									
	10 µg Sm-p80 + 5 µg GLA-SE									
	30 µg Sm-p80 + 5 µg GLA-SE									
	100 µg Sm-p80 + 5 µg GLA-SE									
Study Day 180	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)									
Study Day 187	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)									
Study Day 208	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)									
Max Severity Post Baseline	100 µg Sm-p80 (unadjuvanted)									
	10 µg Sm-p80 + 5 µg GLA-SE									
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)									
	30 µg Sm-p80 + 5 µg GLA-SE									
	100 µg Sm-p80 + 5 µg GLA-SE									

Table 62: Abnormal Laboratory Results Related to Study Treatment by Parameter, Maximum Severity, Time Point, and Treatment Group – Any Chemistry Parameter *(Continued)*

Time Point	Treatment Group	N	None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
			n	%	n	%	n	%	n	%
Note: The "Max Post Baseline" rows indicate the maximum severity experienced by each subject at any time point post baseline. Note: N = Number of subjects in the Safety Population with lab results at the specified visit.										

Tables with similar format to Table 62:

Table 63: Abnormal Laboratory Results Related to Study Treatment by Parameter, Maximum Severity, Time Point, and Treatment Group – Creatinine

Table 64: Abnormal Laboratory Results Related to Study Treatment by Parameter, Maximum Severity, Time Point, and Treatment Group – Alanine Aminotransferase

Table 65: Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Creatinine (mg/dL)

[Implementation Note: Add group name to treatment, e.g. "Group A: 100 µg Sm-p80 (unadjuvanted)".]

Time Point	Treatment Group	N	Mean	Standard Deviation	Median	Min, Max
Study Day 1 (Baseline)	100 µg Sm-p80 (unadjuvanted)	x	xx.x	xx.x	xx.x	xx, xx
	10 µg Sm-p80 + 5 µg GLA-SE					
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)					
	30 µg Sm-p80 + 5 µg GLA-SE					
	100 µg Sm-p80 + 5 µg GLA-SE					
Study Day 8	100 µg Sm-p80 (unadjuvanted)					
	10 µg Sm-p80 + 5 µg GLA-SE					
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)					
	30 µg Sm-p80 + 5 µg GLA-SE					
	100 µg Sm-p80 + 5 µg GLA-SE					
Study Day 8, Change from Baseline	100 µg Sm-p80 (unadjuvanted)					
	…					
Study Day 29	100 µg Sm-p80 (unadjuvanted)					
	10 µg Sm-p80 + 5 µg GLA-SE					
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)					
	30 µg Sm-p80 + 5 µg GLA-SE					
	100 µg Sm-p80 + 5 µg GLA-SE					
Study Day 29, Change from Baseline	100 µg Sm-p80 (unadjuvanted)					
	…					
Study Day 36	100 µg Sm-p80 (unadjuvanted)					
	10 µg Sm-p80 + 5 µg GLA-SE					
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)					

Table 65: Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Creatinine (mg/dL) *(Continued)*

Time Point	Treatment Group	N	Mean	Standard Deviation	Median	Min, Max
	30 µg Sm-p80 + 5 µg GLA-SE					
	100 µg Sm-p80 + 5 µg GLA-SE					
Study Day 36, Change from Baseline	100 µg Sm-p80 (unadjuvanted)					
	…					
Study Day 57	100 µg Sm-p80 (unadjuvanted)					
	10 µg Sm-p80 + 5 µg GLA-SE					
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)					
	30 µg Sm-p80 + 5 µg GLA-SE					
	100 µg Sm-p80 + 5 µg GLA-SE					
Study Day 57, Change from Baseline	100 µg Sm-p80 (unadjuvanted)					
	…					
Study Day 64	100 µg Sm-p80 (unadjuvanted)					
	10 µg Sm-p80 + 5 µg GLA-SE					
	30 µg Sm-p80 + 5 µg GLA-SE					
	100 µg Sm-p80 + 5 µg GLA-SE					
Study Day 64, Change from Baseline	100 µg Sm-p80 (unadjuvanted)					
	…					
Study Day 85	100 µg Sm-p80 (unadjuvanted)					
	10 µg Sm-p80 + 5 µg GLA-SE					
	30 µg Sm-p80 + 5 µg GLA-SE					
	100 µg Sm-p80 + 5 µg GLA-SE					
Study Day 85, Change from Baseline	100 µg Sm-p80 (unadjuvanted)					
	…					
Study Day 180	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)					

Table 65: Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Creatinine (mg/dL) *(Continued)*

Time Point	Treatment Group	N	Mean	Standard Deviation	Median	Min, Max
Study Day 180, Change from Baseline	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)					
Study Day 187	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)					
Study Day 187, Change from Baseline	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)					
Study Day 208	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)					
Study Day 208, Change from Baseline	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)					
Note: N = Number of subjects in the Safety Population with laboratory results at the visit.						

Tables with similar format to Table 65:

Table 66: Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Alanine Aminotransferase (IU/L)

14.3.5.2 Hematology Results

Table 67: Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Any Hematology Parameter

[Implementation Note: Add group name to treatment, e.g. "Group A: 100 µg Sm-p80 (unadjuvanted)".]

Time Point	Treatment Group	N	None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Missing	
			n	%	n	%	n	%	n	%	n	%
Study Day 1 (Baseline)	100 µg Sm-p80 (unadjuvanted)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	10 µg Sm-p80 + 5 µg GLA-SE											
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)											
	30 µg Sm-p80 + 5 µg GLA-SE											
	100 µg Sm-p80 + 5 µg GLA-SE											
Study Day 8	100 µg Sm-p80 (unadjuvanted)											
	10 µg Sm-p80 + 5 µg GLA-SE											
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)											
	30 µg Sm-p80 + 5 µg GLA-SE											
	100 µg Sm-p80 + 5 µg GLA-SE											
Study Day 29	100 µg Sm-p80 (unadjuvanted)											
	10 µg Sm-p80 + 5 µg GLA-SE											
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)											
	30 µg Sm-p80 + 5 µg GLA-SE											
	100 µg Sm-p80 + 5 µg GLA-SE											
Study Day 36	100 µg Sm-p80 (unadjuvanted)											
	10 µg Sm-p80 + 5 µg GLA-SE											
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)											
	30 µg Sm-p80 + 5 µg GLA-SE											
	100 µg Sm-p80 + 5 µg GLA-SE											
Study Day 57	100 µg Sm-p80 (unadjuvanted)											

Table 67: Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Any Hematology Parameter *(Continued)*

Time Point	Treatment Group	N	None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Missing	
			n	%	n	%	n	%	n	%	n	%
	10 µg Sm-p80 + 5 µg GLA-SE											
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)											
	30 µg Sm-p80 + 5 µg GLA-SE											
	100 µg Sm-p80 + 5 µg GLA-SE											
Study Day 64	100 µg Sm-p80 (unadjuvanted)											
	10 µg Sm-p80 + 5 µg GLA-SE											
	30 µg Sm-p80 + 5 µg GLA-SE											
	100 µg Sm-p80 + 5 µg GLA-SE											
Study Day 85	100 µg Sm-p80 (unadjuvanted)											
	10 µg Sm-p80 + 5 µg GLA-SE											
	30 µg Sm-p80 + 5 µg GLA-SE											
	100 µg Sm-p80 + 5 µg GLA-SE											
Study Day 180	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)											
Study Day 187	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)											
Study Day 208	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)											
Max Severity Post Baseline	100 µg Sm-p80 (unadjuvanted)											
	10 µg Sm-p80 + 5 µg GLA-SE											
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)											
	30 µg Sm-p80 + 5 µg GLA-SE											
	100 µg Sm-p80 + 5 µg GLA-SE											

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

Tables with similar format to Table 67:

[Implementation Note: For white blood cells and hemoglobin, columns will be separated into increase and decrease severity. For example, "Mild/Grade 1" will be "Mild/Grade 1 Decrease" and "Mild/Grade 1 Increase".]

Table 68: Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – White Blood Cells

Table 69: Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Hemoglobin

Table 70: Laboratory Results by Parameter, Maximum Severity, Time Point, and Treatment Group – Platelets

Table 71: Abnormal Laboratory Results Related to Study Treatment by Parameter, Maximum Severity, Time Point, and Treatment Group – Any Hematology Parameter

[Implementation Note: Only scheduled time points at which at least one related abnormal lab result is observed in any treatment group will be shown. Add group name to treatment, e.g. "Group A: 100 µg Sm-p80 (unadjuvanted)".]

Time Point	Treatment Group	N	None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
			n	%	n	%	n	%	n	%
Study Day 1 (Baseline)	100 µg Sm-p80 (unadjuvanted)									
	10 µg Sm-p80 + 5 µg GLA-SE									
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)									
	30 µg Sm-p80 + 5 µg GLA-SE									
	100 µg Sm-p80 + 5 µg GLA-SE									
Study Day 8	100 µg Sm-p80 (unadjuvanted)									
	10 µg Sm-p80 + 5 µg GLA-SE									
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)									
	30 µg Sm-p80 + 5 µg GLA-SE									
	100 µg Sm-p80 + 5 µg GLA-SE									
Study Day 29	100 µg Sm-p80 (unadjuvanted)									
	10 µg Sm-p80 + 5 µg GLA-SE									
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)									
	30 µg Sm-p80 + 5 µg GLA-SE									
	100 µg Sm-p80 + 5 µg GLA-SE									
Study Day 36	100 µg Sm-p80 (unadjuvanted)									
	10 µg Sm-p80 + 5 µg GLA-SE									
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)									
	30 µg Sm-p80 + 5 µg GLA-SE									
	100 µg Sm-p80 + 5 µg GLA-SE									
Study Day 57	100 µg Sm-p80 (unadjuvanted)									

Table 71: Abnormal Laboratory Results Related to Study Treatment by Parameter, Maximum Severity, Time Point, and Treatment Group – Any Hematology Parameter *(Continued)*

Time Point	Treatment Group	N	None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3	
			n	%	n	%	n	%	n	%
	10 µg Sm-p80 + 5 µg GLA-SE									
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)									
	30 µg Sm-p80 + 5 µg GLA-SE									
	100 µg Sm-p80 + 5 µg GLA-SE									
Study Day 64	100 µg Sm-p80 (unadjuvanted)									
	10 µg Sm-p80 + 5 µg GLA-SE									
	30 µg Sm-p80 + 5 µg GLA-SE									
	100 µg Sm-p80 + 5 µg GLA-SE									
Study Day 85	100 µg Sm-p80 (unadjuvanted)									
	10 µg Sm-p80 + 5 µg GLA-SE									
	30 µg Sm-p80 + 5 µg GLA-SE									
	100 µg Sm-p80 + 5 µg GLA-SE									
Study Day 180	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)									
Study Day 187	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)									
Study Day 208	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)									
Max Severity Post Baseline	100 µg Sm-p80 (unadjuvanted)									
	10 µg Sm-p80 + 5 µg GLA-SE									
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)									
	30 µg Sm-p80 + 5 µg GLA-SE									
	100 µg Sm-p80 + 5 µg GLA-SE									

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

Tables with similar format to Table 71:

[Implementation Note: For white blood cells and hemoglobin, columns will be separated into increase and decrease severity. For example, "Mild/Grade 1" will be "Mild/Grade 1 Decrease" and "Mild/Grade 1 Increase".]

Table 72: Abnormal Laboratory Results Related to Study Treatment by Parameter, Maximum Severity, Time Point, and Treatment Group – White Blood Cells

Table 73: Abnormal Laboratory Results Related to Study Treatment by Parameter, Maximum Severity, Time Point, and Treatment Group – Hemoglobin

Table 74: Abnormal Laboratory Results Related to Study Treatment by Parameter, Maximum Severity, Time Point, and Treatment Group – Platelets

Table 75: Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – White Blood Cells (10^9 /L)

[Implementation Note: Add group name to treatment, e.g. "Group A: 100 µg Sm-p80 (unadjuvanted)".]

Time Point	Treatment Group	N	Mean	Standard Deviation	Median	Min, Max
Study Day 1 (Baseline)	100 µg Sm-p80 (unadjuvanted)	x	xx.x	xx.x	xx.x	xx.x, xx.x
	10 µg Sm-p80 + 5 µg GLA-SE					
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)					
	30 µg Sm-p80 + 5 µg GLA-SE					
	100 µg Sm-p80 + 5 µg GLA-SE					
Study Day 8	100 µg Sm-p80 (unadjuvanted)					
	10 µg Sm-p80 + 5 µg GLA-SE					
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)					
	30 µg Sm-p80 + 5 µg GLA-SE					
	100 µg Sm-p80 + 5 µg GLA-SE					
Study Day 8, Change from Baseline	100 µg Sm-p80 (unadjuvanted)					
	…					
Study Day 29	100 µg Sm-p80 (unadjuvanted)					
	10 µg Sm-p80 + 5 µg GLA-SE					
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)					
	30 µg Sm-p80 + 5 µg GLA-SE					
	100 µg Sm-p80 + 5 µg GLA-SE					
Study Day 29, Change from Baseline	100 µg Sm-p80 (unadjuvanted)					
	…					
Study Day 36	100 µg Sm-p80 (unadjuvanted)					
	10 µg Sm-p80 + 5 µg GLA-SE					
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)					

Table 75: Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – White Blood Cells (10^9/L) *(Continued)*

Time Point	Treatment Group	N	Mean	Standard Deviation	Median	Min, Max
	30 µg Sm-p80 + 5 µg GLA-SE					
	100 µg Sm-p80 + 5 µg GLA-SE					
Study Day 36, Change from Baseline	100 µg Sm-p80 (unadjuvanted)					
	…					
Study Day 57	100 µg Sm-p80 (unadjuvanted)					
	10 µg Sm-p80 + 5 µg GLA-SE					
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)					
	30 µg Sm-p80 + 5 µg GLA-SE					
	100 µg Sm-p80 + 5 µg GLA-SE					
Study Day 57, Change from Baseline	100 µg Sm-p80 (unadjuvanted)					
	…					
Study Day 64	100 µg Sm-p80 (unadjuvanted)					
	10 µg Sm-p80 + 5 µg GLA-SE					
	30 µg Sm-p80 + 5 µg GLA-SE					
	100 µg Sm-p80 + 5 µg GLA-SE					
Study Day 64, Change from Baseline	100 µg Sm-p80 (unadjuvanted)					
	…					
Study Day 85	100 µg Sm-p80 (unadjuvanted)					
	10 µg Sm-p80 + 5 µg GLA-SE					
	30 µg Sm-p80 + 5 µg GLA-SE					
	100 µg Sm-p80 + 5 µg GLA-SE					
Study Day 85, Change from Baseline	100 µg Sm-p80 (unadjuvanted)					
	…					
Study Day 180	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)					

Table 75: Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – White Blood Cells (10^9/L) *(Continued)*

Time Point	Treatment Group	N	Mean	Standard Deviation	Median	Min, Max
Study Day 180, Change from Baseline	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)					
Study Day 187	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)					
Study Day 187, Change from Baseline	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)					
Study Day 208	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)					
Study Day 208, Change from Baseline	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)					
Note: N = Number of subjects in the Safety Population with laboratory results at the visit.						

Tables with similar format to Table 75:

Table 76: Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Hemoglobin (g/dL)

Table 77: Laboratory Summary Statistics by Parameter, Time Point, and Treatment Group – Platelets (10^9/L)

14.3.6 Displays of Vital Signs

Table 78: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group – Any Assessment

[Implementation Note: For Groups A, B, D, and E, vital signs will be assessed if clinically indicated for study days 85 and 181. For Group C, vital signs will be assessed if clinically indicated for study days 208 and 304. Only include these days if at least one subject assessed on the given day. Add group name to treatment, e.g. "Group A: 100 µg Sm-p80 (unadjuvanted)".]

Time Point	Treatment Group	N	None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Missing	
			n	%	n	%	n	%	n	%	n	%
Study Day 1 (Baseline)	100 µg Sm-p80 (unadjuvanted)	x	x	xx	x	xx	x	xx	x	xx	x	xx
	10 µg Sm-p80 + 5 µg GLA-SE											
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)											
	30 µg Sm-p80 + 5 µg GLA-SE											
	100 µg Sm-p80 + 5 µg GLA-SE											
Study Day 4	100 µg Sm-p80 (unadjuvanted)											
	10 µg Sm-p80 + 5 µg GLA-SE											
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)											
	30 µg Sm-p80 + 5 µg GLA-SE											
	100 µg Sm-p80 + 5 µg GLA-SE											
Study Day 8	100 µg Sm-p80 (unadjuvanted)											
	10 µg Sm-p80 + 5 µg GLA-SE											
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)											
	30 µg Sm-p80 + 5 µg GLA-SE											
	100 µg Sm-p80 + 5 µg GLA-SE											
Study Day 29	100 µg Sm-p80 (unadjuvanted)											

Table 78: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group – Any Assessment *(Continued)*

Time Point	Treatment Group	N	None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Missing	
			n	%	n	%	n	%	n	%	n	%
	10 µg Sm-p80 + 5 µg GLA-SE											
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)											
	30 µg Sm-p80 + 5 µg GLA-SE											
	100 µg Sm-p80 + 5 µg GLA-SE											
Study Day 32	100 µg Sm-p80 (unadjuvanted)											
	10 µg Sm-p80 + 5 µg GLA-SE											
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)											
	30 µg Sm-p80 + 5 µg GLA-SE											
	100 µg Sm-p80 + 5 µg GLA-SE											
Study Day 36	100 µg Sm-p80 (unadjuvanted)											
	10 µg Sm-p80 + 5 µg GLA-SE											
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)											
	30 µg Sm-p80 + 5 µg GLA-SE											
	100 µg Sm-p80 + 5 µg GLA-SE											
Study Day 57	100 µg Sm-p80 (unadjuvanted)											
	10 µg Sm-p80 + 5 µg GLA-SE											
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)											
	30 µg Sm-p80 + 5 µg GLA-SE											
	100 µg Sm-p80 + 5 µg GLA-SE											
Study Day 60	100 µg Sm-p80 (unadjuvanted)											

Table 78: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group – Any Assessment *(Continued)*

Time Point	Treatment Group	N	None		Mild / Grade 1		Moderate/ Grade 2		Severe/ Grade 3		Missing	
			n	%	n	%	n	%	n	%	n	%
	10 µg Sm-p80 + 5 µg GLA-SE											
	30 µg Sm-p80 + 5 µg GLA-SE											
	100 µg Sm-p80 + 5 µg GLA-SE											
Study Day 64	100 µg Sm-p80 (unadjuvanted)											
	10 µg Sm-p80 + 5 µg GLA-SE											
	30 µg Sm-p80 + 5 µg GLA-SE											
	100 µg Sm-p80 + 5 µg GLA-SE											
Study Day 180	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)											
Study Day 183	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)											
Study Day 187	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)											
Max Severity Post Baseline	100 µg Sm-p80 (unadjuvanted)											
	10 µg Sm-p80 + 5 µg GLA-SE											
	30 µg Sm-p80 + 5 µg GLA-SE (delayed booster)											
	30 µg Sm-p80 + 5 µg GLA-SE											
	100 µg Sm-p80 + 5 µg GLA-SE											

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

Tables with similar format to Table 78:

[Implementation Note: For systolic blood pressure, columns will be separated into increase and decrease severity. For example, "Mild/Grade 1" will be "Mild/Grade 1 Decrease" and "Mild/Grade 1 Increase".]

Table 79: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group – Systolic Blood Pressure

Table 80: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group – Diastolic Blood Pressure

Table 81: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group – Heart Rate

Table 82: Vital Signs by Assessment, Maximum Severity, Time Point, and Treatment Group – Oral Temperature

14.4 Summary of Concomitant Medications

Table 83: Number and Percentage of Subjects with Prior and Concurrent Medications by WHO Drug Classification and Treatment Group

WHO Drug Code Level 1, Anatomic Group	WHO Drug Code Level 2, Therapeutic Subgroup	Group A: 100 µg Sm-p80 (unadjuvanted) (N=X)		Group A: 10 µg Sm-p80 + 5 µg GLA-SE (N=X)		Group C: 30 µg Sm-p80 + 5 µg GLA-SE (delayed booster) (N=X)		Group D: 30 µg Sm-p80 + 5 µg GLA-SE (N=X)		Group E: 100 µg Sm-p80 + 5 µg GLA-SE (N=X)		All Subjects (N=X)	
		n	%	n	%	n	%	n	%	n	%	n	%
Any Level 1 Codes	Any Level 2 Codes	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
[ATC Level 1 - 1]	Any [ATC 1 – 1]												
	[ATC 2 - 1]												
	[ATC 2 - 2]												
	[ATC 2 - 3]												
[ATC Level 1 – 2]	[ATC 2 - 1]												
	[ATC 2 - 2]												
	[ATC 2 - 3]												

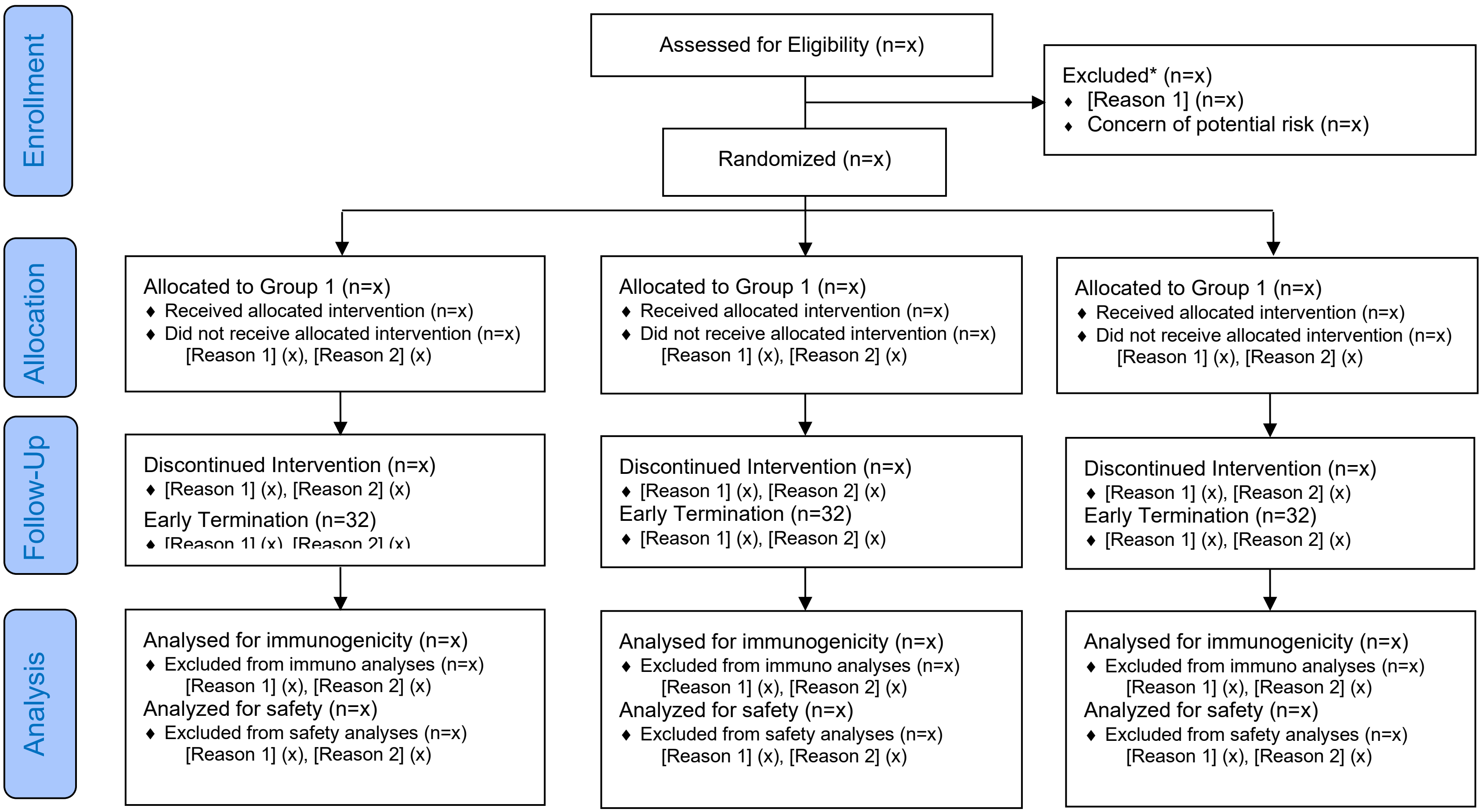
Note: N = Number of subjects in the Safety Population; n=Number of subjects reporting taking at least one medication in the specific WHO Drug Class.
Subjects are counted once per WHO Drug Code Level 2, Therapeutic Subgroup.

APPENDIX 2. FIGURE MOCK-UPS

LIST OF FIGURES

10.1 Disposition of Subjects

Figure 1: CONSORT Flow Diagram



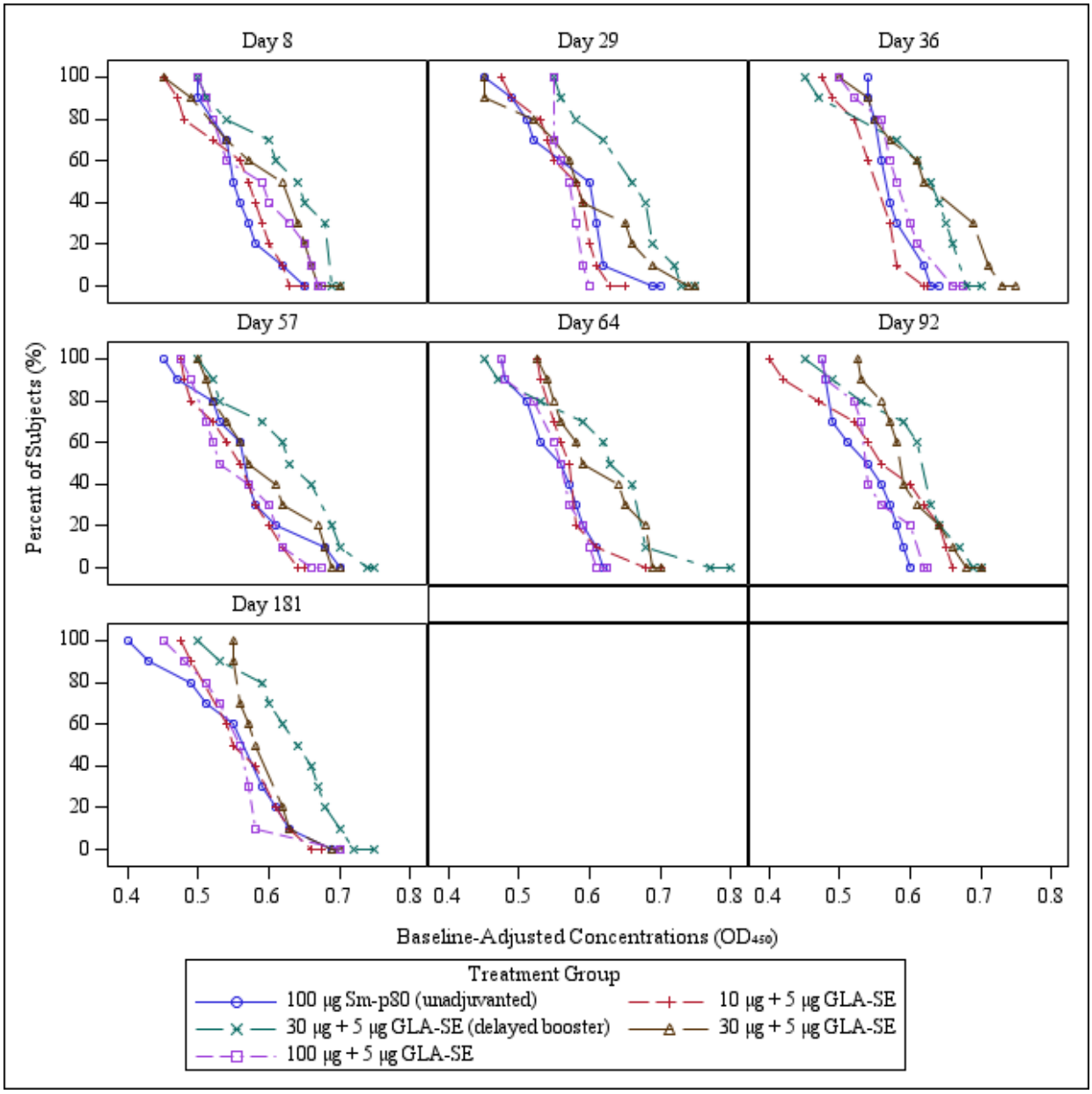
14.2 Efficacy/Immunogenicity Data

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

Figure 2: Reverse Cumulative Distribution of Anti-Sm-p80 ELISA Total IgG Results by Time Point and Treatment Group, mITT Immunogenicity Population

[Implementation Note: Figure will be paneled by scheduled time point: 7 and 28 days after each vaccination, and 124 days after the last vaccination. The y-axis will be the "Percent of Subjects (%)" with a max of 100 and the x-axis will be "Baseline-Adjusted Concentrations (OD_{450})". Each treatment group will have its own marker type and color. A legend will be included containing each treatment group and dosage if enough space available, e.g. Group A would be displayed as "Group A: 100 µg Sm-p80 (unadjuvanted)". Otherwise treatment group only will be shown.]

Figure 2: Reverse Cumulative Distribution of Anti-Sm-p80 ELISA Total IgG Results by Time Point and Treatment Group, mITT Immunogenicity Population *(continued)*



Pseudo Code:

```
ods select CDFPlot;
proc univariate data= dsn;
 by trta stdy;
 cdfplot elisa;                 /*baseline-adjusted results*/
 ods output CDFPlot= _cdf;
data cdf;
 set _cdf;
      cdf  = ecdfy;             /*standard CDF*/
      cdf2 = 100 - cdf;         /*complimentary (reverse) CDF*/
      elisa = ecdfx;            /*baseline-adjusted results*/
run;
```

Figure 2: Reverse Cumulative Distribution of Anti-Sm-p80 ELISA Total IgG Results by Time Point and Treatment Group, mITT Immunogenicity Population *(continued)*

Figure 3: Geometric Mean Anti-Sm-p80 ELISA Total IgG Response Over Time by Treatment Group with 95% Confidence Intervals, mITT Immunogenicity Population

[Implementation Note: The y-axis will be "Baseline-Adjusted Concentrations (OD_{450})", and the x-axis will be actual study day labelled as "Study Day" with tick marks on 7-days post vaccination, 28-days post vaccination, and 124-days post last vaccination. Each treatment group will have its own marker type and color consistent across all figures. A legend will be included containing each treatment group and dosage if enough space available, e.g. Group A would be displayed as "Group A: 100 µg Sm-p80 (unadjuvanted)". Otherwise treatment group only will be shown.]

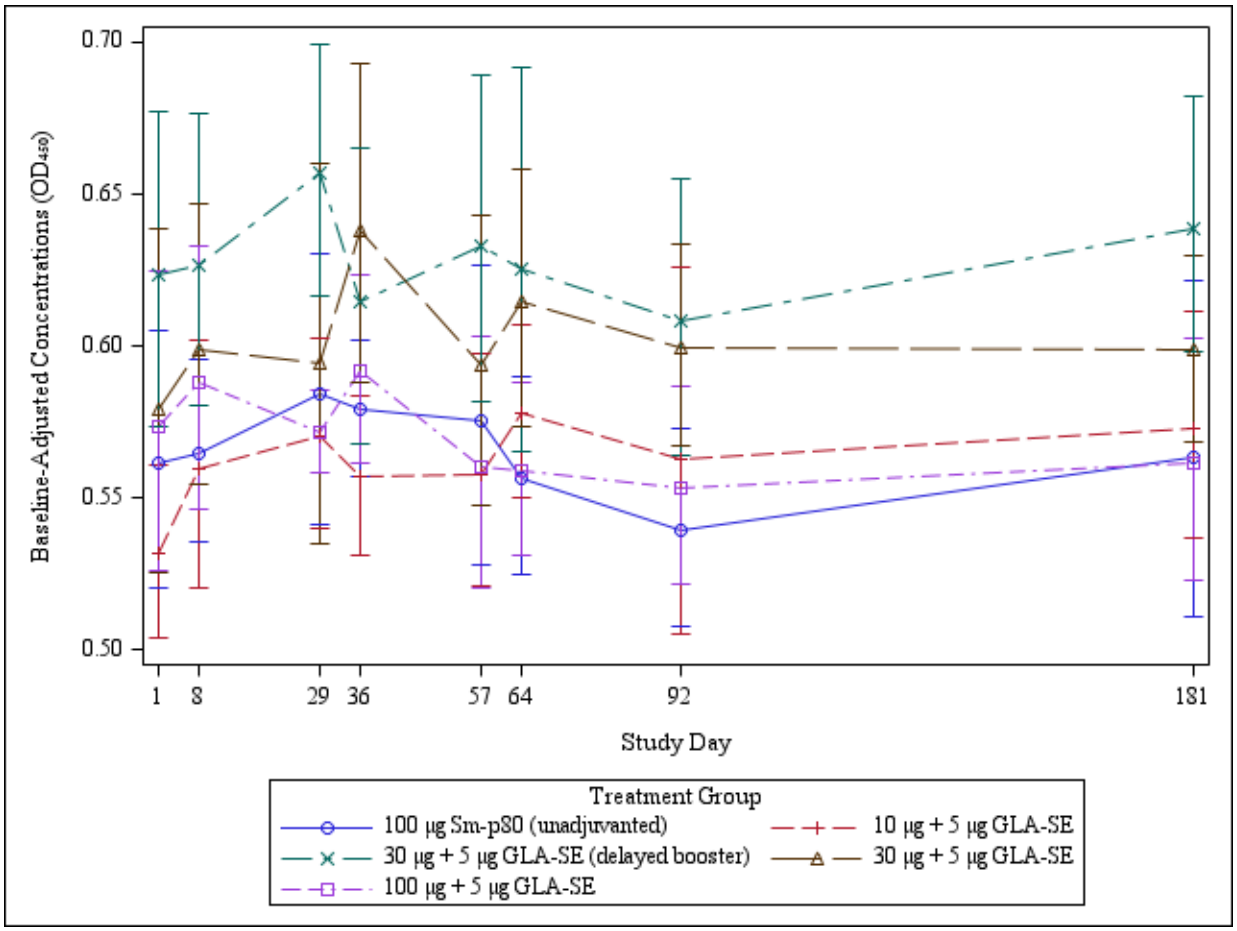
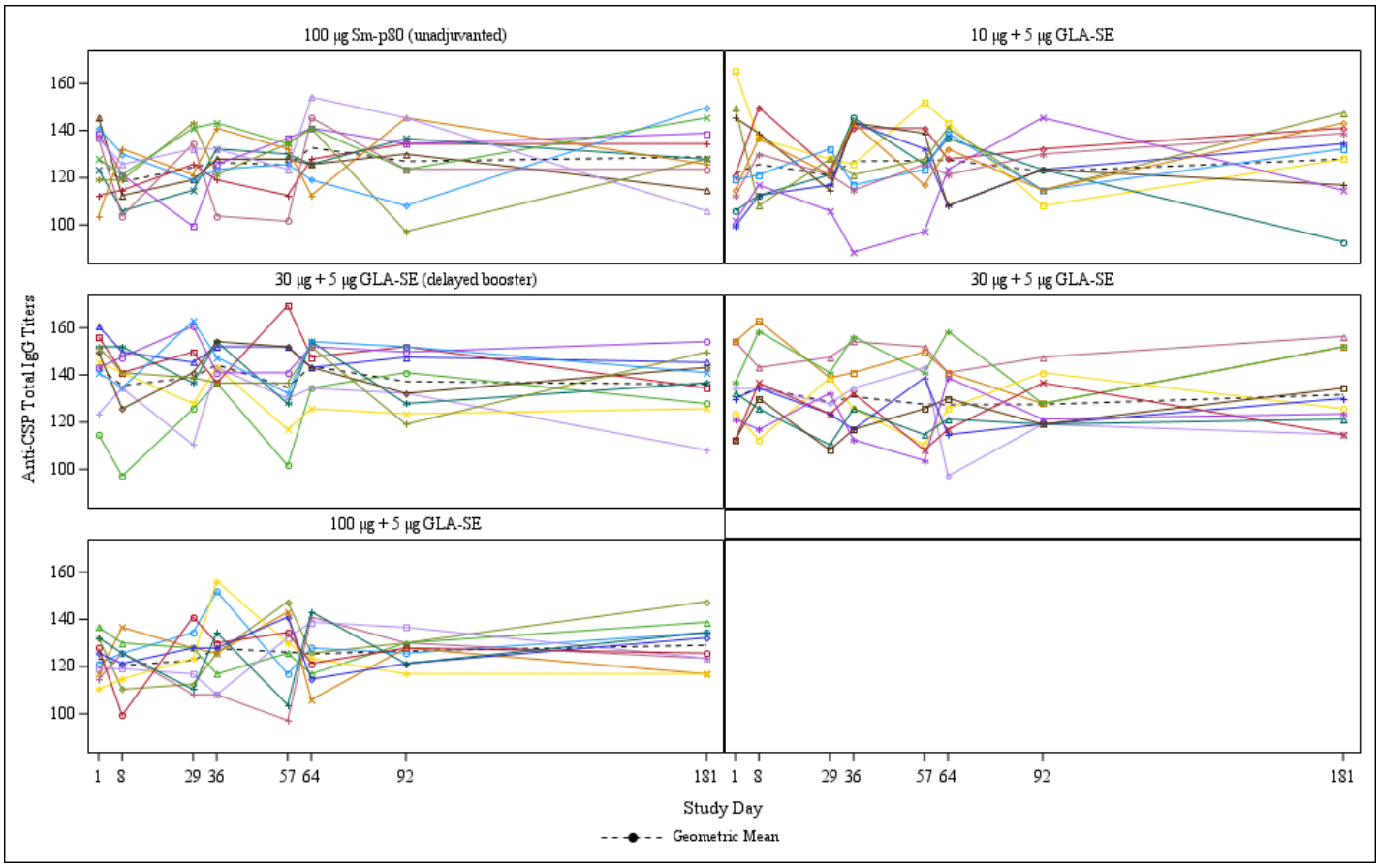


Figure 4: Individual Time Trends of ELISA Total IgG Response by Treatment Group, mITT Immunogenicity Population

[Implementation Note: Figure will be paneled (3 rows and 2 columns) by treatment group. The y-a xis should be labelled “Anti-CSP Total IgG Titers” and range from minimum to maximum values. If titer range exceeds 150, then scale y-axis by log base 2. The x-axis will be labelled “Study Day” with tick marks on 7-days post vaccination, 28-days post vaccination, and 124-days post last vaccination. A dashed black line will be added to show the geometric mean time trend. Add a legend for the dashed black line labelled “Geometric Mean” . Panel labels will include treatment group and dose if enough space available, e.g. "Group A: 100 µg Sm-p80 (unadjuvanted)". Otherwise, treatment group only will be shown.]



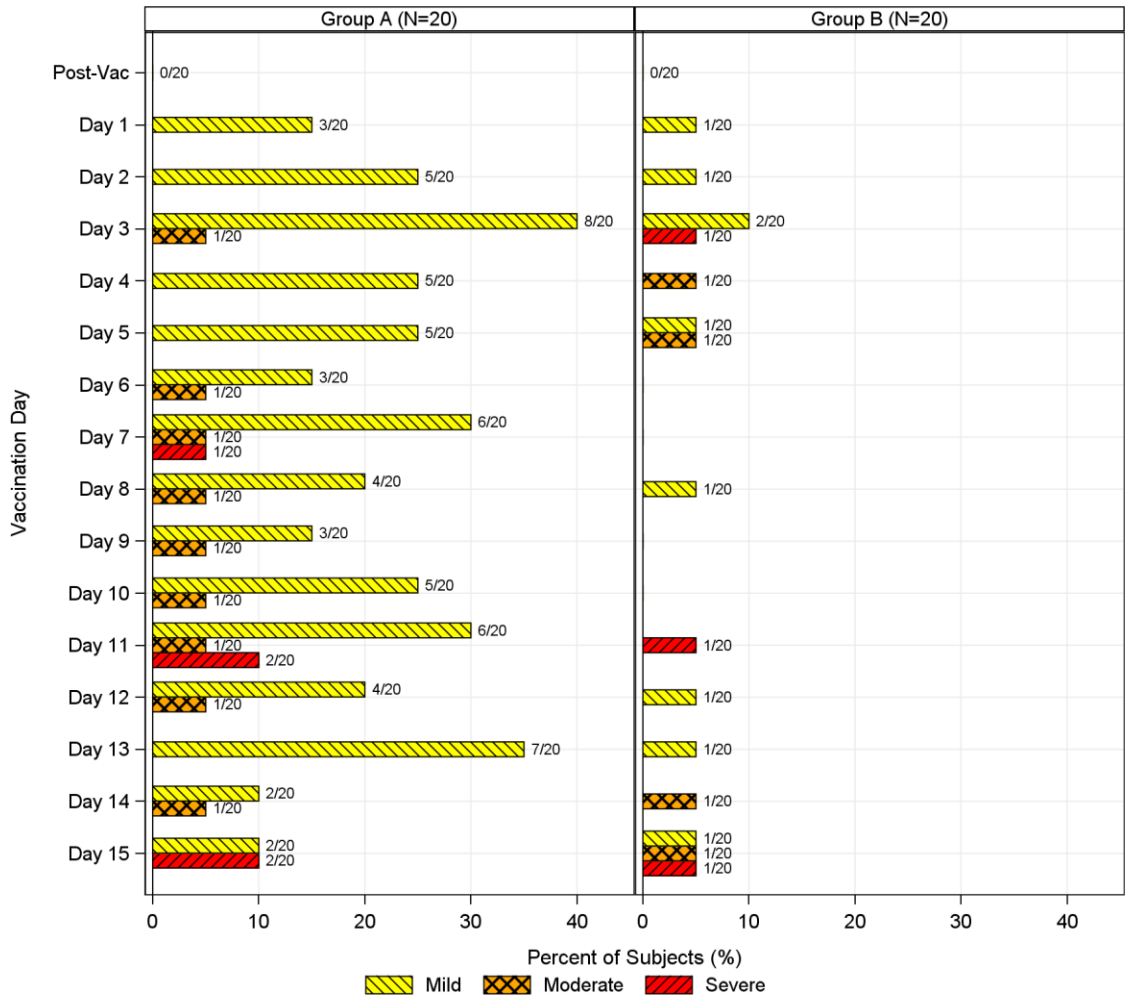
14.3 Safety Data

14.3.1 Adverse Events

14.3.1.1 Solicited Adverse Events

Figure 5: Maximum Severity of Solicited Systemic Symptoms per Subject by Day Post-Vaccination – Post Dose 1

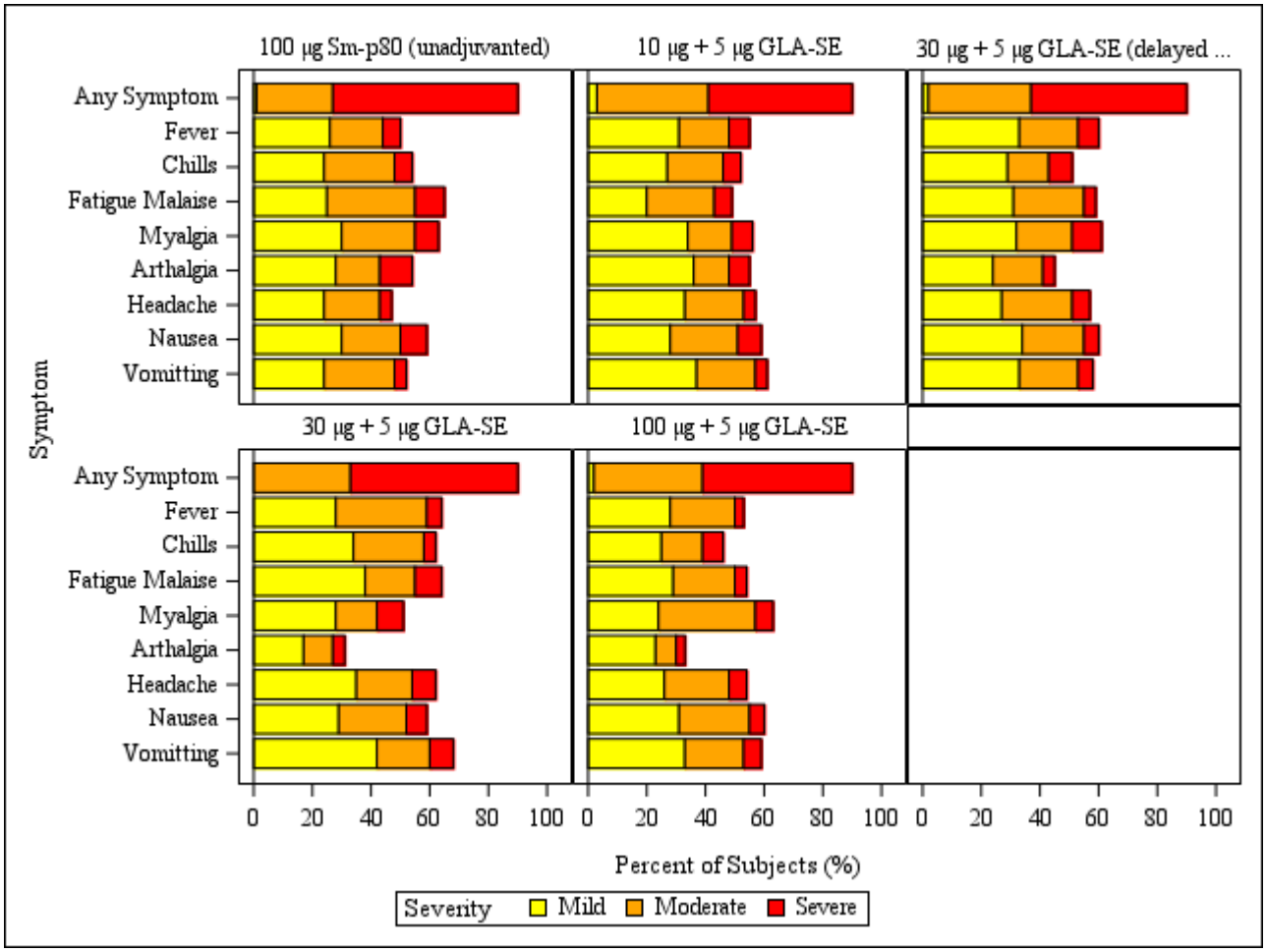
[Implementation Note: This figure will have 3 columns and 2 rows and will be paneled by treatment group and "All Subjects". The y-axis will be "Post Dose Day" and the x-axis will be "Percent of Subjects (%)". This figure will be annotated with the fraction of subjects who experienced the symptom (n/N). Panel labels will include treatment group and dose if enough space available, e.g. "Group A: 100 µg Sm-p80 (unadjuvanted)". Otherwise, treatment group only will be shown.]



Figures with similar format to Figure 5:

Figure 8: Number and Percentage of Subjects Experiencing Solicited Systemic Events by Event, Maximum Severity, and Treatment Group – Post Dose 1

[Implementation Note: The symptoms should start with "Any Symptom" and then in alphabetical order. This figure will have 3 columns and 2 rows and will be paneled by treatment group and "All Subjects". The y-axis will be "Symptom" and the x-axis will be "Percent of Subjects (%)". This figure will be annotated with the fraction of subjects who experienced the symptom (n/N). Panel labels will include treatment group and dose if enough space available, e.g. "Group A: 100 µg Sm-p80 (unadjuvanted)". Otherwise, treatment group only will be shown.]



Figures with similar format to Figure 8:

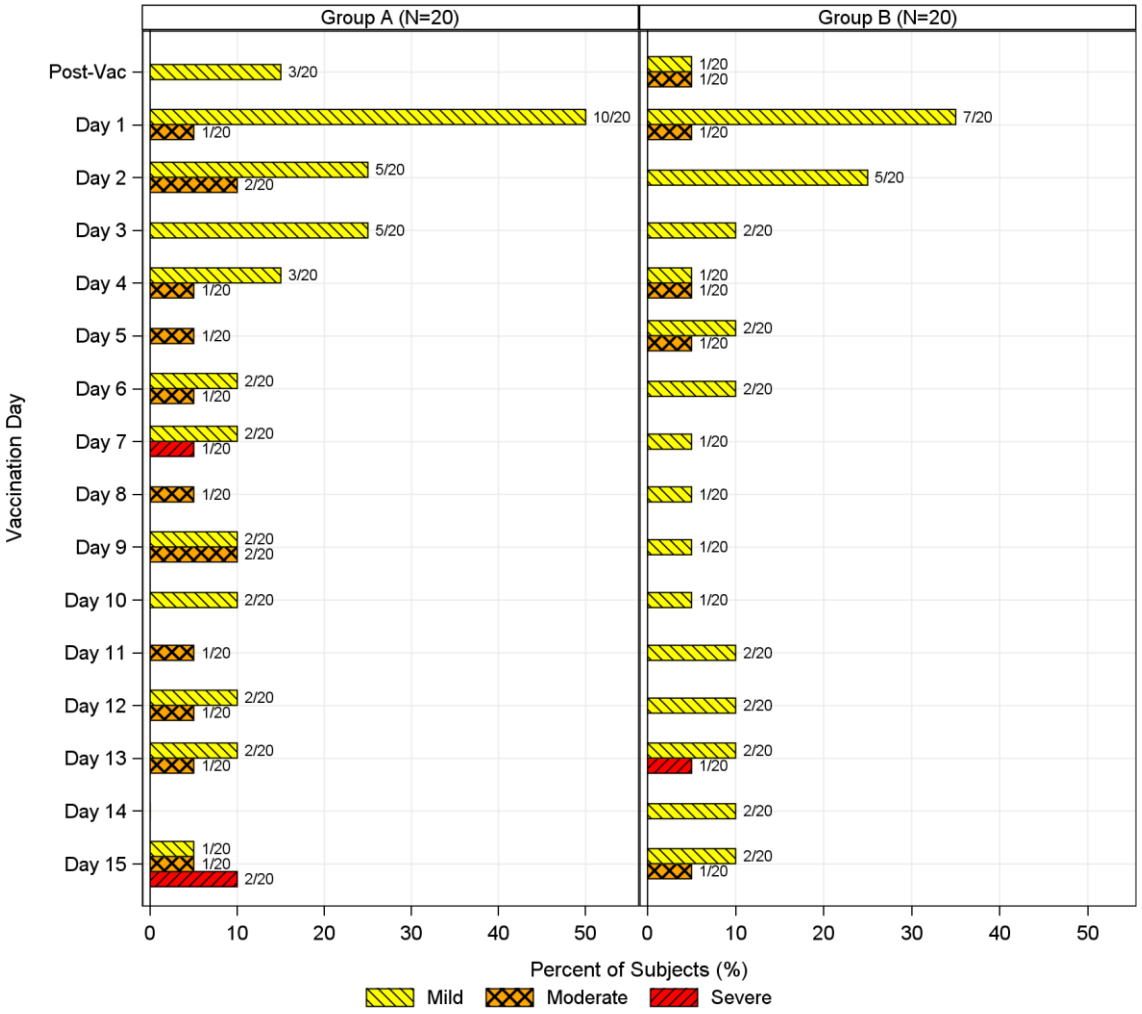
Figure 9: Number and Percentage of Subjects Experiencing Solicited Systemic Events by Event, Maximum Severity, and Treatment Group – Post Dose 2

Figure 10: Number and Percentage of Subjects Experiencing Solicited Systemic Events by Event, Maximum Severity, and Treatment Group – Post Dose 3

Figure 11: Number and Percentage of Subjects Experiencing Solicited Systemic Events by Event, Maximum Severity, and Treatment Group – Post Any Dose

Figure 12: Maximum Severity of Solicited Injection Site Symptoms per Subject by Day Post-Vaccination – Post Dose 1

[Implementation Note: This figure will have 3 columns and 2 rows and will be paneled by treatment group and "All Subjects". The y-axis will be "Post Dose Day" and the x-axis will be "Percent of Subjects (%)". This figure will be annotated with the fraction of subjects who experienced the symptom (n/N). Panel labels will include treatment group and dose if enough space available, e.g. "Group A: 100 µg Sm-p80 (unadjuvanted)". Otherwise, treatment group only will be shown.]



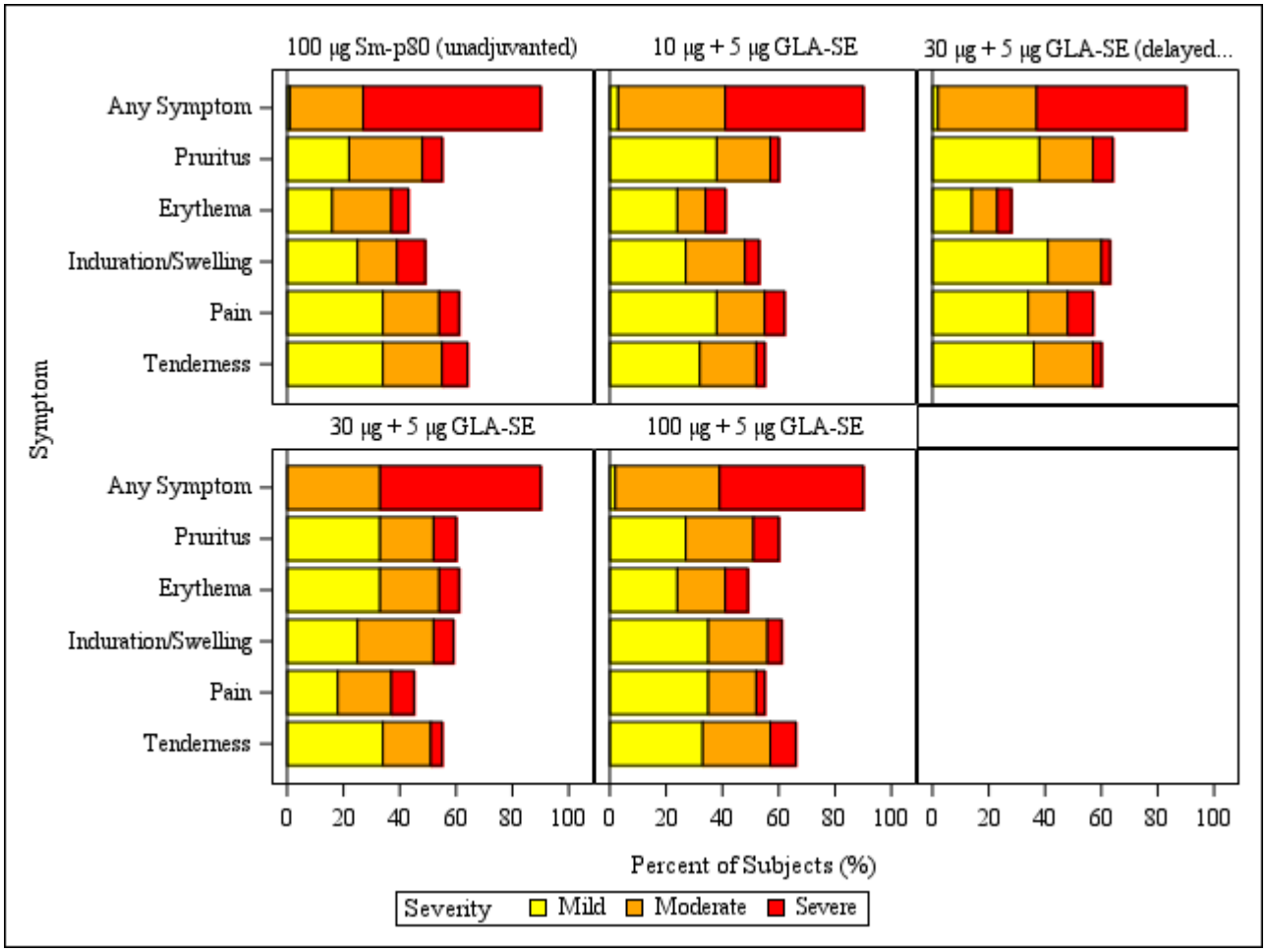
Figures with similar format to Figure 12:

Figure 13: Maximum Severity of Solicited Injection Site Symptoms per Subject by Day Post-Vaccination – Post Dose 2

Figure 14: Maximum Severity of Solicited Injection Site Symptoms per Subject by Day Post-Vaccination – Post Dose 3

Figure 15: Number and Percentage of Subjects Experiencing Solicited Injection Site Events by Event, Maximum Severity, and Treatment Group – Post Dose 1

[Implementation Note: The symptoms should start with "Any Symptom" and then in alphabetical order. This figure will have 3 columns and 2 rows and will be paneled by treatment group and "All Subjects". The y-axis will be "Symptom" and the x-axis will be "Percent of Subjects (%)". This figure will be annotated with the fraction of subjects who experienced the symptom (n/N). Panel labels will include treatment group and dose if enough space available, e.g. "Group A: 100 µg Sm-p80 (unadjuvanted)". Otherwise, treatment group only will be shown.]



Figures with similar format to Figure 15:

Figure 16: Number and Percentage of Subjects Experiencing Solicited Injection Site Events by Event, Maximum Severity, and Treatment Group – Post Dose 2

Figure 17: Number and Percentage of Subjects Experiencing Solicited Injection Site Events by Event, Maximum Severity, and Treatment Group – Post Dose 3

Figure 18: Number and Percentage of Subjects Experiencing Solicited Injection Site Events by Event, Maximum Severity, and Treatment Group – Post Any Dose

14.3.1.2 Unsolicited Adverse Events

Figure 19: Frequency of Related Adverse Events by MedDRA System Organ Class and Severity

[Implementation Note: This figure will include serious and non-serious unsolicited adverse events deemed related to the study product. The SOCs should be sorted "Any SOC" first and then descending frequency. This figure will have 3 columns and 2 rows and will be paneled by treatment group and "All Subjects". The y-axis will be "System Organ Class" and the x-axis will be "Number of Events". This figure will be annotated with the number of events (n). Panel labels will include treatment group and dose if enough space available, e.g. "Group A: 100 µg Sm-p80 (unadjuvanted)". Otherwise, treatment group only will be shown.]

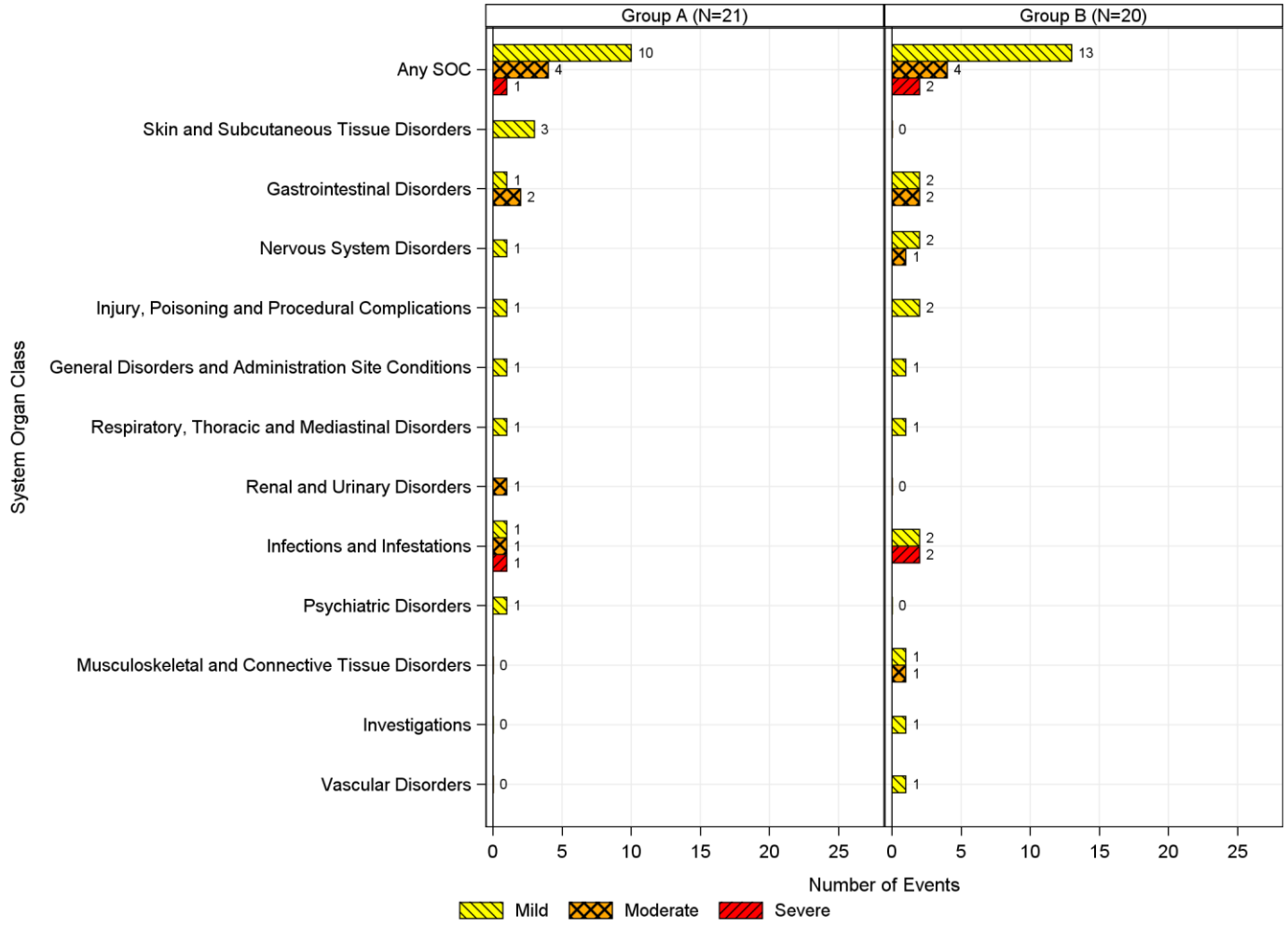
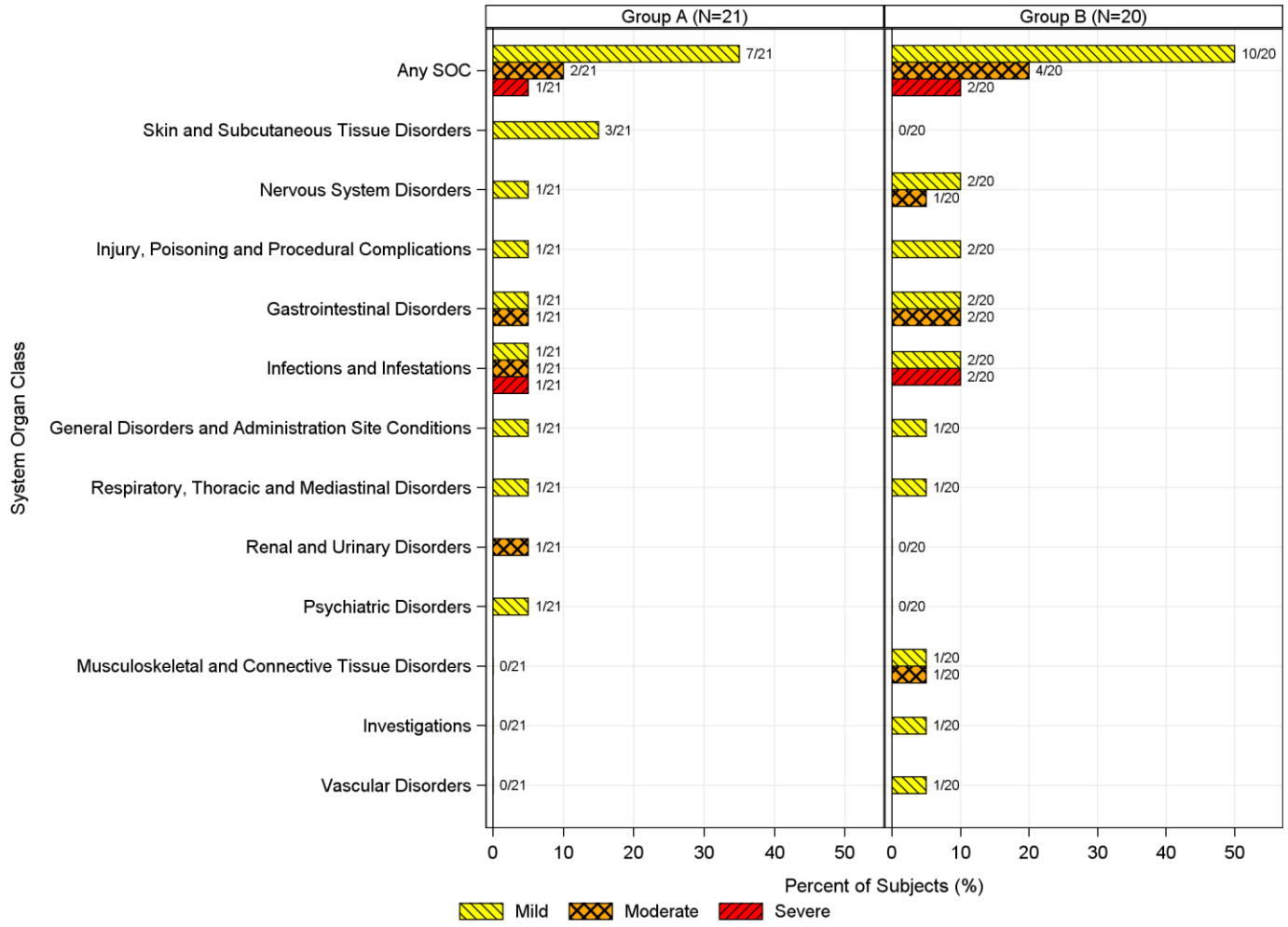


Figure 20: Incidence of Related Adverse Events by MedDRA® System Organ Class and Maximum Severity

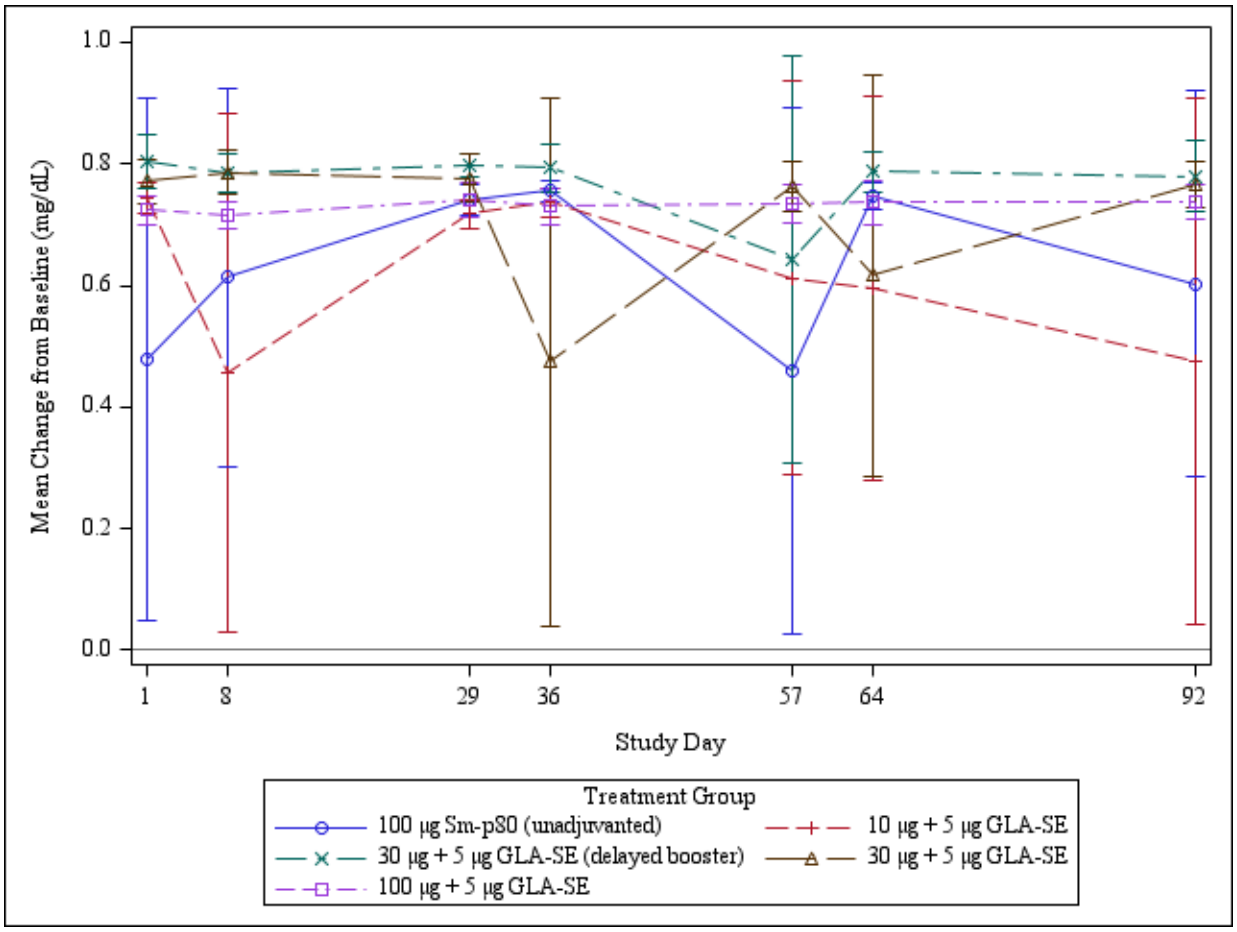
[Implementation Note: This figure will include serious and non-serious unsolicited adverse events deemed related to the study product. The SOCs should be sorted "Any SOC" first and then descending frequency. This figure will have 3 columns and 2 rows and will be paneled by treatment group and "All Subjects". The y-axis will be "System Organ Class" and the x-axis will be "Percent of Subjects (%)". This figure will be annotated with the fraction of subjects who experienced the symptom (n/N). Panel labels will include treatment group and dose if enough space available, e.g. "Group A: 100 µg Sm-p80 (unadjuvanted)". Otherwise, treatment group only will be shown.]



14.3.5 Displays of Laboratory Results

Figure 21: Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter, and Treatment Group – Creatinine

[Implementation Note: The x-axis will be actual study day labelled as "Study Day" with tick marks on vaccination days, 7-days post vaccination, and 28-days post vaccination. The y-axis will be the "Mean Change from Baseline"; include relevant units. For example, creatinine would be "Mean Change from Baseline (mg/dL)". A reference line will be added at Y=0. A legend will be included containing each treatment group and dosage if enough space available, e.g. Group A would be displayed as "Group A: 100 µg Sm-p80 (unadjuvanted)". Otherwise treatment group only will be shown.]



Figures with similar format to Figure 21:

Figure 22: Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter, and Treatment Group – Alanine Aminotransferase

Figure 23: Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter, and Treatment Group – White Blood Cells

Figure 24: Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter, Sex, and Treatment Group – Hemoglobin

[Implementation Note: Panel by sex.]

Figure 25: Laboratory Results by Scheduled Visits: Mean Changes from Baseline by Laboratory Parameter, and Treatment Group – Platelets

APPENDIX 3. LISTINGS MOCK-UPS

LISTINGS

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

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

16.2 Database Listings by Subject

16.2.1 Discontinued Subjects

Listing 2: 16.2.1: Early Terminations or Discontinued Subjects

[Implementation Note: Category will either by “Early Termination” or “Treatment Discontinuation”. Sort by Treatment Group, Subject ID, alphabetically by Category.]

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

16.2.2 Protocol Deviations

Listing 3: 16.2.2.1: Subject-Specific Protocol Deviations

[Implementation Note: Sort by Treatment Group, Subject ID, DV Number.]

Treatment Group	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: Sort by Start Date. Use DATE9 format for all dates.]

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: Exclusion reasons should match the SAP text that describes who will be excluded from analyses. Sort by Treatment Group and Subject ID.]

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

16.2.4 Demographic Data

Listing 6: 16.2.4.1: Demographic Data

[Implementation Note: Sort by Treatment Group and Subject ID.]

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

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. Sort by Treatment Group, Subject ID, MH Number.]

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

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

Listing 8: 16.2.5: Compliance and/or Drug Concentration Data

[Implementation Note: Sort by Treatment Group, Subject ID, and Dose Number.]

Scenario 2

Treatment Group	Subject ID	Dose(s) Missed
		[e.g., Day 3, Day 3 AM, etc.]

16.2.6 Individual Efficacy/Immunogenicity Response Data

Listing 9: 16.2.6: Individual Efficacy/Immunogenicity Response Data

[Implementation Note: Sort by Treatment Group, Subject ID, Planned Time Point.]

Treatment Group	Subject ID	Planned Time Point	Actual Study Day	ELISA Total IgG

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). This listing will include baseline assessments and post-vaccination assessments. Sort by Subject ID, Dose Number, Post Dose Day, Symptom.]

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

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

Listing 11: 16.2.7.2: Solicited Events – Injection Site 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 will include baseline assessments and post-vaccination assessments. Sort by Subject ID, Dose Number, Post Dose Day, Symptom.]

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

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

Listing 12: 16.2.7.3: Unsolicited Adverse Events

[Implementation Note: Sort by Treatment Group, Subject ID, Associated with Dose No., and No. of Days Post Associated Dose. If the table will be multi-page, move the footnote/explanation to the footer so that it repeats for each page of the table.]

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

16.2.8 Individual Laboratory Measurements

Listing 13: 16.2.8.1: Clinical Laboratory Results – Chemistry

[Implementation Note: Severity should be included in parentheses after the result for abnormal results, *e.g.*, 16.2 (Mild). Sort by Treatment Group, Subject ID, and Planned Time Point.]

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

Listing 14: 16.2.8.2: Clinical Laboratory Results – Hematology

[Implementation Note: Sort by Treatment Group, Subject ID, and Planned Time Point.]

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

16.2.9 Vital Signs and Physical Exam Findings

Listing 15: 16.2.9.1: Vital Signs

[Implementation Note: Severity should be included in parentheses after the result for abnormal results, *e.g.*, 16.2 (Mild). Sort by Treatment Group, Subject ID, and Planned Time Point.]

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

Listing 16: 16.2.9.2: Physical Exam Findings

[Implementation Note: If the 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)". Sort by Treatment Group, Subject ID, Planned Time Point.]

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

16.2.10 Concomitant Medications

Listing 17: 16.2.10: Concomitant Medications

[Implementation Note: 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)". Sort by Treatment Group, Subject ID, and CM Number.]

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

16.2.11 Pregnancy Reports

Listing 18: 16.2.11.1: Pregnancy Reports – Maternal Information

[Implementation Note: Sort by Treatment Group, Subject ID, Pregnancy Number.]

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

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

Listing 19: 16.2.11.2: Pregnancy Reports – Gravida and Para

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

Note: Gravida includes the current pregnancy, para events do not.

[a] Preterm Birth

[b] Term Birth

Listing 20: 16.2.11.3: Pregnancy Reports – Live Birth Outcomes

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

Listing 21: 16.2.11.4: Pregnancy Reports – Still Birth Outcomes

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

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

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

APPENDIX 4. NCA TEMPLATE

See separate document, if applicable.