STATISTICAL ANALYSIS PLAN

for

Protocol: RV460 / WRAIR #2672

Study Title:

A Randomized, Double Blind Phase 1 Trial to Evaluate the Safety and Immunogenicity of Priming with Env-C Plasmid DNA Vaccine Alone, with Different Adjuvants, or with an Adjuvanted HIV Env gp145 C.6980 Protein Vaccine and Boosting with the Adjuvanted HIV Env gp145 C.6980 Protein Vaccine with or without the Env-C Plasmid DNA Vaccine in Healthy HIV Uninfected Adults in Kenya

IND #: 21093

Version 1.0

DATE: September 09, 2024

STUDY INFORMATION

Protocol Number Code:	**RV460**
NCT Number	**NCT04826094**
Development Phase:	Phase I
Products or Interventions:	Env-C Plasma DNA Vaccine, HIV-1 Env gp145 C.6980, dmLT adjuvant (recombinant double mutant Escherichia coli heat-labile toxin LT, R192G/L211A), ALF43 adjuvant, Rehydragel®, and saline placebo
Form/Route:	IM Injection (TCI for dmLT adjuvant)
Indication Studied:	Preventative HIV vaccine
Sponsor:	National Institute of Allergy and Infectious Diseases (NIAID) Division of AIDS (DAIDS)
Clinical Trial Initiation Date:	09FEB2021
Clinical Trial Completion Date:	13FEB2024
Date of the Analysis Plan:	09SEP2024
Version Number:	1.0

This study was performed in compliance with Good Clinical Practice.

VERSION HISTORY

SAP Version	Approval Date	Change	Rationale
1.0	09SEP2024	Not Applicable	Original version.

SIGNATURE PAGE

SPONSOR: Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc.

STUDY TITLE: A Randomized, Double Blind Phase 1 Trial to Evaluate the Safety and Immunogenicity of Priming with Env-C Plasmid DNA Vaccine Alone, with Different Adjuvants, or with an Adjuvanted HIV Env gp145 C.6980 Protein Vaccine and Boosting with the Adjuvanted HIV Env gp145 C.6980 Protein Vaccine with or without the Env-C Plasmid DNA Vaccine in Healthy HIV Uninfected Adults in Kenya

PROTOCOL NUMBER: RV460 / WRAIR #2672

Protocol Chair: Merlin Robb, MD

Signature: Merlin Robb DIGITALLY SIGNED Date: 13/Sep/2024 12:18 PM EDT

I am approving this document.

Merlin Robb

Protocol Statistician: Chris Bryant, PhD

Signature: Chris Bryant DIGITALLY SIGNED Date: 09/Sep/2024 02:58 PM EDT

I am approving this document.

Chris Bryant

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LIST OF ABBREVIATIONS

3D-PHAD	3-Deacyl-Phosphorylated Hexa-Acyl Disaccharide
ADC	Antibody-Dependent Complement
ADCC	Antibody-Dependent Cell-Mediated Cytotoxicity
ADCP	Antibody-Dependent Cell-Mediated Phagocytosis
ADCVI	Antibody-Dependent Cell-Mediated Viral Inhibition
AE	Adverse Event
ALF43	Army Liposome Formulation with Monophosphoryl Lipid A and 43% Cholesterol
ALT	Alanine Aminotransferase
ANOVA	Analysis of Variance
AST	Aspartate Aminotransferase
AUC	Area Under the Curve
BMI	Body Mass Index
BP	Blood Pressure
CI	Confidence Interval
cGMP	Current Good Manufacturing Practices
CRF	Circulating Recombinant Forms
DAIDS	Division of AIDS
dmLT	Double Mutant Escherichia Coli Heat Liable Toxin
DNA	Deoxyribonucleic acid
ELISA	Enzyme-Linked Immunosorbent Assay
ELISPOT	Enzyme-Linked Immunospot
Env-C Plasmid DNA	HIV-1 gp120 (93MW965.26) DNA
FDR	False Discovery Rate
GMT	Geometric Mean Titer
HLA	Human Leukocyte Antigen
ICF	Informed Consent Form
ICS	Intracellular Cytokine Staining
IM	Intramuscular
IMM	Immunogenicity (Population)
LN	Lymph Node(s)

List of Abbreviations *(continued)*

MAAE	Medically Attended Adverse Event
MedDRA	Medical Dictionary for Regulatory Activities
mg	Milligram
mL	Milliliter
MPLA	Monophosphoryl Lipid A
N	Number (typically refers to Participants)
NK	Natural Killer (Cell)
NKT	Natural Killer T (Cell)
PBS	Phosphate-Buffered Saline
PIMMC	Potentially Immune-Mediated Medical Condition
PP	Per-Protocol (Population)
PSRT	Protocol Safety Review Team
PT	Preferred Term
RCD	Reverse Cumulative Distribution
RNA	Ribonucleic acid
RNA-Seq	RNA-sequencing
SAP	Statistical Analysis Plan
SAE	Serious Adverse Event
SD	Standard Deviation
SOC	System Organ Class
TCI	Transcutaneous Immunization
Tfh	T follicular helper
µg	Microgram

1. PREFACE

The statistical analysis plan (SAP) for the Phase I study titled "A Randomized, Double Blind Phase 1 Trial to Evaluate the Safety and Immunogenicity of Priming with Env-C Plasmid DNA Vaccine Alone, with Different Adjuvants, or with an Adjuvanted HIV Env gp145 C.6980 Protein Vaccine and Boosting with the Adjuvanted HIV Env gp145 C.6980 Protein Vaccine with or without the Env-C Plasmid DNA Vaccine in Healthy HIV Uninfected Adults in Kenya" expands upon the statistical considerations presented in the protocol. This document includes general statistical principles and planned analyses to address protocol objectives, including sample tables, figures, and listings in appendices.

2. INTRODUCTION

2.1. Purpose and Structure of the Document

The purpose of this study is to explore whether different adjuvant formulations in combination with an Env-C Plasmid DNA and HIV Env gp145 C.6980 protein in a prime-boost combination causes side effects and are tolerable; whether humans respond (develop immune responses) to the vaccines; and how long the effects of study vaccines last in protecting against HIV in healthy adults in Kenya. This study will also compare the effects of the study vaccines with adjuvants and adjuvant patch to those of placebo injections and adjuvant patch. Study objectives will be met via clinical safety assessments and by the testing of blood samples from all participants. Willing and eligible participants have the option to provide lymph node and mucosal secretion samples (semen, cervicovaginal, rectal), which will provide the data for some exploratory objectives. Other exploratory objectives include genetic analysis, such as Human Leukocyte Antigen (HLA) subtyping.This analysis plan has been drafted based on Version 4.0 of the protocol, and any future amendments to the protocol that substantially impact the planned analyses would be addressed in amendments to this SAP.

2.2. Purpose of the Analyses

These analyses will assess the safety, tolerability, and immunogenicity of a vaccine regimen consisting of priming with Env-C Plasmid DNA (with or without adjuvants) with and without admixing with HIV Env gp145 C.6980 protein and boosting with HIV Env gp145 C.6980 protein mixed with Rehydragel®, or ALF43 plus Rehydragel®.

3. STUDY OBJECTIVES AND ENDPOINTS

3.1. Study Objectives

3.1.1. Primary Objective

- To assess the safety and tolerability (including reactogenicity) of HIV Env-C Plasmid DNA given IM, alone, admixed with ALF43 adjuvant, topically applied with dmLT adjuvant, or given with an adjuvanted HIV Env gp145 protein and followed by adjuvanted HIV Env gp145 C.6980 protein boost IM immunizations, with or without Env-C Plasmid DNA

3.1.2. Secondary Objectives

Assess the immunogenicity of the various study vaccine combinations:

- To determine whether the adjuvants under study improve the immunogenicity of the HIV Env-C Plasmid DNA priming
- To determine whether the addition of ALF43 to the Rehydragel® - HIV Env gp145 C.6980 protein boost further improves the immune response to HIV Env gp145 C.6980 protein
- To determine whether adjuvants improve humoral responses across vaccination regimens
- To evaluate the influence of various adjuvants on cellular immune responses
- To describe mucosal humoral responses across vaccination regimens in cervicovaginal and rectal secretions and semen

3.1.3. Exploratory Objectives

- To characterize B-cell functional specificities for each vaccination regimen
- To characterize innate immunity
- To assess the innate/gene expression induced across vaccination regimens (DNA microarray, RNA sequencing) to compare relative influence of various adjuvants in the gene expression profiles of sorted T cell, B cell and innate cell subsets
- To perform systems serology analyses

3.1.4. Sub-Objective

- In participants who elect to undergo lymph node biopsy, characterize HIV-specific responses, T cell activation, T follicular helper (Tfh) cell and B cell distribution in intact lymph nodes (excision of intact peripheral inguinal lymph node) at weeks 14 and 58.

3.2. Endpoints / Outcome Measures

The endpoints below elaborate upon those defined in Section 1.2 of the protocol. All immunogenicity outcome measures will be summarized separately by initial DNA priming dose series (after Doses 1, 2, and 3) or by vaccination group (after Doses 4, 5, and 6), as appropriate depending on the time point(s) for each analysis.

3.2.1. Primary (Safety) Endpoints

Safety will be assessed via solicited AEs (local and systemic reactogenicity), related unsolicited AEs, and SAEs.

Primary safety endpoints will be [the incidence and frequency of]:

- Solicited local reactogenicity adverse events, post-each study dose and post-any study dose, by vaccination group (or by priming series post-prime doses), time point, and severity.
    - Local reactogenicity events assessed in clinic immediate post-vaccination and from self-reported diary cards on Day 2 through Day 7 include: pain/tenderness, itching, warmth, redness/erythema (measurement of largest dimension), and swelling/induration (measurement of largest dimension)
- Solicited systemic reactogenicity adverse events, post-each study dose and post-any study dose, by vaccination group (or by priming series post-prime doses), time point, and severity.
    - Systemic reactogenicity events assessed in clinic immediate post-vaccination and from self-reported diary cards on Day 2 through Day 7 include: fever, tiredness, myalgia, arthralgia, headache, fatigue, chills, rash, nausea, and dizziness.
- Adverse events (AEs) deemed related to the study product(s) by vaccination group (or by priming series post-prime doses) and severity from visit 0 through visit 26.
- Serious adverse events (SAEs) by vaccination group (or by priming series post-prime doses) and severity from visit 0 through visit 26.
- Potentially immune-mediated medical conditions (PIMMCs) by vaccination group (or by priming series post-prime doses) and severity from visit 0 through visit 26.
- Medically attended adverse events (MAAEs) by vaccination group (or by priming series post-prime doses) and severity from visit 0 through visit 26.

3.2.2. Secondary (Immunogenicity) Endpoints

- Plasma IgA binding antibodies to gp120 and V1V2, summarized by time point and by area under the curve over time.
- Neutralizing antibodies and non-neutralizing effector functions such as ADCC and ADCP (with emphasis on RV144 immune correlates of risk of HIV acquisition), summarized by time point and by area under the curve over time.
- Cell-mediated immune responses, such as antigen-specific CD4 and CD8 T cell responses and polyfunctionality scores, induced cytokines and chemokines, and other inflammatory markers, summarized by time point.
- Mucosal humoral responses in cervicovaginal and rectal secretions and semen, including but not limited to plasma IgG and IgA binding antibodies to HIV-1 Env proteins, IgG and IgA subclass, and functional assays, summarized by time point.

3.2.3. Exploratory (Immunogenicity) Endpoints

- Antigen-specific B cell responses as measured via ELISPOT and phenotyping the magnitude and activation status of B cell subsets via flow cytometry, as well as the isolation of monoclonal antibodies from selected vaccine recipients, summarized by time point.
- Innate immune responses, as assessed by the quantification of soluble chemokines and cytokines and the phenotype and function of cellular innate immune subsets such as NK, NKT, and dendritic cells, summarized by time point.
- Gene expression profiles for various sorted T cell, B cell, and innate cell subsets, as measured using RNA-Seq and related methods, described by vaccination group.
- Associations between various immunological measurements, including antibody-binding responses and antibody effector functional assays, via systems serology analysis.

3.2.4. Sub-Endpoint

- The magnitude and frequency of HIV-specific Tfh cells in total lymph nodes and lymph node follicles, Tfh and B cell distributions between intra and extrafollicular LN zones, and levels of cellular activation using ICS, immunohistochemistry, transcriptional analyses, and related techniques at weeks 14 and 58.

3.3. Study Definitions and Derived Variables

The baseline value for immunogenicity data will be defined as the last value obtained prior to the first vaccination. Individual antibody endpoint titers will be reported with values of $C*2^k$, where k=0, 1, 2, etc. and C may vary depending on the dilutions used for a given assay. Values below each assay's limit of detection (LOD) will be imputed as one-half the limit of detection. Where appropriate, values above a reported upper limit of quantification (ULOQ) will be imputed as equal to the ULOQ, and values above the LOD but below a lower limit of quantification (LLOQ) will be imputed as (LOD+LLOQ)/2. For analysis, the arithmetic or geometric mean of replicates for each sample will be computed and used as the response for all subsequent calculations, where applicable.

The magnitude of immune response will be assessed by arithmetic or geometric mean responses at each time point, as well as the peak response. Peak response is defined as the maximum reported immune response by a participant post-vaccination and the week of peak response is defined as the week at which the peak response was observed.

The durability of immune response will be assessed via descriptive statistics of each immune response at later time points.

Total immune responses will be calculated for a given assay via the positive incremental area under the curve (AUC), based on a graph with the analysis value (e.g., log endpoint titer) on the y-axis and visit week on the x-axis. The trapezoidal rule will be applied as follows:

$$\text{AUC}_i = \frac{1}{2} * \sum_{j=1}^{n-1}\left(t_{j+1} - t_j\right) * \left(R_{ij+1} + R_{ij}\right)/(t_n - t_1),$$

where $(t_{j+1} - t_j)$ is the difference between the *j*th and *j*+1th time points, and R*ij* and R*ij*+1 are the assay values measured at the *j*th and *j*+1th time points for the *i*th individual.

4. INVESTIGATIONAL PLAN

4.1. Overall Study Design and Plan

This is an exploratory Phase I randomized, double-blind, placebo-controlled clinical trial to define the safety, tolerability, and immunogenicity of different adjuvant formulations in combination with an Env-C Plasmid DNA and HIV Env gp145 C.6980 protein in a prime-boost combination. Enrolled participants receive 3 doses of Env-C Plasmid DNA as a prime (with or without adjuvants) or admixed with HIV Env gp145 C.6980 protein. The Env-C Plasmid DNA is given alone, formulated with the adjuvant ALF43 (Army Liposome Formulation with Monophosphoryl Lipid A (MPLA) and 43% Cholesterol) adjuvant, or co-administered with the transcutaneous adjuvant dmLT (*E. coli* heat labile enterotoxin) applied at the injection site. The HIV Env gp145 C.6980 protein boost is mixed with Rehydragel® or ALF43 plus Rehydragel®.

Specifications of prime/boost combinations for each study group are presented in **Table 1**. For analysis purposes, participants will be grouped appropriately by vaccination regimen; as such, participants receiving placebo will be considered the eighth vaccination group. Participants will receive prime vaccination at weeks 0, 4, and 12 and boosts at weeks 20, 32, and 56. Some vaccination groups will be combined (by DNA priming regimen or use of ALF43 adjuvant in the boost), depending on the objective or endpoint of interest and the time points utilized in a given analysis.

Table 1: Study Arms

Group	n =		Prime at weeks 0, 4, 12	Boost at weeks 20, 32, 56
	v	p		
1	15	3	Env-C Plasmid DNA (2 mg, IM)	HIV Env gp145 C.6980 protein (100 µg, IM)/ Rehydragel® (500 µg, IM)
2	15	3	Env-C Plasmid DNA (2 mg, IM)	HIV Env gp145 C.6980 protein (100 µg, IM)/ Rehydragel® (500 µg, IM)/ALF43 (200 µg, IM)
3	15	3	Env-C Plasmid DNA (2 mg, IM) + dmLT (50 µg, TCI)	HIV Env gp145 C.6980 protein (100 µg, IM)/ Rehydragel® (500 µg, IM)
4	15	3	Env-C Plasmid DNA (2 mg, IM) + dmLT (50 µg, TCI)	HIV Env gp145 C.6980 protein (100 µg, IM)/ Rehydragel® (500 µg, IM)/ALF43 (200 µg, IM)
5	15	3	Env-C Plasmid DNA (2 mg, IM)/ ALF43 (200 µg, IM)	HIV Env gp145 C.6980 protein (100 µg, IM)/ Rehydragel® (500 µg, IM)
6	15	3	Env-C Plasmid DNA (2 mg, IM)/ALF43 (200 µg, IM)	HIV Env gp145 C.6980 protein (100 µg, IM)/ Rehydragel® (500 µg, IM)/ALF43 (200 µg, IM)
7	15	3	Env-C Plasmid DNA (2 mg, IM)/HIV Env gp145 C.6980 protein (100 µg, IM)/ALF43 (200 µg, IM)	Env-C Plasmid DNA (2 mg, IM)/HIV Env gp145 C.6980 protein (100 µg, IM)/ALF43 (200 µg, IM)/ Rehydragel® (500 µg, IM)

IM = intramuscular, TCI = transcutaneous immunization; ALF43 (Army Liposome Formulation with Monophosphoryl Lipid A (MPLA) and 43% Cholesterol); v = Vaccine Recipient; p = Placebo

Study groups will be assessed for HIV-1 Env-specific antibody responses elicited by boosting with HIV Env gp145 C.6980 protein adjuvated with Rehydragel® with or without ALF43. Group 7 will assess whether the concept of co-delivery of Env-C Plasmid DNA and HIV Env gp145 C.6980 protein simultaneously will increase the frequency and magnitude of immune responses rather than Env-C Plasmid DNA given IM alone.

Group 1 will be fully enrolled first, after which enrollment will begin in Groups 2-7. Once 24 participants in Groups 2-7 have been enrolled (four from each group) and received their first vaccinations, enrollment and vaccinations will be paused for a Protocol Safety Review Team (PSRT) review of blinded safety data from these 24 participants from the day of first vaccination through Day 7. After confirmation of safety from the PSRT, enrollment and vaccinations for the remaining 14 participants in each of Groups 2-7 will resume. Boost vaccinations will be paused (prime vaccinations to continue) when the first 24 participants in Groups 2-7 who had safety data reviewed in the first PSRT review receive their first boost dose, at which point the PSRT will perform another safety review of these newly boosted participants. Boost vaccinations will resume for Groups 2-7 after the PSRT has reviewed boost vaccination data and concluded it is safe to proceed.

The schedule of evaluations is given in **Table 2** below, for reference.

Table 2: Schedule of Evaluations

Visit Number	S1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26 Exit
Visit Day	-45 to -3	0	3 ± 1	7 ± 2	14 ± 3	28 ± 7	35 ± 2	42 ± 3	84 ± 7	87 ± 1	91 ± 2	98 ± 3	140 ± 7	143 ± 1	147 ± 2	154 ± 3	224 ± 7	231 ± 2	238 ± 3	392 ± 7	395 ± 1	399 ± 2	406 ± 3	476 ± 14	560 ± 14	728 ± 14	735 ± 14
Visit week	0	0.5	1	2	4	5	6	12	12.5	13	14	20	20.5	21	22	32	33	34	56	56.5	57	58	68	80	104	105	
Clinical																											
Briefing & contact information	X																										
Informed consents	X																										
Test of understanding	X																										
Complete physical exam, height, weight & review medical history	X																										
Vital signs (BP, pulse, RR, oral temp)	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
Concomitant Medication	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
Targeted physical exam and review of symptoms	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	
HIV risk counseling; pregnancy counseling[11]	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
Vaccination		**X** [6]				**X** [6]			**X** [6]				**X** [6]				**X** [6]			**X** [6]							
Review Eligibility		X				X			X				X				X			X							
Enrollment and randomization[12]		X				X			X				X				X			X							
Assess reactogenicity in clinic 30-60 min post-vaccination		X				X			X				X				X			X							
MAAE documentation[9]		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
Adverse Event documentation		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
Diary card completion/ review[10]			X	X			X			X	X			X	X			X			X	X					
Clinical Laboratory Assessments[5]																											
Urinalysis dipstick for blood, protein and glucose	X																										
Urine pregnancy test[7]	X	X				X		X	X			X2	X			X	X		X	X			X2	X	X	X	
CBC with differential	3				3			3				3				3			3				3				
Creatinine, ALT, AST	3				3			3				3				3			3				3				
Syphilis serology	6																										
HBsAg/HepC	NB																										
Pap smear for Softcup collection participants	X																										
Coagulation and safety tests prior lymph node biopsy[8]											9											9					
HIV testing with Pre/Post HIV test counseling	6	6										6				6			6				6		6	6	

Table 2: Schedule of Evaluations (*continued*)

Visit Number	S1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26 Exit
Visit Day	-45 to -3	0	3 ± 1	7 ± 2	14 ± 3	28 ± 7	35 ± 2	42 ± 3	84 ± 7	87 ± 1	91 ± 2	98 ± 3	140 ± 7	143 ± 1	147 ± 2	154 ± 3	224 ± 7	231 ± 2	238 ± 3	392 ± 7	395 ± 1	399 ± 2	406 ± 3	476 ± 14	560 ± 14	728 ± 14	735 ± 14
Visit week	0	0.5	1	2	4	5	6	12	12.5	13	14	20	20.5	21	22	32	33	34	56	56.5	57	58	68	80	104	105	
Research Laboratory Assessments[3]																											
HIV NAb		6			6	6		6	6			6	6			6	6		6	6			6	6	6	6	6
Binding antibody/ antibody profiling		6		6	6	6	6	6	6		6	6	6		6	6	6	6	6	6		6	6	6	6	6	6
Functional Antibody Assays (ADCC, ADCP, ADCVI, etc.)		NB			NB	NB		NB	NB			NB	NB			NB	NB		NB	NB			NB	NB	NB	NB	NB
Cellular immune analysis		93.5	17	17	42.5		25.5	42.5		17	34	85		17	34	68		34	68		17	34	85	85	85	85	34
Cytokine/soluble factor assays		NB		NB	NB	NB	NB	NB	NB		NB	NB	NB		NB	NB	NB	NB	NB	NB		NB	NB	NB	NB	NB	NB
Gene expression/ transcriptome analysis		34	17						17	17		8.5	17	17						17	17		8.5				
Mucosal secretion collection[1,7]		X							X			X				X			X				X	X	X	X	
Lymph node biopsy[2]	X	X																									
Storage & additional immunogenicity testing (mL)		25.5			17	17			8.5			17	8.5			34	17		34	17		17	51	25.5	25.5	25.5	17
Daily volume (mL)[4,5]	**18**	**171**	**34**	**23**	**77.5**	**29**	**31.5**	**60.5**	**37.5**	**34**	**49**	**134.5**	**37.5**	**34**	**40**	**126**	**29**	**40**	**126**	**46**	**34**	**66**	**168.5**	**122.5**	**128.5**	**128.5**	**63**
Cumulative volume (mL)[4,5]	**18**	**189**	**223**	**246**	**323.5**	**352.5**	**384**	**444.5**	**482**	**516**	**565**	**699.5**	**737**	**771**	**811**	**937**	**966**	**1006**	**1132**	**1178**	**1212**	**1278**	**1446.5**	**1569**	**1697.5**	**1826**	**1889**
8-week cumulative volume[4,5]								**444.5**	**158.5**	**163.5**	**212.5**	**315.5**	**292.5**	**289**	**295**	**372**	**29**	**69**	**195**	**46**	**80**	**146**	**314.5**	**122.5**	**128.5**	**128.5**	**191.5**

NB=No extra blood required

1: Mucosal secretion collections - Rectal secretions collected by sponge. Male participants: semen collection by masturbation. Female participants: cervicovaginal secretions collected by Softcup. For menstruating females, mucosal collection window can be extended to -3 + 14 days.

2: Excisional inguinal lymph node biopsies will be performed in a subset of participants who agree to undergo this procedure. Urine pregnancy testing prior to procedure. Biopsy site assessment at 7 days (+2 days) after each biopsy

3: Research labs may be performed at any visit where sufficient stored samples are available

4: The maximum amount drawn in any 8-week interval is 444.5 mL. The maximum amount drawn in one day is 171 mL

5: Clinical labs may be repeated if clinically significant

6: Phone or clinic visit will be done to assess the participants well-being 24 hours (+1 day) after each vaccination.

7: Pregnancy testing must be performed prior to vaccination and mucosal secretion collection

8: 9 mL should be taken if CBC/Chem results are not available on day of biopsy. Otherwise, 3 mL should be drawn

9: Medically Attended Adverse Events will be followed through the end of the study, a full 12 months following the last vaccination

10: Participants will take home the diary card and complete and the diary card will be reviewed at 7 days after vaccination

11: Additional testing as clinically indicated

12: A participant is considered enrolled into the study once they are randomized into a study group

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

This study uses a factorial, placebo-concurrent control design to assess the safety, tolerability, and immunogenicity of prime-boost combinations of Env-C Plasmid DNA and HIV Env gp145 C.6980 protein with different adjuvant combinations. Sterile saline (0.9% sodium chloride) is the placebo for each study product utilized in this study.

4.3. Selection of Study Population

The study population consists of a targeted 126 healthy, HIV-uninfected male and female participants aged 18 to 40 years in Kericho, Kenya. All study participants must meet the eligibility criteria enumerated in the protocol (Sections 4.2.1, 4.2.2).

4.4. Statistical Considerations for the Study Design

4.4.1. Sample Size Considerations

The safety, reactogenicity, and tolerability of the vaccine regimens are the primary endpoints for this study. Below in **Table 3**, the estimated probability of a participant having at least one of these events (in percent), along with the associated exact Clopper-Pearson 95% confidence interval, is given for various numbers of observed events that correspond to approximate event rates within vaccination groups of possible interest. Note that some event rates cannot be exactly observed within a given vaccination group, depending on the sample size (e.g., 10% of 15 participants is 1.5 participants, which is rounded to 2 in the table below).

Table 3: Estimated Probability (in percent) of a Participant Having at Least One AE, along with the Associated Exact Clopper-Pearson 95% CI, Given Varying Sample Sizes and Numbers of Participants with at Least One Observed AE

Group	n	Approximate AE Rate[1]							
		0%		10%		20%		50%	
		Number of AEs[2]	Estimated Probability (95% CI)	Number of AEs[2]	Estimated Probability (95% CI)	Number of AEs[2]	Estimated Probability (95% CI)	Number of AEs[2]	Estimated Probability (95% CI)
Each Individual Group	15	0	0 (0, 21.8)	2	13.3 (1.7, 40.5)	3	20 (4.3, 48.1)	8	53.3 (26.6, 78.7)
Placebo	21	0	0 (0, 16.1)	2	9.5 (1.2, 30.4)	4	19 (5.4, 41.9)	11	52.4 (29.8, 74.3)
Any DNA Prime with HIV Env gp145 C.6980 /Rehydragel Boosts	105	0	0 (0, 3.5)	11	10.5 (5.3, 18.0)	21	20 (12.8, 28.9)	53	50.5 (40.5, 60.4)
DNA alone (1+2), DNA+TCI (3+4), DNA/ALF43 (5+6)	30	0	0 (0, 11.6)	3	10 (2.1, 26.5)	6	20 (7.7, 38.6)	15	50 (31.3, 68.7)
Any ALF43	75	0	0 (0, 4.8)	8	10.7 (4.7, 20.0)	15	20 (11.6, 30.8)	38	50.7 (38.9, 62.4)

[1] The approximate proportion of participants in a group reporting at least one event of interest.

[2] The number of participants with observed event(s) needed to correspond to the given approximate event rate most closely, with the given sample size.

For illustration, if 2 individuals among the 15 participants in an individual vaccine group experienced at least one event, the estimated event probability would be 13.3%, with an associated exact 95% CI of (1.7%, 40.5%). Eleven individuals reporting at least one event among all active participants (n=105) would lead to a similar estimated event probability of 10.5%, but with a narrower exact 95% CI (5.3%, 18.0%).

Table 4 below gives the probability of observing at least one or more than one event in a group of interest, given underlying per-participant probabilities of at least one event.

Table 4: Probability of Observing at Least One or at Least Two Safety Events in a Given Group, Given Varying Underlying Per-Participant Probabilities of Experiencing at Least One Event

Group	n	Underlying Probability of At Least One Event					
		1%		10%		20%	
		>0	>1	>0	>1	>0	>1
Each Individual Vaccine Group	15	14.0%	1.0%	79.4%	45.1%	96.5%	83.3%
Placebo	21	19.0%	1.9%	89.1%	63.5%	>99%	94.2%
Any Env-C Plasmid DNA Prime with HIV Env gp145 C.6980 /Rehydragel Boosts	105	65.2%	28.3%	>99%	>99%	>99%	>99%
Env-C Plasmid DNA alone (1+2), Env-C Plasmid DNA+TCI (3+4), Env-C Plasmid DNA/ALF43 (5+6)	30	26.0%	3.6%	95.8%	81.6%	>99%	>99%
Any ALF43	75	52.9%	17.3%	>99%	>99%	>99%	>99%

4.4.2. Allocation of Participants to Study Arms (Randomization)

A randomization schedule was centrally generated by the protocol statistician. The study was expected to recruit approximately equal numbers of males and females, but formal targets for randomization were not established. Participants are allocated at a ratio of 15 vaccine : 3 placebo within each vaccination group.

Blocks were used to randomize participants to vaccination status (e.g., vaccine or placebo) for all participants and to vaccination groups for participants in Groups 1 through 7 to maintain balance in assignments over time.

Participants who withdrew, were withdrawn from this study, or lost to follow-up after signing the informed consent form (ICF) and administration of the study product were allowed to be replaced. If a participant withdrew from the study or discontinued vaccination before all slots were filled, the vacated randomization slot was filled with the next available participant.

4.5. Study Products

4.5.1. Study Products Administered

Study products administered include the Env-C Plasmid DNA vaccine (HIV-1 gp120 (93MW965.26) DNA), HIV Env gp145 C.6980 protein, recombinant double mutant Escherichia coli heat labile toxin (dmLT), army liposome formulation – 43% cholesterol (ALF43), and Rehydragel® (aluminum hydroxide fluid gen). Saline (0.9% sodium chloride for injection) was used as placebo for the study.

4.5.2. Identity of Investigational Product(s)

The Env-C Plasmid DNA vaccine is supplied as single-dose vials containing 0.9 mL of solution at a concentration of 4 mg/mL. Each 1 mL of solution contains 4 mg of Env-C Plasmid DNA vaccine and 9 mg of sodium chloride. When thawed, the study product appears as a clear, colorless liquid.

The HIV Env gp145 C.6980 protein vaccine is provided as single-dose vials containing 0.7 mL of solution at a concentration of 600 µg/mL. The buffer is phosphate-buffered saline (PBS), pH 7.4. When thawed, the study product appears as a clear, colorless liquid.

The dmLT adjuvant is administered as a multiple-dose vial (up to two doses can be withdrawn from a vial) containing 0.5 g of lyophilized product. The lyophilized product is formulated at 1 mg/mL in phosphate-buffered saline containing lactose, pH 7.4 and appears as a solid cake, consistent, and white to off-white. Each vial of dmLT is reconstituted with 0.5 mL of sterile water for injection, resulting in a concentration of 1 mg/mL. The reconstituted product appears as a clear, colorless solution.

The ALF43 adjuvant is supplied as single-dose vials containing 240 µg of 3D-PHAD® per vial. ALF43 has a phospholipid to 3D-PHAD® molar ratio of 8.8 to 1. The ALF43 product appears as a white to off-white lyophilized powder, which may be in a cake at the bottom of the vial or dispersed throughout the vial.

The Rehydragel® adjuvant is provided as 3 mL single-dose vials containing 0.7 ± 0.10 mL of aluminum suspension at a concentration of 5 ± 1 mg/mL. The vials are labeled as Aluminum Hydroxide suspension fluid gel (adjuvant). Rehydragel® appears as a white gelatinous precipitate in aqueous suspension; opaque.

Saline (0.9% sodium chloride) serves as the placebo for the trial.

For additional information on the investigational products such as how they relate to the study objectives and endpoints of interest, please refer to Sections 3.1 and 3.2.

4.5.3. Selection of Doses in the Study

All enrolled participants receive three 1 mL doses of placebo or a prime of either 2 mg of Env-C Plasmid DNA (with or without 50 µg of dmLT adjuvant) or 2 mg of Env-C Plasmid DNA with 200 µg of ALF43 adjuvant with or without being admixed with 100 µg of HIV Env gp145 C.6980 protein. Three boosts are administered of either 1 mL of placebo or 100 µg of HIV Env gp145 C.6980 protein boost mixed with 500 µg of Rehydragel®, 200 µg of ALF43 plus 500 µg of Rehydragel®, or 200 µg of ALF43 plus 500 µg of Rehydragel® plus 2 mg of Env-C Plasmid DNA. Doses of each study product are chosen based on one or more of the following: current good manufacturing practices (cGMP) constraints; doses used in a previous clinical trial(s); and the requirement for mixing of vaccine components in the current study.

4.5.4. Selection and Timing of Dose for Each Participant

Participants are randomized to study arm and vaccination status (vaccine vs. placebo) according to the procedure described in Section 4.4.2. Prime immunizations are administered at Weeks 0, 4, and 12 and boost immunizations are administered at Weeks 20, 32, and 56.

4.5.5. Blinding

The PI, clinical staff, and participants are blinded to treatment allocation. Investigators are blinded to participant vaccine versus placebo status within each group but are not blinded to group enrollment. An overlay is applied to dosing syringes by the unblinded pharmacist to avoid unblinding due to the appearance of study products. Placebo syringes are held for the same length of time it would take to prepare and dispense active vaccine syringes to avoid unblinding due to preparation time.

4.5.6. Prior and Concomitant Therapy

Concomitant medications are recorded by participants on diary cards on the day of each study vaccination and then for 7 days following vaccination.

4.5.7. Study Product Compliance

Participants withdrawn are replaced with the next available participant if they withdraw from the study or discontinue treatment before all enrollment slots have been filled. Sensitivity analyses may be performed to assess the impact of protocol non-compliance, based on the Per-Protocol population (defined in Section 5.3.3).

4.6. Safety Variables

Safety will be assessed by laboratory studies, medical history, physical assessment of clinicians, and participant self-assessment recorded on a 7-day diary card. Temperature and solicited local and systemic symptoms are recorded in the clinic before vaccination and 30-60 minutes post-injection, at home approximately 6 hours after vaccination, and then daily by the participant for 7 days. Local reactogenicity symptoms include pain/tenderness, itching, warmth, redness/erythema, and swelling/induration; systemic reactogenicity symptoms include fever, myalgia, arthralgia, headache, fatigue, chills, rash, nausea, and dizziness. Follow-up on participant well-being is performed by telephone (preferred method) or clinic visit on the day following vaccination (and up to 48 hours later). Diary cards are reviewed with the clinician on Day 7 ± 2 days following each vaccination. The incidence of specific post-vaccination reactions and any reaction are used for analysis. For analysis of the incidence of solicited reactogenicity events, the maximum severity reported over the 7-day reactogenicity period will be utilized.

AEs and SAEs, including solicited symptoms that persist after the end of Day 7 and abnormal vital signs measured about 30-60 minutes post-vaccination, will be recorded at all visits along with the associated time point. Possible attribution to the study product is assessed for all AEs except HIV infection. AEs will be summarized by both incidence and frequency. Incidence will be assessed by the maximum severity of AEs reported per-participant within the appropriate MedDRA classification (e.g., MedDRA SOC or PT) for a given table or figure.

Safety laboratory analyses of complete blood count, chemistry (creatinine, alanine aminotransferase [ALT], aspartate aminotransferase [AST]), HIV testing, and pregnancy tests in females are performed according to the SOE (**Table 2**). In addition to abnormal findings reported as AEs, changes from baseline will be computed.

Potentially immune-mediated medical conditions (PIMMCs) and medically attended adverse events (MAAEs) are subsets of adverse events that are determined according to criteria given in the protocol. PIMMCs constitute a group of AEs that includes diseases which are clearly autoimmune in etiology and other inflammatory and/or neurologic disorders which may or may not have autoimmune etiologies. MAAEs are defined as AEs with medically attended visits including hospital, emergency room, urgent care clinic, or other visits to or from medical personnel for any reason. AEs identified at routine study visits will not be considered MAAEs.

4.7. Immunogenicity Variables

Vaccine-induced immune responses will be assessed in study participants as detailed in the SOE (**Table 2**). Depending on the type of assay, different measures will be reported to quantify immune response such as concentrations, background-subtracted fluorescence, endpoint titers, and percent of cell phenotypes. The mean or geometric mean value of the assay outcome measure will be reported for each vaccination group, along with associated confidence intervals and other descriptive statistics, and targeted hypothesis testing as outlined in Section 5.1.

Binding antibody assays will be performed to detect a broad array of HIV-1 antigens in serum or plasma and in mucosal secretion samples. Serum and plasma will also be tested for their ability to block HIV-1 binding to the α4β7 receptor and other possible HIV-1 co-receptors. In addition, antibody isotype, subclass, FC gamma, complement usage, and other antibody profiling tools will be utilized in parallel with antigen specificity. Monoclonal antibodies will also be isolated from selected vaccine recipients and used for analysis as necessary.

ELISA and/or Luminex assays in serum or plasma and in mucosal secretion samples will be performed to detect cytokines and other soluble factors to quantify immune responses after vaccination.

Types of assays to be performed in the study include Antibody-dependent Cell-Mediated Cytotoxicity (ADCC) assays and Antibody-dependent Cell-Mediated Viral Inhibition (ADCVI) assays. ADCC assays will be performed for visits specified in the SOE (**Table 2**) using rapid fluorometric ADCC. Other functional assays include Antibody-dependent Cell-Mediated Phagocytosis (ADCP) and Antibody-dependent Complement (ADC) activation assays.

Neutralization assays will be performed by applying similar techniques from other HIV vaccine trials, such as using cell line-based and PBMC assays with a panel of viruses from different HIV subtypes. HIV Subtypes include A, B, C, D, and other circulating recombinant forms (CRFs) such as AE and AG.

Cryopreserved PBMC and lymph node biopsy samples will be stimulated with HIV-1-specific antigens and tested using standard cellular immune assays which includes, but are not limited to, Intracellular Cytokine Staining (ICS), B-cell, antigen-specific T cells, Tfh, and innate immune cell flow cytometry analysis, ELISPOT, and lymphoproliferation assays.

Immunogenicity variables will be defined according to input from the research laboratory conducting each set of assays, and analysis will be conducted as described in Section 3.3, Section 5, and Section 8. Once additional details on assays are available, if the principles described in this document are insufficient, SAP amendment(s) or addendum(a) to clarify the respective analyses may be drafted.

4.8. Genomic Variables

Other assays include gene expression/transcriptomic analysis using current technologies; genetic analysis including but not limited to Human Leukocyte Antigen (HLA) subtyping and RNA sequencing. Any assay analyses not planned in this document would be accounted for in SAP addenda or other documentation.

4.9. Other Variables

Participant disposition variables will include the number of participants in each vaccination group and overall completing visits and study assessments. Categorical demographic and baseline characteristics to be summarized by vaccination group will include age group, sex, race, ethnicity, tribal classification, marital status, level of education, and occupation. Continuous demographic and baseline characteristics to be summarized by vaccination group will include age and BMI.

5. GENERAL STATISTICAL CONSIDERATIONS

5.1. General Principles

In general, all data listings will be sorted by participant, analysis group, and when appropriate by visit number within participant. Summary tables will be annotated with the total population size relevant to that table/vaccination group, including any missing observations.

Unless otherwise indicated, continuous variables will be summarized using the following descriptive statistics: n (non-missing sample size), mean, standard deviation (SD), minimum, median, and maximum. The frequency and percentages (based on the non-missing sample size) of observed levels will be reported for all categorical measures. The binomial distribution will be assumed for binary endpoints (such as safety events), and exact Clopper-Pearson confidence intervals will be computed, where indicated. To avoid utilizing parametric assumptions and to assess immunogenicity targets consistently regardless of observed distributions, nonparametric methods will be applied for the analysis of continuous immunogenicity variables. Bootstrapping is planned for computing confidence intervals for continuous endpoints, starting with 5,000 samples. These intervals will be compared to intervals generated with 10,000 samples and if the intervals are qualitatively similar enough, then 5,000 samples will be used for analysis to reduce computation time. Confidence intervals based on the t-distribution may be considered as well, if data are approximately normally distributed and/or the sample sizes suffice for the application of the central limit theorem.

For comparisons of safety outcomes, a 5% significance level will be used. Comparisons between groups will be based on the amount of overlap of group-level 95% confidence intervals. No formal hypothesis testing for safety is planned, due to the small sample sizes and challenging interpretation of p-values in that context. For any potential targeted safety hypothesis testing determined to be of post hoc interest, pairwise comparisons would be performed using the Bonferroni-Holm step-down procedure [1] with a 5% significance threshold. For binary endpoints, Barnard's test for pairwise comparisons and Fisher's exact test for global tests would be used as these methods are able to accommodate small sample sizes.

Hypothesis testing will be conducted for immunogenicity analyses to aid the interpretation of results for numerous assays and assay targets. These tests will be considered hypothesis-generating, and the number of tests conducted, the magnitudes of differences observed, and the apparent patterns across various tests and across various immunological endpoints will be considered when interpreting the results. Nonparametric two-sided Mann-Whitney U tests are planned, with the null hypothesis of equivalent distributions of responses across relevant groups. Alternative testing methods may be considered, either for complex assay data, as appropriate depending on the details of those assays, or if the central limit theorem may be applied and simpler t-tests would be appropriate. P-values from tests of immunogenicity variables will be categorized as strong, moderate, or weak evidence based on thresholds of 0.001, 0.01, and 0.05 respectively for comparisons of immunogenicity outcomes; for assays with a large number of targets, p-value adjustments to account for multiplicity may be considered as well (see **Section 5.7**).

Analyses seeking to compare DNA priming regimens will combine individual vaccination groups into the following Priming Dose Groups:

i) Priming Dose Group 1: prime of Env-C Plasmid DNA alone (Vaccination groups 1 and 2)
ii) Priming Dose Group 2: prime of Env-C Plasmid DNA/dmLT (Vaccination groups 3 and 4)
iii) Priming Dose Group 3: prime of Env-C Plasmid DNA/ALF43 (Vaccination groups 5 and 6)
iv) Priming Dose Group 4: prime of Env-C Plasmid DNA/dmLT/HIV Env gp145 C.6980 protein (Vaccination group 7)
v) Pooled Placebo

These combinations of vaccination groups of interest will be utilized for analyses of data prior to the start of boosting doses, as detailed in tables located in the appendix. Further details on the planned analysis of immunogenicity data are given in **Section 8**.

Across analyses, the period from immediately after Dose 1 through the visit where Dose 4 is administered is described as "post-priming doses", "post-prime", "prior to boost doses", or "pre-boost"; the period from the administration of Dose 4 through the end of study is referred to as "post-boost doses", "post-boost", or other similar description.

5.2. Timing of Analyses

The final study report will be completed when all primary objective data and secondary immunogenicity endpoint data are available. Additional exploratory immunogenicity analyses will be presented in separate reports and/or manuscripts, depending on data availability.

Blinded interim immunogenicity analyses are planned while the study is ongoing, but the results of any such analyses will not impact the conduct of the trial.

5.3. Analysis Populations

5.3.1. Safety Populations

The Safety population consists of participants who received at least one vaccination.

5.3.2. Immunogenicity Population

The immunogenicity (IMM) population consists of all participants who received at least one dose of the vaccination or placebo after entry (initial vaccination) and have at least one post-vaccination immunogenicity sample collected with results available for analysis. IMM population analyses are analyzed as-randomized.

5.3.3. Per-Protocol Population

The Per-Protocol (PP) population consists of participants from the IMM population, with the exclusion of participants who missed more than just Dose 2 or Dose 3, or who reported a major protocol deviation determined by the protocol team to potentially impact the evaluation of immune responses, as part of a blinded review. The PP population will be used for sensitivity analyses of peak and total immune responses, to qualitatively compare to analyses utilizing the IMM population. PP analyses will be performed according to the study products received. If results indicate the likelihood of major confounding from varying participant disposition (e.g., missed or out of window study vaccinations, out of window visits, etc.), additional exploratory sensitivity analysis may be conducted to further assess the impact. For more details about potential immunogenicity sensitivity analyses, please refer to Section 8.1.

5.4. Covariates and Subgroups

There are not any protocol-specified covariates of interest. Vaccination groups are combined for some analyses, depending on the endpoint or outcome of interest. See Section 5.1 for more details.

5.5. Missing Data and Outliers

All attempts will be made to collect all data per protocol. No imputation is planned for missing values. Outliers are not expected for primary safety endpoints, however any data point that appears to be erroneous or inexplicable based on clinical judgment will be investigated as a possible outlier. If data points are identified as outliers, sensitivity analysis excluding outliers may be performed to examine the impact of including or excluding the outliers. Any substantive differences will be reported.

The number of non-missing values in each analysis group will be described for all analyses. Participants that missed visits, discontinued the trial, or withdrew from the trial due to COVID-19 will be described in **Listing 20**. The impact of missing data due to COVID-19 will be discussed in the analysis report(s).

5.6. Interim Analyses and Data Monitoring

There are not any formal interim analyses planned. Any interim analysis performed prior to the end of the scheduled follow-up visits will not compromise the integrity of the trial in terms of the maintenance of the study blind, participant retention, safety endpoint assessments, or immunogenicity endpoint assessments. All analyses will be blinded and there will be no plans to publish results from the interim analyses prior to when the final data are collected.

Interim analyses will include analyses of binding antibodies (Luminex and ELISA assays) and HIV neutralization on weeks 0 and 14 in all patients. Blinded comparisons between priming dose groups will be made to facilitate interpretation.

5.7. Multiple Comparisons/Multiplicity

For comparisons of safety outcomes, a 5% significance level will be used. Across objectives, many comparisons between groups will be based on the amount of overlap of group-level confidence intervals. For comparisons of immunogenicity outcomes, targeted hypothesis testing will be conducted, as described in **Section 5.1** and **Section 8**. For any genetic analyses or for endpoints with numerous biomarkers (e.g., array-based assays with many molecular targets), false discovery rate (FDR) correction may be applied to control the proportion of false positive results. Even when not adjusting for multiplicity, the results will be interpreted holistically (e.g., the results across similar biomarkers may be qualitatively compared for a consistent signal) and the number of comparisons will be considered in that interpretation.

6. STUDY PARTICIPANTS

6.1. Demographic and Other Baseline Characteristics

Participant demographics and baseline characteristics, listed in Section 4.9, will be summarized by vaccination group, using the statistics described in Section 5.1. Categorical demographic information such as sex, race, ethnicity, and other baseline characteristics will be summarized and presented by vaccination group in **Table 8**. Continuous demographic information such as age and BMI will be summarized and presented by vaccination group in **Table 9**. Demographic information for individual participants will be provided in **Listing 2**.

6.2. Disposition of Participants

The number of participants who enroll in the trial, overall and stratified by vaccination group, will be presented in **Table 7**, along with the number and percentage of participants who receive each study vaccination, complete all scheduled blood draws, and complete each study visit. Participants who receive study vaccinations will be reported along with the date of the study vaccine injection, the vaccination group they were randomized to, as well as the vaccination injection site (left deltoid or right deltoid) in **Listing 1**.

A flowchart showing the disposition of study participants, adapted from the CONSORT Statement, will be included and will present the number of participants screened, lost to follow up, and analyzed by vaccination group (**Figure 1**).

Participants who discontinue or terminate early from the trial will be reported along with the study date of discontinuation, reason for discontinuation, and completion status in **Listing 3**. Missed visits, discontinuations, and withdrawals due to COVID-19 will be reported in **Listing 20**.

All HIV testing for screening and follow-up visits will be tabulated and reported by participant along with the HIV test result in **Listing 9**.

6.3. Pregnancies

All pregnancies and their outcomes will be presented in **Listing 19**.

6.4. Vital Signs

Vital sign metrics that are evaluated include oral temperature, pulse, respirations, systolic blood pressure, and diastolic blood pressure. A listing of participants who experienced abnormal vital sign results at any point after study dose administration will be presented in **Listing 18**. The number and percentage of participants who experienced a mild, moderate, or severe vital sign result for each time point (including baseline and maximum severity post-baseline) will be presented overall by maximum severity across all vital signs by vaccination group in **Table 10.** Grades for oral temperature, pulse, respirations, systolic blood pressure, and diastolic blood pressure will be presented in **Table 11, Table 12, Table 13, Table 14**, and **Table 15,** respectively.

6.5. Prior and Concurrent Medical Conditions

Any medical condition that is present at the time that the participant is screened is considered as baseline and not reported as an AE. However, if the severity of any pre-existing medical condition increases post-vaccination, according to the DAIDS adverse event severity grading criteria found in **Table 6**, it is then recorded as an AE. Prior and concurrent medical conditions meeting exclusion criteria, collected as part of medical history assessments, will be reported by participant in **Listing 6**. Summaries of participants with prior or concurrent medical conditions will be presented by MedDRA SOC and by vaccination group in **Table 16**.

6.6. Prior and Concomitant Medications

At each vaccination visit, participants are asked to record concomitant medications (along with temperature, local and systemic symptoms) for 7 days post-vaccination, beginning with the day of vaccination on a diary card. Any prior and concomitant medications used by participants, including the status of if the medication is ongoing, will be presented in **Listing 7**.

6.7. Measurements of Study Product Compliance

All participants who were randomized but did not receive a vaccination, received the wrong study vaccination, or missed a vaccination will be presented in **Listing 4**, along with information about each participant's assigned vaccination group, the date of the last completed study visit, and the reason why the study vaccine was not administered. Participant receipt of each study vaccination will be summarized by time point and by vaccination group in **Table 6**.

6.8. Protocol Deviations

The distribution of protocol deviations (quantified by the number of participants and the number of deviations reported) will be summarized by deviation category, deviation type, and vaccination group in **Table 17**. Detailed information on protocol deviations will be presented by vaccination group and deviation category in **Listing 5**.

6.9. Inclusions and Exclusions from Analysis Populations

A tabular summary of participants excluded from analysis populations will be provided in **Table 18**, and all participants included and excluded from the analysis populations will be described in **Listing 8**.

7. SAFETY EVALUATION

All summaries and analysis of safety data will be presented for the safety population. Safety summaries will be presented by vaccination group or priming dose group, depending on the context of the analysis. Post-priming doses, post-any doses, and individual dose periods will be utilized, as appropriate. The denominator for the percentages is based on the number of non-missing observations for an assessment or based on the number of participants in a group and will be described for each exhibit. While the study was not designed with the purpose of detecting safety differences, comparisons between regimens or between groups of interest may be made based on the level of overlap of 95% confidence intervals, as described in Section 5.7.

7.1. Primary Safety Analysis

An overall summary of the incidence of adverse events, including exact 95% CIs for the probability of each event of interest, will be displayed by event type and priming dose or vaccination group in **Table 19**.

Solicited and unsolicited adverse events will be explored further in follow-up tables and figures, as described in subsequent subsections.

7.1.1. Solicited Reactogenicity Events

The number and percentage of participants that experience solicited systemic and local reactogenicity events will be presented by priming dose group along with associated exact 95% confidence intervals, post-any priming dose in **Table 20** and post-each priming dose in **Table 21**, **Table 22**, and **Table 23**. Similar tables will be presented by vaccination group for the reactogenicity periods after boost doses in **Table 24**, **Table 25**, **Table 26**, and **Table 27**. An exploratory analysis will present overall incidence of solicited AEs in **Table 28** for male participants and **Table 29** for female participants.

The maximum severity reported per participant of solicited AEs will be presented graphically in **Figure 2-17**, across any priming dose, or any dose, separately for each dose, and separately for local and systemic reactogenicity.

7.1.2. Unsolicited Adverse Events

Adverse events that exceed a frequency of 5% within any vaccination group during the study will be grouped by MedDRA system organ class and preferred term and displayed by the incidence and frequency of each event in **Table 30**.

The incidence (i.e., number and percentage of participants reporting an event) of unsolicited AEs, including SAEs, PIMMCs, and MAAEs if there are sufficient numbers to warrant summarization, will be tabulated by MedDRA SOC and PT, as well as maximum severity and relationship to study vaccination (separately). This summary will be presented by priming dose group, for AEs occurring during the post-priming doses period in **Table 31**, with the frequencies of each event occurring over the same period summarized by relationship to study vaccination in **Table 32**. The incidence and frequency of related unsolicited AEs over the pre-boost period will be presented graphically in **Figure 20** and **Figure 18**, respectively.

The incidence of unsolicited AEs reported at any point after the initial boost dose (Dose 4) is presented by vaccination group in **Table 33**, and the incidence over the entire study is presented by vaccination group in **Table 34**. The frequencies of unsolicited AEs occurring after administration of Dose 4 are presented in **Table 35** (all AEs, regardless of relationship), with related unsolicited AEs presented in **Table 36**. The incidence and frequency of related unsolicited AEs over the post-boost period will be presented graphically in **Figure 21** and **Figure 19**, respectively

Listings of SAEs, PIMMCs, and MAAEs will be presented separately in **Listing 10, Listing 11,** and **Listing 12,** respectively. Any unanticipated adverse events that occur during the study will be reported by participant in **Listing 13**.

7.1.3. Clinical Laboratory Data

Clinical laboratory values will be summarized by parameter, maximum severity, visit, and analysis group as in **Table 37**. Analysis group is defined as the priming dose groups for any visit prior to Dose 4 and as the individual vaccination group post-Dose 4. The severity grades will be assessed according to the DAIDS Table for Grading the Severity of Adult and Pediatric Adverse Events (**Table 6**), Version 2.1 dated July 2017 and, if clinically significant, summarized separately as AEs (see above).

Laboratory results per participant will be detailed for hematology, chemistry, urinalysis, and serology parameters in **Listing 14**, **Listing 15**, **Listing 16**, and **Listing 17** respectively.

8. IMMUNOLOGICAL EVALUATION

As described in **Section 4.7**, assays will be reported with several possible output measures. Titers measured via serial dilution will be summarized via geometric means; antibody or other analyte concentrations will be summarized via arithmetic means; cell phenotype percentages will be summarized via arithmetic means. Values reported for assay outcomes will be grouped by study arm (see **Table 1**) or by grouped priming dose regimen (i.e., vaccination groups 1 and 2, 3 and 4, and 5 and 6, as outlined in **Section 5.1**), depending on the time point.

Hypothesis testing will be performed for the total (via AUC) and peak responses, with different comparisons specific to those summary measures after the priming dose and after the boost dose, as presented in **Table 5** below. Stepdown procedures may be utilized to limit the number of unnecessary tests, for example, only comparing pairs of groups if the related collapsed comparisons show evidence of differences.

Table 5: Hypothesis Testing Strategy for Immunogenicity Objectives

Secondary Immunogenicity Objective	Relevant Group Comparisons	Scientific Questions Addressed	Time Points (Pre- or Post-boost)
1. To determine whether the adjuvants under study improve the immunogenicity of Env-C Plasmid DNA priming	a. 3+4 vs. 1+2	Impact of dmLT	Pre-boost
	b. 5+6 vs. 1+2	Impact of ALF43	
	c. 3+4 vs. 5+6	Impact of dmLT vs. ALF43	
	d. 3 vs. 1, 4 vs. 2	Impact of dmLT (as part of priming doses, both receive the same boost doses)	Post-boost
	e. 5 vs. 1, 6 vs. 2	Impact of ALF43 (as part of priming doses, both receive the same boost doses)	
	f. 3 vs. 5, 4 vs. 6	Impact of dmLT vs. ALF43 (as part of priming doses, both receive the same boost doses)	
2. To determine whether the addition of ALF43 to the Rehydragel® –HIV Env gp145 C.6980 protein boost further improves the immune response to HIV Env gp145 C.6980 protein	a. 2+4+6 vs. 1+3+5	Impact of ALF43 on gp145 protein boost	Post-boost. Only conducted if 1.a. and 1.b. non-significant
	b. 2 vs. 1, 4 vs. 3, 6 vs. 5		Post-boost
3. To determine whether adjuvants improve humoral responses across vaccine regimens 4. To evaluate the influence of various adjuvants on cellular immune responses 5. To describe mucosal humoral responses across vaccination regimens in cervicovaginal and rectal secretions and semen	Pairwise comparisons (including Group 7)	Impact of gp145 C.6980 as part of priming regimen and Env-C Plasmid DNA as part of boost	Pre-boost: only conducted for Group 7 vs. Groups 5+6, for impact of gp145 C.6980 Post-boost: only conducted for Group 7 vs. Group 6 (other comparisons completed as described above)

P-values generated from hypothesis testing will be categorized as strong, moderate, or weak evidence based on thresholds of 0.001, 0.01, and 0.05 respectively. Comparisons that show no evidence of group differences will be filtered out and not analyzed in follow-up tables or figures. Changes to the methodological approach may be considered based on input from the research laboratories, as appropriate, and these changes would be described and justified in the analysis report(s).

8.1. Secondary Immunogenicity Analysis

Immunogenicity endpoints will be analyzed in the IMM population, with sensitivity analyses conducted in the PP population. Those will be conducted for peak and total immune responses, for qualitative comparison with results in IMM. Additional sensitivity analysis may be conducted on a post hoc basis, if it appears likely that missed or out of window study vaccinations, out of window visits, intercurrent events, or other deviations from the protocol are substantially confounding estimates and inference. These would be done in targeted fashion and, as with the planned analysis, multiplicity will be considered in interpretation.

For antibody assays, geometric mean titers (GMTs) or mean responses (as appropriate for each assay measure) and the associated 95% confidence intervals will be presented along with minimum, median, and maximum values, at baseline, individual time points, and peak responses. This will be done separately for the pre-boost period by priming dose group, as displayed in **Table 38**, and for all time points by vaccination group, as displayed in **Table 42**. The timing of peak responses will be summarized by priming dose group over the pre-boost period as in **Table 39** and by vaccination group over the entire study as in **Table 43**. Furthermore, the total immune response over the pre-boost period will be summarized by priming dose group as in **Table 40**, and the total response over the entire study will be summarized as in **Table 44**. Statistical comparisons of total and peak responses, specific to the study period as described in Section 8 above, will be presented by priming dose group for pre-boost comparisons in **Table 41** and by vaccination group for post-boost comparisons in **Table 45**.

Cellular endpoints will be summarized similarly to antibody results, with appropriate adjustments to the statistics presented, by priming dose group as in **Table 46** and **Table 47**, for CD4+ T cells and CD8+ T cells, respectively. They will also be summarized across all time points by vaccination groups, as in **Table 48** and **Table 49**. If the number of cell subsets assessed is comparable to the antigens tested for antibody assays, targeted hypothesis testing may be conducted as described above.

Figures will be generated for assay/antigen combinations (and potentially T or B cell subsets) with statistical comparisons meeting the $p<0.05$ threshold for "weak evidence" of a difference between groups. These would include presentations of central tendency, as in **Figure 22**, with corresponding 95% CIs, as well as representations of the entire distribution of responses within each vaccination group, via boxplots as in **Figure 23**. Scatterplots and associated Spearman correlation estimates may be generated for peak responses from multiple assay targets or assays, on a post hoc basis depending on other results (**Figure 24**).

8.2. Exploratory Immunogenicity Analysis

Exploratory immunogenicity analyses will be primarily descriptive in nature but would follow a similar approach as described for secondary immunogenicity endpoints in Section 8.1.

A listing of participants who consented to optional specimen collection will be presented in **Listing 21**.

8.3. Sub-Objective Analyses

Analyses of lymph node biopsies will be performed on the subset of participants in the IMM population who elect to undergo lymph node biopsies. Analyses will be primarily descriptive with summaries provided by visit and vaccination group as described above. If the sample size of the sub-analyses population is adequate, hypothesis testing may be performed as outlined in Section 8.

9. 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 one decimal place beyond the analysis data. The minimum and maximum use the same number of decimal places as the analysis data. Proportions will be presented as two decimal places; values greater than zero but less than 0.01 will be presented as "<0.01". Percentages for safety endpoints will be reported to the nearest whole number; values greater than zero but less than 1% will be presented as "<1"; values greater than 99% but less than 100% will be reported as ">99%"; for cell phenotyping endpoints, significant digits will be determined based on the observed precision of the measurements. Estimated parameters, not on the same scale as raw observations (e.g., regression coefficients) will be reported to 3 significant figures.

10. TECHNICAL DETAILS

SAS version 9.4 or above and R version 3.6 or above will be used to generate all tables, figures, and listings. Other software may be used for processing of assays, and further details will be presented in the final report if they are available.

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

The protocol stated that Wald confidence intervals would be computed for continuous immunogenicity endpoints, but to avoid making distributional assumptions and to consistently assess immunological targets with varying observed distributions, bootstrapping is planned instead. Since the study is exploratory in nature and was not powered to detect any pre-specified group differences based on assumptions about utilizing a specific statistical methodology, discretion will be applied to allow for appropriate methods to be applied based on the details of the varied immunological assay outputs.

The protocol also stated that no multiplicity adjustments were planned, but the number of comparisons and antigens will be considered when determining whether p-value adjustment would be helpful for interpretation.

12. REFERENCES

1. Holm, S. (1979). A simple sequentially rejective multiple test procedure. *Scandinavian Journal of Statistics*, **6**, 65–70. http://www.jstor.org/stable/4615733

13. TABLES, FIGURES, AND LISTINGS

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

APPENDICES

APPENDIX 1. TABLE SHELLS

LIST OF TABLES

List of Tables (*continued*)

List of Tables (*continued*)

REFERENCE TABLES

Table 6: DAIDS Table for Grading the Severity of Adverse Events

See https://rsc.niaid.nih.gov/sites/default/files/daidsgradingcorrectedv21.pdf for the DAIDS Table for Grading the Severity of Adult and Pediatric Adverse Events (DAIDS AE Grading Table), Version 2.1 dated July 2017.

DISPOSITION SUMMARY

Table 7: Participant Disposition by Vaccination Group

Participant Disposition	Group 1: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)		Group 2: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)		Group 3: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)		Group 4: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)		Group 5: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)		Group 6: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)		Group 7: Env-C Plasmid DNA / HIV Env gp145 C.6980 protein/ ALF43 + Env-C Plasmid DNA / HIV Env gp145 C.6980 protein / ALF43 / Rehydragel® (N=X)		Pooled Placebo (N=X)		All Participants (N=X)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Screened	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Enrolled/ Randomized	x	100	x	100	x	100	x	100	x	100	x	100	x	100	x	100	x	100
Received Study Vaccination (Visit 1, Day 0)	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Completed Visit 2 (Day 3 ± 1)	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Completed Visit 3 (Day 7 ± 2)	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Completed Visit 4 (Day 14 ± 3)	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Received Study Vaccination (Visit 5, Day 28 ± 7)	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Completed Visit 6 (Day 35 ± 2)	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Completed Visit 7 (Day 42 ± 3)	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Received Study Vaccination (Visit 8, Day 84 ± 7)	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Completed Visit 9 (Day 87 ± 1)	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Completed Visit 10 (Day 91 ± 2)	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Completed Visit 11 (Day 98 ± 3)	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Received Study Vaccination (Visit 12, Day 140 ± 7)	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Completed Visit 13 (Day 143 ± 1)	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx

Table 7: Participant Disposition by Vaccination Group (*continued*)

Participant Disposition	Group 1: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)		Group 2: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)		Group 3: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)		Group 4: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)		Group 5: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)		Group 6: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)		Group 7: Env-C Plasmid DNA / HIV Env gp145 C.6980 protein/ ALF43 + Env-C Plasmid DNA / HIV Env gp145 C.6980 protein / ALF43 / Rehydragel® (N=X)		Pooled Placebo (N=X)		All Participants (N=X)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Completed Visit 14 (Day 147 ± 2)	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Completed Visit 15 (Day 154 ± 3)	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Received Study Vaccination (Visit 16, Day 224 ± 7)	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Completed Visit 17 (Day 231 ± 2)	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Completed Visit 18 (Day 238 ± 3)	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Received Study Vaccination (Visit 19, Day 392 ± 7)	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Completed Visit 20 (Day 395 ± 1)	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Completed Visit 21 (Day 399 ± 2)	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Completed Visit 22 (Day 406 ± 3)	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Completed Visit 23 (Day 476 ± 14)	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Completed Visit 24 (Day 560 ± 14)	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Completed Visit 25 (Day 728 ± 14)	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Completed Follow-up (Visit 26, Day 725 ± 14)	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Received All Study Vaccinations	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Completed All Scheduled Blood Draws	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Note: N = Number of randomized participants																		

Table 8: Summary of Categorical Demographic and Baseline Characteristics by Vaccination Group

Variable	Statistic	Group 1: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)		Group 2: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)		Group 3: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)		Group 4: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)		Group 5: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)		Group 6: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)		Group 7: Env-C Plasmid DNA / HIV Env gp145 C.6980 protein/ ALF43 + Env-C Plasmid DNA / HIV Env gp145 C.6980 protein / ALF43 / Rehydragel® (N=X)		Pooled Placebo (N=X)		All Participants (N=X)	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Age	18-25	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	26-30	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	31-35	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	35-40	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Sex	Male	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Female	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Race	White	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Black or African American	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Asian	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	American Indian/ Alaskan Native	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Multi-racial	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Native Hawaiian or other Pacific Islander	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Other	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Ethnicity	Non-Hispanic/ Latino	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Hispanic/Latino	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Tribe	Kalenjin	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Kisii	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Luya	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Luo	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Kikuyu	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Refuse to Answer	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Other	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx

Table 8: Summary of Categorical Demographic and Baseline Characteristics by Vaccination Group (*continued*)

Variable	Statistic	Group 1: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)		Group 2: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)		Group 3: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)		Group 4: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)		Group 5: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)		Group 6: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)		Group 7: Env-C Plasmid DNA / HIV Env gp145 C.6980 protein/ ALF43 + Env-C Plasmid DNA / HIV Env gp145 C.6980 protein / ALF43 / Rehydragel® (N=X)		Pooled Placebo (N=X)		All Participants (N=X)	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Marital Status	Single, never married	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Married or living as a couple	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Divorced / Separated	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Widowed	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Married but living apart	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
Level of Education	No formal education	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Primary school not completed	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Primary school completed	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Secondary school not completed	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Secondary school completed	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	College/university	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Advanced degree	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx

Table 8: Summary of Categorical Demographic and Baseline Characteristics by Vaccination Group (*continued*)

Variable	Statistic	Group 1: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)		Group 2: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)		Group 3: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)		Group 4: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)		Group 5: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)		Group 6: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)		Group 7: Env-C Plasmid DNA / HIV Env gp145 C.6980 protein/ ALF43 + Env-C Plasmid DNA / HIV Env gp145 C.6980 protein / ALF43 / Rehydragel® (N=X)		Pooled Placebo (N=X)		All Participants (N=X)	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Occupation	Student	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Housewife	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Personal or domestic services	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Unskilled laborer	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Farmer	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Entertainment / Services / Hospitality	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Skilled Trade	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Professional / managerial	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Commerce / business	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Sex worker	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Fisher / Fish trader	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Truck driver	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Military officer	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Military enlisted	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx
	Other	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx	x	xx

Note: N = Number of randomized participants

Table 9: Summary of Continuous Demographic and Baseline Characteristics by Vaccination Group

Variable	Characteristic	Group 1: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)	Group 2: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)	Group 3: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)	Group 4: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)	Group 5: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)	Group 6: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)	Group 7: Env-C Plasmid DNA / HIV Env gp145 C.6980 protein/ ALF43 + Env-C Plasmid DNA / HIV Env gp145 C.6980 protein / ALF43 / Rehydragel® (N=X)	Pooled Placebo (N=X)	All Participants (N=X)
Age (years)	Mean	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Standard Deviation	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Minimum	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Median	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Maximum	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
BMI (kg/cm^2)	Mean	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Standard Deviation	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Minimum	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Median	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
	Maximum	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx
Note: N = Number of randomized participants										

Table 10: Vital Signs by Vaccination Group, Time Point, and Severity – Any Assessment

Vaccination Group	Time Point	N	None		Mild		Moderate		Severe		Missing	
			n	%	n	%	n	%	n	%	n	%
Group 1: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/Rehydragel® (N=X)	Baseline	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Visit 1	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Visit 2	x	x	xx	x	xx	x	xx	x	xx	x	xx
	[Other Visits]	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Max Severity Post Baseline	x	x	xx	x	xx	x	xx	x	xx	x	xx
Group 2: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/Rehydragel® /ALF43 (N=X)	Baseline	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Visit 1	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Visit 2	x	x	xx	x	xx	x	xx	x	xx	x	xx
	[Other Visits]	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Max Severity Post Baseline	x	x	xx	x	xx	x	xx	x	xx	x	xx
Group 3: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/Rehydragel® (N=X)	Baseline	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Visit 1	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Visit 2	x	x	xx	x	xx	x	xx	x	xx	x	xx
	[Other Visits]	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Max Severity Post Baseline	x	x	xx	x	xx	x	xx	x	xx	x	xx
Group 4: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/Rehydragel® /ALF43 (N=X)	Baseline	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Visit 1	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Visit 2	x	x	xx	x	xx	x	xx	x	xx	x	xx
	[Other Visits]	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Max Severity Post Baseline	x	x	xx	x	xx	x	xx	x	xx	x	xx
Group 5: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/Rehydragel® (N=X)	Baseline	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Visit 1	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Visit 2	x	x	xx	x	xx	x	xx	x	xx	x	xx
	[Other Visits]	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Max Severity Post Baseline	x	x	xx	x	xx	x	xx	x	xx	x	xx

Table 10: Vital Signs by Vaccination Group, Time Point, and Severity – Any Assessment (*continued*)

Vaccination Group	Time Point	N	None		Mild		Moderate		Severe		Missing	
			n	%	n	%	n	%	n	%	n	%
Group 6: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/Rehydragel® /ALF43 (N=X)	Baseline	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Visit 1	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Visit 2	x	x	xx	x	xx	x	xx	x	xx	x	xx
	[Other Visits]	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Max Severity Post Baseline	x	x	xx	x	xx	x	xx	x	xx	x	xx
Group 7: Env-C Plasmid DNA / HIV Env gp145 C.6980 protein/ ALF43 + Env-C Plasmid DNA / HIV Env gp145 C.6980 protein / ALF43 / Rehydragel® (N=X)	Baseline	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Visit 1	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Visit 2	x	x	xx	x	xx	x	xx	x	xx	x	xx
	[Other Visits]	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Max Severity Post Baseline	x	x	xx	x	xx	x	xx	x	xx	x	xx
Pooled Placebo (N=X)	Baseline	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Visit 1	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Visit 2	x	x	xx	x	xx	x	xx	x	xx	x	xx
	[Other Visits]	x	x	xx	x	xx	x	xx	x	xx	x	xx
	Max Severity Post Baseline	x	x	xx	x	xx	x	xx	x	xx	x	xx

Note: The "Max Post Baseline" rows indicate the maximum severity experienced by each participant at any time point post baseline, including unscheduled assessments.
N= Number of randomized participants

Tables with similar format:

Table 11: Vital Signs by Vaccination Group, Time Point, and Severity – Oral Temperature

Table 12: Vital Signs by Vaccination Group, Time Point, and Severity – Pulse

Table 13: Vital Signs by Vaccination Group, Time Point, and Severity – Respirations

Table 14: Vital Signs by Vaccination Group, Time Point, and Severity – Systolic Blood Pressure

Table 15: Vital Signs by Vaccination Group, Time Point, and Severity – Diastolic Blood Pressure

Table 16: Summary of Participants with Prior or Concurrent Medical Conditions by MedDRA System Organ Class and Vaccination Group

MedDRA System Organ Class	Group 1: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/Rehydragel® (N=X)		Group 2: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/Rehydragel® /ALF43 (N=X)		Group 3: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/Rehydragel® (N=X)		Group 4: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/Rehydragel® /ALF43 (N=X)		Group 5: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/Rehydragel® (N=X)		Group 6: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/Rehydragel® /ALF43 (N=X)		Group 7: Env-C Plasmid DNA / HIV Env gp145 C.6980 protein/ ALF43 + Env-C Plasmid DNA / HIV Env gp145 C.6980 protein / ALF43 / Rehydragel® (N=X)		Pooled Placebo (N=X)		All Participants (N=X)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Any SOC	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
[SOC 1]	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
[SOC 2]	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

Note: N = Number of randomized participants

n = Number of participants reporting medical history within the specified SOC. A participant is only counted once per SOC

Table 17: Distribution of Protocol Deviations by Category, Type, and Vaccination Group

[Implementation Note: Example categories and deviation types given.]

Category	Deviation Type	Group 1: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)		Group 2: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)		Group 3: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)		Group 4: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)		Group 5: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)		Group 6: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)		Group 7: Env-C Plasmid DNA / HIV Env gp145 C.6980 protein/ ALF43 + Env-C Plasmid DNA / HIV Env gp145 C.6980 protein / ALF43 / Rehydragel® (N=X)		Pooled Placebo (N=X)		All Participants (N=X)	
		# Part.	# Dev.	# Part.	# Dev.	# Part.	# Dev.	# Part.	# Dev.	# Part.	# Dev.	# Part.	# Dev.	# Part.	# Dev.	# Part.	# Dev.	# Part.	# Dev.
Eligibility / enrollment	Any type	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Did not meet inclusion criterion	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Met exclusion criterion	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	ICF not signed prior to study procedures	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Follow-up visit schedule	Any type	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Out of window visit	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Missed visit/visit not conducted	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Protocol procedure / assessment	Any type	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Incorrect version of ICF signed	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Blood not collected	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Urine not collected	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	[Insert other deviation types observed]	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x

Table 17: Distribution of Protocol Deviations by Category, Type, and Vaccination Group (*continued*)

Category	Deviation Type	Group 1: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)		Group 2: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)		Group 3: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)		Group 4: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)		Group 5: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)		Group 6: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)		Group 7: Env-C Plasmid DNA / HIV Env gp145 C.6980 protein/ ALF43 + Env-C Plasmid DNA / HIV Env gp145 C.6980 protein / ALF43 / Rehydragel® (N=X)		Pooled Placebo (N=X)		All Participants (N=X)	
		# Part.	# Dev.	# Part.	# Dev.	# Part.	# Dev.	# Part.	# Dev.	# Part.	# Dev.	# Part.	# Dev.	# Part.	# Dev.	# Part.	# Dev.	# Part.	# Dev.
Vaccine administration	Any type	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Required procedure done incorrectly	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Study product temperature excursion	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Blinding policy / procedure	Any type	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Study assignment unblinded	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
	Other	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x

Notes: N = Number of participants enrolled; Part = Participants; Dev = Deviations.

Table 18: Analysis Population Exclusions

Analysis Population	Reason Participants Excluded	Group 1: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)		Group 2: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)		Group 3: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)		Group 4: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)		Group 5: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)		Group 6: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)		Group 7: Env-C Plasmid DNA / HIV Env gp145 C.6980 protein/ ALF43 + Env-C Plasmid DNA / HIV Env gp145 C.6980 protein / ALF43 / Rehydragel® (N=X)		Pooled Placebo (N=X)		All Participants (N=X)	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Safety population	Did not receive study vaccination																		
Immunogenicity population	Did not receive study vaccination																		
	Did not have at least one post-vaccination sample collected																		
Per Protocol population	Did not receive study vaccination																		
	Did not have at least one post-vaccination sample collected with results available for analysis																		
	[other reasons]																		

Notes: N = Number of participants enrolled; n = Number of participants excluded from each analysis population for the given reason.

SAFETY SUMMARY

Table 19: Overall Summary of Adverse Events by Event Type and Group

Event Type	Group	N	None		Mild / Grade 1		Moderate / Grade 2		Severe / Grade 3		Potentially Life-Threatening / Grade 4		Any Incidence		
			n	%	n	%	n	%	n	%	n	%	n	%	95% CI
At least one local solicited AE	Priming Dose Group 1: Prime of Env-C Plasmid DNA alone	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	xx.x, xx.x
	Group 1: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel®	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	xx.x, xx.x
	Group 2: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	xx.x, xx.x
	Priming Dose Group 2: Prime of Env-C Plasmid DNA/dmLT	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	xx.x, xx.x
	Group 3: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel®	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	xx.x, xx.x
	Group 4: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	xx.x, xx.x
	Priming Dose Group 3: Prime of Env-C Plasmid DNA/ALF43	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	xx.x, xx.x
	Group 5: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel®	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	xx.x, xx.x
	Group 6: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	xx.x, xx.x
	Priming Dose Group 4: Prime of Env-C Plasmid DNA/dmLT/HIV Env gp145 C.6980 protein (Group 7)	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	xx.x, xx.x
	Pooled Placebo	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	xx.x, xx.x
At least one systemic solicited AE	[Analysis Groups]	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	xx.x, xx.x
At least one severe or greater solicited AE		x	N/A	N/A	N/A	N/A	N/A	N/A	x	x.x	x	x.x	x	x.x	xx.x, xx.x
At least one related unsolicited AE	[Analysis Groups]	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	xx.x, xx.x

Table 19: Overall Summary of Adverse Events by Event Type and Group (*continued*)

Event Type	Group	N	None		Mild / Grade 1		Moderate / Grade 2		Severe / Grade 3		Potentially Life-Threatening / Grade 4		Any Incidence		
			n	%	n	%	n	%	n	%	n	%	n	%	95% CI
At least one SAE[a]	[Analysis Groups]	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	xx.x, xx.x
At least one Grade 3+ unsolicited AE	[Analysis Groups]	x	N/A	N/A	N/A	N/A	N/A	N/A	x	x.x	x	x.x	x	x.x	xx.x, xx.x
At least one PIMMC	[Analysis Groups]	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	xx.x, xx.x
At least one MAAE	[Analysis Groups]	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x	xx.x, xx.x

Notes: N = Number of participants in the Safety population; n = Number of participants reporting each event type; AE = Adverse Event; SAE = Serious Adverse Event; PIMMC = Potentially Immune Mediated Medical Condition; MAAE = Medically Attended Adverse Event. Participants are counted once for each category regardless of the number of events.

[a] See Listing of Serious Adverse Events

SOLICITED ADVERSE EVENTS

Table 20: Number and Percentage of Participants Experiencing Solicited Reactogenicity Events Post-Any Priming Dose by Event, Maximum Severity, and Priming Dose Group

Event	Severity	Priming Dose Group 1: Prime of Env-C Plasmid DNA alone (N = X)		Priming Dose Group 2: Prime of Env-C Plasmid DNA/dmLT (N = X)		Priming Dose Group 3: Prime of Env-C Plasmid DNA/ALF43 (N = X)		Priming Dose Group 4: Prime of Env-C Plasmid DNA/dmLT/HIV Env gp145 C.6980 protein (N = X)		Pooled Placebo (N=X)		All Participants Receiving Env-C Plasmid DNA (N=X)	
		n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI
Any Solicited Reactogenicity Event	None	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Mild (Grade 1)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Moderate (Grade 2)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Severe (Grade 3)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Potentially Life-Threatening (Grade 4)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Any Incidence	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
Systemic Reactogenicity													
Any Solicited Systemic Reactogenicity Event	None	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Mild (Grade 1)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Moderate (Grade 2)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Severe (Grade 3)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Potentially Life-Threatening (Grade 4)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Any Incidence	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
[Systemic Events]	None	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Mild (Grade 1)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Moderate (Grade 2)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Severe (Grade 3)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Potentially Life-Threatening (Grade 4)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-

Table 20: Number and Percentage of Participants Experiencing Solicited Reactogenicity Events Post-Any Priming Dose by Event, Maximum Severity, and Priming Dose Group (*continued*)

Event	Severity	Priming Dose Group 1: Prime of Env-C Plasmid DNA alone (N = X)		Priming Dose Group 2: Prime of Env-C Plasmid DNA/dmLT (N = X)		Priming Dose Group 3: Prime of Env-C Plasmid DNA/ALF43 (N = X)		Priming Dose Group 4: Prime of Env-C Plasmid DNA/dmLT/HIV Env gp145 C.6980 protein (N = X)		Pooled Placebo (N=X)		All Participants Receiving Env-C Plasmid DNA (N=X)	
		n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI
Local Reactogenicity													
Any Solicited Local Reactogenicity Event	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 (Grade 1)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Moderate (Grade 2)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Severe (Grade 3)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Potentially Life-Threatening (Grade 4)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Any Incidence	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
[Local Events]	None	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Mild (Grade 1)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Moderate (Grade 2)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Severe (Grade 3)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Potentially Life-Threatening (Grade 4)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-

Notes: N = Number of participants in the Safety population; n = Number of participants reporting each symptom; Severity is the maximum severity reported post-any priming vaccination (Doses 1-3) for each participant.

Tables with similar format:

Table 21: Number and Percentage of Participants Experiencing Solicited Reactogenicity Events Post-Dose 1 by Event, Maximum Severity, and Priming Dose Group

Table 22: Number and Percentage of Participants Experiencing Solicited Reactogenicity Events Post-Dose 2 by Event, Maximum Severity, and Priming Dose Group

Table 23: Number and Percentage of Participants Experiencing Solicited Reactogenicity Events Post-Dose 3 by Event, Maximum Severity, and Priming Dose Group

Table 24: Number and Percentage of Participants Experiencing Solicited Reactogenicity Events Post-Any Boost Dose by Event, Maximum Severity, and Vaccination Group

Event	Severity	Group 1: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)		Group 2: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)		Group 3: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)		Group 4: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)		Group 5: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)		Group 6: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)		Group 7: Env-C Plasmid DNA / HIV Env gp145 C.6980 protein/ ALF43 + Env-C Plasmid DNA / HIV Env gp145 C.6980 protein / ALF43 / Rehydragel® (N=X)		Pooled Placebo (N=X)		All Participants Receiving Env-C Plasmid DNA (N=X)	
		n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI
Any Solicited Reactogenicity Event	None	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Mild (Grade 1)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Moderate (Grade 2)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Severe (Grade 3)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Potentially Life-Threatening (Grade 4)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Any Incidence	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	x (xx)	x.x, x.x	x (xx)	x.x, x.x	x (xx)	x.x, x.x
Systemic Reactogenicity																			
Any Solicited Systemic Reactogenicity Event	None	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Mild (Grade 1)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Moderate (Grade 2)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Severe (Grade 3)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Potentially Life-Threatening (Grade 4)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Any Incidence	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	x (xx)	x.x, x.x	x (xx)	x.x, x.x	x (xx)	x.x, x.x
[Systemic Events]	None	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Mild (Grade 1)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Moderate (Grade 2)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Severe (Grade 3)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Potentially Life-Threatening (Grade 4)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-

Table 24: Number and Percentage of Participants Experiencing Solicited Reactogenicity Events Post-Any Boost Dose by Event, Maximum Severity, and Vaccination Group

Event	Severity	Group 1: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)		Group 2: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)		Group 3: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)		Group 4: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)		Group 5: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)		Group 6: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)		Group 7: Env-C Plasmid DNA / HIV Env gp145 C.6980 protein/ ALF43 + Env-C Plasmid DNA / HIV Env gp145 C.6980 protein / ALF43 / Rehydragel® (N=X)		Pooled Placebo (N=X)		All Participants Receiving Env-C Plasmid DNA (N=X)	
		n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI	n (%)	95% CI
Local Reactogenicity																			
Any Solicited Local Reactogenicity Event	None	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Mild (Grade 1)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Moderate (Grade 2)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Severe (Grade 3)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Potentially Life-Threatening (Grade 4)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Any Incidence	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	x (xx)	x.x, x.x	x (xx)	x.x, x.x	x (xx)	x.x, x.x
[Local Events]	None	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Mild (Grade 1)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Moderate (Grade 2)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Severe (Grade 3)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-
	Potentially Life-Threatening (Grade 4)	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-	x (xx)	-

Notes: N = Number of participants in the Safety population; n = Number of participants reporting each event; Severity is the maximum severity reported post-any boost vaccination (Doses 4-6) for each participant.

Tables with similar format:

Table 25: Number and Percentage of Participants Experiencing Solicited Reactogenicity Events Post-Dose 4 by Event, Maximum Severity, and Vaccination Group

Table 26: Number and Percentage of Participants Experiencing Solicited Reactogenicity Events Post-Dose 5 by Event, Maximum Severity, and Vaccination Group

Table 27: Number and Percentage of Participants Experiencing Solicited Reactogenicity Events Post-Dose 6 by Event, Maximum Severity, and Vaccination Group

Table 28: Number and Percentage of Male Participants Experiencing Solicited Reactogenicity Events Post-Any Dose, by Event and Vaccination Group

Event	Group 1: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)		Group 2: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)		Group 3: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)		Group 4: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)		Group 5: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)		Group 6: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)		Group 7: Env-C Plasmid DNA / HIV Env gp145 C.6980 protein/ ALF43 + Env-C Plasmid DNA / HIV Env gp145 C.6980 protein / ALF43 / Rehydragel® (N=X)		Pooled Placebo (N=X)		All Male Participants (N=X)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Any Solicited Reactogenicity Event	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
Any Solicited Systemic Reactogenicity Event	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
[Systemic Event 1]	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
[Systemic Event 2]	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
Any Solicited Local Reactogenicity Event	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
[Local Event 1]	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx
[Local Event 2]	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx	xx

Notes: N = Number of male participants in the Safety Population; n = Number of participants reporting each symptom

Table with similar format:

Table 29: Number and Percentage of Female Participants Experiencing Solicited Reactogenicity Events Post-Any Dose, by Event and Vaccination Group

UNSOLICITED ADVERSE EVENTS

Table 30: Unsolicited Adverse Events Occurring in 5% of Participants in Any Analysis Group by MedDRA System Organ Class and Preferred Term, and Vaccination Group

MedDRA System Organ Class	MedDRA Preferred Term	Group 1: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)		Group 2: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)		Group 3: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)		Group 4: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)		Group 5: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)		Group 6: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)		Group 7: Env-C Plasmid DNA / HIV Env gp145 C.6980 protein/ ALF43 + Env-C Plasmid DNA / HIV Env gp145 C.6980 protein / ALF43 / Rehydragel® (N=X)		Pooled Placebo (N=X)		All Participants Receiving Env-C Plasmid DNA (N=X)	
		n (%)	Events	n (%)	Events	n (%)	Events	n (%)	Events	n (%)	Events	n (%)	Events	n (%)	Events	n (%)	Events	n (%)	Events
All	All	x (xx)	x	x (xx)	x	x (xx)	x	x (xx)	x	x (xx)	x	x (xx)	x	x (xx)	x	x (xx)	x	x (xx)	x
SOC1	PT1	x (xx)	x	x (xx)	x	x (xx)	x	x (xx)	x	x (xx)	x	x (xx)	x	x (xx)	x	x (xx)	x	x (xx)	x
Etc.	Etc.	x (xx)	x	x (xx)	x	x (xx)	x	x (xx)	x	x (xx)	x	x (xx)	x	x (xx)	x	x (xx)	x	x (xx)	x

Notes: N = Number of participants in the Safety Population; n = Number of participants reporting event; Events = Total frequency of events reported.

Table 31: Number and Percentage of Participants Experiencing Unsolicited Adverse Events Prior to Boost Doses, by MedDRA® System Organ Class and Preferred Term, Maximum Severity, Relationship, and Priming Dose Group

MedDRA® System Organ Class	MedDRA® Preferred Term	Any Incidence			Severity[a]								Relationship to Vaccination[b]			
					Mild		Moderate		Severe		Potentially Life-Threatening		Not Related		Related	
		n	%	95% CI	n	%	n	%	n	%	n	%	n	%	n	%
Priming Dose Group 1: Prime of Env-C Plasmid DNA alone (N = X)																
Any SOC	Any PT	x	x.x	xx.x, xx.x	x	x.x	x	xx	x	x.x	x	x.x	x	x.x	x	xx
[SOC 1]	Any PT	x	x.x	xx.x, xx.x	x	x.x	x	xx	x	x.x	x	x.x	x	x.x	x	xx
	[PT 1]	x	x.x	xx.x, xx.x	x	x.x	x	xx	x	x.x	x	x.x	x	x.x	x	xx
	[PT 2]	x	x.x	xx.x, xx.x	x	x.x	x	xx	x	x.x	x	x.x	x	x.x	x	xx
[SOC 2]	Any PT	x	x.x	xx.x, xx.x	x	x.x	x	xx	x	x.x	x	x.x	x	x.x	x	xx
	[PT 1]	x	x.x	xx.x, xx.x	x	x.x	x	xx	x	x.x	x	x.x	x	x.x	x	xx
	[PT 2]	x	x.x	xx.x, xx.x	x	x.x	x	xx	x	x.x	x	x.x	x	x.x	x	xx
Priming Dose Group 2: Prime of Env-C Plasmid DNA/dmLT (N = X)																
[Repeat for all Priming Dose Groups]																

Notes: N = Number of participants in the Safety population; n = Number of participants reporting each SOC/PT.

[a] For severity, a participant is counted once per preferred term and is summarized according to the highest reported severity.

[b] For relationship, a participant is only counted once per preferred term and is summarized according to the closest reported relationship.

Severity and relationship are counted independently, prior to administration of any boost vaccinations (Dose 4).

[Implementation note: If there are sufficient counts of SAEs, PIMMCs, or MAAEs, sections will be included for each of those, separately from non-serious unsolicited AEs.]

Table 32: Frequency of Unsolicited Adverse Events Reported Prior to Boost Doses by MedDRA System Organ Class and Preferred Term, Relatedness, and Priming Dose Group

MedDRA® System Organ Class	MedDRA® Preferred Term	Priming Dose Group 1: Prime of Env-C Plasmid DNA alone (N = X)		Priming Dose Group 2: Prime of Env-C Plasmid DNA/dmLT (N = X)		Priming Dose Group 3: Prime of Env-C Plasmid DNA/ALF43 (N = X)		Priming Dose Group 4: Prime of Env-C Plasmid DNA/dmLT/HIV Env gp145 C.6980 protein (N = X)		Pooled Placebo (N=X)		All Participants Receiving Env-C Plasmid DNA (N=X)	
		Related	Not Related	Related	Not Related	Related	Not Related	Related	Not Related	Related	Not Related	Related	Not Related
All Unsolicited Adverse Events - AEs													
Any SOC	Any PT	x	x	x	x	x	x	x	x	x	x	x	x
[SOC 1]	Any PT	x	x	x	x	x	x	x	x	x	x	x	x
	[PT 1]	x	x	x	x	x	x	x	x	x	x	x	x
	[PT 2]	x	x	x	x	x	x	x	x	x	x	x	x
[SOC 2]	Any PT	x	x	x	x	x	x	x	x	x	x	x	x
	[PT 1]	x	x	x	x	x	x	x	x	x	x	x	x
	[PT 2]	x	x	x	x	x	x	x	x	x	x	x	x
Unsolicited Serious Adverse Events - SAEs													
Any SOC	Any PT	x	x	x	x	x	x	x	x	x	x	x	x
[SOC 1]	Any PT	x	x	x	x	x	x	x	x	x	x	x	x
	[PT 1]	x	x	x	x	x	x	x	x	x	x	x	x
	[PT 2]	x	x	x	x	x	x	x	x	x	x	x	x
[SOC 2]	Any PT	x	x	x	x	x	x	x	x	x	x	x	x
	[PT 1]	x	x	x	x	x	x	x	x	x	x	x	x
	[PT 2]	x	x	x	x	x	x	x	x	x	x	x	x
Unsolicited Adverse Events of Special Interest - PIMMCs													
Any SOC	Any PT	x	x	x	x	x	x	x	x	x	x	x	x
[SOC 1]	Any PT	x	x	x	x	x	x	x	x	x	x	x	x
	[PT 1]	x	x	x	x	x	x	x	x	x	x	x	x
	[PT 2]	x	x	x	x	x	x	x	x	x	x	x	x
[SOC 2]	Any PT	x	x	x	x	x	x	x	x	x	x	x	x
	[PT 1]	x	x	x	x	x	x	x	x	x	x	x	x
	[PT 2]	x	x	x	x	x	x	x	x	x	x	x	x

Table 32: Frequency of Unsolicited Adverse Events Reported Prior to Boost Doses by MedDRA System Organ Class and Preferred Term, Relatedness, and Priming Dose Group (*continued*)

MedDRA® System Organ Class	MedDRA® Preferred Term	Priming Dose Group 1: Prime of Env-C Plasmid DNA alone (N = X)		Priming Dose Group 2: Prime of Env-C Plasmid DNA/dmLT (N = X)		Priming Dose Group 3: Prime of Env-C Plasmid DNA/ALF43 (N = X)		Priming Dose Group 4: Prime of Env-C Plasmid DNA/dmLT/HIV Env gp145 C.6980 protein (N = X)		Pooled Placebo (N=X)		All Participants Receiving Env-C Plasmid DNA (N=X)	
		Related	Not Related	Related	Not Related	Related	Not Related	Related	Not Related	Related	Not Related	Related	Not Related
Unsolicited Adverse Events of Special Interest - MAAEs													
Any SOC	Any PT	x	x	x	x	x	x	x	x	x	x	x	x
[SOC 1]	Any PT	x	x	x	x	x	x	x	x	x	x	x	x
	[PT 1]	x	x	x	x	x	x	x	x	x	x	x	x
	[PT 2]	x	x	x	x	x	x	x	x	x	x	x	x
[SOC 2]	Any PT	x	x	x	x	x	x	x	x	x	x	x	x
	[PT 1]	x	x	x	x	x	x	x	x	x	x	x	x
	[PT 2]	x	x	x	x	x	x	x	x	x	x	x	x
Other Non-Serious Unsolicited Adverse Events													
Any SOC	Any PT	x	x	x	x	x	x	x	x	x	x	x	x
[SOC 1]	Any PT	x	x	x	x	x	x	x	x	x	x	x	x
	[PT 1]	x	x	x	x	x	x	x	x	x	x	x	x
	[PT 2]	x	x	x	x	x	x	x	x	x	x	x	x
[SOC 2]	Any PT	x	x	x	x	x	x	x	x	x	x	x	x
	[PT 1]	x	x	x	x	x	x	x	x	x	x	x	x
	[PT 2]	x	x	x	x	x	x	x	x	x	x	x	x

Notes: N = Number of participants in the Safety population; n = Number of events reported within each SOC/PT. Only events prior to administration of any boost vaccinations (Dose 4) are included.

Table 33: Number and Percentage of Participants Experiencing Unsolicited Adverse Events Post-Boost Doses, by MedDRA® System Organ Class and Preferred Term, Maximum Severity, Relationship, and Vaccination Group

MedDRA® System Organ Class	MedDRA® Preferred Term	Any Incidence			Severity[a]								Relationship to Treatment[b]			
					Mild		Moderate		Severe		Potentially Life-Threatening		Not Related		Related	
		n	%	95% CI	n	%	n	%	n	%	n	%	n	%	n	%
Group 1: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)																
Any SOC	Any PT	x	x.x	xx.x, xx.x	x	x.x	x	xx	x	x.x	x	x.x	x	x.x	x	xx
[SOC 1]	Any PT	x	x.x	xx.x, xx.x	x	x.x	x	xx	x	x.x	x	x.x	x	x.x	x	xx
	[PT 1]	x	x.x	xx.x, xx.x	x	x.x	x	xx	x	x.x	x	x.x	x	x.x	x	xx
	[PT 2]	x	x.x	xx.x, xx.x	x	x.x	x	xx	x	x.x	x	x.x	x	x.x	x	xx
[SOC 2]	Any PT	x	x.x	xx.x, xx.x	x	x.x	x	xx	x	x.x	x	x.x	x	x.x	x	xx
	[PT 1]	x	x.x	xx.x, xx.x	x	x.x	x	xx	x	x.x	x	x.x	x	x.x	x	xx
	[PT 2]	x	x.x	xx.x, xx.x	x	x.x	x	xx	x	x.x	x	x.x	x	x.x	x	xx
Group 2: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)																
[Repeat for all Vaccination Groups]																

Notes: N = Number of participants in the Safety population; n = Number of participants reporting each SOC/PT.

[a] For severity, a participant is counted once per preferred term and is summarized according to the highest reported severity.

[b] For relationship, a participant is only counted once per preferred term and is summarized according to the closest reported relationship.

Severity and relationship are counted independently, after the administration of Dose 4.

Table with similar format:

Table 34: Number and Percentage of Participants Experiencing Unsolicited Adverse Events, by MedDRA® System Organ Class and Preferred Term, Maximum Severity, Relationship, and Vaccination Group

[Implementation note: This table will present the incidence of all unsolicited AEs across all time points. The last footnote from above will be updated to remove the last clause on timing.]

Table 35: Frequency of Unsolicited Adverse Events Reported Post-Boost, by MedDRA System Organ Class and Preferred Term, and Vaccination Group

MedDRA® System Organ Class	MedDRA® Preferred Term	Group 1: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)	Group 2: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)	Group 3: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)	Group 4: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)	Group 5: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)	Group 6: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)	Group 7: Env-C Plasmid DNA / HIV Env gp145 C.6980 protein/ ALF43 + Env-C Plasmid DNA / HIV Env gp145 C.6980 protein / ALF43 / Rehydragel® (N=X)	Pooled Placebo (N=X)	All Participants Receiving Env-C Plasmid DNA (N=X)
		Events	Events	Events	Events	Events	Events	Events	Events	Events
All Unsolicited Adverse Events - AEs										
Any SOC	Any PT	x	x	x	x	x	x	x	x	x
[SOC 1]	Any PT	x	x	x	x	x	x	x	x	x
	[PT 1]	x	x	x	x	x	x	x	x	x
	[PT 2]	x	x	x	x	x	x	x	x	x
[SOC 2]	Any PT	x	x	x	x	x	x	x	x	x
	[PT 1]	x	x	x	x	x	x	x	x	x
	[PT 2]	x	x	x	x	x	x	x	x	x
Unsolicited Serious Adverse Events - SAEs										
Any SOC	Any PT	x	x	x	x	x	x	x	x	x
[SOC 1]	Any PT	x	x	x	x	x	x	x	x	x
	[PT 1]	x	x	x	x	x	x	x	x	x
	[PT 2]	x	x	x	x	x	x	x	x	x
[SOC 2]	Any PT	x	x	x	x	x	x	x	x	x
	[PT 1]	x	x	x	x	x	x	x	x	x
	[PT 2]	x	x	x	x	x	x	x	x	x
Unsolicited Adverse Events of Special Interest - PIMMCs										
Any SOC	Any PT	x	x	x	x	x	x	x	x	x
[SOC 1]	Any PT	x	x	x	x	x	x	x	x	x
	[PT 1]	x	x	x	x	x	x	x	x	x
	[PT 2]	x	x	x	x	x	x	x	x	x
[SOC 2]	Any PT	x	x	x	x	x	x	x	x	x
	[PT 1]	x	x	x	x	x	x	x	x	x
	[PT 2]	x	x	x	x	x	x	x	x	x

Table 35: Frequency of Unsolicited Adverse Events Reported Post-Boost, by MedDRA System Organ Class and Preferred Term, and Vaccination Group (*continued*)

MedDRA® System Organ Class	MedDRA® Preferred Term	Group 1: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)	Group 2: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)	Group 3: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)	Group 4: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)	Group 5: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)	Group 6: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)	Group 7: Env-C Plasmid DNA / HIV Env gp145 C.6980 protein/ ALF43 + Env-C Plasmid DNA / HIV Env gp145 C.6980 protein / ALF43 / Rehydragel® (N=X)	Pooled Placebo (N=X)	All Participants Receiving Env-C Plasmid DNA (N=X)
		Events	Events	Events	Events	Events	Events	Events	Events	Events
Unsolicited Adverse Events of Special Interest - MAAEs										
Any SOC	Any PT	x	x	x	x	x	x	x	x	x
[SOC 1]	Any PT	x	x	x	x	x	x	x	x	x
	[PT 1]	x	x	x	x	x	x	x	x	x
	[PT 2]	x	x	x	x	x	x	x	x	x
[SOC 2]	Any PT	x	x	x	x	x	x	x	x	x
	[PT 1]	x	x	x	x	x	x	x	x	x
	[PT 2]	x	x	x	x	x	x	x	x	x
Other Non-Serious Unsolicited Adverse Events										
Any SOC	Any PT	x	x	x	x	x	x	x	x	x
[SOC 1]	Any PT	x	x	x	x	x	x	x	x	x
	[PT 1]	x	x	x	x	x	x	x	x	x
	[PT 2]	x	x	x	x	x	x	x	x	x
[SOC 2]	Any PT	x	x	x	x	x	x	x	x	x
	[PT 1]	x	x	x	x	x	x	x	x	x
	[PT 2]	x	x	x	x	x	x	x	x	x
Notes: N = Number of participants in the Safety Population; Events = Total frequency of events reported.										

Table with similar format:

Table 36: Frequency of Related Unsolicited Adverse Events Occurring Post-Boost, by MedDRA System Organ Class and Preferred Term, and Vaccination Group

Table 37: Summary of Laboratory Results by Parameter, Maximum Severity, Visit, and Analysis Group – [Parameter]

[Implementation note: Any visit before boosting regimen begins (Dose 4) will analyze priming dose groups. Any visit during or after boosting regimen will analyze vaccination groups]

Visit	Analysis Group	N	None		Mild / Grade 1		Moderate / Grade 2		Severe / Grade 3		Potentially Life-Threatening / Grade 4	
			n	%	n	%	n	%	n	%	n	%
Baseline (Day 0)	Priming Dose Group 1: Prime of Env-C Plasmid DNA alone	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Priming Dose Group 2: Prime of Env-C Plasmid DNA/dmLT	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Priming Dose Group 3: Prime of Env-C Plasmid DNA/ALF43	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Priming Dose Group 4: Prime of Env-C Plasmid DNA/dmLT/HIV Env gp145 C.6980 protein	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Pooled Placebo	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
[Additional visits prior to Dose 4]	Priming Dose Group 1: Prime of Env-C Plasmid DNA alone	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Priming Dose Group 2: Prime of Env-C Plasmid DNA/dmLT	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Priming Dose Group 3: Prime of Env-C Plasmid DNA/ALF43	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Priming Dose Group 4: Prime of Env-C Plasmid DNA/dmLT/HIV Env gp145 C.6980 protein	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Pooled Placebo	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
[Additional visits post-Dose 4]	Group 1: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel®	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Group 2: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Group 3: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel®	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Group 4: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Group 5: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel®	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x

Table 37: Summary of Laboratory Results by Parameter, Maximum Severity, Visit, and Analysis Group (*continued*)

Visit	Analysis Group	N	None		Mild / Grade 1		Moderate / Grade 2		Severe / Grade 3		Potentially Life-Threatening / Grade 4	
			n	%	n	%	n	%	n	%	n	%
	Group 6: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Group 7: Env-C Plasmid DNA / HIV Env gp145 C.6980 protein/ ALF43 + Env-C Plasmid DNA / HIV Env gp145 C.6980 protein / ALF43 / Rehydragel®	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Pooled Placebo	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
Max Severity Post Baseline	Group 1: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel®	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Group 2: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Group 3: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel®	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Group 4: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Group 5: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel®	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Group 6: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Group 7: Env-C Plasmid DNA / HIV Env gp145 C.6980 protein/ ALF43 + Env-C Plasmid DNA / HIV Env gp145 C.6980 protein / ALF43 / Rehydragel®	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x
	Pooled Placebo	x	x	x.x	x	x.x	x	x.x	x	x.x	x	x.x

Notes: N = Number of participants in the Safety Population with available samples; n = Number of participants reporting each severity. The “Max Post Baseline” rows indicate the maximum severity experienced by each participant at any time point post baseline, including unscheduled assessments.

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Table 38: Summary of [Assay/Immune Response] Responses Pre-Boost by Antigen, Time Point, and Priming Dose Group

Antigen	Priming Dose Group	Time Point	n	Minimum	Median	Maximum	[GMT/Mean (95% CI)]
[Antigen 1]	Priming Dose Group 1: Prime of Env-C Plasmid DNA alone (Vaccination Groups 1+2) (N=X)	Baseline (Day 0)	xx	xx	xx	xx	xx.x (xx.x, xx.x)
		[Additional visits, pre-Dose 4]	xx	xx	xx	xx	xx.x (xx.x, xx.x)
		Week 20 (Prior to First Boost)	xx	xx	xx	xx	xx.x (xx.x, xx.x)
		Peak Response, Pre-Boost	xx	xx	xx	xx	xx.x (xx.x, xx.x)
	Priming Dose Group 2: Prime of Env-C Plasmid DNA/dmLT (Vaccination Groups 3+4) (N=X)	Baseline (Day 0)	xx	xx	xx	xx	xx.x (xx.x, xx.x)
		[Additional visits, pre-Dose 4]	xx	xx	xx	xx	xx.x (xx.x, xx.x)
		Week 20 (Prior to First Boost)	xx	xx	xx	xx	xx.x (xx.x, xx.x)
		Peak Response, Pre-Boost	xx	xx	xx	xx	xx.x (xx.x, xx.x)
	[Additional Groups]		xx	xx	xx	xx	xx.x (xx.x, xx.x)
[Additional antigens]							

Notes: N = Number of participants in the Immunogenicity population; n = Number of participants with available results; [GMT = Geometric Mean Titer]. 95% confidence intervals for [GMTs] calculated using [empirical bootstrapping, based on 5000 samples]. Results summarized here are pre-boost, up to and including Week 20 prior to administration of Dose 4.

Table 39: Summary of the Timing of Peak [Assay/Immune Response] Response Pre-Boost, by Antigen and Priming Dose Group

Priming Dose Group	Study Week of Peak Response			Maximum	Mean (SD)
	n	Minimum	Median		
Priming Dose Group 1: Prime of Env-C Plasmid DNA alone (Vaccination Groups 1+2) (N=X)	xx	xx	xx	xx	xx.x (xx.x)
Priming Dose Group 2: Prime of Env-C Plasmid DNA/dmLT (Vaccination Groups 3+4) (N=X)	xx	xx	xx	xx	xx.x (xx.x)
Priming Dose Group 3: Prime of Env-C Plasmid DNA/ALF43 (Vaccination Groups 5+6) (N=X)	xx	xx	xx	xx	xx.x (xx.x)
Priming Dose Group 4: Prime of Env-C Plasmid DNA/dmLT/HIV Env gp145 C.6980 protein (Vaccination Group 7) (N=X)	xx	xx	xx	xx	xx.x (xx.x)
Pooled Placebo (N=X)	xx	xx	xx	xx	xx.x (xx.x)

Notes: N = Number of participants in the Immunogenicity population; n = Number of participants with available results; SD = Standard Deviation. **Time is summarized in weeks**; if the same peak response was reached at multiple time points, the first time point is utilized for this analysis. Results up to and including Week 20 are considered here.

Table 40: Normalized Total [Assay/Immune Response] Responses per Study Day Pre-Boost, by Antigen and Priming Dose Group

Antigen	Priming Dose Group	n	Minimum	Median	Maximum	Mean AUC (95% CI)
[Antigen 1]	Priming Dose Group 1: Prime of Env-C Plasmid DNA alone (Vaccination Groups 1+2) (N=X)	xx	xx	xx	xx	xx.x (xx.x, xx.x)
	Priming Dose Group 2: Prime of Env-C Plasmid DNA/dmLT (Vaccination Groups 3+4) (N=X)	xx	xx	xx	xx	xx.x (xx.x, xx.x)
	Priming Dose Group 3: Prime of Env-C Plasmid DNA/ALF43 (Vaccination Groups 5+6) (N=X)	xx	xx	xx	xx	xx.x (xx.x, xx.x)
	Priming Dose Group 4: Prime of Env-C Plasmid DNA/dmLT/HIV Env gp145 C.6980 protein (Vaccination Group 7) (N=X)	xx	xx	xx	xx	xx.x (xx.x, xx.x)
	Pooled Placebo (N=X)	xx	xx	xx	xx	xx.x (xx.x, xx.x)
[Additional antigens]	[Groups]	xx	xx	xx	xx	xx.x (xx.x, xx.x)

Notes: N = Number of participants in the Immunogenicity population; n = Number of participants with data available for analysis. AUC computed through Week 20 (Visit 12), the last observation prior to boost doses, and is normalized by the number of days between first and last observations per participant, to account for varying time on study. 95% confidence intervals for the mean calculated using [empirical bootstrapping, based on 5000 samples].

Table 41: Statistical Comparisons of Peak Responses and Normalized Total [Assay/Immune Response] Responses Pre-Boost, by Antigen

[Implementation note: False Discovery Rate (FDR) correction may be made via p-value adjustment, depending on the number of assay targets. Otherwise the final column will not be included.]

Antigen	Measure	Comparison	Description	p-value[a]	[Adjusted p value[b]]
[Antigen 1]	Normalized Total Immune Response, Through Week 20 (Pre-boost)	Groups 3+4 vs. Groups 1+2	Impact of dmLT	0.xx	0.xx
		Groups 5+6 vs. Groups 1+2	Impact of ALF43	0.xx	0.xx
		Groups 3+4 vs. Groups 5+6	Impact of dmLT vs. ALF43	0.xx	0.xx
		Group 7 vs. Groups 5+6	Impact of HIV Env gp145 C.6980 protein	0.xx	0.xx
	Peak Response, Through Week 20 (Pre-Boost)	Groups 3+4 vs. Groups 1+2	Impact of dmLT	0.xx	0.xx
		Groups 5+6 vs. Groups 1+2	Impact of ALF43	0.xx	0.xx
		Groups 3+4 vs. Groups 5+6	Impact of dmLT vs. ALF43	0.xx	0.xx
		Group 7 vs. Groups 5+6	Impact of HIV Env gp145 C.6980 protein	0.xx	0.xx

[a]Two-sided Mann-Whitney U test used to compare distributions of responses between analysis groups

[[b]Benjamini-Hochberg procedure used to calculate adjusted p-values, to control the false discovery rate]

Table 42: Summary of [Assay/Immune Response] Responses, by Antigen, Time Point, and Vaccination Group

Antigen	Vaccination Group	Time Point	n	Minimum	Median	Maximum	[GMT/Mean (95% CI)]
[Antigen 1]	Group 1: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)	Baseline (Day 0)	xx	xx	xx	xx	xx.x (xx.x, xx.x)
		[Visits post-priming doses]	xx	xx	xx	xx	xx.x (xx.x, xx.x)
		Week 20 (Prior to First Boost)	xx	xx	xx	xx	xx.x (xx.x, xx.x)
		[Additional visits, post-Dose 4]	xx	xx	xx	xx	xx.x (xx.x, xx.x)
		Peak Response, Post-Week 20 (Post-Boost)	xx	xx	xx	xx	xx.x (xx.x, xx.x)
		Peak Response, Through the End of the Study	xx	xx	xx	xx	xx.x (xx.x, xx.x)
	Group 2: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)	Baseline (Day 0)	xx	xx	xx	xx	xx.x (xx.x, xx.x)
		[Visits post-priming doses]	xx	xx	xx	xx	xx.x (xx.x, xx.x)
		Week 20 (Prior to First Boost)	xx	xx	xx	xx	xx.x (xx.x, xx.x)
		[Additional visits, post-Dose 4]	xx	xx	xx	xx	xx.x (xx.x, xx.x)
		Peak Response, Post-Week 20 (Post-Boost)	xx	xx	xx	xx	xx.x (xx.x, xx.x)
		Peak Response, Through the End of the Study	xx	xx	xx	xx	xx.x (xx.x, xx.x)
	[Additional Groups]		xx	xx	xx	xx	xx.x (xx.x, xx.x)
[Additional antigens]			xx	xx	xx	xx	xx.x (xx.x, xx.x)

Notes: N = Number of participants in the Immunogenicity population; n = Number of participants with available results; [GMT = Geometric Mean Titer]. 95% confidence intervals for [GMTs] calculated using [empirical bootstrapping, based on 5000 samples].

Table 43: Summary of the Timing of Peak [Assay/Immune Response] Response, by Antigen and Vaccination Group

Analysis group	n	Minimum	Median	Maximum	Mean (SD)
Group 1: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel®	xx	xx	xx	xx	xx.x (xx.x)
Group 2: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel®/ALF43	xx	xx	xx	xx	xx.x (xx.x)
Group 3: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel®	xx	xx	xx	xx	xx.x (xx.x)
Group 4: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43	xx	xx	xx	xx	xx.x (xx.x)
Group 5: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel®	xx	xx	xx	xx	xx.x (xx.x)
Group 6: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43	xx	xx	xx	xx	xx.x (xx.x)
Group 7: Env-C Plasmid DNA / HIV Env gp145 C.6980 protein/ ALF43 + Env-C Plasmid DNA / HIV Env gp145 C.6980 protein / ALF43 / Rehydragel®	xx	xx	xx	xx	xx.x (xx.x)
Pooled Placebo	xx	xx	xx	xx	xx.x (xx.x)

Notes: N = Number of participants in the Immunogenicity population; n = Number of participants with available results; SD = Standard Deviation. **Time is summarized in weeks**; if the same peak response was reached at multiple time points, the first time point is utilized for this analysis. Results through the entire study are considered here. 95% confidence intervals for the mean calculated using [empirical bootstrapping, based on 5000 samples].

Table 44: Normalized Total [Assay/Immune Response] Responses per Study Day, by Antigen and Vaccination Group

Antigen	Vaccination Group	n	Minimum	Median	Maximum	Mean AUC (95% CI)
[Antigen 1]	Group 1: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)	xx	xx	xx	xx	xx.x (xx.x, xx.x)
	Group 2: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)	xx	xx	xx	xx	xx.x (xx.x, xx.x)
	Group 3: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)	xx	xx	xx	xx	xx.x (xx.x, xx.x)
	Group 4: Env-C Plasmid DNA + dmLT + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)	xx	xx	xx	xx	xx.x (xx.x, xx.x)
	Group 5: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)	xx	xx	xx	xx	xx.x (xx.x, xx.x)
	Group 6: Env-C Plasmid DNA / ALF43 + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)	xx	xx	xx	xx	xx.x (xx.x, xx.x)
	Group 7: Env-C Plasmid DNA / HIV Env gp145 C.6980 protein/ ALF43 + Env-C Plasmid DNA / HIV Env gp145 C.6980 protein / ALF43 / Rehydragel® (N=X)	xx	xx	xx	xx	xx.x (xx.x, xx.x)
	Pooled Placebo (N=X)	xx	xx	xx	xx	xx.x (xx.x, xx.x)
[Additional antigens]	[Groups]	xx	xx	xx	xx	xx.x (xx.x, xx.x)

Notes: N = Number of participants in the Immunogenicity population; n = Number of participants with data available for analysis; AUC = Area Under the Curve. AUC computed through the end of the study, normalized by the number of days between first and last observations per participant, to account for varying time on study. 95% confidence intervals for the mean calculated using [empirical bootstrapping, based on 5000 samples].

Table 45: Statistical Comparisons of Peak and Normalized Total [Assay/Immune Response] Responses, by Antigen

[Implementation note: False Discovery Rate (FDR) correction may be made via p-value adjustment, depending on the number of assay targets. Otherwise the final column will not be included.]

Antigen	Measure	Comparison	Description	p-value[a]	[Adjusted p-value[b]]
[Antigen 1]	Normalized Total Immune Response, Through the End of the Study	Group 3 vs. Group 1	Impact of dmLT (as part of priming doses, both receive the same boost doses)	0.xx	0.xx
		Group 4 vs. Group 2	-	0.xx	0.xx
		Group 5 vs. Group 1	Impact of ALF43 (as part of priming doses, both receive the same boost doses)	0.xx	0.xx
		Group 6 vs. Group 2	-	0.xx	0.xx
		Group 5 vs. Group 3	Impact of dmLT vs. ALF43 (as part of priming doses, both receive the same boost doses)	0.xx	0.xx
		Group 6 vs. Group 4	-	0.xx	0.xx
		Group 2 vs. Group 1	Impact of ALF43 on gp145 protein boost	0.xx	0.xx
		Group 4 vs. Group 3	-	0.xx	0.xx
		Group 6 vs. Group 5	-	0.xx	0.xx
		Group 7 vs. Group 6	Impact of HIV Env gp145 C.6980 protein as part of priming doses, Env-C Plasmid DNA as part of boost doses	0.xx	0.xx
	Peak Response, Through the End of the Study	Group 3 vs. Group 1	Impact of dmLT (as part of priming doses, both receive the same boost doses)	0.xx	0.xx
		Group 4 vs. Group 2	-	0.xx	0.xx
		Group 5 vs. Group 1	Impact of ALF43 (as part of priming doses, both receive the same boost doses)	0.xx	0.xx
		Group 6 vs. Group 2	-	0.xx	0.xx
		Group 5 vs. Group 3	Impact of dmLT vs. ALF43 (as part of priming doses, both receive the same boost doses)	0.xx	0.xx
		Group 6 vs. Group 4	-	0.xx	0.xx
		Group 7 vs. Group 6	Impact of HIV Env gp145 C.6980 protein as part of priming doses, Env-C Plasmid DNA as part of boost doses	0.xx	0.xx
	Peak Response, Post-Boost	Group 2 vs. Group 1	Impact of ALF43 on gp145 protein boost	0.xx	0.xx
		Group 4 vs. Group 3	-	0.xx	0.xx
		Group 6 vs. Group 5	-	0.xx	0.xx

[a]Two-sided Mann-Whitney U test used to compare distributions of responses between analysis groups
[[b]Benjamini-Hochberg procedure used to calculate adjusted p-values, to control the false discovery rate across antigens]

Table 46: Summary of CD4+ T Cells Pre-Boost, by Cell Population, Time Point, and Priming Dose Group

Cell Population (Child Cell Markers/Parent Cell Markers)	Priming Dose Group	Time Point	n	Minimum (%)	Median (%)	Maximum (%)	Mean Frequency (%) (95% CI)
[e.g., Cell population label (IL-10+CD4+/CD4+)]	Priming Dose Group 1: Prime of Env-C Plasmid DNA alone (Vaccination Groups 1+2) (N=X)	Baseline (Day 0)	xx	xx	xx	xx	xx.x (xx.x, xx.x)
		[Additional visits, pre-Dose 4]	xx	xx	xx	xx	xx.x (xx.x, xx.x)
		Week 20 (Prior to First Boost)	xx	xx	xx	xx	xx.x (xx.x, xx.x)
		Peak Response, Through Week 20 (Pre-Boost)	xx	xx	xx	xx	xx.x (xx.x, xx.x)
	Priming Dose Group 2: Prime of Env-C Plasmid DNA/dmLT (Vaccination Groups 3+4) (N=X)	Baseline (Day 0)	xx	xx	xx	xx	xx.x (xx.x, xx.x)
		[Additional visits, pre-Dose 4]	xx	xx	xx	xx	xx.x (xx.x, xx.x)
		Week 20 (Prior to First Boost)	xx	xx	xx	xx	xx.x (xx.x, xx.x)
		Peak Response, Through Week 20 (Pre-Boost)	xx	xx	xx	xx	xx.x (xx.x, xx.x)
	[Additional Groups]		xx	xx	xx	xx	xx.x (xx.x, xx.x)
[Additional cell subsets]			xx	xx	xx	xx	xx.x (xx.x, xx.x)

Notes: N = Number of participants in the Immunogenicity population; n = Number of participants with data available for analysis. 95% confidence intervals for the mean calculated using [empirical bootstrapping, based on 5000 samples].

Similar Table:

Table 47: Summary of CD8+ T Cells Pre-Boost, by Cell Population, Time Point, and Priming Dose Group

Table 48: Summary of CD4+ T Cells, by Cell Population, Time Point, and Vaccination Group

Cell Population (Child Cell Markers/Parent Cell Markers)	Priming Dose Group	Time Point	n	Minimum (%)	Median (%)	Maximum (%)	Mean Frequency (%) (95% CI)
[e.g., Cell population label (IL-10+CD4+/CD4+)]	Group 1: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® (N=X)	Baseline (Day 0)	xx	xx	xx	xx	xx.x (xx.x, xx.x)
		[Additional visits, pre-Dose 4]	xx	xx	xx	xx	xx.x (xx.x, xx.x)
		Week 20 (Prior to First Boost)	xx	xx	xx	xx	xx.x (xx.x, xx.x)
		[Additional visits, post-Dose 4]	xx	xx	xx	xx	xx.x (xx.x, xx.x)
		Peak Response, Post-Week 20 (Post-Boost)	xx	xx	xx	xx	xx.x (xx.x, xx.x)
		Peak Response, Through the End of the Study	xx	xx	xx	xx	xx.x (xx.x, xx.x)
	Group 2: Env-C Plasmid DNA + HIV Env gp145 C.6980 protein/ Rehydragel® /ALF43 (N=X)	Baseline (Day 0)	xx	xx	xx	xx	xx.x (xx.x, xx.x)
		[Additional visits, pre-Dose 4]	xx	xx	xx	xx	xx.x (xx.x, xx.x)
		Week 20 (Prior to First Boost)	xx	xx	xx	xx	xx.x (xx.x, xx.x)
		[Additional visits, post-Dose 4]	xx	xx	xx	xx	xx.x (xx.x, xx.x)
		Peak Response, Post-Week 20 (Post-Boost)	xx	xx	xx	xx	xx.x (xx.x, xx.x)
		Peak Response, Through the End of the Study	xx	xx	xx	xx	xx.x (xx.x, xx.x)
	[Additional Groups]		xx	xx	xx	xx	xx.x (xx.x, xx.x)
[Additional cell subsets]			xx	xx	xx	xx	xx.x (xx.x, xx.x)

Notes: N = Number of participants in the Immunogenicity population; n = Number of participants with data available for analysis. 95% confidence intervals for the mean calculated using [empirical bootstrapping, based on 5000 samples].

Similar Table:

Table 49: Summary of CD8+ T Cells, by Cell Population, Time Point, and Vaccination Group

APPENDIX 2. FIGURES

LIST OF FIGURES

List of Figures (*continued*)

Figure 1: CONSORT Flow Diagram

[Implementation Note: This is an example figure. Changes made include enrollment of participants into each of the vaccination groups arms, the follow-up schedule with associated participant counts, and number of participants in the analysis population(s).]

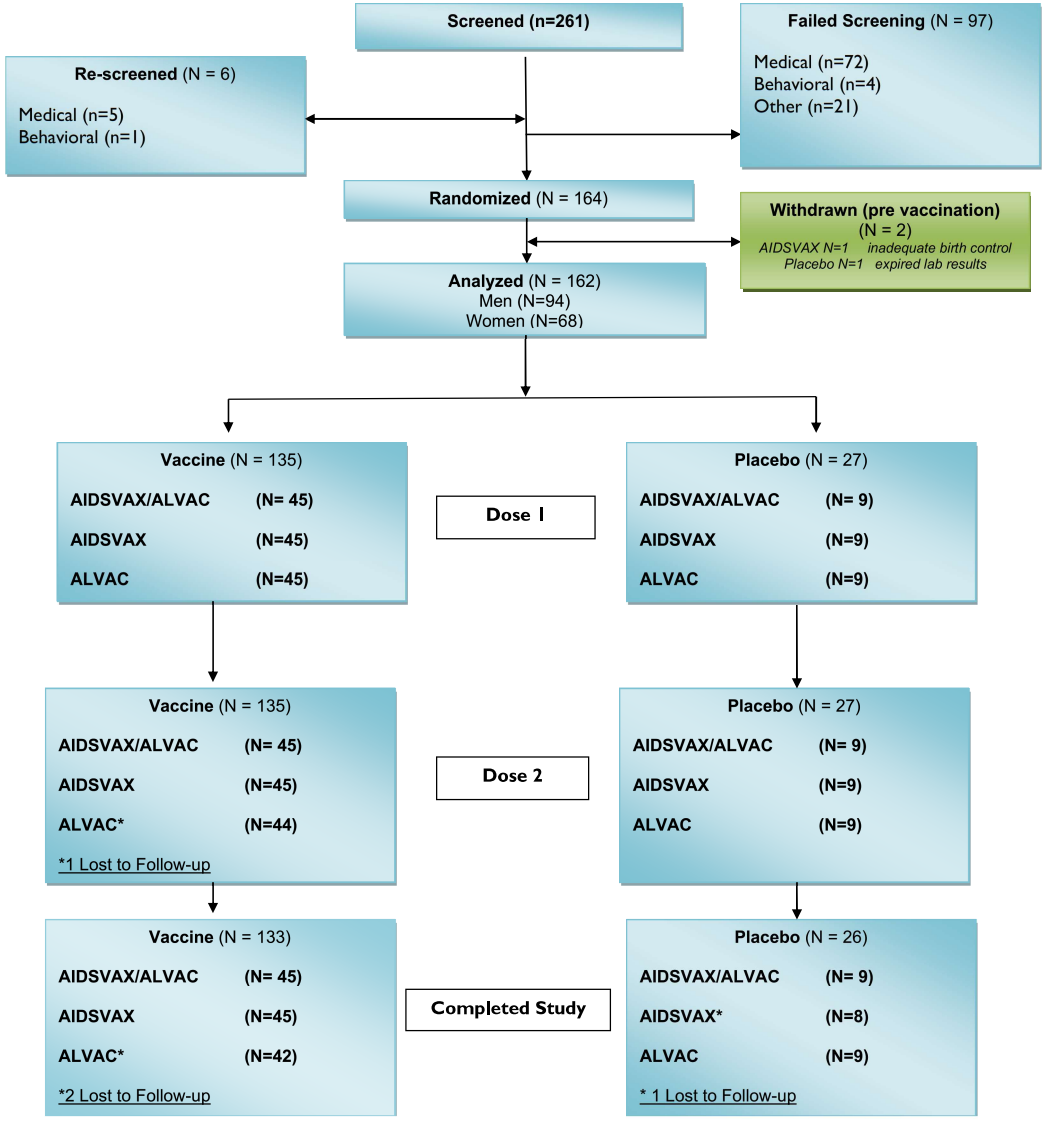
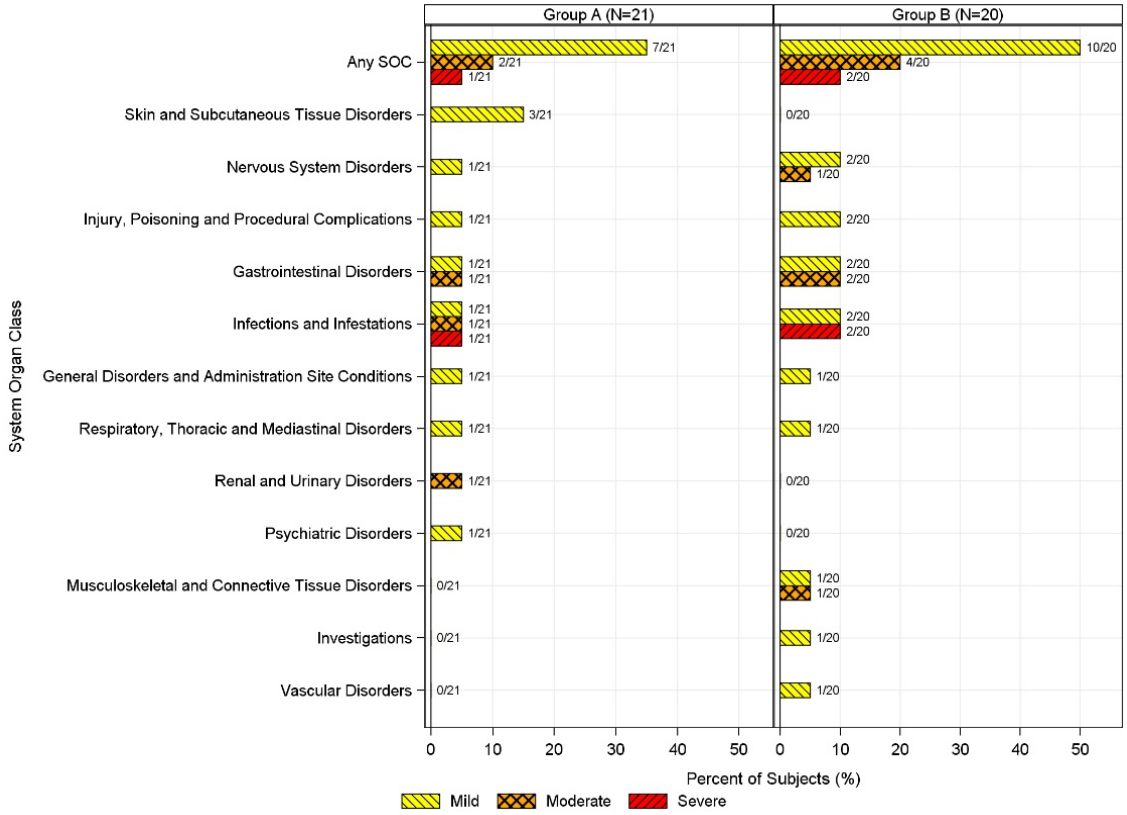


Figure 2: Maximum Severity of Solicited Systemic Reactogenicity Events per Participant Post-Any Priming Dose by Priming Dose Group

[Implementation Note: This is an example figure. Priming dose groups will be in separate panels, each systemic event and "Any Systemic Reactogenicity" will be on the y-axis, and the percent of participants reporting each maximum severity over the reactogenicity period will be on the x-axis.]



Figures with similar format:

Figure 3: Maximum Severity of Solicited Systemic Reactogenicity Events per Participant Post-Dose 1 by Priming Dose Group

Figure 4: Maximum Severity of Solicited Systemic Reactogenicity Events per Participant Post-Dose 2 by Priming Dose Group

Figure 5: Maximum Severity of Solicited Systemic Reactogenicity Events per Participant Post-Dose 3 by Priming Dose Group

Figure 6: Maximum Severity of Solicited Systemic Reactogenicity Events per Participant Post-Any Dose by Vaccination Group

[Implementation Note: Vaccination dose groups will be in separate panels, each systemic event and "Any Systemic Reactogenicity" will be on the y-axis, and the percent of participants reporting each maximum severity over the reactogenicity period will be on the x-axis. Similar for the figures below.]

Figure 7: Maximum Severity of Solicited Systemic Reactogenicity Events per Participant Post-Dose 4 by Vaccination Group

Figure 8: Maximum Severity of Solicited Systemic Reactogenicity Events per Participant Post-Dose 5 by Vaccination Group

Figure 9: Maximum Severity of Solicited Systemic Reactogenicity Events per Participant Post-Dose 6 by Vaccination Group

Figure 10: Maximum Severity of Solicited Local Symptoms per Participant Post-Any Priming Dose by Priming Dose Group

[Implementation Note: Priming dose groups will be in separate panels, each local event and "Any Local Reactogenicity" will be on the y-axis, and the percent of participants reporting each maximum severity over the reactogenicity period will be on the x-axis.]

Figure 11: Maximum Severity of Solicited Local Symptoms per Participant Post-Dose 1 by Priming Dose Group

[Implementation Note: Same as Figure 10.]

Figure 12: Maximum Severity of Solicited Local Symptoms per Participant Post-Dose 2 by Priming Dose Group

[Implementation Note: Same as Figure 10.]

Figure 13: Maximum Severity of Solicited Local Symptoms per Participant Post-Dose 3 by Priming Dose Group

[Implementation Note: Same as Figure 10.]

Figure 14: Maximum Severity of Solicited Local Symptoms per Participant Post-Any Dose by Vaccination Group

[Implementation Note: Vaccination groups will be in separate panels, each local event and "Any Local Reactogenicity" will be on the y-axis, and the percent of participants reporting each maximum severity over the reactogenicity period will be on the x-axis.]

Figure 15: Maximum Severity of Solicited Local Symptoms per Participant Post-Dose 4 by Vaccination Group

[Implementation Note: Same as Figure 14.]

Figure 16: Maximum Severity of Solicited Local Symptoms per Participant Post-Dose 5 Period by Vaccination Group

[Implementation Note: Same as Figure 14.]

Figure 17: Maximum Severity of Solicited Local Symptoms per Participant Post-Dose 6 by Vaccination Group

[Implementation Note: Same as Figure 14.]

Figure 18: Frequency of Related Unsolicited Adverse Events Occurring Prior to Boost Dose, by MedDRA® System Organ Class and Priming Dose Group

[Implementation Note: This is an example figure. Priming dose groups will be presented in separate panels, each SOC and Any SOC will be on the y-axis, and the total number of events of each severity will be on the x-axis.]

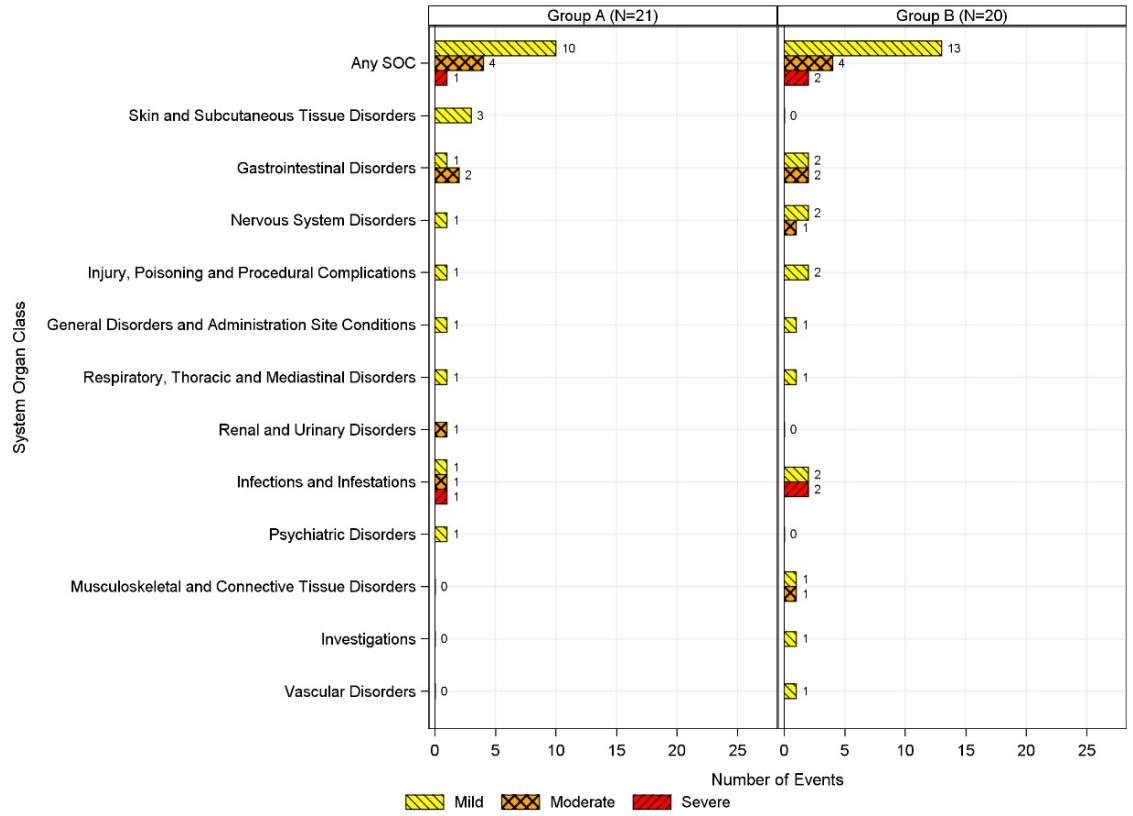


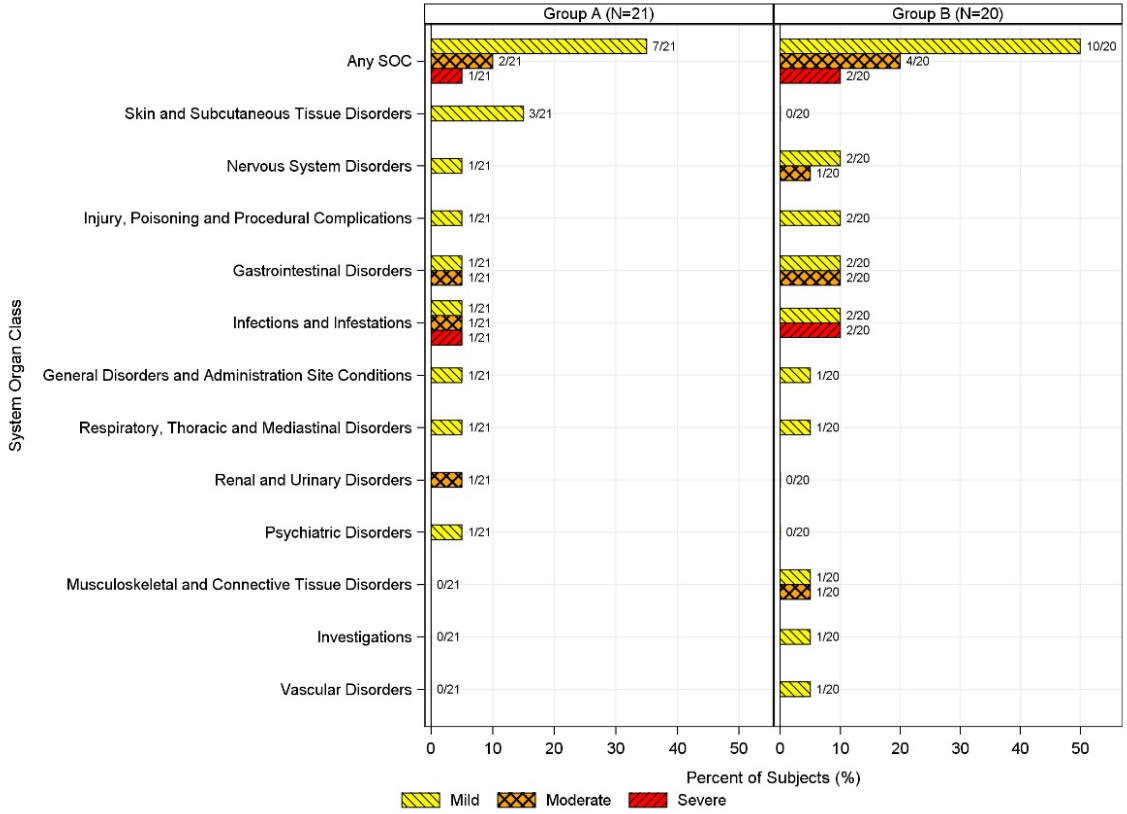
Figure with similar format:

Figure 19: Frequency of Related Unsolicited Adverse Events Post-Boost by MedDRA® System Organ Class and Vaccination Group

[Implementation Note: Vaccination groups will be presented in separate panels, each SOC and Any SOC will be on the y-axis, and the total number of events of each severity will be on the x-axis.]

Figure 20: Number and Percentage of Participants Reporting Related Unsolicited Adverse Events Prior to Boost Dose, by MedDRA® System Organ Class, Maximum Severity, and Priming Dose Group

[Note: This is an example figure. Priming dose groups will be in separate panels, each SOC and "Any SOC" will be on the y-axis, and the percent of participants reporting each maximum severity will be on the x-axis.]



Figures with similar format:

Figure 21: Number and Percentage of Participants Reporting Related Unsolicited Adverse Events Post-Boost, by MedDRA® System Organ Class, Maximum Severity, and Vaccination Group

[Note: Vaccination groups will be in separate panels, each SOC and "Any SOC" will be on the y-axis, and the percent of participants reporting each maximum severity will be on the x-axis.]

Figure 22: [Geometric Mean Titers] and 95% CIs for [Assay Name/Immune Response] Responses [Prior to/Post- Boost Doses], by Antigen, Study Day, and [Priming Dose Group / Vaccination Group]

[Implementation Note: This is a generic example figure. GMTs and associated 95% CIs are shown on the y-axis and Study Day is shown on the x-axis, with colors and line shapes denoting analysis group. The connecting lines will be dashed. Figures of this type will be presented for titer values. For assays with continuous analysis values, analogous figures will show mean values and associated CIs on the y-axis instead.]

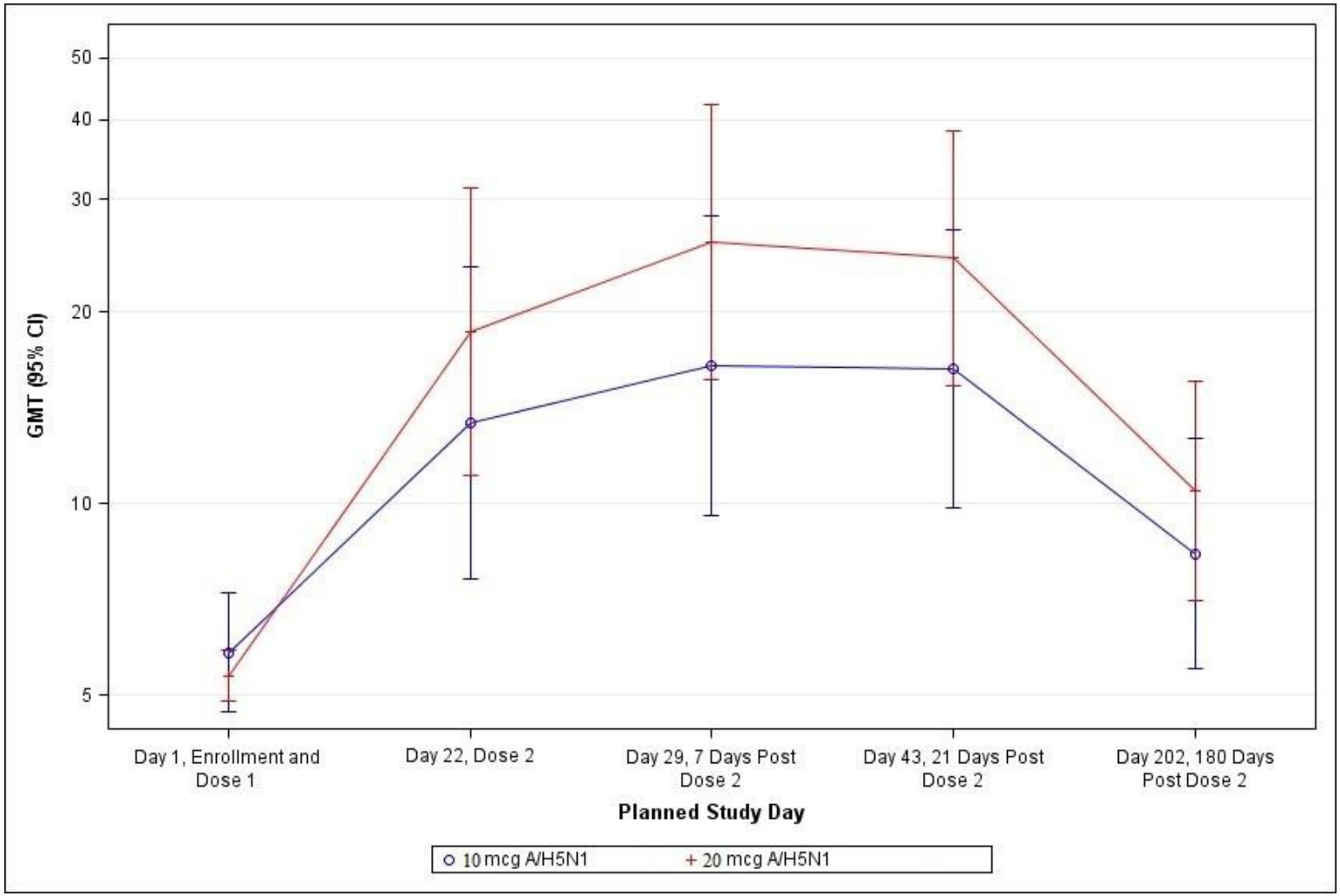


Figure 23: [Non-Titer Assay Name] Responses by Vaccination Group and Time Point

[Implementation Note: Boxplots will be generated, per the plan described in Section 8. This is an example figure. Separate panels will be presented for each visit. Analysis values will be displayed on the y-axis and priming dose groups or vaccination groups along the x-axis]

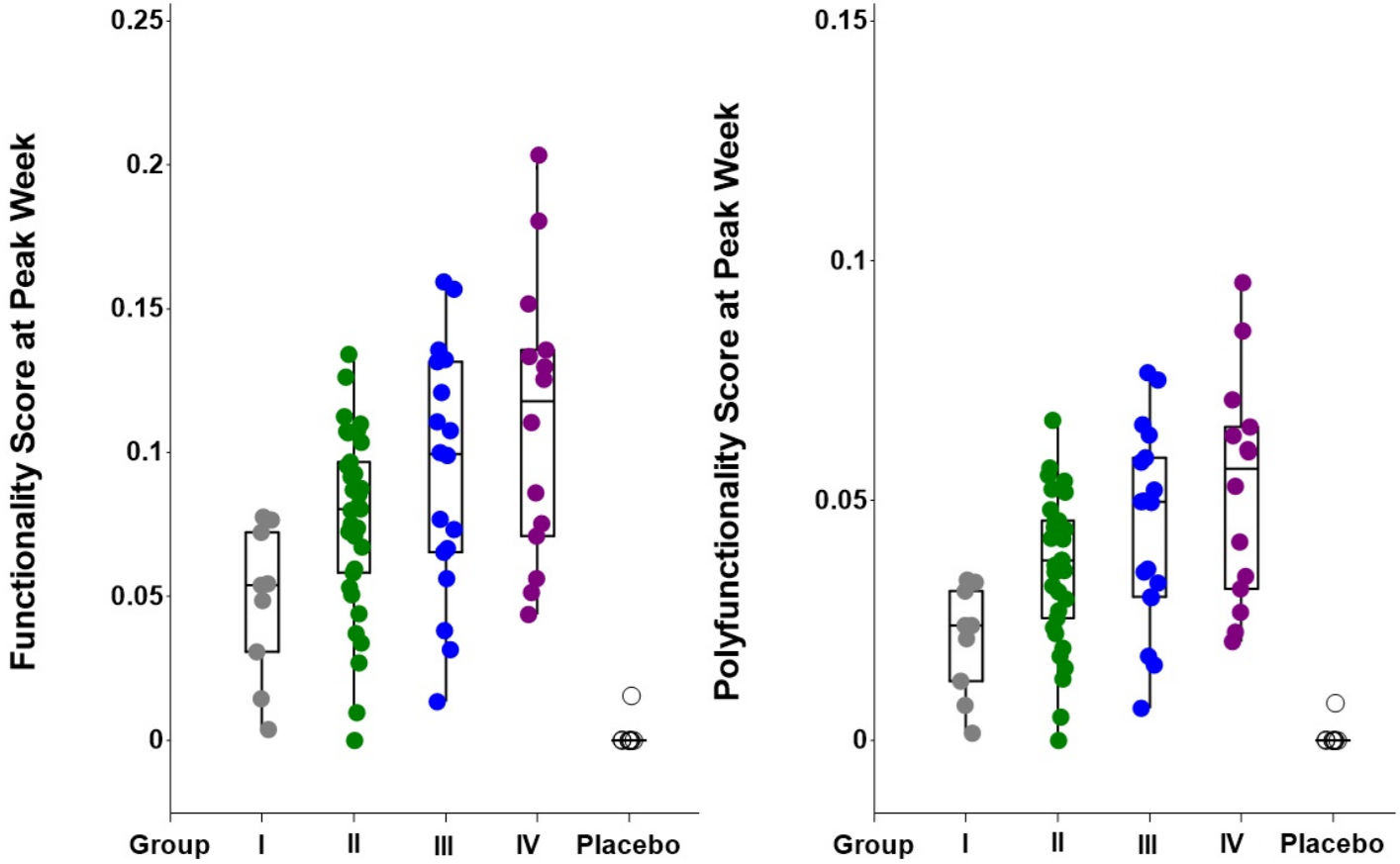
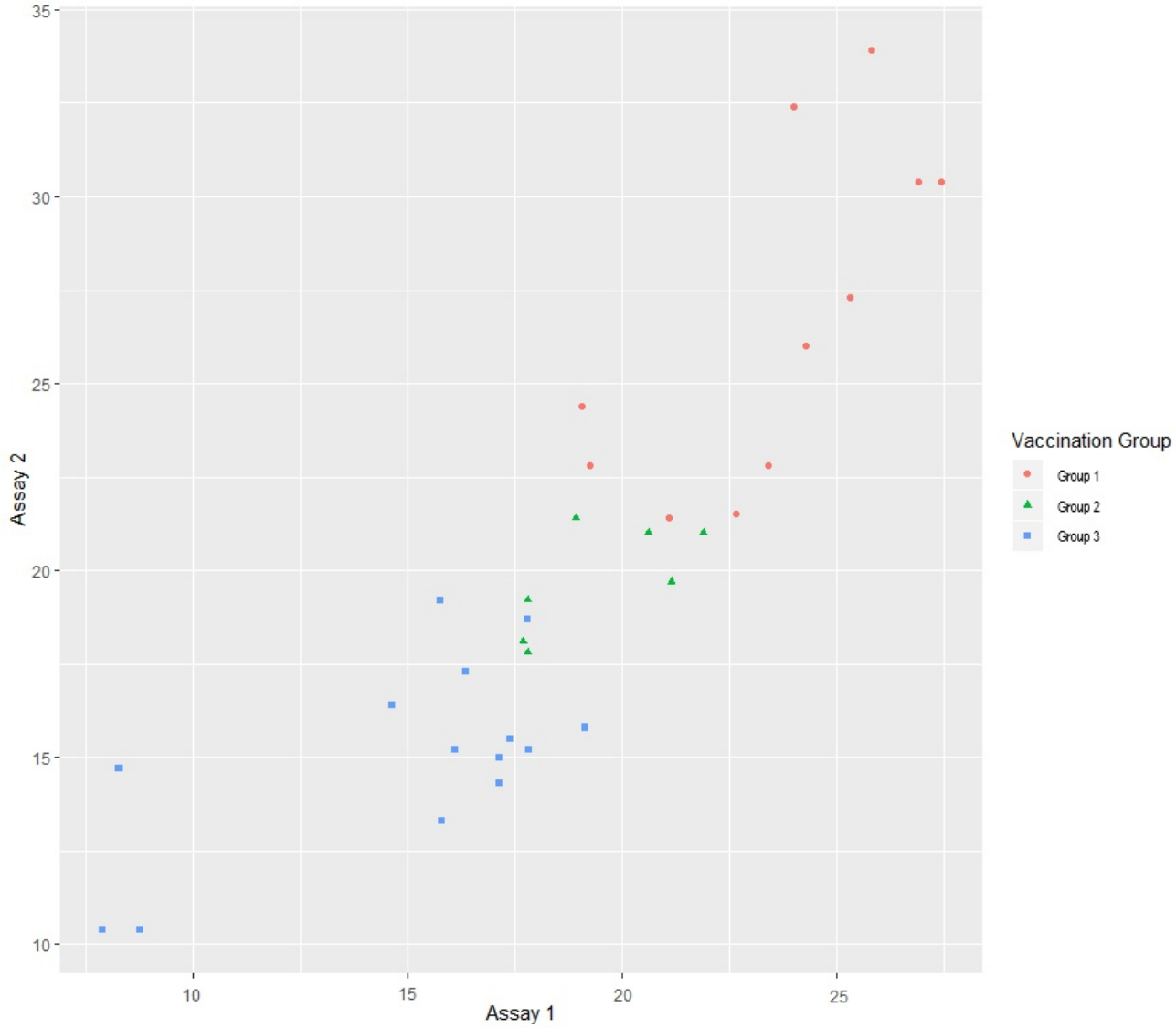


Figure 24: Correlation of Peak [Assay Name] Response with Peak [Assay Name] Response by Vaccination Group

[Implementation Note: This is an example figure. Vaccination groups will be represented by different shapes each with their own distinct color. The Spearman rank-order correlation estimates will be presented as well.]



APPENDIX 3. LISTINGS

LIST OF LISTINGS

Listing 1: Participants Receiving Study Vaccination

[Implementation Note: Listing will be sorted by vaccination group (ascending), participant ID, and visit number within participant]

Vaccination Group	Participant ID	Visit Number	Injection Date	Injection Site (Left Deltoid / Right Deltoid)

Listing 2: Participant Demographic Data

Participant ID	Vaccination Group	Age	Sex	Race	Ethnicity	Tribe	Marital Status	Level of Education	Occupation	BMI

Listing 3: Discontinuations and Early Terminations

Participant ID	Date Form Started	Date of Completion / Discontinuation from Study	Reason for Discontinuation

Listing 4: Participants Not Receiving Assigned Study Vaccination

Participant ID	Vaccination Group	Date of Last Completed Study Visit	Study Vaccine Not Administered, Reason

Listing 5: Protocol Deviations

Participant ID	Vaccination Group	Deviation Date	Deviation Category	Deviation Grade	Description of Deviation	Site Awareness Date	IRB/IEC Notification Date	Corrective Action Taken?	Explanation of Corrective Action
[N/A if screening failure]									

Listing 6: Prior and/or Concurrent Medical Conditions

Participant ID	Vaccination Group	Does the participant have past medical or surgical history and/or current conditions?	Diagnosis	Year Started	Year Ended	Ongoing?

Listing 7: Prior and Concomitant Medications

Participant ID	Vaccination Group	Date Form Started	CM Number	Generic Name – Med/Product	Start Date	Stop Date	Ongoing?	Dose	Unit	Route Code	Frequency Code	Indication	Comments
	[N/A if screening failure]												

Listing 8: Participants Analysis Population Inclusion and Exclusion Status

Participant ID	Vaccination Group	Analyses in which Participant is Included	Analyses from which Participant is Excluded	Results Available?	Reason Participant Excluded
		[e.g., Safety, ITT, PP]	[e.g., Safety, ITT, PP, Day x]		

Listing 9: Incident HIV Infections

Participant ID	Visit Number	Reason HIV Testing Not Collected	HIV Testing Collection Date	HIV Test for a Screening or Follow-up Visit?	HIV Test Result	Comments

Listing 10: Serious Adverse Events

Participant ID	Vaccination Group	Adverse Event Number	Adverse Event	Start Date	Stop Date	Intensity	Outcome	Is this an SAE?	If yes, Reason	Related to Vaccine?	Related to Optional Study Procedure?	Study Vaccine Change	Event Summary

Listing 11: Potentially Immune-Mediated Medical Conditions

Participant ID	Vaccination Group	Adverse Event Number	Adverse Event	Start Date	Stop Date	Intensity	Outcome	Is this AE a PIMMC?	Related to Vaccine?	Related to Optional Study Procedure?	Study Vaccine Change	Event Summary

Listing 12: Medically Attended Adverse Events

Participant ID	Vaccination Group	Adverse Event Number	Adverse Event	Start Date	Stop Date	Intensity	Outcome	Is this AE a MAAE?	Related to Vaccine?	Related to Optional Study Procedure?	Study Vaccine Change	Event Summary

Listing 13: Unanticipated Adverse Events

Participant ID	Vaccination Group	Adverse Event Number	Adverse Event	Start Date	Stop Date	Intensity	Outcome	Related to Vaccine?	Related to Optional Study Procedure?	Study Vaccine Change	Event Summary

Listing 14: Hematology Laboratory Values

Participant ID	Vaccination Group	Visit Number	Hematology Collection Date	If not collected, Reason	Hematology Parameter	Result	Severity Grade	Comments

Listing 15: Chemistry Laboratory Values

Participant ID	Vaccination Group	Visit Number	Chemistry Collection Date	If not collected, Reason	Chemistry Parameter	Result	Severity Grade	Comments

Listing 16: Urinalysis Laboratory Values

Participant ID	Vaccination Group	Visit Number	Urinalysis Collection Date	If not collected, Reason	Urinalysis Parameter	Result	Severity Grade	Comments

Listing 17: Serology Laboratory Values

Participant ID	Vaccination Group	Visit Number	Serology Collection Date	If not collected, Reason	Serology Parameter	Result	Severity Grade	Comments

Listing 18: Abnormal Vital Signs

Participant ID	Study Group	Visit Number	If not done, Reason	Oral Temperature (°C)	Pulse (beats/min)	Respiratory Rate (breaths/min)	Systolic BP (mmHg)	Diastolic BP (mmHg)

Listing 19: Pregnancies

Participant ID	Study Group	Visit Number	Pregnancy Result	Date of Delivery	Date of Termination	Comments

Listing 20: Missed Visits, Discontinuations, and Withdrawals due to COVID-19

Participant ID	Missed Study Visit Number	Date of Last Completed Study Visit	Date of most recent participant contact	Missed visit/ discontinuation / withdrawal caused by COVID?	Comments

Listing 21: Participants Who Consented to Optional Specimen Collection

Participant ID	Date of Informed Consent Signed	Consent for optional procedures obtained?	Optional procedures consented to	If no, reason	Consent for future use of samples?	Future use samples consented to	Consent for future genetic testing of samples?	Future genetic testing samples consented to