SCHARP
Statistical Center for HIV/AIDS Research and Prevention

STATISTICAL ANALYSIS PLAN FOR HVTN SAFETY

Protocol HVTN 303 (v2.0)

A Phase 1, Open-Label Clinical Trial to Evaluate Safety, Tolerability, and Immunogenicity of Adjuvanted HIV-1 Fusion Peptide Conjugate Vaccine (VRC-HIVVCP0108-00-VP) Alone or in Prime-Boost Regimens with Adjuvanted HIV-1 Envelope Trimer 4571 (VRC-HIVRGP096-00-VP) and HIV-1 Trimer 6931 (VRC-HIVRGP0106-00-VP) Vaccines in Healthy Adults

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Statistical Analysis Plan for Safety

Protocol: HVTN 303 (v2.0)

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SAP Modification History

The version history of, and modifications to, this statistical analysis plan are described below.

SAP Version	Modification
1.0	Initial
2.0	Update the safety SAP based on protocol version 2.0

Table of Contents

1 LIST OF ABBREVIATIONS AND ACRONYMS

Ab	antibody
AE	adverse event
AESI	adverse event of special interest
Ag	antigen
ALT	Alanin aminotransferase
AoU	Assessment of Understanding
ART	antiretroviral therapy
AUC-MB	area under the magnitude breadth curve
β-HCG	beta human chorionic gonadotropin
BAMA	binding antibody multiplex assay
bnAb	broadly neutralizing antibody
BP	blood pressure
CAB	community advisory board
CBC	complete blood count
cGMP	current Good Manufacturing Practice
CI	confidence interval
CMIA	chemiluminescent microparticle immunoassay
ConC	consensus clade C sequence
COVID-19	corona virus disease – 2019
CRF	case report form
CRPMC	Clinical Research Product Management Center
CRS	clinical research site
CSS	clinical safety specialist
CTL	CD8+ T lymphocyte(s)
DAERS	DAIDS Adverse Experience Reporting System
DAIDS	Division of AIDS
DHHS	Department Health & Human Services
d/v	dose per volume
DS	disulfide mutation
DSMB	data and safety monitoring board
EAE	expedited adverse event
EC	ethics committee
eGFR	estimated glomerular filtration rate

EIA	enzyme immunoassay
ELICA	electrochemiluminescence
Env	HIV-1 envelope glycoprotein
EUA	emergency use authorized
EUL	emergency use listing
FDA	food and drug administration
FP	fusion peptide
FP8v1-rTTHC	fusion peptide conjugate vaccine
FP8v2	eight N-terminal FP residues
FS	functionality score
FSR	Final Study Report
GCP	Good Clinical Practice
GEE	generalized estimating equations
GLP	good laboratory practice
GPP	Good Participatory Practices
HA	hemagglutinin
HCV	hepatitis C virus
IB	investigator's brochure
ICS	intracellular cytokine staining
IDR	immunodominant region
IM	intramuscular
IND	investigational new drug (application)
IRB	institutional review board
IV	intravenous
KLH	keyhole limpet hemocyanin
MAAE	medically attended adverse events
MAR	missing at random
MCAR	missing completely at random
Mcg	microgram
mg	milligram
mL	milliliter
MOP	manual of procedures
MPL	monophosphoryl lipid A
MSD	Meso Scale Discovery

MSM	person born male with partner(s) born male
NAb	neutralizing antibody
NAT	nucleic acid test
NIAID	National Institute of Allergy and Infectious Diseases
NIH	National Institute of Health
OHRP	Office for Human Research Protections
PAB	Pharmaceutical Affairs Branch
PBMC	peripheral blood mononuclear cells
PBS	phosphate buffered saline
PCA	principal component analysis
PCR	polymerase chain reaction
PEF	peak expiratory flow
PFS	polyfunctionality score
PI	Principal Investigator
PrEP	pre-exposure prophylaxis
PSRT	protocol safety review team
RAB	regulatory affairs board
RE	Regulatory Entity
RSC	Regulatory Support Center
rTTHC	recombinant tetanus toxoid heavy chain fragment C
SAE	serious adverse event
SAP	statistical analysis plan
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SAS	statistical analysis system
SC	subcutaneous
SD	standard deviation
SICF	sample informed consent form
SMB	safety monitoring board
SOP	Standard Operating Procedure
SPT	safety and pharmacovigilance team
SSP	study specific procedures
SUSAR	suspected unexpected serious adverse reaction
ULN	Upper limit of normal
VCMP	vaccine clinical materials program

VISP	vaccine-induced seropositivity
VRC	Vaccine Research Center
WBC	white blood cell
WHO	World Health Organization

2 OVERVIEW

The following describes the Statistical Analysis Plan (SAP) for the analysis of safety data from HVTN 303 for Safety Monitoring Board (SMB) reports and the Final Study Report (FSR) for Safety.

3 PROTOCOL SUMMARY

3.1 Title

A Phase 1, Open-Label Clinical Trial to Evaluate Safety, Tolerability, and Immunogenicity of Adjuvanted HIV-1 Fusion Peptide Vaccine (VRC- HIVVCP0108-00-VP) Alone or in Prime-Boost Regimens with Adjuvanted HIV-1 Envelope Trimer 4571 (VRC-HIVRGP096-00-VP) and HIV-1 Trimer 6931 (VRC-HIVRGP0106-00-VP) Vaccines in Healthy Adults.

3.2 Design

This is a phase 1, open-label, dose-escalation study to evaluate the dose, safety, tolerability and immunogenicity of adjuvanted HIV-1 Fusion Peptide (FP) conjugate vaccine (FP8v1-rTTHC) alone or in prime-boost regimens with adjuvanted HIV-1 Trimer 4571 and adjuvanted HIV-1 Trimer 6931. The primary hypothesis is that FP8v1-rTTHC, HIV-1 Trimer 4571, and HIV-1 Trimer 6931 adjuvanted vaccines are safe and tolerable when administered alone and when co-administered with HIV-1 Trimer 4571, in prime-boost regimens.

3.3 Study products

- FP8v1-rTTHC (FP conjugate vaccine) is an HIV-1 fusion peptide conjugated to recombinant tetanus toxoid heavy chain fragment C (rTTHC) via sulfo-SIAB chemical linker. FP8v1 corresponds to the amino-terminal eight residues of the most prevalent HIV fusion peptide sequence. FP conjugate vaccine will be provided at a 1-milligram (mg)/milliliter (mL) concentration in 3-mL glass vials filled to 0.7 mL.
- HIV-1 Trimer 4571 (Trimer 4571) is a synthetic soluble HIV-1 envelope product that consists of an HIV-1 envelope (Env) trimer variant, derived from clade A, strain BG505. Trimer 4571 is provided at a 500-mcg/mL concentration in 3-mL glass vials filled to 1.2 mL
- HIV-1 Trimer 6931 (Trimer 6931) is a synthetic soluble HIV-1 envelope product that consists of an HIV-1 envelope (Env) trimer variant, derived from consensus clade C sequence (ConC). Trimer 6931 will be provided at a 1-mg/mL concentration in 3-mL glass vials filled to 1.2 mL
- Adjuplex is the adjuvant and will be provided in a sterile, pyrogen-free, homogeneous suspension at 0.7 mL in 3-mL glass vials. Adjuplex will be mixed with study products in the pharmacy during preparation prior to vaccination at a 20% dose by volume
- PBS (labeled as Phosphate Buffered Saline pH 7.2): Diluent

3.4 Study population

Healthy adults aged 18 to 50 years, inclusive

3.5 Study plans and schema table

This study has two parts. Part A will evaluate the safety, tolerability, and immunogenicity of single doses of the FP conjugate, Trimer 4571 and Trimer 6931 vaccines, in a dose-escalation design. Each product must be assessed as safe prior to use in Part B. Trimer 4571 with alum adjuvant has been previously evaluated in humans but will be tested in Part A with Adjuplex. Part B will evaluate the safety, tolerability, and immunogenicity of FP conjugate prime, Trimer 4571 prime, or an FP plus Trimer 4571 prime, all followed by subsequent doses of Trimer 4571, Trimer 6931 and both Trimers combined. Study vaccines will be administered intramuscularly (IM) via needle and syringe in two injection sites. The study schema is below:

Table 2-1 Schema

Part A: Dose Escalation**											
Group	**N**	**W0**									
1	3	25 mcg FP conjugate vaccine									
2	3	200 mcg FP conjugate vaccine									
3	3	100 mcg Trimer 6931									
4	3	200 mcg Trimer 6931									
5	3	200 mcg Trimer 4571									
Part A Total	**15***										
Part B: Prime Boost Regimen**											
Group	**N**	**W0**	**W4**	**W8*****	**W12*****	**W20*****	**W24*****	**W32*****	**W36*****	**W44*****	**W48*****
6	~~15~~ 10	200 mcg Trimer 4571			~~200 mcg Trimer 4571~~		~~200 mcg Trimer 6931~~		~~100 mcg Trimer 4571 + 100 mcg Trimer 6931~~		~~100 mcg Trimer 4571 + 100 mcg Trimer 6931~~
7	~~15~~ 10	200 mcg FP conjugate vaccine	200 mcg FP conjugate vaccine	~~200 mcg FP conjugate vaccine~~	~~200 mcg Trimer 4571~~		~~200 mcg Trimer 4571~~		~~200 mcg Trimer 6931~~		~~100 mcg Trimer 4571 + 100 mcg Trimer 6931~~
8	~~15~~ 9	200 mcg FP conjugate vaccine + 200 mcg Trimer 4571	200 mcg FP conjugate vaccine + 200 mcg Trimer 4571	~~200 mcg FP conjugate vaccine + 200 mcg Trimer 4571~~		~~200 mcg Trimer 6931~~		~~100 mcg Trimer 4571 + 100 mcg Trimer 6931~~		~~100 mcg Trimer 4571 + 100 mcg Trimer 6931~~	
Part B total	**~~45~~[$] 29**										
Overall Total	**~~60~~[‡] 44**										

Table 1-1 Footnotes:

**Adjuplex adjuvant will be mixed with all study products in Part A and Part B at 20% by volume in the pharmacy during product preparation for all vaccinations. Once mixed, all study injections will be divided into 2 syringes, and each syringe will be administered intramuscularly to one of the deltoids.

* In Part A, up to 20 participants may be enrolled if needed for safety or immunogenicity evaluations. Additional participants may be enrolled to ensure the availability of 2-week safety data from at least 3 participants per group.

§ In Part B, up to 50 participants may be enrolled if needed for safety or immunogenicity evaluations. Additional participants may be enrolled to ensure the availability of 2-week safety data from at least 15 participants per group.

† Total up to 70 participants can be enrolled if needed for safety or immunogenicity evaluations.

Notes:

***Vaccination in Part B starting from Week 8 onwards did not take place.

Actual Ns for Group 6, 7 and 8 were 10, 10 and 9 respectively. In Part B total 29 participants were enrolled

Part A of the study may begin with direct enrollment of participants into the following groups simultaneously:

• Group 1 with no more than 1 participant enrolled per day for the 3 participants.

• Group 3 with no more than 1 participant enrolled per day for the 3 participants.

After Groups 1 and 3 have been fully enrolled, the study will be placed on a safety hold. No additional enrollments will proceed until the Protocol Safety Review Team (PSRT) has determined it is safe to do so. Once all of the reactogenicity and 2-week safety data from at least 6 participants have been submitted to the database, the PSRT must assess the accumulated product-specific data as showing no significant safety concerns before proceeding with enrollment of Groups 2, 4 and 5. If the PSRT has determined it is safe to proceed after reviewing data from Groups 1 and 3, the following groups may begin simultaneously:

• Group 2 with no more than 1 participant enrolled per day for the 3 participants

• Group 4 with no more than 1 participant enrolled per day for the 3 participants

• Group 5 with no more than 1 participant enrolled per day for the 3 participants

Once Groups 2, 4 and 5 have been fully enrolled, the study will be placed on a safety hold before proceeding with Part B. Once all of the reactogenicity and 2-week safety data from at least 9 participants have been submitted to the database, the PSRT must assess the accumulated product-specific data as showing no significant safety concerns before proceeding with enrollment of Part B.

Part B enrollments may only proceed if no safety concerns have been identified for any of the product administrations in Part A of the study.

If at any time there is insufficient data to conduct a formal PSRT Safety Review because of participant discontinuations from the study before sufficient data are collected, then additional participants may be enrolled into that group to acquire the requisite data on the required number of participants specified above. Moreover, the PSRT may recommend additional participants be enrolled into a given treatment group if additional safety evaluations are requested.

Consultation with the HVTN Safety Monitoring Board (SMB), Institutional Review Board (IRB) and Food and Drug Administration (FDA), if needed, as specified by study pause criteria (per Section 9.5.1), will occur if indicated.

3.6 Duration per participant

For participants in Part A (Groups 1-5): 52 weeks of scheduled clinic visits

~~For participants in Part B (Groups 6 and 7): 100 weeks of scheduled clinic visits~~

~~For participants in Part B (Group 8): 96 weeks of scheduled clinic visits~~

On January 13, 2023, a protocol memo was distributed informing the clinical research sites that all vaccinations in HVTN 303 were permanently discontinued. Procedures specified for remaining follow-up visits have been revised. Duration for Part A participants remained unchanged. Duration for Part B participants (for Groups 6 -8) is 56 weeks.

3.7 Estimated total study duration

~~Total study duration is 36 months (includes enrollment, planned safety holds and follow-up).~~

Following cessation of vaccination and reduction of follow-up duration the estimated total study duration is reduced to approximately 18 months.

3.8 Study Sites

HVTN Clinical Research Sites (HVTN CRSs) to be specified in the Site Announcement Memo.

4 SAFETY OBJECTIVES AND ENDPOINTS

Primary objective 1:

To evaluate the safety and tolerability of the following regimens in healthy adults:

- Adjuvanted FP conjugate vaccine administered IM at a dose of 25 or 200 mcg,
- Adjuvanted Trimer 6931, administered IM at a dose of 100 or 200 mcg,
- Adjuvanted Trimer 4571 administered IM at 200 mcg, or
- Prime-boost vaccination regimens of FP conjugate, Trimer 4571, and Trimer 6931 vaccines.

Primary endpoint 1:

Local and systemic reactogenicity signs and symptoms, laboratory measures of safety, and adverse and serious adverse events.

SAEs, medically attended adverse events (MAAEs), adverse events of special interest (AESIs) and AEs leading to early participant withdrawal or permanent discontinuation which will be collected throughout the study and for 12 months following any receipt of study product. Additionally, all adverse events will be collected for 28 days after any receipt of study vaccination. All safety lab related adverse events will be collected throughout duration of study.

5 COHORT DEFINITION

Recruitment will target 60 (up to 70) healthy adult participants 18 to 50 years of age. However, due to the early termination, the study enrolled a total of 44 participants (15 in Part A and 29 in Part B). The primary goal of this study is to identify safety concerns that may be associated with the study products.

Since enrollment is concurrent with receiving the first study vaccination, all enrolled participants will provide some safety data. For immunogenicity analyses, the sample calculations are based on the available samples..

6 POTENTIAL CONFOUNDERS

Characterization of the safety of the vaccine is susceptible to confounding by adverse events not related to the vaccine that by chance occur more often in one arm of the trial than another. Therefore analyses involving adverse events will incorporate the reported relationship to product as assessed by HVTN staff.

7 RANDOMIZATION

In Part A, Groups 1 and 3 will be randomized and will enroll no more than 1 participant per day for 3 participants per group. Contingent on the safety data from Groups 1 and 3, Groups 2, 4, and 5 will be randomized and may enroll simultaneously with no more than 1 participant per day for 3 participants for each group. Contingent on the safety data from Groups 1-5 in Part A, Groups 6-8 in Part B will be randomized and stratified by whether or not participants will be willing to consent to leukapheresis. A maximum of 7 participants per group that do NOT consent to leukapheresis collection will be enrolled. A participant's randomization assignment will be computer generated and provided to the HVTN CRS pharmacist through a Web-based randomization system. At each institution, the pharmacist with primary responsibility for dispensing study products is charged with maintaining security of the treatment assignments (except in emergency situations as specified in the HVTN manual of procedures [MOP]).

8 BLINDING

Participants and site staff will be unblinded to participants' group assignments. Laboratory program staff will be unblinded to whether a sample is from Part A or Part B but will remain blinded to the treatment assignment within Part A or Part B during assay analysis.

9 SAMPLE SIZE

The goal of the safety evaluation for this study is to identify safety concerns associated with product administration. The ability of the study to detect SAEs can be expressed by the true event rate above which at least 1 SAE would likely be observed and the true event rate below which no events would likely be observed. Specifically, for each vaccine arm of the study (n = 3) in Part A, there is a 90% chance of observing at least 1 event if the true rate of such an event is 53.6% or more; and there is a 90% chance of observing no events if the true rate is 1% or less. For a vaccine arm in Part B (n = 9 or 10), there is a 90% chance of observing at least 1 event if the true rate of such an event is 22.6% or 20.6% or more; and there is a 90% chance of observing no events if the true rate is 1% or less For a combined vaccine arm (Groups 1-5 in Part A and Groups 6-8 in Part B) of the study (n = 44), there is a 90% chance of observing at least 1 event if the true rate of such an event is 5.1% or more; and there is a 90% chance of observing no events if the true rate is 0.2% or less. As a reference, in HVTN vaccine trials from April 2008 through March 2018, about 1.7% of participants who received placebos experienced an SAE.

Binomial probabilities of observing 0, 1 or more, and 2 or more events among arms of size 3, 9, 10, and 44 are presented in Table 6-1 for a range of possible true adverse event rates. These calculations provide a more complete picture of the sensitivity of this study design to identify potential safety problems with the vaccine.

Table 6-1 Probability of observing 0 events, 1 or more events, and 2 or more events, among arms of size 3, 9, 10, and combined arms of size 44, for different true event rates

True event rate (%)	Pr(0/3)	Pr(1+/3)	Pr(2+/3)	Pr(0/10)	Pr(1+/10)	Pr(2+/10)	Pr(0/9)	Pr(1+/9)	Pr(2+/9)	Pr(0/44)	Pr(1+/44)	Pr(2+/44)
1	97	3	0	90.4	9.6	0.4	91.4	8.6	0.3	64.3	35.7	7.2
4	88.5	11.5	0.5	66.5	33.5	5.8	69.3	30.7	4.8	16.6	83.4	53
5	85.7	14.3	0.7	59.9	40.1	8.6	63	37	7.1	10.5	89.5	65.3
10	72.9	27.1	2.8	34.9	65.1	26.4	38.7	61.3	22.5	1	99	94.3
20	51.2	48.8	10.4	10.7	89.3	62.4	13.4	86.6	56.4	<0.1	>99.9	99.9
30	34.3	65.7	21.6	2.8	97.2	85.1	4	96	80.4	<0.1	>99.9	>99.9
40	21.6	78.4	35.2	0.6	99.4	95.4	1	99	92.9	<0.1	>99.9	>99.9
50	12.5	87.5	50	0.1	99.9	98.9	0.2	99.8	98	<0.1	>99.9	>99.9
60	6.4	93.6	64.8	0	>99.9	99.8	0	>99.9	99.6	<0.1	>99.9	>99.9

An alternative way of describing the statistical properties of the study design is in terms of the 95% confidence interval (CI) for the true rate of an adverse event based on the observed data. Table 6-2 shows the 2-sided 95% confidence intervals for the probability of an event based on a particular observed rate. Calculations are done using the score test method (52). If none of the participants in a group of size of 3 (eg, Groups 1-5 in Part A) or in a group of size of 9 or 10 (eg, the Groups 6-8 in Part B) are experiencing a safety event, the 95% 2-sided upper confidence bound for the true rate of such events in the total vaccinated population is 56.1% or 29.9% or 29.2%, respectively. For the combined vaccine arms in Part A and Part B (Groups 1-8, n = 44), the 95% 2-sided upper confidence bound for this rate is 9.8%.

Table 6-2 Two-sided 95% confidence intervals based on observing a particular rate of safety endpoints for arms of size 3, 9, 10 or combined arms of size 44

Observed event rate	95% Confidence interval (%)
0/3	[0, 56.1]
1/3	[6.1, 79.2]
2/3	[20.8, 93.9]
0/9	[0, 29.9]
1/9	[2, 43.5]
2/9	[6.3, 54.7]
0/10	[0, 29.2]
1/10	[0.1, 30.5]
2/10	[0.2, 31.9]
0/44	[0.1, 9.8]
1/44	[0.3, 11.4]
2/44	[0.6, 12.9]

10 STATISTICAL ANALYSIS

10.1 Statistical analyses

This section describes the final study analyses, unblinded as to treatment arm assignment. All data from enrolled participants will be analyzed according to the initial randomization assignment regardless of how many vaccinations they received. In the rare instance that a participant receives the wrong treatment at a specific vaccination time, the Statistical Analysis Plan (SAP) will address how to analyze the participant's safety data. Analyses are modified intent-to-treat in that individuals who are randomized but not enrolled do not contribute data and hence are excluded. Because of the brief length of time between randomization and enrollment (typically no more than 4 working days), very few such individuals are expected.

Analyses for primary endpoints will be performed using statistical analysis system (SAS) and R. All other descriptive and inferential statistical analyses will be performed using SAS, StatXact, or R statistical software.

No formal multiple comparison adjustments will be employed for multiple safety endpoints, multiple primary immunogenicity endpoints, or secondary endpoints. However, multiplicity adjustments will be made for certain immunogenicity assays, as discussed below, when the assay endpoint is viewed as a collection of hypotheses (eg, testing multiple peptide pools to determine a positive response).

10.2 Analysis variables

The analysis variables consist of baseline participant characteristics, safety, and immunogenicity for primary- and secondary-objective analyses.

10.3 Baseline comparability

Treatment arms will be compared for baseline participant characteristics using descriptive statistics.

10.4 Safety/tolerability analysis

Since enrollment is concurrent with receiving the first vaccination, all participants will have received at least 1 vaccination and therefore will provide some safety data.

10.4.1 Reactogenicity

The number and percentage of participants experiencing each type of reactogenicity sign or symptom will be tabulated by severity and treatment arm in Part A and Part B and the percentages displayed graphically by arm. For a given sign or symptom, each participant's reactogenicity will be counted once under the maximum severity for all injection visits. In addition, to the individual types of events, the maximum severity of local pain or tenderness, induration or erythema, and of systemic symptoms will be calculated. Kruskal-Wallis tests will be used to test for differences in severity across arms and Wilcoxon rank sum test will be used to test for difference in severity between 2 arms in Part B.

10.4.2 AEs and SAEs

AEs will be summarized using Medical Dictionary for Regulatory Activities (MedDRA) System Organ Class and preferred terms. Tables will show by treatment arm (in Part A and Part B) the number and percentage of participants experiencing an AE within a System Organ Class or within preferred term category by severity or by relationship to study product. For the calculations in these tables, a participant with multiple AEs within a category will be counted once under the maximum severity or the strongest recorded causal relationship to study product. Formal statistical testing comparing arms is not planned since interpretation of differences must rely heavily upon clinical judgment.

A listing of SAEs reported to the Division of AIDS (DAIDS) Regulatory Support Center (RSC) Safety Office will provide details of the events including severity, relationship to study product, time between onset and last vaccination, and number of vaccinations received.

10.4.3 Local laboratory values

Box plots of local laboratory values will be generated for baseline values and for values measured during the course of the study by treatment arm (Part A and Part B) and visit. Each box plot will show the first quartile, the median, and the third quartile. Outliers (values outside the box plot) will also be plotted. If appropriate, horizontal lines representing boundaries for abnormal values will be plotted.

For each local laboratory measure, summary statistics will be presented by treatment arm and time point, as well as changes from baseline for post enrollment values. In addition, the number (percentage) of participants with local laboratory values recorded as meeting Grade 1 AE criteria or above as specified in the Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events will be tabulated by treatment arm for each post vaccination time point. Reportable clinical laboratory abnormalities without an associated clinical diagnosis will also be included in the tabulation of AEs described above.

10.4.4 Reasons for vaccination discontinuation and early study termination

The number and percentage of participants who discontinue vaccination and who terminate the study early will be tabulated by reason and treatment arm (Part B).

10.5 Analyses prior to end of scheduled follow-up visits

Any analyses conducted prior to the end of the scheduled follow-up visits should not compromise the integrity of the trial in terms of participant retention or safety or immunogenicity endpoint assessments. In particular, early unblinded analyses by treatment assignment require careful consideration and should be made available on a need-to-know basis only.

10.5.1 Safety

During the course of the trial, unblinded analyses of safety data will be prepared approximately every 4 months during the main study for review by the SMB. Ad hoc safety reports may also be prepared for SMB review at the request of the HVTN 303 PSRT. The HVTN leadership must approve any other requests for unblinded safety data prior to the end of the scheduled follow-up visits.

11 SAFETY TABLES, PARTICIPANT LISTINGS, AND FIGURES

11.1 List of Tables

The following tables are included in the SMB reports and FSR for Safety:

11.2 List of Tables

The following tables are included in the SMB reports and FSR for Safety:

- Enrollment Report
- Demographics and Study Product Administration Frequencies
- Study Product Administration Errors
- Maximum Local and Systemic Reactogenicity Summaries
- Adverse Events by Treatment – Listed by Body System and Severity – By Decreasing Frequency
- Adverse Events by Preferred Term and Severity – by Decreasing Frequency – Includes Severe, Potentially Life-threatening or Fatal Events only
- Adverse Events by Preferred Term and Severity – by Decreasing Frequency – Includes All Severities
- Adverse Events by Preferred Term and Severity – by Decreasing Frequency – Includes Related Events only
- Adverse Events by Preferred Term and Relationship to Study Product – by Decreasing Frequency – Includes Events of Any Relationship

Additional tables included in the FSR for Safety:

- Social Impact Summary
- End of Study HIV Diagnostic Testing Results (Vaccine-Induced Seropositivity/Reactivity)

11.3 List of Participant Listings

These participant listings are included in the SMB reports:

- Discontinuation Status
- Severe or Life-Threatening Local and Systemic Reactogenicities
- Moderate, Severe or Life-threatening Erythema / Induration
- Serious Adverse Events (SAEs)/Expedited Adverse Events (EAEs)
- Severe, Life-Threatening, or Fatal Adverse Events
- Adverse Events of Special Interest (AESI)
- Medically Attended Adverse Events (MAAE)
- Study Product Related Events
- Pregnancies
- HIV Infections

11.4 List of Figures

These graphs are included in the SMB reports and FSR for Safety:

- Maximum Local Reactogenicities
- Maximum Systemic Reactogenicities
- Boxplots for Laboratory Measures

12 REFERENCES

1. Agresti A, Coull BA. Approximate is better than "exact" for interval estimation of binomial proportions. Am Stat. 1998;52(2):119-26.