STATISTICAL ANALYSIS PLAN FOR PROTOCOLS

HVTN 703/HPTN 081

A phase 2b study to evaluate the safety and efficacy of VRC01 broadly neutralizing monoclonal antibody in reducing acquisition of HIV-1 infection in women in sub-Saharan Africa

HVTN 704/HPTN 085

A phase 2b study to evaluate the safety and efficacy of VRC01 broadly neutralizing monoclonal antibody in reducing acquisition of HIV-1 infection among men and transgender persons who have sex with men

JULY 7, 2020

HVTN 704/HPTN 085 and HVTN 703/HPTN 081 Antibody Mediated Prevention Trials Statistical Analysis Plan for Safety, Trial Monitoring, and Prevention Efficacy Analysis

July 7, 2020

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Version 3.2

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1 Overview of the Antibody Mediated Prevention Trials

The Antibody Mediated Protection (AMP) trials consist of two harmonized protocols, HVTN 704/HPTN 085 and HVTN 703/HPTN 081, which evaluate the safety and efficacy of VRC01, a broadly neutralizing monoclonal antibody (mAb) against the CD4 binding site of the HIV-1 envelope glycoprotein administered in 10 IV infusions every 8 weeks, in reducing acquisition of HIV-1 infection. HVTN 704/HPTN 085 enrolls 2700 HIV-uninfected men and transgender persons (TG) in North and South America (U.S., Switzerland, Peru, Brazil) who have anal sex with men or TG, and HVTN 703/HPTN 081 enrolls 1900 HIV-uninfected sexually active women in sub-Saharan Africa (South Africa, Botswana, Malawi, Kenya, Zimbabwe, Mozambique, and Tanzania). Study participants are randomized to receive a 10 mg/kg or a 30 mg/kg dose of VRC01 or a control preparation. Participants are tested for HIV-1 infection every 4 weeks and at any time following participant report of possible HIV-1 exposure during the study. Enrollment in both AMP trials is completed by the earliest event of reaching full enrollment or September 30, 2018.

2 Objectives and Endpoints of the AMP Trials

HVTN 704/HPTN 085 and HVTN 703/HPTN 081 are two randomized, double-blind, placebo-controlled Phase 2b test-of-concept HIV prevention trials, conducted in HIV-uninfected adults at risk for HIV infection.

2.1 Primary Objectives and Endpoints

Primary objective 1:
To evaluate the safety and tolerability of VRC01 mAb administered through IV infusion

Primary endpoint 1:
Local and systemic reactogenicity signs and symptoms, laboratory measures of safety, AEs, SAEs, and rates of discontinuation

Primary objective 2:
To determine if the VRC01 mAb prevents HIV-1 infection and to estimate the level of efficacy

Primary endpoint 2:
Documented HIV-1 infection by the Week 80 study visit

2.2 Secondary Objectives and Endpoints

Planned statistical analyses for secondary objective 1 is described in the separate Correlates of Prevention Efficacy Statistical Analysis Plan.

Secondary objective 1:
To develop a marker(s) of the VRC01 mAb that correlates with the level and antigenic specificity of protection against HIV-1 infection and to provide insight into the mechanistic correlates of protection

Secondary endpoints 1:
Serum concentration of VRC01 in participants assigned to receive the mAb (ELISA, neutralizing assay)

Serum mAb effector functions to HIV-1 Envs representing variability of the VRC01 antibody footprint

Sequences of breakthrough HIV infections from the earliest available HIV-positive plasma samples

VRC01 neutralization-sensitivity of, and effector function against, HIV strains from infected trial participants from the earliest available postHIV-infection serum samples

2.3 Exploratory Objectives

Exploratory objective 1:
To assess use of FTC/TDF in the study cohort

Exploratory objective 2:
To assess if prevention efficacy is modified by FTC/TDF use

Exploratory objective 3:
To understand changes in risk behavior and the potential for risk compensation for all study participants

Exploratory objective 4:
To measure anti-idiotype antibodies to VRC01

3 Follow-Up Period

All participants will be followed for 104 weeks (i.e., 2 years) post-enrollment. Week 80 is the last study visit for the primary efficacy endpoint analysis. To allow retrospective testing of any infection diagnoses detected up until Week 88 as primary endpoints by Week 80, the final efficacy analysis will be triggered when the last enrolled participant reaches the Week 88 visit. Week 104 is the last study visit for the co-primary endpoint analysis of safety and

tolerability. Participants who are diagnosed with HIV-1 infection during the study will be followed for approximately 6 months following infection diagnosis.

4 Study Populations

We define three study cohorts that are analyzed for addressing various study objectives. This terminology is used throughout this SAP.

- **Safety Cohort**: all randomized participants who receive the first infusion
- **Modified Intent-to-Treat (MITT) Cohort**: participants in the Safety Cohort who are not later discovered to have been HIV-infected on the date of the first infusion (Day 0) and who are not involved in a duplicate enrollment
- **Per-Protocol (PP) Cohort**: MITT participants who receive all planned infusions within the target infusion-visit windows

The Safety Cohort and the MITT Cohort are very similar but not identical to a full Intention-to-Treat Cohort (i.e., all randomized participants); the Safety Cohort differs by excluding randomized volunteers who do not enroll; and the MITT Cohort is a subset of the Safety Cohort that also excludes randomized participants discovered later to have been HIV-positive by Day 0. Due to blinding and the brief length of time between randomization and enrollment (typically no more than 4 working days), we expect almost all randomized participants to be in the Safety Cohort. Given that eligibility for the study requires recent evidence of being HIV-1 uninfected (within 30 days prior to enrollment), we expect almost all enrolled participants to be in the MITT Cohort.

The PP Cohort membership status is defined at each fixed study time point for a participant, with inclusion defined by receiving all planned infusions within the target infusion-visit windows up to that point of time or up to the time of HIV-1 infection diagnosis, whichever occurs earlier. This time-dependent cohort definition is necessary given that participants experiencing the HIV infection primary endpoint are not given infusions post HIV infection diagnosis. Consequently, the analyses for assessing prevention efficacy in the MITT and PP cohorts handle time differently—the former compare infection rates between treatment groups in the fixed MITT cohort defined at baseline whereas the latter compare infection rates between treatment groups whose membership changes over time based on infusion adherence data. In particular, at a given study time a participant is in the PP cohort if they have received all planned infusions within the target infusion-visit windows up to that point of time or up to the time of HIV-1 infection diagnosis, whichever occurs earlier.

All analyses of safety objectives are based on the Safety Cohort. All analyses of prevention efficacy are based on the MITT cohort unless explicitly demarcated otherwise. Analyses of

correlates of prevention efficacy are based on participants in cohorts defined in the Correlates of Prevention Efficacy SAP.

Prevention efficacy analyses will be based on data from MITT participants treated according to the initial randomization assignment regardless of how many infusions they received (i.e., treated "as randomized"). Additionally, secondary efficacy analyses will be performed in the PP Cohort, which will be analyzed on the "as-treated" basis (actually received treatments).

In the unexpected event of a duplicate enrollment, the interim safety and infusion discontinuation data will be reported for each enrollment, considering these as separate participants, while noting in the report that a duplicate enrollment occurred. The final safety report will include only the safety and infusion discontinuation data following the first randomization, analyzed according to the randomized treatment assignment. The immunogenicity and prevention efficacy analyses will exclude all data from participants with a duplicate enrollment regardless of whether also duplicate randomization occurred or not.

5 Definition of the Primary Efficacy Endpoint (Documented HIV-1 Infection)

5.1 HIV Testing Postinfusion

The prevention efficacy endpoint is diagnosis of HIV-1 infection during the follow-up period. Following enrollment, HIV testing will take place at scheduled clinic visits.

HIV testing is performed using the protocol-specific HIV testing algorithms (see Study-Specific Procedures). At scheduled visits that include HIV testing, specimens will be tested with an FDA-approved 4^{th} generation HIV-1/2 enzyme immunoassay (EIA) or chemiluminescent microparticle immunoassay (CMIA). If the participant has a reactive test result, an HIV RNA test and an HIV-1/2 discriminatory test will be performed as indicated in the algorithm. Further HIV testing is required using a second specimen drawn on a later date to confirm a diagnosis of HIV infection. The second specimen may be collected at an interim visit. Samples to be stored for future studies will also be collected at this time.

A 'case' is defined as a participant who is confirmed to have acquired HIV-1 infection after enrollment based on the protocol-specific diagnostic algorithms (see SSP). Before informing a participant that they are infected at or after enrollment, all HIV test results will be reviewed by a blinded, independent Endpoint Adjudicator(s) or designee(s). Only HIV-1 infection cases confirmed by the Endpoint Adjudicator(s) will be counted as HIV-1 infections in the analysis.

5.2 Endpoint Adjudication

The general diagnostic criteria for HIV infection are well accepted. However, definitive diagnosis of HIV infection in the context of having received a study product that is even partially effective may be more difficult. Specifically, if VRC01 is capable of completely suppressing viral replication, or if the antibody alters the normal serological response upon exposure to HIV, standard diagnostic tests may be more difficult to assess. Therefore, the Endpoint Adjudicator(s) will review all serological and virological test results in a blinded manner for each participant who tests positive per the trials' diagnostic testing algorithms. The Endpoint Adjudicator(s) will also review HIV test results in cases where HIV infection status is not clearly resolved using the HIV testing algorithm. The assessment of the Endpoint Adjudicator(s) or designee(s) will be reported to the SDMC and to the HIV diagnostics laboratory.

The Endpoint Adjudicator(s) or designee(s) must notify the SDMC within 1 working day of any confirmed HIV infection. The HIV diagnostics lab will inform the clinic of the outcome of the HIV testing algorithm (i.e., HIV-infected, HIV-uninfected, or redraw required).

The Endpoint Adjudicator(s) or designee(s) will be expert in the fields of infectious diseases or laboratory medicine independent of the Vaccine Research Center and clinical investigators participating in this trial. A separate Standard Operating Procedure will govern the activities of the Endpoint Adjudicator(s) or designee(s).

5.3 Date of the Primary Efficacy Endpoint

The Endpoint Adjudicator(s) will define the date of diagnosis based on his/her judgment of all of the available diagnostic data. This date is assigned based only on diagnostic results collected prospectively over time; it does not consider the results of HIV-specific PCR tests that may be performed on earlier samples that are tested later. The date of HIV-1 infection diagnosis will be used as the event-date for primary time-to-event analyses of Primary Endpoint 2 (documented HIV-1 infection) and for all secondary time-to-event analyses of Primary Endpoint 2 that analyze time since enrollment as the failure time variable.

5.4 Estimated Date of HIV-1 Infection

For all participants diagnosed with HIV-1 infection, the sample available at the nearest date before the diagnosis date will be tested using HIV-specific PCR. If it is positive, then the sample at the second nearest date before the diagnosis date will be tested using HIV-specific PCR. This 'look-back' procedure will be repeated until an HIV-specific PCR negative test result is obtained or until a test is done for a Day 0 sample. The complete HIV diagnostic test history including retrospective testing is used to estimate the date of infection as described in detail in Section 4.2 of the Correlates of Prevention Efficacy SAP. The estimated infection

date will be used as the event-date for secondary analyses of Primary Endpoint 2 that analyze time since last infusion received prior to the estimated infection date as well as for marker correlates and sieve analyses of breakthrough HIV-1 infections (see the Correlates of Prevention Efficacy SAP for details) and may also be used for exploratory analyses of the primary efficacy endpoint. The estimator for the date of HIV-1 infection may be refined to be based on additional data beyond the diagnostic testing information (details of this estimator are described in the Correlates of Prevention Efficacy SAP).

6 Interactions of Study Statisticians with the Data and Safety Monitoring Board

At each 6-monthly Data and Safety Monitoring Board (DSMB) meeting, the study statisticians will present Open and Closed Reports separately for each AMP trial; all tables and figures included in the Closed Report are specified in Appendix A with statistical analyses of safety further described in Section 7. For a subset of tables and figures in the Closed report, the Open Report includes tables and figures with the same information except with trial information presented pooled across the three treatment groups to preserve blinding to treatment assignment. In addition, the following trial monitoring reports will be presented at each DSMB meeting, separately for each AMP trial:

- feasibility monitoring report per Section 9.1 starting after approximately and not fewer than 120 enrolled participants have expected follow-up through to the end of the Week 32 visit;
- monitoring report of prevention efficacy for potential harm, non-efficacy, and high efficacy per Section 9.2, where
  - potential harm monitoring is commenced at the 20^{th} pooled primary efficacy endpoint and is continually performed with each additional endpoint until the time non-efficacy/high efficacy monitoring is triggered,
  - non-efficacy monitoring is commenced at at least 45 but no more than 67 pooled primary efficacy endpoints, and
  - high efficacy monitoring is commenced at the same time as non-efficacy monitoring;
- monitoring report for the use of Truvada as pre-exposure prophylaxis per Section 9.3;
- monitoring report for futility to assess prevention efficacy per Section 9.4 starting after at least 12 months after the first participant is enrolled; and
- monitoring report for performance standards of quality of trial conduct per Section 9.5.

7 Statistical Analysis of Safety

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

7.1 Baseline Comparability

Treatment groups will be compared for baseline characteristics including demographics and laboratory measurements, using descriptive statistics (percentages, means, ranges).

7.1.1 Reactogenicity

The number and percentage of participants experiencing each type of reactogenicity sign or symptom will be tabulated by severity and treatment arm and the percentages displayed graphically by arm. For a given sign or symptom, each participants reactogenicity will be counted once under the maximum severity for all infusion 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 between arms.

7.1.2 AEs and SAEs

AEs will be summarized using MedDRA System Organ Class and preferred terms. Tables will show by treatment arm 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. A listing of SAEs reported to the DAIDS Regulatory Support Center (RSC) Safety Office will provide details of the events including severity, relationship to study product, time between onset and last infusion, and number of infusions received.

7.1.2.1 Infusion Reactions

A descriptive analysis of infusion reactions is provided for DSMB review at the 6-monthly meetings. The analysis includes the assessment of cumulative incidence of *the first occurrence* of (i) any infusion reaction, and (ii) each of the four clinical categories (also referred to as types) of an infusion reaction (urticarial reaction, dyspnea with rash, dyspnea without rash, and other reaction) as a function of the number of received infusions. For both (i) and (ii), time to an infusion reaction is measured in terms of the number of infusions received by the onset time.

We estimate the first occurrence of (i) using the complement of the Kaplan-Meier estimator for the survival function and pointwise 95% Wald confidence intervals (CIs). Participants who did not experience an infusion reaction contribute partial (i.e., right-censored) information in the analysis. In addition, sample proportions of received infusions that led to a first infusion reaction as a function of the infusion number are reported with 95% exact binomial CIs.

We estimate the first occurrence of (ii) using the Aalen-Johansen estimator for the type-specific cumulative incidence function within the competing risks survival analysis framework.

Note that an estimated cumulative incidence function, overall or type-specific, can only be reliably interpreted at timepoints with sufficiently large numbers at risk to ensure stability of the estimators.

7.1.3 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 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 timepoint, as well as changes from baseline for postenrollment 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 DAIDS AE Grading Table will be tabulated by treatment arm for each postinfusion timepoint. Reportable clinical laboratory abnormalities without an associated clinical diagnosis will also be included in the tabulation of AEs described above.

7.1.4 Reasons for Infusion Discontinuation and Early Study Termination

The number and percentage of participants who permanently discontinue infusions and who terminate the study early will be tabulated by reason and treatment arm.

8 Statistical Analysis of Prevention Efficacy

Except where specified, all prevention efficacy endpoint analyses are performed in the MITT cohort. All analyses only use samples and data collected prior to study unblinding. Unless either of the trials is stopped prematurely, the common data cut date for the final prevention

efficacy analysis in both trials is set to be May 1, 2020, which includes more than 80 weeks of follow-up for the last enrolled participant in each trial (80 weeks after the last enrollment falls on April 2, 2020 in HVTN 703/HPTN 081 and April 17, 2020 in HVTN 704/HPTN 085).

All analyses specified in Sections 8.1, 8.2, and 8.3 are conducted in each AMP trial separately, as well as pooled over the two AMP trials. The statistical methods are the same, except the pooled analyses additionally stratify for study. For cumulative incidence-based pooled analyses, stratification is performed by estimating the cumulative hazard separately within each combination of study and treatment group (requiring at least 10 total primary HIV-1 infection endpoints within each combination of study and treatment group), and, for Cox model-based pooled analyses, stratification is performed by using a separate baseline hazard for each study (requiring at least 10 total primary HIV-1 infection endpoints within each study to include the trial as a stratification covariate).

8.1 Primary Analysis of Prevention Efficacy

The time between enrollment and the date of HIV-1 infection diagnosis determined according to Section 5.3 is evaluated in the MITT cohort. The failure times of participants never observed to be diagnosed with HIV-1 infection are right-censored at the date of the last HIV-negative test or the Week 80 visit, whichever occurs earlier.

Let PE denote the overall prevention efficacy by the Week 80 visit of the 10 mg/kg and 30 mg/kg mAb groups pooled together compared to the control group. We define the primary PE parameter as

$$PE = \big\{1 - \text{cumulative incidence ratio (pooled mAb groups/control group) of the primary efficacy endpoint by the Week 80 visit}\big\} \times 100\%, \quad (1)$$

where the cumulative incidence ratio is the probability of the primary efficacy endpoint by the Week 80 visit for participants assigned to receive the mAb divided by the probability of the primary efficacy endpoint by the Week 80 visit for participants assigned to receive control. More specifically, the primary PE parameter, $PE(t)$, will be estimated at a fixed time point t chosen to be the latest possible time point when stable estimation using follow-up data through the Week 80 visit can be achieved; this is operationalized by defining t as the maximum time point with 150 participants at risk for the primary endpoint in each of the placebo and individual VRC01 groups. All times-to-event will be right-censored at the Week 80 visit or earlier following the operational rules summarized in Table 1. Note that the fixed time point t will likely differ for the two AMP trials given the dynamic visit windows. By definition of the stratified estimator, the trial-pooled analysis will use the smaller of the two fixed time points t. Additionally, note that, due to differences between Schedules 1 and 4, the operational rules in Table 1 imply that an infection endpoint observed in Schedule 4 after the hypothetical Schedule 4 Week 80 visit would be excluded from primary endpoints,

Table 1: Operational rules for right-censoring of times-to-event at the Week 80 visit

HIV status	Visit attendance scenario			Censoring rule
HIV-Uninfected	Attended s1 wk 80 visit			Censor at s1 wk 80 sample draw date
	Missed s1 wk 80 visit	Attended s1 post-wk 80 visit		Censor at target s1 wk 80 visit date
		Attended s4 post-wk 80 visit		Censor at maximum of (hypothetical s4 wk 80 visit[1], last s1 sample draw date)
		Did not attend post-week 80 visit in s1 or s4		Censor at last HIV-uninfected sample draw date
HIV-Infected	Infected in s1 on or before s1 wk 80 visit			Infected, use adjudicated diagnosis date
	Infected in s1 after s1 wk 80 visit	Attended s1 wk 80 visit		Censor at s1 wk 80 sample draw date
		Missed s1 wk 80 visit	Evidence of HIV-negative status at post-s1 wk 80 visit	Censor at target s1 wk 80 visit date
			No evidence of HIV-negative status at post-s1 wk 80 visit	Censor at last HIV-uninfected sample draw date
	Entered s4 at or before hypothetical s4 wk 80 visit[1]	Infected on or before hypothetical s4 wk 80 visit		Infected, use adjudicated diagnosis date
		Infected after hypothetical s4 wk 80 visit	Evidence of HIV-negative status at post-hypothetical s4 wk 80 visit	Censor at hypothetical s4 wk 80 visit[1] date
			No evidence of HIV-negative status at post-hypothetical s4 wk 80 visit	Censor at last HIV-uninfected sample draw date
	Entered s4 after the hypothetical s4 wk 80 visit and diagnosed after the first s4 visit			Censor at maximum of (hypothetical s4 wk 80 visit, last s1 HIV-uninfected sample draw date)
	Entered s4 after the hypothetical s4 wk 80 visit and diagnosed immediately			Censor at last s1 HIV-uninfected sample draw date[2]

- Abbreviations: wk = visit label for target visit week as defined in the study protocol (Appendix J for Schedule 1 and Appendix M for Schedule 4), s1 = Schedule 1, s4 = Schedule 4.
- Actual visit dates may differ from the implied week in the target visit label due to (1) dynamic visit scheduling in schedule 1, and (2) visit windows in schedules 1 and 4.
- All censoring times are based on sample draw dates or target visit dates (where appropriate). Visit windows are not used because (1) Schedule 1 and Schedule 4 visit windows are quite different (s1 allowable wk 80 visit window is +/- 7 days, s4 allowable windows are -41/+42 days), and (2) since a hypothetical wk 80 visit is constructed in s4, unnecessarily complicated to construct a hypothetical s4 wk 80 visit window, which would overlap with other s4 visit windows if the same pattern were followed and would be an entirely unique visit window if no overlap were ensured.
- [1]Hypothetical s4 week 80 visit is defined as exactly 560 days post-enrollment. Justification: unlike s1, s4 visits are all relative to enrollment and occur independently of each other, so it's preferable to define a hypothetical wk 80 visit as 560 days post-enrollment than to use a midpoint estimator and/or some other dynamic method which doesn't correspond to s4's structure.
- [2]If a participant enters s4 at wk 88 or wk 104 and is immediately diagnosed, cannot determine whether infection occurred in s1 (clearly before the target s1 wk 80 visit) or in s4 (clearly after the hypothetical s4 wk 80 visit).

while an infection endpoint observed in Schedule 1 at the same time post-enrollment would be included as a primary endpoint if the endpoint was registered before or at the Schedule 1 Week 80 visit.

Each of the two cumulative incidence parameters in (1) will be estimated using the transformed Nelson-Aalen estimator for the cumulative hazard function evaluated at time t defined in the preceding paragraph. We will use the delta method to obtain the asymptotic 95% CI for the log cumulative incidence ratio (pooled mAb/control) and then back-transform these confidence bounds to the PE scale. Both the point estimate and the 95% CI for PE will be reported. If there are more than 10 HIV-1 primary endpoints in each of the VRC01 dose groups, then the Nelson-Aalen estimator for the cumulative hazard function will be computed separately for each dose group and the weighted average of the dose group-specific estimates, with the weight 0.5 assigned to each dose group, will be transformed for inference about PE. The variance estimate of the overall averaged cumulative hazard estimator will

be used to obtain the variance estimate on the log cumulative incidence ratio scale for calculating confidence intervals. For trial-pooled analyses, if there are more than 10 primary endpoints in each stratum defined by trial and treatment group, the Nelson-Aalen estimator will be computed separately in each of the 6 strata (4 VRC01 dose group strata and 2 control group strata), and separate weighted averages of the VRC01 dose-group and control-group stratum-specific estimates, with weights 0.25 assigned to each VRC01 dose-group stratum and weights 0.5 assigned to each control-group stratum, will be transformed for inference about the trial-pooled PE.

PE is the target parameter for the primary analysis of overall PE. The primary analysis tests the null hypothesis

$$H_0 : PE = 0\% \text{ versus the alternative hypothesis } H_1 : PE \neq 0\% \tag{2}$$

using a 2-sided $\alpha = 0.05$ level Wald test of the equality of log cumulative hazard functions at 80 weeks for the pooled mAb group and the control group. Note that the critical value for determining whether the effect of VRC01 on prevention of HIV-1 acquisition is significant at the two-sided 0.05 level will not require adjustment for the interim monitoring of PE for potential harm, non-efficacy, and high efficacy described in Section 9.2. This is because this monitoring is designed to have minimal impact on the type-I error/power of the study. Moreover, whereas interim monitoring for positive PE would mean that the actual type-I error of the study is inflated above the nominal level, interim monitoring for potential harm, non-efficacy, and high efficacy has the effect of decreasing the actual type-I error rate below the nominal level. In other words, use of the unadjusted critical value leads to conservative (as opposed to anti-conservative) inference, and our simulations show that the degree of conservatism is minimal.

The timing of infections will be described separately for the pooled mAb group and the control group by the respective cumulative incidence curves of the time between first infusion and the date of HIV-1 infection diagnosis. Each curve will be estimated by a transformed Nelson-Aalen estimator for the cumulative hazard function. To obtain a pointwise 95% CI, we will use the delta method to obtain the asymptotic 95% CI for the log cumulative incidence over time and then exponentiate the confidence bounds. As for PE, if there are more than 10 HIV infection events in each of the VRC01 dose groups, then the above estimators will be computed separately for each dose group and aggregated for inference on the pooled mAb group cumulative incidence.

Additionally, cumulative PE over time will be reported. To obtain pointwise 95% CIs, first we will use the delta method to obtain asymptotic 95% CIs for the log cumulative incidence ratio (pooled VRC01/control) over time and then back-transform the confidence bounds to the PE scale. The simultaneous 95% confidence interval for cumulative PE over time will be obtained following the method of Parzen, Wei, and Ying (1997). The same method will be applied to obtain an estimate of cumulative PE on the additive difference-scale (control group minus pooled VRC01 group) with pointwise and simultaneous 95% confidence intervals. This analysis is informative because it communicates about benefits and risk on an absolute scale:

for example under the assumption that assignment to a VRC01 arm does not increase the risk of infection for any participant, the estimate at a given time t is interpreted as the probability a participant assigned to a VRC01 arm has their infection averted compared to, counter to fact, had they been assigned to placebo.

8.2 Secondary Analyses of Prevention Efficacy

Secondary analyses assess PE parameters for the mAb dose groups separately. Let PE10 be the overall prevention efficacy of the 10 mg/kg mAb group and let PE30 be the overall prevention efficacy of the 30 mg/kg mAb group, defined as

$$PE10 = \big\{1 - \text{cumulative incidence ratio (mAb 10 mg/kg group/control group)} \\ \text{of the primary efficacy endpoint by 80 weeks}\big\} \times 100\%,$$

and

$$PE30 = \big\{1 - \text{cumulative incidence ratio (mAb 30 mg/kg group/control group)} \\ \text{of the primary efficacy endpoint by 80 weeks}\big\} \times 100\%.$$

The PE10 and PE30 parameters will be assessed using the same estimation method as described in Section 8.1.

We will conduct secondary analyses to test the null hypotheses

$$H_0 : PE10 = 0\% \text{ versus the alternative hypothesis } H_1 : PE10 \neq 0\%$$

and

$$H_0 : PE30 = 0\% \text{ versus the alternative hypothesis } H_1 : PE30 \neq 0\%$$

using 2-sided $\alpha = 0.05$ level Wald tests described in Section 8.1. Both unadjusted p-values and Holm–Bonferroni-adjusted p-values (Holm, 1979) will be reported for each of the individual dose versus control group analyses.

In addition, the following secondary analyses of PE will be conducted:

(i) Assess a dose-response effect by testing the null hypothesis

$H0$: cumulative HIV-1 incidence by 80 weeks is equal in the three study groups versus $H1 : 0\% \leq PE10 \leq PE30$ with at least one strict inequality.

(ii) Test the null hypothesis that the cumulative HIV-1 incidence by 80 weeks is equal in the three study groups versus the alternative hypothesis that there are some differences.

(iii) Test the null hypothesis that the cumulative HIV-1 incidence by 80 weeks is equal in the two mAb groups versus the alternative hypothesis that PE30 is greater than PE10, which would demonstrate that assignment to a higher mAb dose level causes higher PE.

Hypotheses (i)–(iii) will be tested using cumulative hazard function based Wald tests. Define the Wald test statistic

$$W_{i,j} = \frac{\log \widehat{\Lambda}_i(80 \text{ weeks}) - \log \widehat{\Lambda}_j(80 \text{ weeks})}{\sqrt{\widehat{\text{var}}\{\log \widehat{\Lambda}_i(80 \text{ weeks})\} + \widehat{\text{var}}\{\log \widehat{\Lambda}_j(80 \text{ weeks})\}}},$$

where $\widehat{\Lambda}(\cdot)$ is the Nelson-Aalen estimator and $i, j \in \{c, 10, 30\}$, $i \neq j$, represent the control, 10 mg/kg mAb, and 30 mg/kg mAb group, respectively. The test statistic considers the estimated variance of the Nelson-Aalen estimator proposed in Aalen (1978).

The alternative hypothesis in (i) is equivalent to $\widetilde{H}_1 : \Lambda_c(t_0) \geq \Lambda_{10}(t_0) \geq \Lambda_{30}(t_0)$, $t_0 =$ 80 weeks, with at least one strict inequality, and therefore the test of (i) will reject H_0 if both $W_{c,10} \geq \Phi^{-1}(0.975)$ and $W_{10,30} \geq \Phi^{-1}(0.975)$, where Φ^{-1} is the quantile function of the standard normal distribution. The test of (ii) will reject H_0 if at least one of $|W_{c,10}| \geq \Phi^{-1}(0.975)$ and $|W_{10,30}| \geq \Phi^{-1}(0.975)$ holds. The test of (iii) will reject H_0 if $W_{10,30} \geq \Phi^{-1}(0.975)$.

As a supportive analysis of the hypotheses in (2), targeted minimum loss-based estimation (TMLE) may be used to estimate cumulative incidences of the primary efficacy endpoint over time for the pooled mAb arm and the control arm. Iterative mean-based TMLE is used for this analysis as described in Benkeser, Carone, and Gilbert (2016). The Super Learner (van der Laan, Polley, and Hubbard, 2007) is used to generate initial estimates of the conditional censoring distribution and the iterated conditional means. The Super Learner library includes both parametric and nonparametric algorithms: generalized linear models, generalized additive models with 2 or 3 degrees of freedom, a regression tree (Breiman et al., 1984), and a random forest (Breiman, 2001) (specified in Table 2). Each method considers adjustment for baseline demographic covariates, the baseline behavioral risk score built via supervised learning as described in Section 8.6, and two-way interactions of these terms. The baseline demographics to adjust for are country (if there are at least 10 total primary HIV-1 infection endpoints in a country – otherwise categories are collapsed) and AMP study (for analyses that pool the two AMP trials). The candidate algorithms in the Super Learner library consider various adjustments for time, as shown in Table 2. TMLE analyses will produce plots of estimated cumulative PE on both the multiplicative mAb efficacy and additive-difference scales, as done for the primary analyses. The TMLE analyses will be implemented using the *survtmle* R package available at CRAN.

PE parameters will be estimated by 1 minus the ratio (pooled mAb groups/control group) of these tMLE estimators. Influence-curve based variance estimators of each cumulative incidence is used, and the delta method applied to obtain the variance estimator of the log

Table 2: Models included in the Super Learner library. Z denotes a mAb group assignment, B baseline behavioral risk score as described in Section 8.6, and W a vector of baseline demographic covariates. The columns indicate what type of model was used (glm = generalized linear model, step = stepwise glm using both AIC and BIC as selection criteria, and gam = generalized additive model), how time was modeled ($\emptyset$ denotes time was omitted from the model, `factor(t)` indicates dummy variables were used), and what covariates were included ($x * y$ indicates a cross product between covariates x and y). We use $s(x; df = d)$ to denote that variable x was modeled using a polynomial spline of degree d.

Model type	Time	Covariates
Conditional mean estimates		
glm	$\emptyset$	Z
glm	$\emptyset$	$Z + B + W$
glm	$\emptyset$	$Z * B$
step	$\emptyset$	$Z * B + W$
Censoring estimates		
glm	`factor(t)`	$\emptyset$
glm	`factor(t)`	$Z * t$
glm	$\emptyset$	Z
glm	$\emptyset$	$Z + B + W$
glm	t	Z
glm	t	$Z + B + W$
glm	$\log(t)$	Z
glm	$\log(t)$	$Z + B + W$
step	`factor(t)`	$Z + B + W$
step	t	$Z + B + W$
step	$\log(t)$	$Z + B + W$
gam	$s(t, 3)$	Z
gam	$s(t, 3)$	$Z + B + W$
gam	$s(t, 2)$	Z
gam	$s(t, 2)$	$Z + B + W$

cumulative incidence ratio. Point estimates and 95% pointwise and simultaneous Wald CIs for cumulative incidence curves and $PE(t)$ curves will be plotted. For the final timepoint of 80 weeks, 2-sided Wald p-values will be reported.

In addition to studying PE based on cumulative incidences of the primary efficacy endpoint over time, secondary analyses will assess hazard ratio based PE defined as

$$PE = \big\{1 - \text{hazard ratio (pooled mAb groups/control group)} \\ \text{of the primary efficacy endpoint at 80 weeks}\big\} \times 100\%. \quad (3)$$

The PE parameter in (3) will be estimated using a Cox proportional hazards model with the indicator of assignment to a mAb group versus the control group as the sole covariate. The score test will be used to evaluate whether hazard ratio PE differs from zero. This analysis uses the same failure time as used for the primary analysis of the cumulative-incidence based PE. Goodness-of-fit diagnostics including the complementary log-log endpoint-free survival curves and the Grambsch and Therneau (1994) test will be applied to assess veracity of the proportional hazards assumption.

This Cox model analysis will be repeated, conducted as an as-treated analysis of the per-protocol (PP) cohort. This analysis is done using the same Cox model except that participants are right-censored by the event of no longer qualifying for membership in the PP cohort.

An additional secondary analysis of PE based on the Cox proportional hazards model will be done that uses as the failure time variable the time from the most recent infusion to the estimated date of HIV-1 infection. This analysis is conducted in the MITT cohort. This analysis can have increased power to detect prevention efficacy compared to the primary analysis of the cumulative incidence based parameter PE, if instantaneous prevention efficacy is higher when VRC01 concentrations are higher. Goodness-of-fit diagnostics will be applied as described above.

The Cox models are selected for the secondary analysis instead of the primary analysis in order that the validity and interpretation of the primary analysis does not depend on the proportional hazards assumption.

The Cox model may also be used for a secondary analysis to assess PE in the MITT cohort by modeling full cumulative infusion adherence (i.e., at study time t, all infusions up to and including time t received within target visit windows) or lack thereof as a binary time-varying covariate. In addition, to study the dose-response in the association of infusion adherence with PE, we will assess PE in subgroups defined by the level of cumulative infusion adherence over time, with adherence levels defined, at time t, as missing zero infusions by time t, missing at most 1 infusion by time t, missing at most 2 infusions by time t, etc., included in the model as binary time-varying covariates. If there is a time-varying covariate prognostic for subsequent HIV-1 infection that also predicts the probability of subsequently taking infusions, and taking infusions predicts subsequent values of this prognostic factor, then the Cox model described above provides biased inference (Hernán et al., 2000). Based on this, diagnostics will be done to check if there are any measured time-varying covariates strongly associated with both infection and taking subsequent infusions. If such covariates are identified, then the standard Cox model analysis described above will be supplemented with a causal structural nested Cox model analysis, which is designed to correct for time-varying confounding.

Sensitivity analyses of the primary analysis will test $H0 : PE = 0\%$ with a log-rank test and with a Gehan-Wilcoxon test stratified by VRC01 dose group.

To further explore potential time-variations in PE from Week 0 through to Week 80, in-

stantaneous PE over time, defined as one minus the instantaneous hazard ratio (pooled VRC01/control) over time, will be estimated using the nonparametric kernel estimation method with optimal bandwidth selection for the instantaneous hazard ratio as described in Andersen et al. (1993), with an asymptotic pointwise 95% CI. The simultaneous 95% confidence interval for instantaneous PE will be calculated following the method of Gilbert et al. (2002).

8.2.1 Analyses of Prevention Efficacy for HIV-1 Infections After the Week 80 Visit

The primary analyses of prevention efficacy and the Cox model secondary analyses of prevention efficacy will be repeated including all MITT HIV-1 infections in the analysis occurring through to the Week 104 terminal study visit. These analyses are relevant because the right-tail of VRC01 concentration may be long enough that protection against infection could occur even against HIV-1 infections many weeks or months after the last VRC01 infusion.

8.3 Prevention Efficacy Against Measured Neutralization Sensitive Viruses

8.3.1 Final Analyses Also Included in Interim Analyses

For each primary HIV-1 infection endpoint, neutralization sensitivity of the majority breakthrough founding virus (and of other founding minor viral variants with frequency greater than 10%) at the first HIV-1 RNA positive time point to the VRC01 clinical lot is measured by three independent replicates of IC50 and IC80 from the TZM-bl target cell assay. (A 'founder virus' is an HIV-1 variant that is measured/observed based on sequencing the earliest available post-infection sample.) For each geometric mean readout (across the three replicates) of IC50 and IC80 separately, majority founder viruses are divided into five categories of sensitivity level ("sensitivity type"): Sensitive = < 0.3 μg/mL; Moderately Sensitive = 0.3–1 μg/mL; Intermediate = 1–3 μg/mL; Moderately Resistant = 3–10 μg/mL; and Resistant = > 10 μg/mL. For infected cases with multiple assayed HIV-1 variants, the geometric mean IC50 and IC80 pertaining to the most sensitive variant is used for analysis. The report will include a table of the distributions of the number of HIV-1 infected cases (and/or assayed variants) by treatment assignment and sensitivity type, and boxplots of the distributions of geometric mean IC50 and IC80 readouts for infected cases by treatment assignment.

In addition, for each sensitivity type category, for IC50 and IC80 separately, the following results are presented:

- Estimated cumulative incidence curves of each HIV-1 sensitivity type by treatment assignment (Aalen-Johansen estimator)

- Estimated cumulative prevention efficacy curve for each HIV-1 sensitivity type (contrast of Aalen-Johansen estimates)
- Estimated proportional hazards prevention efficacy by quantitative $\log_{10}$ IC50 or $\log_{10}$ IC80 (method of Juraska and Gilbert (2013))

If the number of primary endpoint counts in some sensitivity type categories is small, then adjacent categories may be combined, to ensure at least 5 endpoints total per analyzed category.

8.3.2 Additional Analyses Included in the Final Analysis

All of the primary and secondary analyses of overall prevention efficacy specified in Sections 8.1 and 8.2 will be repeated for the endpoint HIV-1 infection with sensitivity type Sensitive or Moderately Sensitive according to the definitions above. The statistical methods are the same, except cumulative incidence estimators are replaced with cause-specific cumulative incidence estimators and Cox model analyses right-censor primary HIV-1 infection endpoints of a different sensitivity type.

8.3.3 Prevention Efficacy Accounting for Number of Founding Viruses

Another secondary analysis may be conducted to assess the effect of VRC01 on prevention of HIV-1 acquisition over 80 weeks using the method of Follmann and Huang (2015) that incorporates information on the number of HIV-1 founder viruses in HIV-1-infected participants. The method has increased efficiency relative to Cox proportional hazards regression if VRC01 reduces the number of founders.

8.4 Analysis of Exploratory Objective 1

The use of oral FTC/TDF as PrEP will be assessed as described in Section 9.3.

8.5 Analysis of Exploratory Objective 2

If there is substantial PrEP use detection at baseline, then the Cox model will be used to assess whether prevention efficacy significantly differs in subgroups with detectable versus undetectable baseline PrEP use, and to make inferences on prevention efficacy separately in each subgroup. In addition, if there is substantial PrEP use detected over the course of the study, then a marginal structural Cox model will be used to assess prevention efficacy in the sub-population not using PrEP.

More specifically, the primary analysis will be repeated where only MITT infection endpoints with no evidence of PrEP use at the time of HIV-1 diagnosis and at the time of the earliest evidence of infection will be included in the analysis. Intracellular TFV concentration (see Section 8.4) will be used to determine eligibility for this analysis. A participant is eligible if the TFV concentration is below the lower limit of detection as defined above at the diagnosis visit and at the visit with earliest evidence of HIV-1 infection (if different from the diagnosis visit). Since the ARVs are only detectable in plasma for roughly 14 days (Patterson et al. 2010) and some participants may have become infected before the 14-day window, with this approach we are not assured that all those included in the analysis were not using prophylactic ARVs at the time of infection. Therefore an additional analysis may be conducted that addresses this issue by also excluding participants from the HIV-1 acquisition analysis if they self-reported ARV use in the last 30 days at either the diagnosis visit or the last visit prior to diagnosis. These analyses will evaluate uninfected participants without accounting for data on their TFV concentrations.

8.6 Analysis of Exploratory Objective 3

Several analyses will make use of components of a 2-dimensional predicted HIV-1 risk score, which refers to identified best models predicting the conditional probability that a participant who is HIV-1-negative at $t_0 = 0$ weeks becomes HIV-1-positive by a fixed time point $t_1 =$ 80 weeks (and $t_1 = 104$ weeks) given a set of baseline input variables W and treatment stratum $Z \in \{\text{control, pooled VRC01}\}$.

The first step in the prediction problem involves, for each $Z = z$ separately, estimating

$$\psi_{0,z}(W) = P_0(T \leq 80 \text{ weeks} \mid T > 0 \text{ weeks}, W, Z = z),$$

where T is a time from enrollment to the primary endpoint event (the parameter of interest for $t_1 = 104$ weeks is defined analogously). It has been shown that this parameter is identifiable based on observed data in a trial with a time-to-event endpoint. The procedure for estimating $\psi_{0,z}(W)$ is fully described in the "Statistical Analysis Plan for HIV-1 Risk Prediction in KwaZulu-Natal via Superlearner" developed by Alex Luedtke and Ernesto Ulloa (downloadable from `https://www.overleaf.com/read/bkycmxsdzzvm`), with all modifications described in the following paragraphs.

All estimators will be trained and applied separately in each AMP trial given major differences in demographics, risk behavior, and viral transmission and epidemiology between the two trial populations. Moreover, in the control-group risk prediction in HVTN 703/HPTN 081, two data sets will be used for training all estimators: Initially, we will restrict the training set to primary follow-up in HVTN 703/HPTN 081 control recipients only. Subsequently, we will enrich this training set by including 80 weeks of blinded follow-up in the HVTN 702 trial's combined control and vaccine female recipients who were enrolled at overlapping sites with HVTN 703/HPTN 081. We will refer to these as the restricted and enriched control groups, respectively, in HVTN 703/HPTN 081.

In each AMP trial, the estimation will be carried out separately in the control (restricted and enriched for HVTN 703/HPTN 081) and pooled VRC01 groups, i.e., the estimators will be trained separately on data from participants in the control and pooled VRC01 groups (estimation in individual VRC01 dose groups is not considered due to potential convergence failures and limited precision). The best-performing estimator $\widehat{\psi}_z$ for $\psi_{0,z}$ will also be identified independently for each $z \in \{\text{control, pooled VRC01}\}$ in each trial. For the control-group prediction in HVTN 703/HPTN 081, the candidate estimators including the superlearner trained on the restricted control-group data and the candidate estimators including the superlearner trained on the enriched control-group data will be all evaluated together for prediction accuracy, identifying a single best-performing estimator across both the restricted and enriched control-group data sets. For the i-th enrolled participant with a baseline covariate vector W_i, the predicted HIV-1 risk score is then defined as the ordered pair $\left(\widehat{\psi}_{\text{control}}(W_i), \widehat{\psi}_{\text{pooledVRC01}}(W_i)\right)$ of the best-performing estimators.

In more detail, within each combination of trial and treatment stratum, a set of candidate estimators $\{\widehat{\psi}_1, \ldots, \widehat{\psi}_K\}$, specified in Table 5 in the KwaZulu-Natal risk prediction SAP, and a superlearner estimator $\widehat{\psi}_{SL}$ for $\psi_{0,z}$ will first be constructed following Algorithm 1 below. The best-performing estimator $\widehat{\psi}_z$ is defined as an estimator from the set $\{\widehat{\psi}_1, \ldots, \widehat{\psi}_K, \widehat{\psi}_{SL}\}$ with maximal cross-validated AUC in the treatment stratum $Z = z$ (see Algorithm 2 below). Following identification of the best-performing estimator in each treatment stratum, we will compute the estimated/predicted HIV-1 risk score for all enrolled participants.

The covariate vector W will consist of participant-level baseline demographic characteristics and baseline behavioral survey responses. The baseline demographic characteristics include clinical site, country of residence, race, ethnicity, and age in both trials, and, in addition, gender identity in HVTN 704/HPTN 085. The behavioral risk survey consists of 88 questions that aim to assess the risk of HIV infection and can be previewed in Appendix B. HVTN 703/HPTN 081 participants enrolled at clinical sites outside of South Africa were administered an abbreviated form of the behavioral survey consisting of a subset of 60 questions (Appendix C). In order to maximize the use of covariate information, missing responses in the full set of survey questions selected for inclusion in W (a subset of the 88 questions) will be imputed using the missForest method (Stekhoven and Bühlmann, 2011), implemented in the `missForest` R function, for participants outside of South Africa using observed responses from participants enrolled in South Africa. The missForest method uses random forests to multiply impute mixed-type data. This method does not require tuning parameters or distributional assumptions and has been shown to perform comparably to or better than other commonly used multiple imputation methods such as multivariate imputation by chained equations or k-nearest neighbors. Since this analysis considers a large fraction of imputed responses for some behavioral risk variables, another set of superlearner estimators will be fit using only the abbreviated survey, and the best-fitting model will be identified from the pooled set of estimators based on the full/imputed and the abbreviated behavioral risk covariate vectors in this trial.

The risk score computation involves the following steps: Initially, baseline variables with a

large portion of missing responses or sparse response levels will be excluded upfront from the input covariate data set, and for a given $\widehat{\psi}_z(W)$, only a subset of the 88 behavioral survey variables and the aforementioned demographic variables will be included in W. Then, the missForest method will be used to multiply impute missing covariate values in W. Next, to accommodate a high-dimensional W, dimension-reducing screening methods will be used for "classical" algorithms. Modified versions of screening methods in `SuperLearner`'s R functions `screen.glmnet` and `screen.randomforest` for the time-to-event outcome will be used as two screening algorithms combined with each prediction algorithm. More specifically, a Cox model with lasso penalty will be used in `screen.glmnet`, and a survival forest (R function `rsfc`) will be used in `screen.randomforest`. In `screen.randomforest`, the top 20 variables with the greatest variable importance index will be screened in. Lastly, the estimators will be trained using the screened-in covariates, the prediction accuracy will be evaluated, and the best-performing estimators will be used for predicting HIV-1 risk in each treatment stratum.

For the HVTN 703/HPTN 081 enriched control-group candidate estimators, W will consist of the baseline demographic characteristics specified above and the questionnaire data from the HVTN 702 behavioral risk assessment. The HVTN 702 behavioral risk assessment consists of 23 questions which, like the HVTN 703/HPTN 081 behavioral risk survey, aim to assess risk of HIV infection. Some questions in the HVTN 702 assessment correspond, in part, to questions in the full HVTN 703/HPTN 081 survey but are structured differently. Questions between the two assessments which capture similar information (e.g., number of sex partners) will be consolidated into a single feature where possible. Survey items in the HVTN 702 survey that were not included in the full HVTN 703/HPTN 081 survey (e.g., age at sexual debut) will be multiply imputed using the missForest method. No other covariates from the full HVTN 703/HPTN 081 survey will be used in fitting the enriched control-group candidate estimators. Note that imputation of the enriched data set will be performed separately from the imputation of the restricted HVTN 703/HPTN 081 survey described above. Since this analysis considers a large fraction of imputed responses, another set of candidate estimators will be fit using only the questions that are shared between the HVTN 702 and the full HVTN 703/HPTN 081 surveys. The best-fitting estimator will be identified from the pooled set of estimators based on the complete/imputed and the restricted/enriched control-group data sets in HVTN 703/HPTN 081.

Internal validation of $\widehat{\psi}_z(W)$ (see Algorithm 2 below) will be based on cross-validated predictions using only data from the AMP trials (with no additional external training set to train the learners). External validation will not be performed. Computation time of `survtmle` scales with the resolution of T. To limit computation time, person-time will be rounded up to the nearest month.

Pseudocode for Superlearner and Candidate Estimators

Let A_z denote observed data from participants in treatment stratum z in a single AMP trial.

Algorithm 1 Superlearner and candidate estimators

Input: A_z and $\widehat{\psi}_1, ..., \widehat{\psi}_K$ prediction algorithms

Use A_z to impute A_z^* via package `missForest`
Use package `survtmle` on A_z^* to obtain $\widehat{D}_i^{(1)}$ and $\widehat{D}_i^{(2)}, \forall i \in A_z^*$ †
Partition A_z^* into 10 folds, with $A_{z,1}^*, ..., A_{z,10}^*$ denoting validation sets
for $j = 1, ..., 10$ **do**
  for $k = 1, ..., K$ **do**
    Fit $\widehat{\psi}_{k,j}$ on training set $A_{z,-j}^*$ pertaining to $A_{z,j}^*$ ‡
    Let $j(i) = j$ for all $i \in A_{z,j}^*$
  end for
end for
Using $\left\{\widehat{\psi}_{k,j(i)}(W_i), \widehat{D}_i^{(1)}, \widehat{D}_i^{(2)} : i \in A_z^*,\ k \in \{1, ..., K\}\right\}$, obtain optimal $\boldsymbol{\alpha} = (\alpha_1, ..., \alpha_K)$ using package `nloptr`
Repeat steps 3–10 five times to obtain $\boldsymbol{\alpha}^* = \frac{1}{5}\sum_{r=1}^{5} \boldsymbol{\alpha}^{(r)}$
for $k = 1, ..., K$ **do**
  Fit algorithm $\widehat{\psi}_k$ on A_z^* ‡
end for
Let $\widehat{\psi}_{SL}(w) = \sum_{k=1}^{K} \alpha_k^* \widehat{\psi}_k(w)$

Output: $\widehat{\psi}_k(W_i)$, $k = 1, ..., K$, and $\widehat{\psi}_{SL}(W_i)$ for all $i \in A_z^*$

† Following Section 3 in the KwaZulu-Natal risk prediction SAP, `survtmle` is run twice to obtain the individual i-specific quantities $\widehat{D}_i^{(1)}$ and $\widehat{D}_i^{(2)}$, defined as the sum of the point estimate of the marginal survival probability $P(T \in (t_0, t_1])$ and $P(T > t_1)$, respectively, plus the corresponding individual i-specific efficient influence function estimate output by `survtmle`. $\widehat{D}_i^{(1)}$ and $\widehat{D}_i^{(2)}$ are then used to estimate the cross-validated risk, which is minimized with respect to the superlearner weights.

‡ Some data adaptive algorithms such as `glmnet` may require another layer of cross-validation.

Pseudocode for Internal Validation Algorithm

Let A_z denote observed data from participants in treatment stratum z in a single AMP trial.

Algorithm 2 Internal Cross-validation

Input: A_z and $\widehat{\psi}_1, ..., \widehat{\psi}_K$ prediction algorithms

Partition A_z^* into 10 folds, with $A_{z,1}^*, ..., A_{z,10}^*$ denoting validation sets
for $s = 1, ..., 10$ **do**
  Use training set $A_{z,-s}$ to impute $A_{z,-s}^*$ via package `missForest`
  Use package `survtmle` on $A_{z,-s}^*$ to obtain $\widehat{D}_{s,i}^{(1)}$ and $\widehat{D}_{s,i}^{(2)}, \forall i \in A_{z,-s}^*$ †
  Partition $A_{z,-s}^*$ into 10 folds, with $A_{z,-s,1}^*, ..., A_{z,-s,10}^*$ denoting validation sets
  for $j = 1, ..., 10$ **do**
    for $k = 1, ..., K$ **do**
      Fit $\widehat{\psi}_{k,j}$ on training set $A_{z,-s,-j}^*$ pertaining to $A_{z,-s,j}^*$ ‡
      Let $j(i) = j$ for all $i \in A_{z,-s,j}^*$
    end for
  end for
  Using $\left\{\widehat{\psi}_{k,j(i)}(W_i), \widehat{D}_{s,i}^{(1)}, \widehat{D}_{s,i}^{(2)} : i \in A_{z,-s}^*, k \in \{1, ..., K\}\right\}$, obtain optimal $\boldsymbol{\alpha} = (\alpha_1, ..., \alpha_K)$ using package `nloptr`
  Repeat steps 5–12 five times to obtain $\boldsymbol{\alpha}_s^* = \frac{1}{5}\sum_{r=1}^{5} \boldsymbol{\alpha}^{(r)}$
  for $k = 1, ...K$ **do**
    Fit algorithm $\widehat{\psi}_k$ on $A_{z,-s}^*$ ‡
  end for
  Let $\widehat{\psi}_{SL,s}(w) = \sum_{k=1}^{K} \alpha_{s,k}^* \widehat{\psi}_k(w)$
  Let $s(i) = s$ for all $i \in A_{z,s}$
end for
Use A_z to impute A_z^* via package `missForest`
Use package `survtmle` on A_z^* to obtain $\widehat{D}_i^{(1)}$ and $\widehat{D}_i^{(2)}, \forall i \in A_z^*$ †
Compute $\widehat{AUC}_{CV}$ for each $\widehat{\psi}_k$ and $\widehat{\psi}_{SL}$ using $\left\{\widehat{\psi}_{k,s(i)}(W_i), \widehat{\psi}_{SL,s(i)}(W_i), \widehat{D}_i^{(1)}, \widehat{D}_i^{(2)} : i \in A_z^*\right\}$

Output: $\widehat{AUC}_{CV}$ for $\widehat{\psi}_k$, $k = 1, ..., K$, and $\widehat{\psi}_{SL}$ for A_z^*

† Following Section 3 in the KwaZulu-Natal risk prediction SAP, `survtmle` is run twice to obtain the individual i-specific quantities $\widehat{D}_i^{(1)}$ and $\widehat{D}_i^{(2)}$, defined as the sum of the point estimate of the marginal survival probability $P(T \in (t_0, t_1])$ and $P(T > t_1)$, respectively, plus the corresponding individual i-specific efficient influence function estimate output by `survtmle`. $\widehat{D}_i^{(1)}$ and $\widehat{D}_i^{(2)}$ are then used to estimate the cross-validated risk, which is minimized with respect to the superlearner weights.

‡ Some data adaptive algorithms such as `glmnet` may require another layer of cross-validation.

9 Trial Monitoring

The AMP trials are monitored in four ways: (1) feasibility monitoring for retention and adherence to infusions; (2) sequential monitoring of prevention efficacy; (3) monitoring for futility to assess prevention efficacy, defined as an inability to answer the primary efficacy objective in a timely manner; and (4) operational monitoring for other performance standards of quality of trial conduct. Data on these monitoring activities are collated into interim reports and are presented to the independent DSMB every 6 months. While guidelines for trial modifications based on the monitoring operate separately for the two AMP trials, the same multinational DSMB monitors the two trials, facilitating its ability to account for all information when making recommendations. Following each DSMB meeting, the DSMB reports to the Oversight Committee (OC) a summary of the trial review, which may include recommendations to modify or terminate the trial for one or both study cohorts. The following descriptions apply to each trial separately.

9.1 Feasibility Check and Guideline for Continuing Enrollment as Planned

A feasibility monitoring report is developed as soon as approximately and not fewer than 120 enrolled participants have expected follow-up through to the end of the Week 32 visit window. This feasibility monitoring is based on the first four 8-week infusion intervals (Weeks 1 through 32) and evaluates whether an adequately high percentage of participants attend clinical visits and receive the infusions per the protocol.

The guideline is based on an adequately high rate of study participation (participants remain engaged in the trial and have not declined further infusions) supplemented by data on visit attendance, which corresponds to adherence to receipt of infusions.

As stated in the protocol, the following guideline is used for continuing enrollment as planned:

- Continued participation by the Week 32 visit pooled over the three treatment groups is greater than 80%.

If this treatment group-blinded criterion fails to be met, the Protocol Team, in discussions with the DSMB and OC, will discuss whether modification or termination of the trial is warranted.

Here we expand upon the details of the feasibility guideline and on the output included in the feasibility check monitoring report.

Discontinued participation is assessed using multiple event definitions indicating discontinued participation, in order to capture different reasons for discontinuation that have different

impacts on the ability of the trials to meet their primary efficacy objectives. In particular, the following five definitions (with their purposes summarized) will be analyzed:

1. CRF-confirmed permanent discontinuation of study product administration prior to study completion, with discontinuation due to a safety issue or refusal to continue taking infusions. [*Addresses if infusions are too onerous*]

2. The same as Definition 1 except only including discontinuation due to a safety issue [*Addresses if infusions are too onerous due to a safety issue*]

3. The same as Definition 1 except only including discontinuation due to refusal to continue undergoing infusions. [*Addresses if infusions are considered too onerous due to a non-safety reason*]

4. Permanent discontinuation of study product administration for any reason other than a safety issue or refusal to continue taking infusions. This definition includes CRF-confirmed study termination due to lost contact with participant or 20 consecutive weeks without any participant contact. [*Addresses discontinued infusions or loss to follow-up for reasons other than safety or refusal, with no information available on whether the loss was related to infusions being onerous*]

5. The first event of Definitions 1 and 4 [*Addresses discontinued infusions for any reason including loss to follow-up*]

Definition 1 aims to measure discontinued participation due to the infusion process being too onerous, which could occur either because of a safety issue or because of refusal to continue receive infusions. Definitions 2 and 3 measure discontinued participation due to the two component events comprising Definition 1 (safety and refusal, respectively), thereby isolating two reasons for discontinued infusions. These types of discontinued participation are the most serious in that a high rate would indicate an infeasibility of the VRC01 intervention, and therefore Definitions 1, 2, 3 are the most important for measuring feasibility of the intervention. As such the 80% feasibility guideline is interpreted primarily for Definition 1.

Definition 4 measures discontinued participation due to reasons other than safety or refusal including loss to follow-up, which is based on either CRF-confirmed loss or an operational definition of a loss to follow-up event not captured on a CRF. Given that loss to follow-up is expected to frequently occur for reasons different from the infusion process being too onerous (i.e., for reasons that would occur in efficacy trials of other HIV prevention interventions, such as moving), this type of discontinued participation is less serious, where the study could still be made feasible under moderate rates of loss to follow-up, by enrolling additional study participants.

Definition 5 counts as discontinued participation any reason for discontinuation or loss to follow-up, whichever occurs first. Thus this definition measures permanent ceasing of infusions without distinguishing the reason.

For each definition of discontinued participation, the analysis counts discontinued participation events. First, we define discontinued participation as a record on a CRF confirming permanent discontinuation of study product administration prior to study completion, with discontinued participation by Week 32 defined as this date occurring before or on the Week 32 visit date, or, if the visit was not yet attended, before or on the date defining the end of the Week 32 visit window. For Definition 5, the Kaplan-Meier estimator will be used to estimate and display the probability of discontinued participation over time, starting at study entry through to the time period during which data are available (which will extend at least through the Week 32 visit window). For all other definitions, a competing risks failure time analysis is used that studies the time until the first event of a type specified in a given definition. For these competing risks analyses a participants follow-up is right-censored by the occurrence of another discontinuation event type that is not included in the definition under consideration. For these competing risks analyses each time-to-event curve is estimated using the Aalen-Johansen estimator, which in particular yields an estimate of the probability of discontinuation due to the event type by the Week 32 visit. For Definition 1 right-censoring is by loss to follow-up (using the operational Definition 4); for Definition 2 right-censoring is by loss to follow-up (using the operational Definition 4) and by discontinuation due to refusal; for Definition 3 right-censoring is by loss to follow-up (using the operational Definition 4) and by discontinuation due to a safety issue; and for Definition 4 right-censoring is by discontinuation due to Definition 1 (a safety issue or refusal).

Appendix A includes mock tables on expected versus observed visit attendance (Table 5A) and on infusion adherence (Table 5B) patterns that will be reported at the 6-monthly DSMB meetings. All of this output will be included in the feasibility check monitoring report, focusing on the first five infusion visits (Week 0, 8, 16, 24, 32).

9.2 Sequential Monitoring of Prevention Efficacy for Potential Harm, Non-Efficacy, and High Efficacy

For each trial, PE is monitored by the independent DSMB at each DSMB meeting, with triggers based on numbers of primary HIV-1 infection endpoints for when the DSMB meetings begin to include formal evaluation of the potential harm, non-efficacy, and high efficacy stopping boundaries (these triggers are described below). The approach to sequential monitoring of PE is similar to that described in Gilbert, Grove et al. (2011). The monitoring of PE in the AMP trials is also similar to that used for the HVTN 505 phase 2b HIV-1 vaccine efficacy trial (Hammer et al., 2013). Each of the AMP trials uses sequential monitoring of the pooled mAb groups versus control to stop early for:

- potential harm [establish that PE (pooled over the mAb groups) $< 0\%$ based on a 2-sided monitoring-adjusted 90% confidence interval lying below 0%]
- non-efficacy [establish that PE (pooled over the mAb groups) $< 40\%$ based on a 2-sided 95% nominal confidence interval lying below 40%]

Table 3: Summary of sequential monitoring of PE for each AMP trial

Monitoring Type	Hypotheses	Testing Approach	Size/ Power	Monitoring Plan	Number of Interim Analyses
Potential Harm	$H_0 : PE \geq 0\%$ vs. $H_1 : PE < 0\%$	Exact 1-sided binomial test of the proportion of infections assigned to a mAb group	1-sided $\alpha = 0.05$	Near-constant* 1-sided p-value cut-off controlling the FWER at $\alpha = 0.05$	After every infection from 20^{th} total until first non-efficacy analysis
Non-Efficacy	$H_0 : PE \geq 40\%$ vs. $H_1 : PE < 40\%$	Wald test	1-sided $\alpha = 0.025$	Nominal 2-sided 95% CI supplemented with conditional power	6-monthly starting after at least 45 but no more than 67 total infections†
High Efficacy	$H_0 : PE \leq 70\%$ vs. $H_1 : PE > 70\%$	Wald test	1-sided $\alpha = 0.025$	Nominal 2-sided 95% CI	6-monthly starting at the same time as for non-efficacy

*An increasing per-test alpha until a constant level is reached that, if applied to all subsequent tests, maintains the specified FWER

†The first non-efficacy/high efficacy interim analysis occurs either at the scheduled DSMB meeting at which there are 45 or more primary endpoint events across the three study groups or when 67 total primary endpoint events are observed, whichever occurs earlier.

- high efficacy [establish that PE (pooled over the mAb groups) $> 70\%$ based on a 2-sided 95% nominal confidence interval lying above 70%].

The sequential monitoring for non-efficacy and high-efficacy is based on 2-sided 95% confidence intervals in order that the result of the study that would be reported in the abstract of a journal article would convey convincing evidence supporting the conclusion of non-efficacy or high efficacy. Freidlin, Korn, and Gray (2010) discuss a rationale for this approach to non-efficacy monitoring. The sequential monitoring for potential harm is based on 2-sided 90% confidence intervals for prudence to protect the safety of study participants, i.e., less precision is required to meet a guideline for potential harm than to meet guidelines about non-efficacy or high efficacy. The sequential monitoring plan for each AMP trial is summarized in Table 3.

The potential harm monitoring is done after every primary endpoint event starting at the 20^{th} total pooled over the three treatment groups, through to the time at which the non-efficacy/high efficacy monitoring commences. Once the non-efficacy/high efficacy monitoring begins, the non-efficacy monitoring serves the purpose of detecting a harmful effect of the mAb to elevate the endpoint rate compared to control. The details of the procedures used for the three monitoring guidelines are described next. In addition to these monitoring guidelines that are based on parameters aggregating all primary HIV-1 infection events over follow-up,

the statistical reports including non-efficacy/high efficacy monitoring will also graphically report estimates of cumulative HIV-1 incidence over time by study arm and estimates of cumulative prevention efficacy over time for high dose vs. placebo and for low dose vs. placebo.

9.2.1 Potential harm monitoring

Heyse et al. (2008) and the HVTN 505 phase 2b HIV-1 vaccine efficacy trial (Hammer et al., 2013) are examples of randomized, placebo-controlled efficacy trials that used continuous monitoring for an elevation in the endpoint rate in the active versus control treatment arm. Continuous monitoring means that an unblinded statistician has visibility to the treatment assignment of each diagnosed MITT HIV-1 infection as they are determined in real-time, and, after each confirmed HIV-1 infection diagnosis, this statistician notes whether a stopping boundary is reached that indicates that the relative cumulative rate of HIV-1 infection (RR, pooled mAb group/control) exceeds one. If the stopping boundary is met, then the unblinded statistician immediately informs the Chair of the DSMB and the Executive Secretary of the DSMB through secure communication procedures. As such, the potential harm monitoring is in real-time, with a result possible at any time, whereas in contrast the non-efficacy and high efficacy monitoring is conducted only at the 6-monthly scheduled DSMB meetings or at any extra DSMB meetings requested by the DSMB (with exception that the first non-efficacy analysis would be done and reported to the DSMB by secure means prior to a scheduled DSMB meeting if the 67^{th} total primary endpoint event occurs prior to a non-efficacy analysis triggered by at least 45 endpoints by a scheduled DSMB meeting, as described in Table 3).

The potential harm monitoring is done using an exact one-sided binomial test of the null hypothesis $H_0 : p \leq 2/3$ versus the alternative hypothesis $H_1 : p > 2/3$, where p is the probability that an HIV-1-infected participant was assigned to either of the two mAb groups (as compared to being assigned to the control group). The tests start at the 20^{th} total infection through to the infection count at which the non-efficacy/high efficacy monitoring commences, which is a minimum of 45 and is a random variable that depends on the timing of DSMB meetings (this value is referred to as the $n^{*\text{th}}$ infection). Based on protocol projections we assume that n^* is at most 67, which is useful for setting the critical values of the test. (If the highly unlikely result occurs that n^* exceeds 67, then the first non-efficacy analysis would be conducted based on 67 infections, which would serve the purpose of potential harm monitoring. The number 67 is chosen because that is the infection count at which a point estimate of zero PE would just correspond to an upper nominal 95% confidence bound for PE equal to 0.40; this approach to starting non-efficacy monitoring was suggested by Freidlin, Korn, and Gray (2010).) Each test is performed at a prespecified nominal/unadjusted alpha-level, which may vary over the multiple tests. The alpha-level used for each test is determined indirectly as follows: we must first choose the overall type I error rate we are willing to accept over the course of the monitoring (the overall probability that we reach a stopping boundary during the trial, when the mAb is actually safe, i.e., true $RR = 1$, equivalently $p = 2/3$); and secondly we must choose whether/how to vary the alpha-level from test-to-test. Using

Table 4: Potential harm monitoring stopping boundaries for each AMP trial: One-sided p-value cut-offs for rejecting $H_0 : p \leq 2/3$ in favor of $H_1 : p > 2/3$ with an exact 1-sided binomial test where p is the probability that an HIV-1-infected participant was assigned to one of the two mAb groups

No. of Infections in VRC01 Groups	No. of Infections in Control Groups	Per-Test Type I Error Rate (1-Sided P-value Cut-off)
20	0	0.003
20	1	0.013
20	2	0.018
22	3	0.018
25	4	0.018
28	5	0.018
31	6	0.018
34	7	0.018
37	8	0.018
40	9	0.018
43	10	0.018
45	11	0.018
48	12	0.018
54	13	0.018

these pieces of information we determine the exact alpha-levels to be used for each test.

An overall 1-sided type I error rate of 0.05 is chosen for the family-wise error rate of the multiple hypothesis tests starting at the 20^{th} HIV-1 infection endpoint through to the 67^{th}. This type I error rate is chosen to balance the competing goals of participant safety and preventing false positive results. To prevent stopping too early, perhaps due to spurious results caused by wide sampling variability, stopping prior to the accumulation of 20 total infections was ruled out (the 2:1 mAb:control allocation ratio leads to this choice; in contrast a 1:1 allocation ratio would lead to starting at about 12 total infections). Table 4 shows the potential harm stopping boundaries in terms of the one-sided p-value cut-offs for a selected set of potential harm interim analyses starting at the 20^{th} HIV-1 infection event.

9.2.2 Non-efficacy monitoring

For each AMP trial, the first non-efficacy analysis will be reported to the DSMB at the first scheduled 6-monthly meeting at which at least a total of 45 HIV-1 infection endpoints have occurred, combined over the three study groups. The analysis is based on all HIV-1 infection endpoints up until the time of data lock, and if this number exceeds 67, then the first non-efficacy analysis would be done based on 67 events and the report provided to the

DSMB by secure means prior to the scheduled DSMB meeting (as noted above).

At each non-efficacy interim analysis PE is estimated with a 2-sided 95% nominal confidence interval using the same method as for the final analysis of PE described in Section 8.1. Cumulative prevention efficacy through time t, $PE(t)$, will be estimated at time point t chosen to be the latest possible time point when stable estimation with follow-up data through the Week 80 visit (or earlier if necessary) can be achieved; this is operationalized by defining t as the maximum time point when 150 participants are observed to be at risk for the primary endpoint in each of the placebo and pooled VRC01 groups. The timepoint t will be chosen for evaluation of whether the stopping boundary is crossed or not. All times-to-event will be right-censored at the Week 80 visit or earlier following the operational rules summarized in Table 1. As stated in Table 3, the non-efficacy stopping boundary is defined by the 2-sided upper 95% confidence limit for PE being at 40%, where the 95% CI lying below 40% with the lower 95% confidence limit lying below 0% constitutes meeting the guideline for non-efficacy.

The 2-sided 95% confidence intervals for PE, estimated in the same way as described for the final analysis, are reported for sequential monitoring of PE at every DSMB meeting through to the end of the trial.

In addition, a supplemental analysis will estimate the proportional-hazards PE parameter (defined in (3)) with a 2-sided 95% confidence interval and a two-sided p-value for whether proportional-hazards PE differs from unity, following the same statistical procedures described for the final analysis plan (see Section 8.2).

9.2.2.1 Unblinded conditional power assessment at an interim analysis

Interim monitoring of PE for non-efficacy will be supplemented with an unblinded conditional power assessment using the actual observed control-group incidence, and the following levels of PE in the future data are assumed: $PE = 0\%$, $PE = \widehat{PE}$ in the observed data, and $PE = 60\%$.

9.2.2.2 Estimated prevention efficacy by measured VRC01 neutralization sensitivity

The analyses specified in Section 8.3.1 will be reported at interim analyses that included non-efficacy monitoring.

9.2.3 High efficacy monitoring

The 2-sided 95% confidence interval for PE used for non-efficacy monitoring is also used for high efficacy monitoring, where it is compared to PE = 70% instead of PE = 40% as a

stopping boundary. High-efficacy monitoring is conducted at each interim analysis at which non-efficacy analysis is conducted.

9.2.4 Rationale for starting non-efficacy/high efficacy monitoring at at least 45 total infections

Freidlin, Korn, and Gray (2010) suggested beginning non-efficacy monitoring as soon as a point estimate of PE equal to zero would correspond to the nominal 95% confidence interval of a hazard ratio based efficacy parameter under a Cox proportional hazards model just barely ruling out the design alternative (PE = 40% in the AMP trials). This approach implies starting the non-efficacy monitoring at the 67^{th} total infection in each AMP trial. However, based on protocol projections of accrual and incidence, between about 60 and 100 total HIV-1 infection events are expected in each trial, for PE varying over the range 0% to 60%. Therefore it would not be unlikely that no non-efficacy interim analysis would occur if the Freidlin, Korn, and Gray (2010) recommendation were strictly followed. Moreover, a high efficacy analysis would not occur, as its timing is synchronized to the non-efficacy monitoring timing, which could be problematic if the PE is very high. Accordingly, the monitoring starts at at least 45 infections, which is judged to be large enough to have reasonable precision and small enough to make it likely that some non-efficacy/high efficacy interim analyses would occur during the trial. Note that if the first non-efficacy interim analysis occurred at 45 total infections, then stopping for non-efficacy, which would occur if the nominal 2-sided 95% confidence interval lies below 40%, would correspond to a negative PE estimate. This is an advantageous property in that a result of early non-efficacy would be an unambiguous result about absence of prevention efficacy.

9.3 Monitoring of the Use of PrEP

The use of oral FTC/TDF as PrEP (either off-study or provided in the study) may impact study outcomes (e.g., by lowering HIV-1 incidence rendering a loss of study power). Dried blood spot (DBS) samples will be used for assessment of quantitative concentrations of intracellular TFV-DP.

Prevalence of oral FTC/TDF will be reported both as any detectable use and estimated effective use. Estimated percentages of person-years at-risk during any detectable FTC/TDF use and during inferred effective FTC/TDF use will be reported. We summarize how inferred effective use is measured. Current knowledge about PrEP in MSM indicates consistent use of at least 4 doses a week is required to achieve substantial levels of protection. The lower quartile of simulated tenofovir diphosphate (TFV-DP) levels in DBS at 4 doses per week is 719 fmol/punch (Castillo-Mancilla et al., 2013). In iPrEx OLE, the protective levels of TFV-DP in DBS were quantified as 700 fmol/punch (Grant et al., 2014), that is, there were no infections at visits where TFV-DP concentration was 700 fmol per punch or greater. Current knowledge about PrEP in women indicates consistent use of 6–7 doses a week is required to

achieve protection. The lower quartile of simulated TFV-DP levels in DBS at 6 doses per week is 1064 fmol/punch (Castillo-Mancilla et al., 2013). In the HVTN 704/HPTN 085 study we will use 700 fmol/punch as the cut-off to define effective PrEP use based on the lower quartile cited above. For the HVTN 703/HPTN 081 study we will use 1,000 fmol/punch since current knowledge suggests that at least 6 doses of PrEP per week is required for effective PrEP use in women based similarly on the lower quartile. Ongoing work with calibration of DBS from directly observed dosing studies may refine these thresholds. PrEP use measures will be reported by arm to the DSMB; in addition both the OC and the protocol team leadership will see pooled estimates of FTC/TDF use.

HVTN 704/HPTN 085 collects and stores DBS samples at every study visit, whereas HVTN 703/HPTN 081 collects and stores DBS samples at pre-specified DBS sample collection days. The sample collection days can vary by study site; however, it is expected that the collection days will occur once per month. Furthermore, in order to tune the precision of PrEP use estimation, the frequency of collection may be increased. While the storage and collection differs by protocol, the selection of stored samples to assay will be similar. We refer to the method of selecting participant samples for assaying DBS samples for prospective monitoring of PrEP as the DBS sampling plan.

At a given calendar time T (e.g., a fixed date prior to a scheduled DSMB meeting), we are interested in the population-level parameter, percent person-years at-risk for HIV on effective PrEP use between initiation of DBS storage, and time T. Definition of this parameter makes the assumption that we have an assay readout from stored samples that accurately measures effective PrEP use as a binary outcome at the time the sample was drawn; importantly it does not require an accurate measurement of effective PrEP use the day before or for any period of time earlier than the sampling day. In addition to estimating percent person-years on effective PrEP use we define a similar parameter, percent person-years exposed to detectable PrEP using the lower limit of quantitation (LLOQ) of the DBS assay.

Define the target parameter of interest as

$$\Phi(T) = \frac{\int_{T_0}^{T} p(t)E[Y(t)]dt}{\int_{T_0}^{T} E[Y(t)]dt}$$

where T_0 is the time since the first person enrolled after DBS storage commenced, $p(t)$ is the percent of participants on effective PrEP use at time $t \in [T_0, T]$, and $E[Y(t)]$ is the expected number of participants with DBS storage at-risk for HIV at time t.

We estimate $\Phi(T)$ based on the binary PrEP use readout from the DBS assay and the DBS sampling plan. Let i ranging from 1 to N index study participants and let j ranging from 1 to M_i index participant serum collection dates that are sampled for assaying. For each sample collected, we have an indicator x_{ij} of effective PrEP use which is only measured if the DBS sampling indicator, Δ_{ij}, is equal to 1. The estimated percent person-years on effective

Table 5: Estimated rates of PrEP use and estimated percent person-years on effective PrEP use

Number of DBS specimens collected over the 1st batch period	N_1
Number of DBS specimens assayed over the 1st batch period	N_2
Proportion of assayed specimens with TFV-DP above LLOQ (95% CI)	N_3/N_2 (x.xx, x.xx)
Proportion of assayed specimens with TFV-DP above effective use threshold* (95% CI)	N_4/N_2 (x.xx, x.xx)
Percent person years on detectable PrEP through date T=xx (95% CI)#	$\widehat{\Phi}(T)_d$ (x.xx, x.xx)
Percent person years on effective PrEP through date T=xx (95% CI)#	$\widehat{\Phi}(T)_e$ (x.xx, x.xx)
Repeat through Nth batch period	

*threshold defined by study (700 fmol/punch MSM+TG, 1000 fmol/punch sub-Saharan African Women)
#$\widehat{\Phi}(T)_d$ is an estimate of the target parameter of interest based on measured TFV-DP above the LLOQ. Similarly, $\widehat{\Phi}(T)_e$ is based on TFV-DP above the study specific threshold for effective PrEP use.

PrEP use from the initiation of PrEP monitoring time T_0 until time T is defined as

$$\widehat{\Phi}(T) = \frac{\Sigma_{i=1}^{N}\Sigma_{j=1}^{M_i}\Delta_{ij}x_{ij}\pi_{ij}^{-1}P_{ij}}{\Sigma_{i=1}^{N}\Sigma_{j=1}^{M_i}P_{ij}}$$

where the sampling probability, π_{ij}, and person-years, P_{ij}, are defined below.

Let k ranging from 1 to K index the DBS sampling plan collection intervals $[T_0, T_1]$, $(T_1, T_2]$, ..., $(T_{K-1}, T_K]$ where the right endpoint of each interval is a sample collection date (with $T_K \equiv T$) and define $\mathcal{T}_k$ as the k^{th} interval. Let $t_{i1} < t_{i2} < \ldots < t_{iM_i}$ be the sampling times in $[T_0, T]$ for the i^{th} participant and define t_{i0} as the maximum of T_0 and the i^{th} participants enrollment time. The DBS sampling plan determines which samples, collectively across participants, will be assayed for PrEP use. Define the set of samples, S_{ij}, as all samples collected during the same collection interval $\mathcal{T}_k$ as the sample i, j. That is, $S_{ij} \equiv \{i', j' | t_{i'j'} \in \mathcal{T}_k \text{ for } k \text{ s.t. } t_{ij} \in \mathcal{T}_k\}$. Define the sampling probability as

$$\pi_{ij} \equiv \frac{\Sigma_{i',j' \in S_{ij}}\Delta_{i'j'}}{|S_{ij}|}$$

where $|S_{ij}|$ is the number of samples in set S_{ij}. Define person-years, P_{ij}, as $t_{ij} - t_{i(j-1)}$. Note that our parameter of interest can be defined and estimated for the entire study cohort, as well as for sub-regions (e.g., North America for the HVTN 704/HPTN 085 study). We will report bootstrap 95% confidence intervals for $\Phi(T)$.

The same approach is used for point and confidence interval estimation of the percent person-years exposed to detectable PrEP use.

An example of PrEP use report statistics are shown in Table 5.

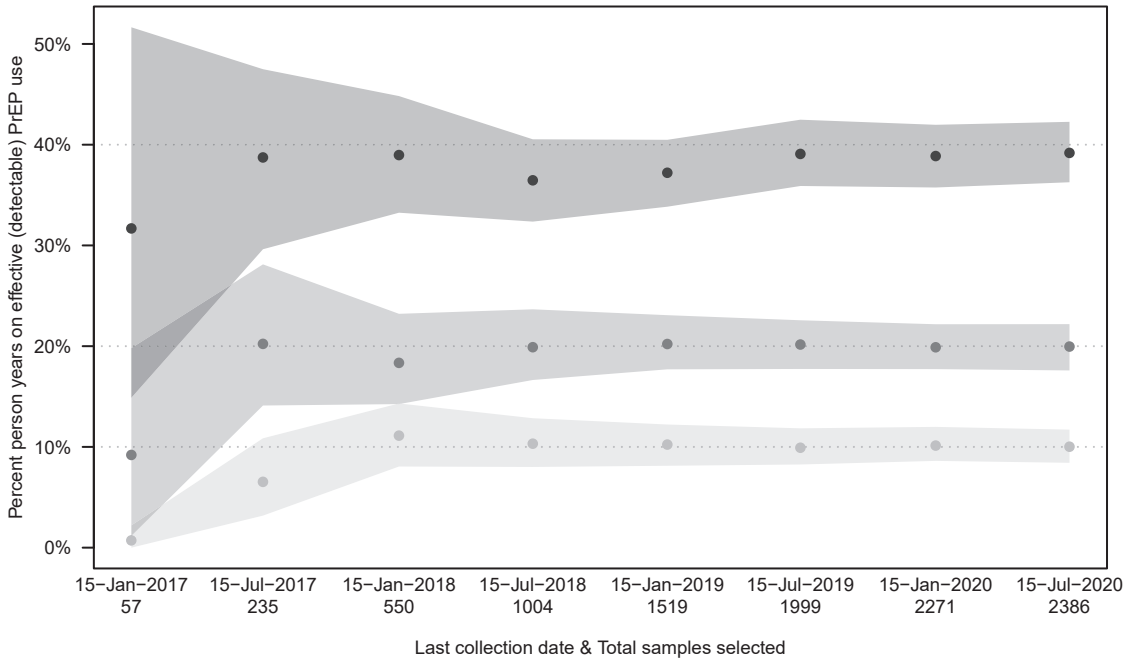

Figure 1: PrEP use Monitoring under three PrEP use scenarios (40%, 20% and 10% per person year) in the HVTN704/085 trial. For 6-monthly intervals shown on the x-axis all samples assayed to date are used to estimate PrEP use prevalence from the beginning of monitoring until that time using the estimator described in Section 8.4. Below each date is the total number of samples that would be assayed according to the simulation study. Estimates are shown as a dots of varying color intensity corresponding to the three PrEP use scenarios. Corresponding color bands are used to show the 95% bootstrap confidence interval for each estimate.

9.3.1 Simulation Study for PrEP Monitoring

A simulation study was conducted to help determine the number of DBS samples that should be collected and assayed a simulation study was run. For a simulated AMP trial, the PrEP monitoring plan was implemented based on the following assumptions: 1) Enrollment falls randomly between Monday and Friday; 2) Follow-up visits follow the visit schedule exactly; 3) Missed visits are distributed uniformly at a rate of 10%; 4) Dropout is 10% per person year based on an exponential distribution; 5) HIV-infection is 3% for HVTN 704/HPTN 085 (or 5.5% for HVTN 703/HPTN 081) per person year based on an exponential distribution; and, 6) Initiation of DBS sample collection begins as of November 1, 2016 in both protocols. PrEP use was simulated at various constant rates among trial participants and participants are assumed to be either on (or off) PrEP during the entire trial. Simulation results for each trial are presented for the number of samples collected spaced at 6 month intervals. The

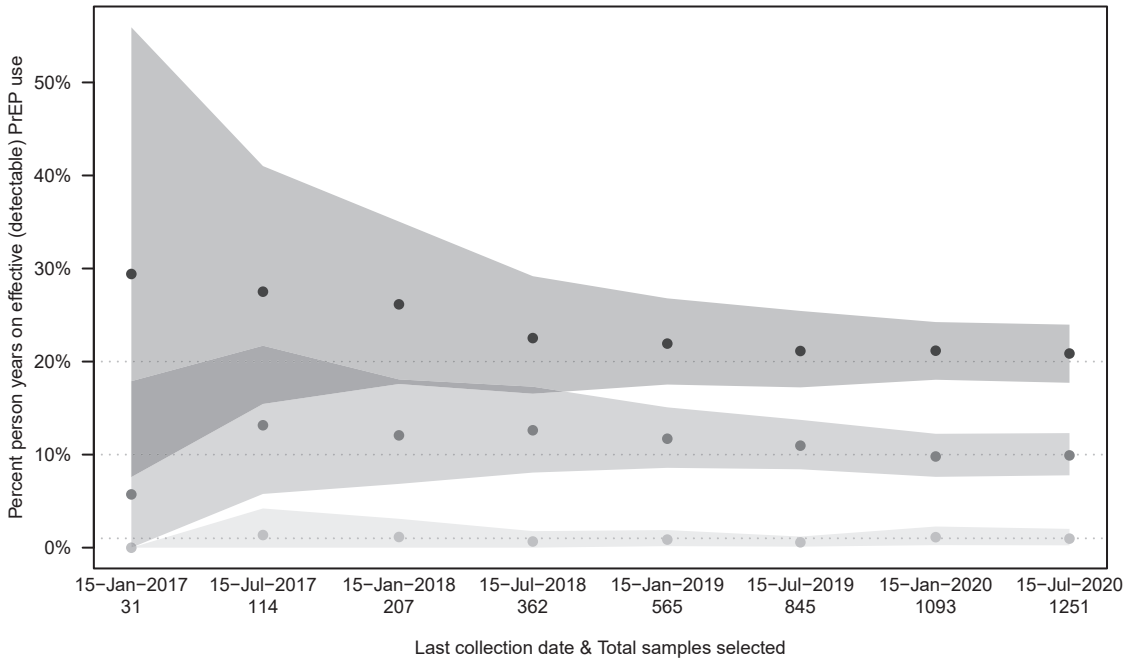

Figure 2: PrEP use Monitoring under three PrEP use scenarios (20%, 10% and 1% per person year) in the HVTN703/081 trial. For 6-monthly intervals shown on the x-axis all samples assayed to date are used to estimate PrEP use prevalence from the beginning of monitoring until that time using the estimator described in Section 8.4. Below each date is the total number of samples that would be assayed according to the simulation study. Estimates are shown as a dots of varying color intensity corresponding to the three PrEP use scenarios. Corresponding color bands are used to show the 95% bootstrap confidence interval for each estimate.

intervals are spaced such that the last collection time point is approximately 3.5 months prior to the next DSMB meeting to allow the intracellular TFV-DP assay to be run and a report generated. In this simulation, all samples collected per protocol HVTN703/HPTN081 version 2.0 would be assayed. For the HVTN704/HPTN085 trial, all samples collected the clinic business day closest to the 15^{th} of each month would be assayed. Simulation results are shown in Figures 2 and 1.

The simulation study results show that by the time 200 samples have been selected the confidence intervals around the estimate of PrEP use are reasonably tight and by the time 500 samples have been selected the extra gain in precision as more samples are assayed becomes limited. However, continuing to assay samples over the course of the trial will allow estimation of temporal trends in PrEP use. The simulation also shows that when PrEP prevalence is very low the bootstrap confidence interval is unlikely to provide proper

coverage.

9.4 Monitoring for Futility to Assess Prevention Efficacy

The objective of monitoring the trial for futility to assess PE is to monitor progress toward the minimal needed target number of treatment arm-pooled HIV-1 primary endpoint infections by the Week 80 visit in the MITT cohort. Two targets are monitored for:

1. the total number of HIV-1 infections needed to achieve the planned 90% power to detect PE = 60%, and
2. the total number of HIV-1 infections needed to achieve 50% power to detect PE = 60%,

each using a 1-sided 0.025-level Wald test of $H_0 : PE \leq 0\%$ against $H_1 : PE > 0\%$, assuming proportional hazards of HIV-1 infection in the pooled VRC01 and control groups. The target numbers in 1. and 2. are 57 and 21, respectively (calculated by solving equation (1) in Schoenfeld (1983)). The rationale for considering the two targets is as follows: (i) if the trial cannot achieve the planned 90% power to detect PE = 60%, considerations about enrollment modification or expansion are warranted, and (ii) if the trial cannot achieve even 50% power to detect PE = 60%, considerations about completing the trial early for futility to assess PE are warranted.

Two versions of the futility monitoring report will be generated. A report provided to the DSMB will be included in 6-monthly closed DSMB reports, starting in November 2017 for HVTN 703/HPTN 081 and in April 2018 for HVTN 704/HPTN 085, and will report:

(a) the estimated distribution of the total (i.e., treatment arm-pooled) number of HIV-1 infections, with corresponding power to reject $H_0 : PE \leq 0\%$ using a 1-sided 0.025-level Wald test under the alternative hypothesis $PE = 60\%$ throughout the trial,

(b) the estimated probability that the total number of HIV-1 infections is ≥ 57 (target 1) with 95% credible intervals,

(c) the estimated probability that the total number of HIV-1 infections is ≥ 21 (target 2) with 95% credible intervals,

(d) the estimated distribution of the number of HIV-1 infections in each of the three treatment arms.

The distributions in (a) and (d) will also be summarized by the mean number of HIV-1 infections with a Wald 95% confidence interval. The estimation procedures for (a)–(d) will be conducted under each of the following three scenarios:

(i) the treatment arm-pooled infection rate in (a)–(c) and the three treatment arm-specific infection rates in (d) used for generating future data are based on a Bayesian model and the prior assumption that $PE = 60\%$ (the design alternative),

(ii) the treatment arm-pooled infection rate in (a)–(c) and the three treatment arm-specific infection rates in (d) used for generating future data are based on a Bayesian model and the prior assumption that $PE = 0\%$ (the null hypothesis), and

(iii) the treatment arm-pooled infection rate in (a)–(c) used for generating future data is based on a Bayesian model and the prior assumption that the infection rate equals the observed to-date infection rate.

The reason for conducting the estimation procedure under (i)–(iii) is that the purpose of the results for the 57 endpoint target (b) is to trigger considerations about enrollment modifications, whereas the purpose of the results for the 21 endpoint target (c) is to trigger considerations about early trial completion due to futility, where it is desired to reach a guideline based on (b) more easily/readily than a guideline based on (c). Accordingly, the results for (b) are interpreted focusing on the prior of PE = 60% (i.e., scenario (i)), which makes it more likely to reach a guideline than the prior of PE = 0%, and the results for (c) are interpreted focusing on the prior of $PE = 0\%$ (i.e., scenario (ii)), which makes it less likely to reach a guideline than the prior of $PE = 60\%$. Results for (b) and (c) based on carrying forward the observed to-date infection rate in scenario (iii) provide additional guidance to the DSMB regarding considerations about enrollment modification or early trial completion.

Furthermore, a treatment-blinded report will be generated for distribution to the Leadership Group before each DSMB meeting takes place and will report estimates listed in (a)–(c) above calculated based only on treatment-blinded data in scenarios (i)–(iii). The reported results pertaining to estimates (a)–(c) under scenarios (i)–(iii) will be identical to those in the DSMB report.

While it is the primary responsibility of the Leadership Group to make decisions regarding trial operations and modifications based on the monitoring of treatment-blinded primary endpoints, given the resource issues involved, DSMB review is also needed because issues of scientific integrity are also involved. More specifically, the DSMB can evaluate the progress toward primary endpoint targets in the context of the treatment-unblinded data, and based on this review may recommend to the Leadership Group to complete the trial early due to reaching a guideline for futility to assess PE (specified below).

The monitoring for futility to assess PE includes the following guidelines for trial modifications:

- **Guideline for enrollment modifications.** If, in the $PE = 60\%$ scenario for the prior distribution in (i), the estimated probability of reaching at least 57 total infections is less than 25%, the Leadership Group may consider enrollment modifications with the intention to be able to conduct the primary PE analysis with adequate power.

- **Guideline for futility.** If, in the PE = 0% scenario for the prior distribution in (ii), the estimated probability of reaching at least 21 total infections is less than 25%, the DSMB may recommend completing the trial early based on the inability to conduct the primary PE analysis with adequate power. However, since this is a proof-of-concept trial, a high bar is desired for completing the trial early for futility, and therefore if this event occurs yet the non-efficacy monitoring has not started or the non-efficacy boundary has not been reached, then this guideline for futility also requires that the estimated PE for the pooled VRC01 vs. control arm is $< 30\%$ and the estimated PE for the VRC01 30 mg/kg vs. control arm is $< 30\%$.

If enrollment is incomplete at the time of an interim futility analysis, then the outlined estimation procedures will use the average observed enrollment rate in approximately the last 6 months for generating future enrollment data. A Bayesian approach will be used for generating future HIV-1 incidence data, conditional on observed data to-date. More specifically, the estimates in (a)–(c) will condition on the observed to-date treatment arm-pooled HIV-1 incidence rate, whereas the estimates in (d) will condition on the three observed to-date treatment arm-specific HIV-1 incidence rates. All estimates in (a)–(d) will also use the observed to-date treatment arm-pooled dropout rate for generating future dropout data. Further details of these calculations, including the prior distributions, are described in Section 9.4.1.

If, at any time, these guidelines for futility to assess PE are met and yet it appears that value exists in continuing the trial, the statisticians will provide the DSMB and the Leadership Group with additional information, as appropriate, for use in their consideration of whether to recommend early trial completion.

9.4.1 Estimation of the number of HIV-1 infection endpoints at an interim analysis

The method for estimating the probability distribution of the number of HIV-1 infection endpoints by the Week 80 visit is based on the following approach to simulating this trial. The trial is modeled as a combination of three processes—enrollment, dropout, and HIV-1 infection—and a large number of trials is simulated. The three processes are assumed to be independent, and their distributions are taken to be Poisson, exponential, and exponential, respectively. Data are generated at the level of the individual participant, such that, for each participant, we obtain an enrollment time, an (underlying true) infection time, and a dropout time. Only the minimum of the infection and dropout times is observable, and the average value for this minimum is beyond the duration of the trial, such that neither event will be observed for most participants.

In the absence of observed trial data, the treatment arm-pooled as well as the treatment arm-specific parameters for the infection and dropout processes are chosen to match our pre-trial assumptions about these rates. In addition, the infection rate considers both the

design alternative of $PE = 60\%$ and the null hypothesis of $PE = 0\%$ in the calculation of the total and treatment arm-specific numbers of endpoints. More specifically, in HVTN 704/HPTN 085, treatment arm-pooled calculations in (a)–(c) assume

- pooled infection rate ($PE = 60\%$ scenario): $(1/3) \times 0.03 + (2/3) \times 0.4 \times 0.03 = 0.018$ infections/person-year at-risk, and
- pooled infection rate ($PE = 0\%$ scenario): 0.03 infections/person-year at-risk,

and, in HVTN 703/HPTN 081,

- pooled infection rate ($PE = 60\%$ scenario): $(1/3) \times 0.055 + (2/3) \times 0.4 \times 0.055 = 0.033$ infections/person-year at-risk, and
- pooled infection rate ($PE = 0\%$ scenario): 0.055 infections/person-year at-risk.

Both trials assume a treatment arm-pooled dropout rate of 0.10 dropouts/person-year at-risk.

In HVTN 704/HPTN 085, treatment arm-specific calculations in (d) assume

- infection rate in the control arm: 0.03 infections/person-year at-risk,
- infection rate in each VRC01 arm ($PE = 60\%$ scenario): $0.4 \times 0.03 = 0.012$ infections/person-year at-risk, and
- infection rate in each VRC01 arm ($PE = 0\%$ scenario): 0.03 infections/person-year at-risk,

and, in HVTN 703/HPTN 081,

- infection rate in the control arm: 0.055 infections/person-year at-risk,
- infection rate in each VRC01 arm ($PE = 60\%$ scenario): $0.4 \times 0.055 = 0.022$ infections/person-year at-risk, and
- infection rate in each VRC01 arm ($PE = 0\%$ scenario): 0.055 infections/person-year at-risk.

In the absence of observed data, in both trials and each of the three treatment arms, the dropout rate is assumed to be 0.10 dropouts/person-year at-risk.

The first step in simulating each trial is to enroll a certain number of participants per week according to a random draw from a Poisson distribution with rate parameter as listed above. Enrollment continues week-by-week until a total of 2700 participants in HVTN

704/HPTN 085 or 1900 participants in HVTN 703/HPTN 081 is reached. Second, each participant is assigned an exact enrollment day, uniformly distributed within their enrollment week. Following enrollment, the infection and dropout times are drawn from their respective exponential distributions, and the lesser of the two is recorded as occurring at the given time (possibly outside the time-window of the trial). We consider dropout events to have occurred at the dropout time (in weeks) that was generated (assuming it was less than the infection time). For participants who become HIV-1 infected, we record their time of diagnosis as the time of the first study visit following the true infection time. It is this time of diagnosis that we observe for infected participants.

A modification of the above procedure for simulating an efficacy trial is used for estimating metrics of futility to assess PE at a given interim analysis. The modification entails using the observed trial data to estimate parameters of the processes, rather than relying entirely on pre-trial assumptions. In particular:

- enrollment rate: if enrollment is incomplete, estimated based on the treatment arm-pooled rate observed in approximately the last 6 months in the study,
- infection rate: drawn from a posterior distribution of the infection rate formed by combining the observed data with our prior specification about the infection rate based on the pre-trial assumptions, and
- dropout rate: estimated based on the treatment arm-pooled rate observed to date.

The rationale for a Bayesian approach for the infection rate (see Section 9.4.2 for details) is to help stabilize the infection rate early in the trial when insufficient time will have passed to accrue many infections. If we were to rely solely on the observed infections, we might by chance obtain very low rates, which would lead to an unrealistic prediction of the number of endpoints.

We consider three different gamma prior distributions for the infection rate in each of scenarios (i)–(iii) reflecting different weights assigned to the prior distribution (see Section 9.4.2 for details). Gamma distributions are considered because they are conjugate to the exponential distribution used for generating future infection data.

At a given interim analysis, 10^5 trials are simulated using the above procedure and treatment arm-pooled infection and dropout rates for estimates in (a)–(c). Separately, another set of 10^5 trials is simulated using the above procedure, treatment arm-specific infection rates, and the treatment arm-pooled dropout rate for estimates in (d). Each of these trials yields a projected number of infections by the Week 80 visit. These projected numbers of infections from each trial will be used to estimate the entire distribution of the number of infections. The probability of reaching at least the target number of infections will be estimated as the proportion of trials with the projected number of infections greater than or equal to the target.

Figures on enrollment, HIV-1 incidence and dropout over time will also be included to aid interpretation of the results.

9.4.2 A Bayesian model for the HIV-1 incidence rate in estimation of the number of HIV-1 infection endpoints at an interim analysis

Let n_k and T_k denote, respectively, the infection count and the observed total person-time at risk at the time of the k-th futility analysis, pooling over all treatment arms. Additionally, let T^* denote the estimated total person-time at risk for the primary efficacy analysis. Let the prior distribution of the pooled HIV-1 incidence rate p be $\mathsf{Ga}(\alpha, \beta)$ parametrized such that the prior mean $E\,p = \alpha/\beta$ (the same Bayesian method applies to the treatment arm-specific HIV-1 incidence rate).

Generally, assuming that, conditional on p, the times to infection follow $\mathsf{Exp}(p)$, the posterior mean of p at the time of the k-th analysis equals

$$\begin{aligned} E[p \,|\, \text{data}] &= \frac{\alpha + n_k}{\beta + T_k} \\ &= \frac{\alpha}{\beta}\,\frac{\beta}{\beta + T_k} + \frac{n_k}{T_k}\,\frac{T_k}{\beta + T_k}, \end{aligned} \tag{4}$$

i.e., the posterior mean can be interpreted as a convex combination of the prior mean and the observed incidence rate. For a given $\beta > 0$, the weight on the prior mean at the first analysis depends on the accumulated person-time at risk (T_1), and the weight will decrease in subsequent analyses because $\beta/(\beta+T_k)$ is a decreasing function of T_k, which is a desirable Bayesian property.

In order to identify α and β, it is desirable that the prior mean equals the pre-trial assumed treatment arm-pooled incidence rate p^* (e.g., under $PE = 60\%$, $p^* = (1/3) \times 0.055 + (2/3) \times 0.4 \times 0.055 = 0.033$ in HVTN 703/HPTN 081), i.e.,

$$\frac{\alpha}{\beta} = p^*.$$

Furthermore, we propose to consider three values of β that correspond to the weights $w = \frac{1}{2}$, $\frac{1}{3}$ and $\frac{1}{4}$ on the prior mean at the time when 50% of the estimated total person-time at risk has been accumulated, i.e., for each value of w, β is defined as the solution to the equation

$$\frac{\beta}{\beta + T^*/2} = w.$$

It follows that

$$\beta = \beta(w, T^*) = \frac{wT^*}{2(1-w)}\,,$$

and the estimation of T^* is described in Section 9.4.2.1. For $w = \frac{1}{2}$, $\frac{1}{3}$ and $\frac{1}{4}$, we obtain $\beta = \frac{T^*}{2}$, $\frac{T^*}{4}$, and $\frac{T^*}{6}$, respectively.

At the k-th futility analysis and for each of the three values of β, we will sample the HIV-1 incidence rate from $\mathsf{Ga}(\alpha+n_k, \beta+T_k)$ for generating future data and report the weight $\frac{\beta}{\beta+T_k}$ on the prior mean in the convex combination (4).

9.4.2.1 Estimation of the total person-years at risk (T^*)

We will use HVTN 703/HPTN 081 to illustrate the calculation. In this trial, the total target sample size is $N = 1900$, the duration of follow-up per participant is $\tau = 80/52$ years, the pre-trial assumed dropout rate is $d^* = 0.1$ dropouts per person-year at risk (PYR), and, in the $PE = 60\%$ scenario, the pre-trial assumed treatment arm-pooled HIV-1 incidence rate is $p^* = (1/3) \times 0.055 + (2/3) \times 0.4 \times 0.055 = 0.033$ cases per PYR.

We consider the standard right-censored failure time analysis framework. Denoting the failure and censoring times as T and C, respectively, we assume that T is independent of C, $T \sim \mathsf{Exp}(p^*)$, and $C \sim \mathsf{Exp}(d^*)$. It follows that $X := \min(T, C) \sim \mathsf{Exp}(p^* + d^*)$ and

$$\begin{aligned} T^* &= N \times E[\min(X, \tau)] \\ &= N \times \left\{ E[X \mid X \le \tau]\, P(X \le \tau) + \tau\, P(X > \tau) \right\} \\ &= N \times \left\{ (p^* + d^*) \int_0^\tau x \exp^{-(p^*+d^*)x}\, \mathrm{d}x + \tau \exp^{-(p^*+d^*)\tau} \right\} \\ &= N \times \frac{1 - \exp^{-(p^*+d^*)\tau}}{p^* + d^*}\,. \end{aligned}$$

In HVTN 703/HPTN 081, this amounts to $T^* = 2643.42$ PYRs. For comparison, if all N participants were followed for τ years, the total PYRs would be $N\tau = 2923.08$ years.

Subsequently, for $T^* = 2643.42$ PYRs, if $T_1 = 0.2\, T^*$, the weights $\frac{\beta}{\beta+T_1}$ on the prior mean at the first futility analysis corresponding to $w = \frac{1}{2}$, $\frac{1}{3}$, and $\frac{1}{4}$ are 0.71, 0.56, 0.45, respectively. If $T_1 = 0.3\, T^*$, the respective weights on the prior mean are 0.63, 0.45, and 0.36.

9.5 Monitoring for Performance Standards of Quality of Trial Conduct

The protocol team and study investigators will have performance standards regarding the quality of trial conduct in addition to the study endpoint rate. Some of these use standard metrics detailed in the Network Evaluation Metrics and Standards document, whereas others are specific to the AMP trials. Some of these standards will relate to achievement of targeted levels of:

1. participant enrollment into the trial (targets based on protocol assumptions);

2. retention of participants (target 5% annual dropout or less, with minimally acceptable level of no more than 10% annual dropout; also target 90% visit attendance among participants under follow-up [NEC standard]).

3. adherence to receipt of infusions (target 90% of infusions received, with minimally acceptable level of 70% of infusions received).

4. quality and timeliness of HIV-1 diagnostic testing.

5. quality and timeliness of data collected on case report forms.

Appendix A describes the output that is used to evaluate items 1 (Figure 17), 2 (Table 5A and Figure 1), and 3 (Table 5B and Figure 3), and Section 9.1 provides additional information about 3 in terms of the feasibility check monitoring.

9.5.1 Expanded details for reporting on item 4: quality and timeliness of HIV-1 diagnostic testing

1. **Timeliness:** Turnaround time from blood collection to diagnostic reporting is summarized. This process monitors the site, the site-processing lab, the shipping company and the actual diagnostics lab. In addition the turnaround time from arrival in the lab to reporting is monitored, which isolates the turnaround time to the lab.

2. **Quality:** No additional monitoring for HIV-1 diagnostic quality is done beyond the fact that the labs participate in CAP and VQA and they are all audited annually by DAIDS.

9.5.2 Expanded details for reporting on item 5: quality and timeliness of data collected on case report forms

This reporting will use NEC standard metrics, as detailed in the Network Evaluation Metrics and Standards document (pages 12-14). In summary, the reporting outputs are as follows:

1. **For Quality:** For **QC Rate**, the standard metric for satisfactory quality is < 10 QCs per 100 pages. The denominator for this metric includes the total number of pages entered in the database during the time period. For refaxes, only the most recent page faxed is included. All CRF pages faxed to SCHARP are included in this calculation. Total CRF pages are labeled (Total Pages1) in the DMQ table.

   For **QC Resolution**, the standard metric is $> 80\%$ of QCs resolved in < 7 calendar days.

   For **Percent EDCd**, note that quality tends to be higher when pages are submitted via EDC (real time validation, faster submissions, etc), and this metric incentivizes sites to use EDC.

2. **Timeliness:** The standard metric for CRF Submission Rate (% pages faxed/EDCd on time) is $> 90\%$ of pages submitted within < 4 calendar days. The denominator for this metric is not total pages, as it excludes pages that, according to study operations, may not be completed and/or faxed immediately following a study visit (e.g., screening visit forms). Log-based forms are also not included. For refaxes, only the initial page faxed is included. Only time-critical CRF forms are calculated. Screening and log based forms are excluded. CRFs included in this calculation are labeled (Total Pages2). HIV test results are excluded.

The DSMB and the leadership of the AMP trials will monitor whether the trials are achieving at least minimally acceptable levels of key performance standards. The DSMB will make recommendations to improve areas that are deficient. Termination of a trial would be considered if it appears unlikely that minimally acceptable performance will be achieved.

10 Statistical Software

All analyses described in this SAP will be conducted in *R*.

11 Roles of Study Statisticians

HVTN SDMC statisticians will be blinded or unblinded to treatment group. During protocol development and after primary follow-up is completed, there will be no distinction between the roles; both types of statisticians will be responsible for designing and analyzing the study. During the primary follow-up period, however, only the treatment-unblinded statistician(s) will see interim data broken down by treatment group. Their role will be to conduct the interim monitoring and to produce and present reports on accruing data to the study DSMB. During the primary follow-up period, treatment-blinded statisticians will see only the interim data pooled across study groups. This way, treatment-blinded statisticians can assist protocol leadership in making decisions about modifications to the protocol without being influenced by interim efficacy results.

Appendix A

Mock tables and figures for the DSMB Closed Report are included below. The Closed Report summarizes trial information pooled across the treatment groups (labeled Total) and by masked treatment assignment (labeled A, B, and C). At the request of the DSMB, protocol statisticians will unmask treatment labels. A subset of these tables and figures will

form the Open Report, in which trial information is reported pooled across the treatment groups.

DRAFT

HVTN xxx/ HPTN xxx

Data and Safety Monitoring Board (DSMB)
CLOSED Report

Tables and Figures

HVTNxxx/HPTNxxx:
Closed DSMB Report for DSMB meeting on [Date].
Data Cutoff date:[Date].

Table 1. Disposition of Study Participants by Treatment Assignment^

	Total	A	B	C
Number Randomized	xxx (100.0%)	xxx (100.0%)	xxx (100.0%)	xxx (100.0%)
Enrolled	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Not Enrolled	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Pending Enrollment	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Number Enrolled*	xxx (100.0%)	xxx (100.0%)	xxx (100.0%)	xxx (100.0%)
On Study (in Primary Follow-Up)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Completed Primary Follow-up	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Early Study Termination	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)

^ Enrolled implies receipt of the first study product
* Primary Follow-Up is 92 weeks for uninfected participants and 24-weeks post-diagnosis for infected participants

Table 2. Baseline Participant Characteristics by Treatment Assignment

	Total	A	B	C
Total Enrolled	xxx (100.0%)	xxx (100.0%)	xxx (100.0%)	xxx (100.0%)
Gender Identity				
Male	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Female	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Transgender Male	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Transgender Female	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Gender Queer	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Other	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Age (years)				
18 - 20	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
21 - 30	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
31 - 40	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
41 - 50	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Missing	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Median	xx	Xx	xx	xx
Min, Max	xx - xx	xx – xx	xx - xx	xx - xx
Race				
White	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Black or African American	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Asian	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Hawaiian/Pacific Islander	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Native Am./Alaska Native	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Other Race	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Multi-racial	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Missing	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)

NOTE: Participants may self-report more than 1 gender identity, thus numbers and percentages may total to more than 100%

HVTNxxx/HPTNxxx:
Closed DSMB Report for DSMB meeting on [Date].
Data Cutoff date:[Date].

Table 3. Baseline Risk Behaviors by Treatment Assignment

	Total	A	B	C
Total Enrolled	xxx (100.0%)	xxx (100.0%)	xxx (100.0%)	xxx (100.0%)
Number Sex Partners in the Last Month				
0	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
1	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
2	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
3-4	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
>=5	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Median	xxx	xxx	xxx	xxx
Min, Max	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx
Had an HIV+ Partner				
Yes	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Unprotected Receptive Vaginal Sex with a Partner				
Yes	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Unprotected Insertive Vaginal Sex with a Partner				
Yes	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Unprotected Insertive Anal Sex with a Partner				
Yes	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Unprotected Receptive Anal Sex with a Partner				
Yes	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Exchange of Sex for Money/Gifts				
Yes	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)

HVTNxxx/HPTNxxx:
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Data Cutoff date:[Date].

Table 3. Baseline Risk Behaviors by Treatment Assignment

	Total	A	B	C
Total Enrolled	xxx (100.0%)	xxx (100.0%)	xxx (100.0%)	xxx (100.0%)
Alcohol Use				
Never	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Monthly or less	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
2-4 times a month	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
2-3 times a week	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
4 or more times a week	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Prefer not to answer				
Injection Drug Use				
Yes	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Marijuana Use				
Yes	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Crack cocaine use				
Yes	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Powder cocaine use				
Yes	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Amphetamine/Methamphetamine/Crystal Meth Use				
Yes	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Methaqualone or Mandrax Use?				
Yes	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)

HVTNxxx/HPTNxxx:
Closed DSMB Report for DSMB meeting on [Date].
Data Cutoff date:[Date].

Table 3. Baseline Risk Behaviors by Treatment Assignment

	Total	A	B	C
Total Enrolled	xxx (100.0%)	xxx (100.0%)	xxx (100.0%)	xxx (100.0%)
Heroin, Prescription Pain Killers/Medications Use				
Yes	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
MDMA or Ecstasy Use				
Yes	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Popper Use				
Yes	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)

Table 4. Study Status and Reasons for Early Study Termination by Treatment Assignment

	Total	A	B	C
Total Enrolled	xxx (100.0%)	xxx (100.0%)	xxx (100.0%)	xxx (100.0%)
Status				
In Infusion Phase	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
In FU, Completed Infusions	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
In FU, Discontinued Infusions	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Completed FU and Infusions	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Completed FU, Discontinued Infusions	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Early Termination, Completed Infusions	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Early Termination, Discontinued Infusions	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Reasons for Early Termination	(n=x)	(n=x)	(n=x)	(n=x)
Death	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Participant refused	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Unable to adhere to visit schedule	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Participant relocated	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Unable to contact	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Investigator decision	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Inappropriate enrollment	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Duplicate screening/enrollment	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Early study closure	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Participant incarcerated	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Study product infusions	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Other	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Early Termination Due to an Adverse Experience	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Early Termination Due to Study Product infusions	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)

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Data Cutoff date:[Date].

Table 5A. Visit Retention by Treatment Assignment

	Total	A	B	C
Total Enrolled	xxx	xxx	xxx	xxx
Week 4 / 28 days post Infusion 1				
Expected and/or Completed visit	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Retained	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Missed visit	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Terminated	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Permanently discontinued infusion	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
.				
.				
Week 92 / 140 days Post Infusion 10				
Expected and/or Completed visit	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Retained	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Missed visit	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Terminated	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Permanently discontinued infusion	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)

Post-infusion visits are not expected if the infusion visit was not done.

Retention = # Participants who completed the visit / # Participants expected for and./or completed the visit.
A visit is considered expected if the participant is in Schedule 1 at the time of the visit and the visit window has closed.
A visit is considered completed once the Post-Enrollment IV Infusion Administration or Specimen Collection form is entered in the study database.

HVTNxxx/HPTNxxx:
Closed DSMB Report for DSMB meeting on [Date].
Data Cutoff date:[Date].

Table 5B. Infusion Adherence by Treatment Assignment

	Total	A	B	C
Total Enrolled	xxx	xxx	xxx	xxx
Week 0 / Infusion 1				
Retained	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Received Infusion	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Missed Infusion	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Week 8 / Infusion 2				
Retained	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Received Infusion	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Missed Infusion	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
.				
.				
Week 72 / Infusion 10				
Retained	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Received Infusion	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Missed Infusion	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)

Retained = # Participants who completed the visit

A visit is considered completed once the Post-Enrollment IV Infusion Administration or Specimen Collection form is entered in the study database

A participant has received infusion once the Post-Enrollment IV Infusion Administration is entered in the study database

.

HVTNxxx/HPTNxxx:
Closed DSMB Report for DSMB meeting on [Date].
Data Cutoff date:[Date].

Table 6. Permanent Discontinuation of Infusions by Treatment Assignment

	Total	A	B	C
Infusion Status				
In Infusion Phase	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Completed Infusions Phase	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Permanently Discontinued Infusions	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Reasons For Discontinuation	xxx	xxx	xxx	xxx
Pregnancy	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
HIV infection	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Death	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Clinical event	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Reactogenicity symptom	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Investigator reason	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Participant refused study product infusion	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Co-enrollment in a study	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Two reactive HIV tests	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Other	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)

HVTNxxx/HPTNxxx:
Closed DSMB Report for DSMB meeting on [Date].
Data Cutoff date:[Date].

Figure 1A. Cumulative Incidence of Dropout by Treatment Assignment

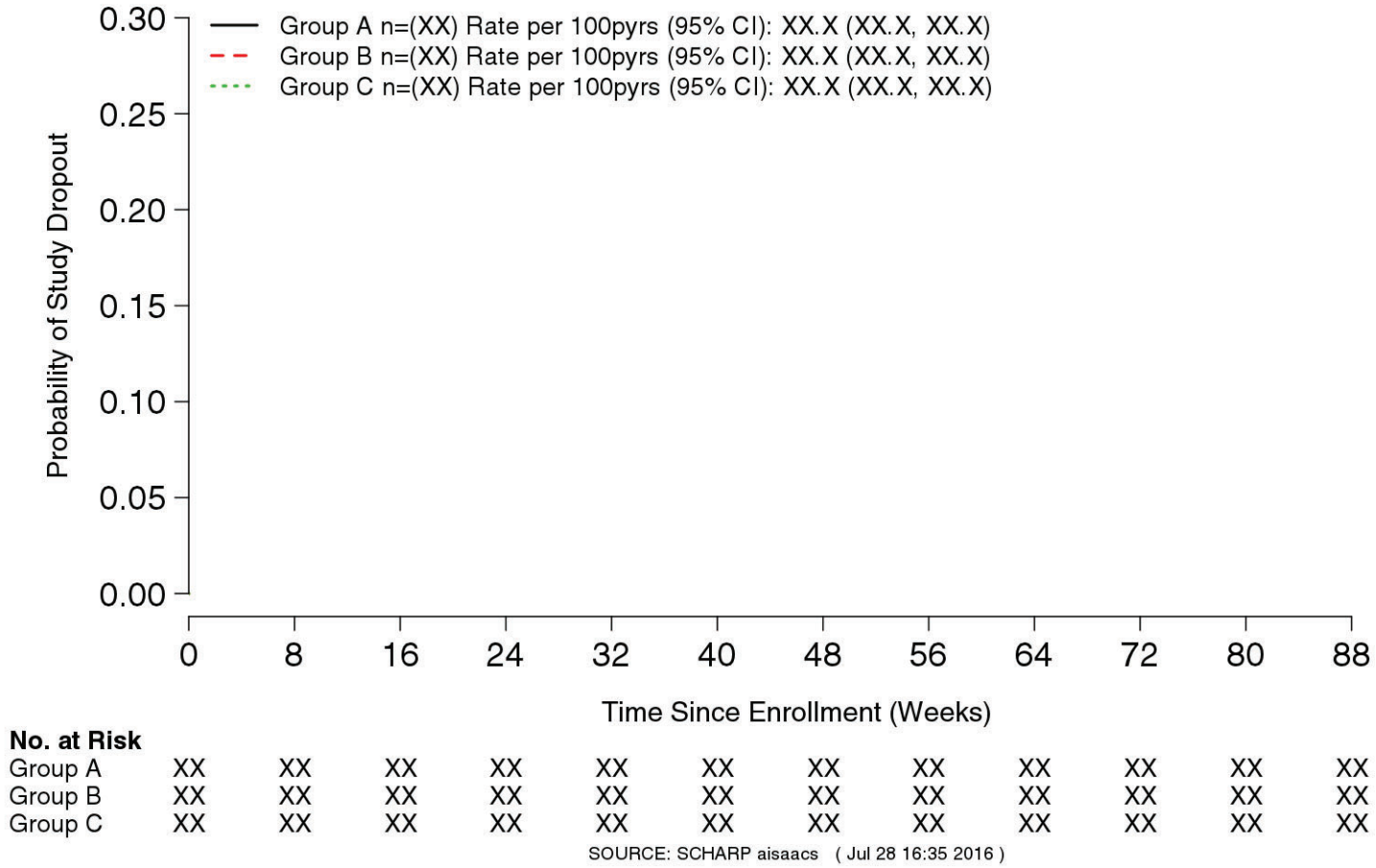
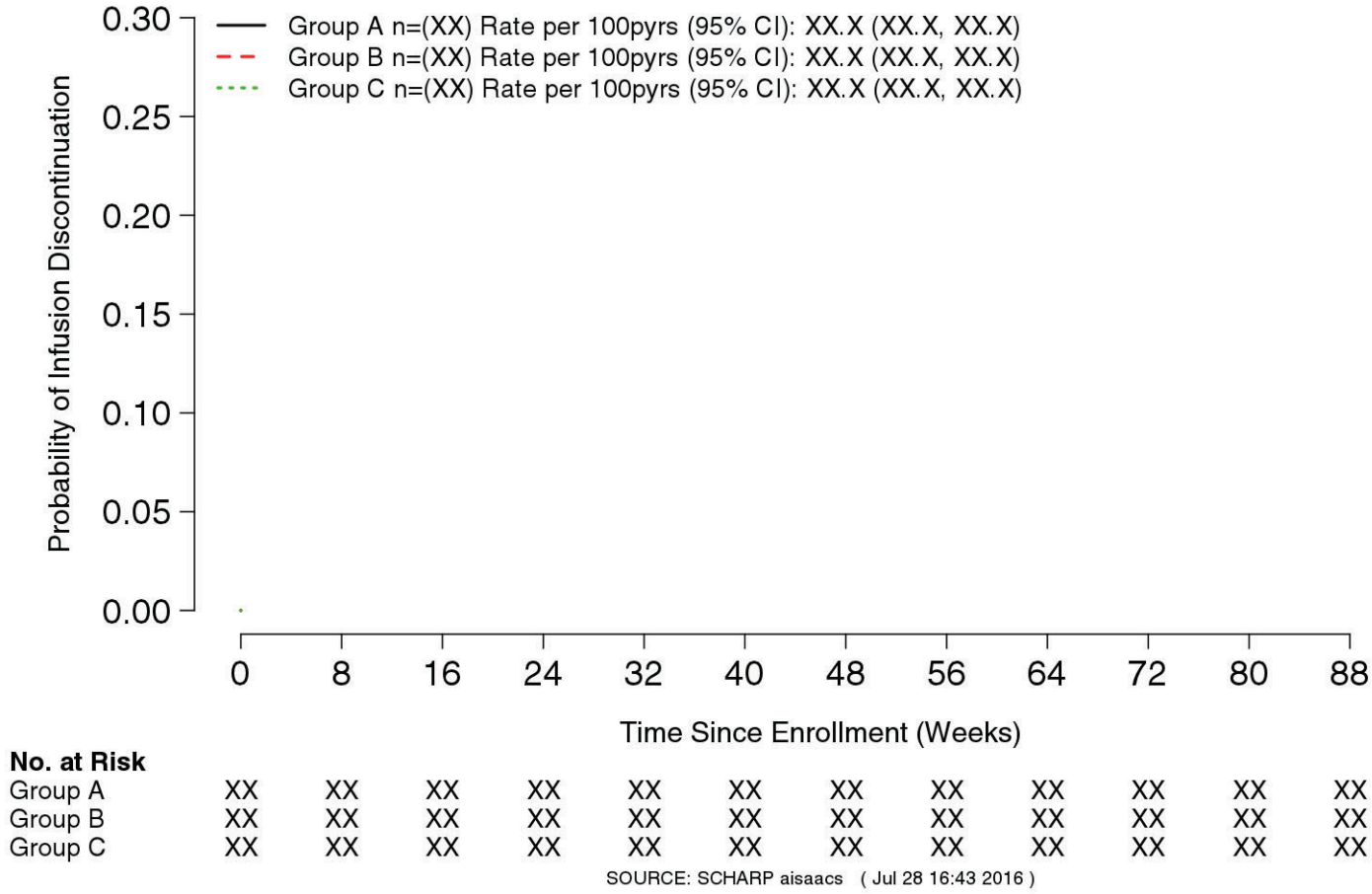
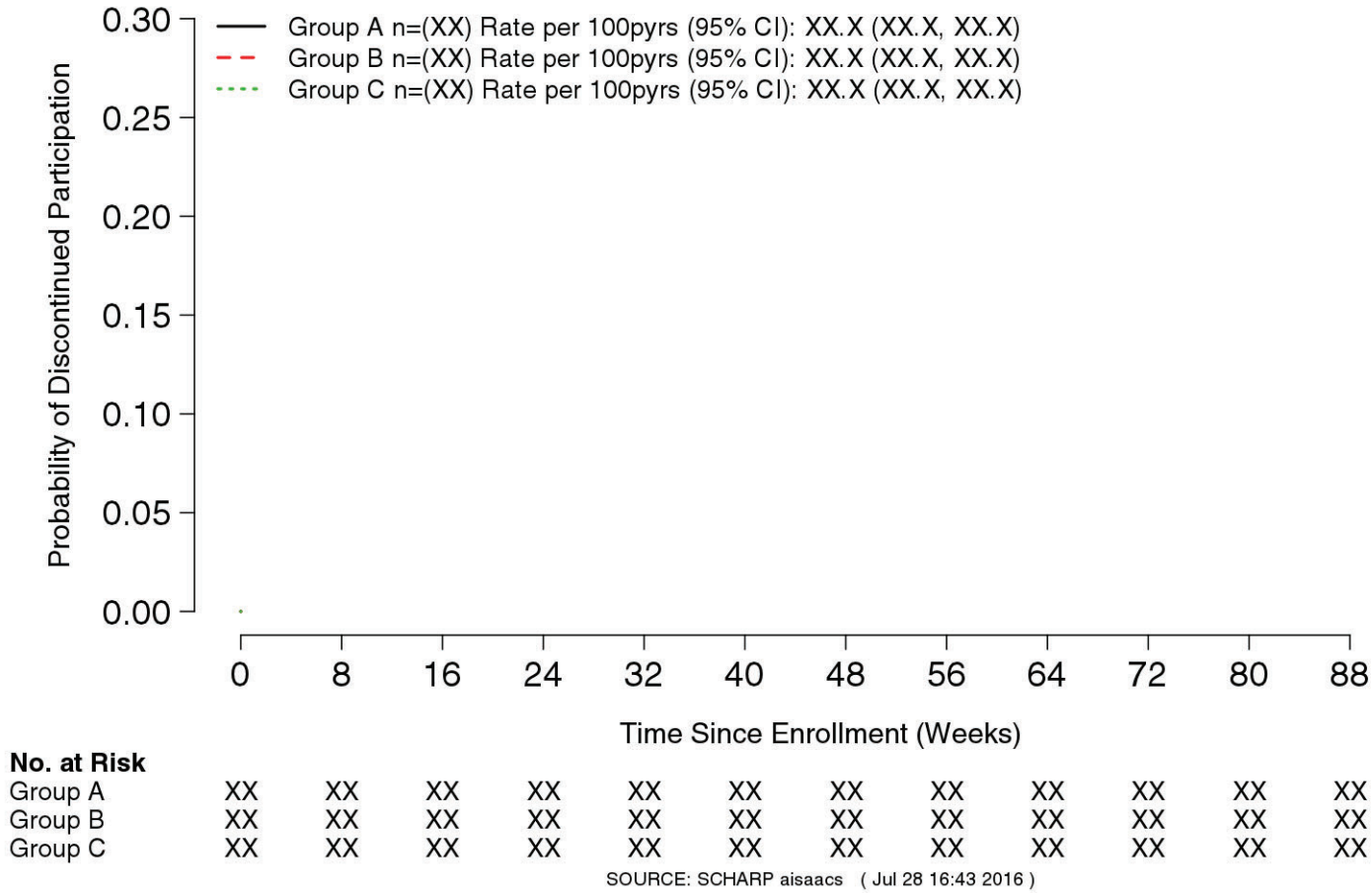


Figure 1B. Cumulative Incidence of Infusion Discontinuation by Treatment Assignment



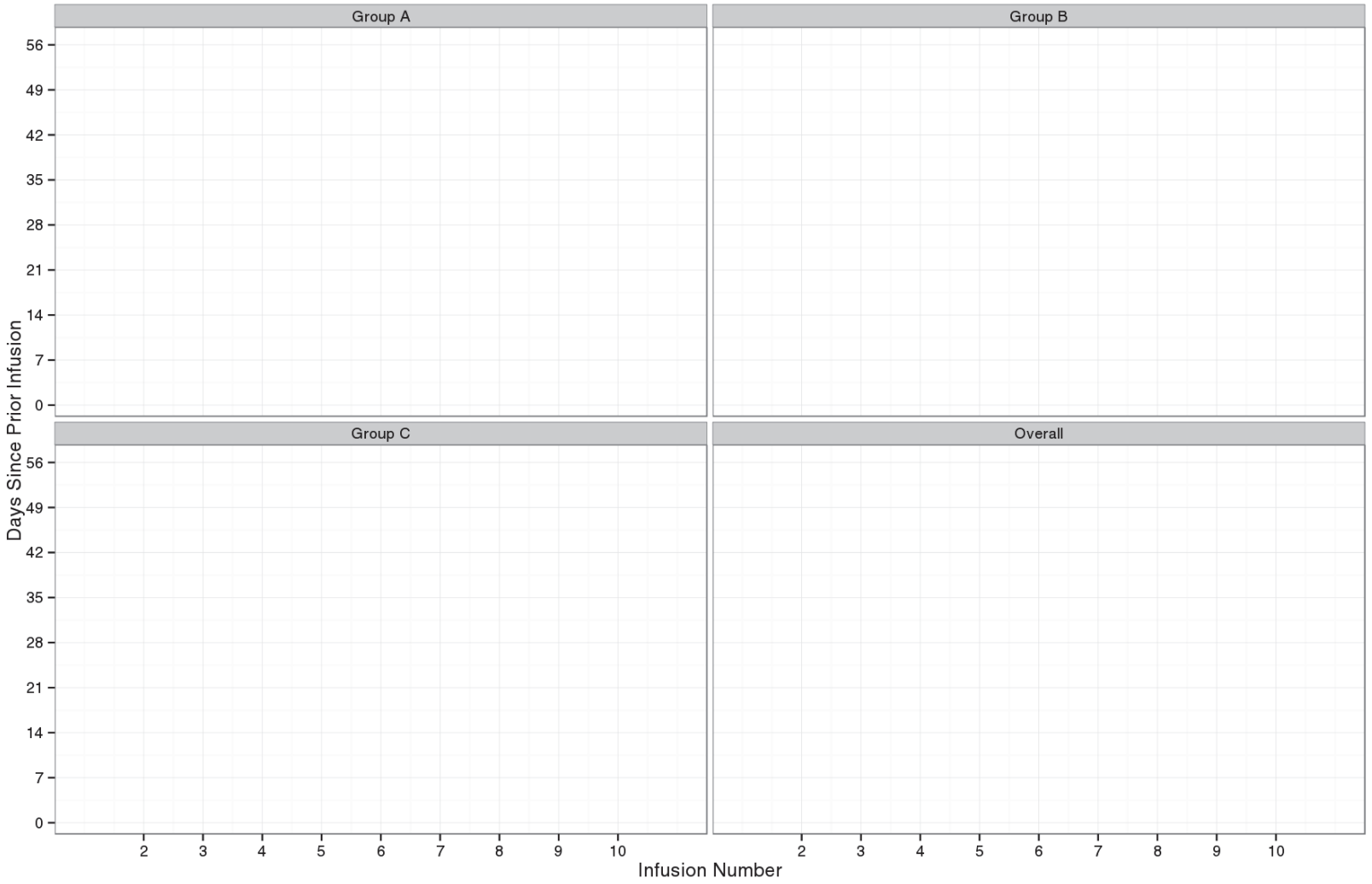
HVTNxxx/HPTNxxx:
Closed DSMB Report for DSMB meeting on [Date].
Data Cutoff date:[Date].

Figure 1C. Cumulative Incidence of Discontinued Participation (Dropout or Infusion Discontinuation) by Treatment Assignment



HVTNxxx/HPTNxxx:
Closed DSMB Report for DSMB meeting on [Date].
Data Cutoff date:[Date].

Figure 2. Boxplot for Time Between Infusions by Treatment Assignment



HVTNxxx/HPTNxxx:
Closed DSMB Report for DSMB meeting on [Date].
Data Cutoff date:[Date].

Figure 3. Sample of Adherence Patterns over Study Time by Treatment Assignment

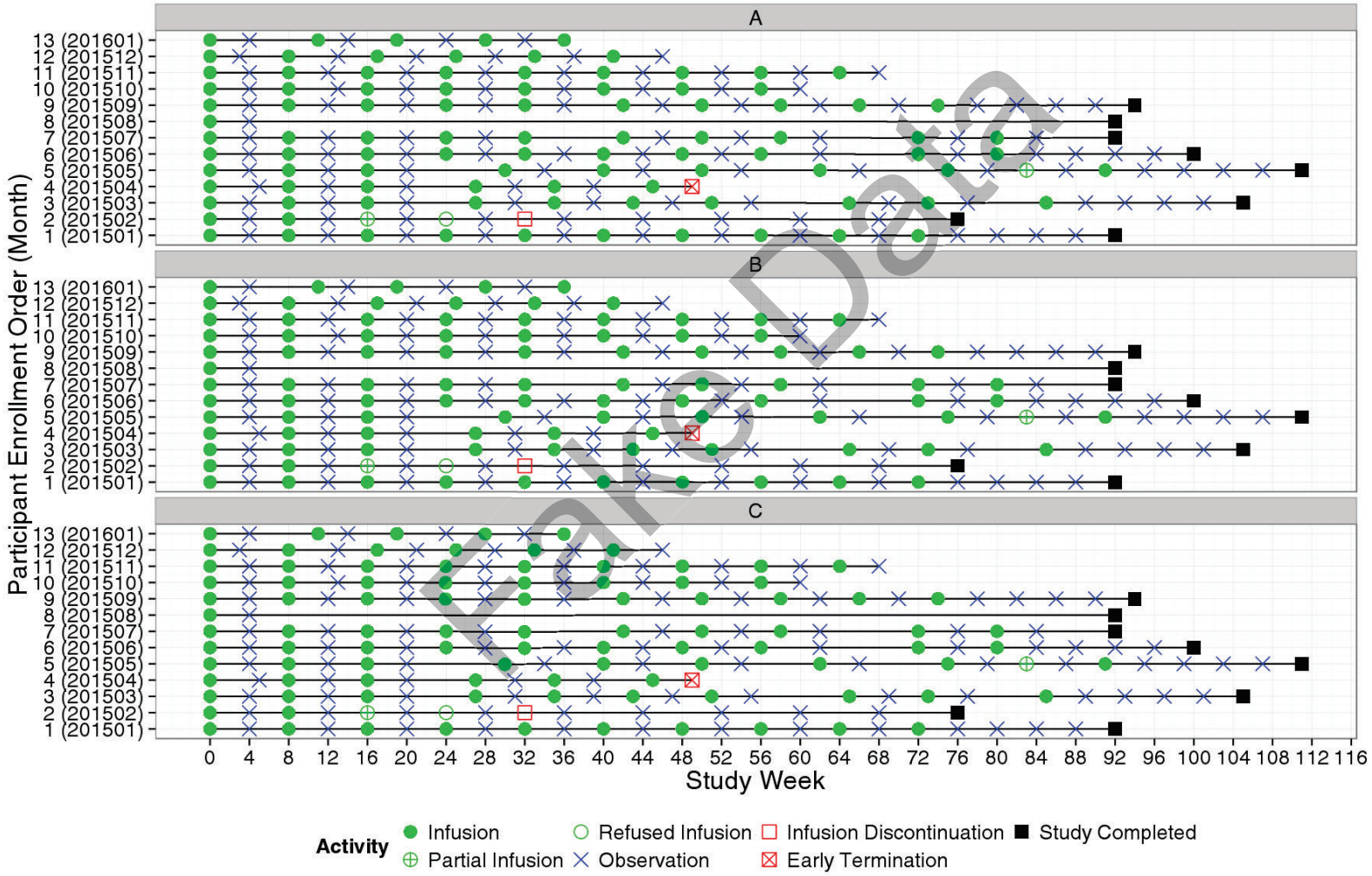


Table 7A. Maximum Local Reactogenicity Summary By Treatment Assignment

	Total		A		B		C	
Number Infused	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Pain								
None	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Mild	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Moderate	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Severe	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Potentially Life-Threatening	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Tenderness								
None	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Mild	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Moderate	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Severe	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Potentially Life-Threatening	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Pain and/or Tenderness								
None	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Mild	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Moderate	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Severe	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Potentially Life-Threatening	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Erythema								
None or not gradeable	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
6.25 to < 25 cm^2 or 2.5 to <5 cm single dim (Gr 1)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
25 to < 100 cm^2 or 5 to <10 cm single dim (Gr2)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
>= 100 cm^2 or >= 10 cm single dim or severe complication (Gr 3)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
> Potentially life threatening complication (Gr 4)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)

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NOTE: Events are noted in the category of highest severity grade reported.

HVTNxxx/HPTNxxx:
Closed DSMB Report for DSMB meeting on [Date].
Data Cutoff date:[Date].

Table 7B. Maximum Systemic Reactogenicity Summary By Treatment Assignment

	Total		A		B		C	
Number Infused	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Malaise and/or Fatigue								
None	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Mild	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Moderate	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Severe	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Potentially Life-Threatening	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Myalgia								
None	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Mild	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Moderate	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Severe	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Potentially Life-Threatening	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Headache								
None	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Mild	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Moderate	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Severe	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Potentially Life-Threatening	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Nausea								
None	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Mild	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Moderate	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Severe	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Potentially Life-Threatening	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)

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Events are noted in the category of highest severity grade reported.

Figure 4. Maximum Local Reactogenicity, by Treatment Assignment

Boxplots of local reactogenicity events defined as specific surveyed adverse events that are commonly associated with infusion administration and that have an onset within 3 days following an infusion. Local reactogenicity events assessed in this study are: local pain to the infusion site, local tenderness to the infusion site, erythema at the infusion site, and induration/swelling at the infusion site. Severity definitions are based on The Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events (DAIDS AE Grading Table), Version 2.0 (January 2010).

Figure 5: Maximum Systemic Reactogenicity, by Treatment Assignment

Boxplots of systemic reactogenicity events defined as specific surveyed adverse events that are commonly associated with infusion administration and that have an onset within 3 days following an infusion. Systemic reactogenicity events are: malaise and/or fatigue, myalgia, headache, nausea, vomiting, chills, arthalgia and body temperature. Severity definitions are based on The Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events (DAIDS AE Grading Table), Version 2.0 (January 2010).

HVTNxxx/HPTNxxx:
Closed DSMB Report for DSMB meeting on [Date].
Data Cutoff date:[Date].

Table 8. Expedited Adverse Experiences (EAEs) Reported to the Regulatory Support Center (RSC) by Treatment Assignment, Participant and Decreasing Severity NOTE: * in column 'Non Rept.' indicates non−reportable EAE by DAIDS criteria, as determined by RSC.

Trt.	Publication ID	Severity	EAE Number	Adverse Experience	Onset Date	Relation to Study Product	Medical Officer's Relation to Study Product	Number of Previous Infusions	Days Since Last Infusion	Non Reportable
A	XXX-XXXX	text	XXXXXX	text	dd-MMM-yyyy	text	text	X	XX	
	XXX-XXXX	text	XXXXXX	text	dd-MMM-yyyy	text	text	X	XX	
.										
.										
B	XXX-XXXX	text	XXXXXX	text	dd-MMM-yyyy	text	text	X	XX	
	XXX-XXXX	text	XXXXXX	text	dd-MMM-yyyy	text	text	X	XX	
.										
.										
C	XXX-XXXX	text	XXXXXX	text	dd-MMM-yyyy	text	text	X	XX	
	XXX-XXXX	text	XXXXXX	text	dd-MMM-yyyy	text	text	X	XX	
	..									
	XXX-XXXX	text	XXXXXX	text	dd-MMM-yyyy	text	text	X	XX	
	XXX-XXXX	text	XXXXXX	text	dd-MMM-yyyy	text	text	X	XX	

HVTNxxx/HPTNxxx:
Closed DSMB Report for DSMB meeting on [Date].
Data Cutoff date:[Date].

Table 9. Adverse Events (AEs) by System Organ Class and Severity and Treatment Assignment Sorted by Decreasing Frequency

	Total (N=XXXX)		A (N=XXXX)		B (N=XXXX)		C (N=XXXX)	
System Organ Class/ Severity	n	(%)	n	(%)	n	(%)	n	(%)
Participants with one or more AEs								
Mild and Greater	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Moderate and Greater	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Severe and Greater	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Life Threatening and Greater	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Fatal	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Infections and infestations								
Mild and Greater	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Moderate and Greater	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Severe and Greater	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Life Threatening and Greater	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Fatal	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Gastrointestinal disorders								
Mild and Greater	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Moderate and Greater	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Severe and Greater	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Life Threatening and Greater	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Fatal	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
General disorders and administration Country conditions								
Mild and Greater	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Moderate and Greater	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Severe and Greater	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Life Threatening and Greater	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Fatal	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
Respiratory, thoracic and mediastinal disorders								
Mild and Greater	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)	xxx	(xx.x%)
.								
.								

N's are the number of participants enrolled.
n's are the number of participants reporting one or more AEs within a specific system organ class.
Incidence is calculated by n divided by the number enrolled x 100.
AE records included in the table have been coded into MedDRA codes by SCHARP clinical staff.

HVTNxxx/HPTNxxx:
Closed DSMB Report for DSMB meeting on [Date].
Data Cutoff date:[Date].

Table 10. Grade 3-5 Adverse Events (AEs) by High Level Term and Severity and Treatment Assignment, Sorted by Decreasing Frequency

	Total (N=XXXX) n (%)	A (N=XXXX) n (%)	B (N=XXXX) n (%)	C (N=XXXX) n (%)
Participants with one or more AEs				
Severe and Greater	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Life Threatening and Greater	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Fatal	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Poisoning and toxicity				
Severe and Greater	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Life Threatening and Greater	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Fatal	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Abdominal and gastrointestinal disorders				
Severe and Greater	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Life Threatening and Greater	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Fatal	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Streptococcal Infections				
Severe and Greater	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Life Threatening and Greater	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Fatal	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Pain and discomfort NEC				
Severe and Greater	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Life Threatening and Greater	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Fatal	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Viral infections NEC				
Severe and Greater	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Life Threatening and Greater	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
.				
.				

N's are the number of participants enrolled.
n's are the number of participants reporting one or more AEs within a specific system organ class.
Incidence is calculated by n divided by the number enrolled x 100. AE records included in the table have been coded into MedDRA codes by SCHARP clinical staff.

HVTNxxx/HPTNxxx:
Closed DSMB Report for DSMB meeting on [Date].
Data Cutoff date:[Date].

Table 11. Adverse Events (AEs) by High Level Term and Severity and Treatment Assignment, Sorted by Decreasing Frequency

	Total (N=XXXX) n (%)	A (N=XXXX) n (%)	B (N=XXXX) n (%)	C (N=XXXX) n (%)
Participants with one or more AEs				
Mild and Greater	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Moderate and Greater	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Severe and Greater	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Life Threatening and Greater	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Fatal	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Poisoning and Toxicity				
Mild and Greater	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Moderate and Greater	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Severe and Greater	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Life Threatening and Greater	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Fatal	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Streptococcal Infections				
Mild and Greater	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Moderate and Greater	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Severe and Greater	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Life Threatening and Greater	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Fatal	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Allergies to foods, food additives, drugs and other chemicals				
Mild and Greater	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Moderate and Greater	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Severe and Greater	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
.				
.				

N's are the number of participants enrolled.
n's are the number of participants reporting one or more AEs within a specific system organ class.
Incidence is calculated by n divided by the number enrolled x 100.
AE records included in the table have been coded into MedDRA codes by SCHARP clinical staff.

Table 12. Adverse Events (AEs) Related to Study Product by High Level Term and Treatment Assignment

High Level Term/Relationship	Total (N=XXXX) n	(%)	A (N=XXXX) n	(%)	B (N=XXXX) n	(%)	C (N=XXXX) n	(%)
Paricipants with one or more AEs								
Related	xx	(xx.x%)	xx	(xx.x%)	xx	(xx.x%)	xx	(xx.x%)
Viral Infections NEC								
Related	xx	(xx.x%)	xx	(xx.x%)	xx	(xx.x%)	xx	(xx.x%)
Gastrointestinal disorders								
Related	xx	(xx.x%)	xx	(xx.x%)	xx	(xx.x%)	xx	(xx.x%)
Poisoning and Toxicity								
Related	xx	(xx.x%)	xx	(xx.x%)	xx	(xx.x%)	xx	(xx.x%)
Allergies to foods, food additives, drugs and other chemicals								
Related	xx	(xx.x%)	xx	(xx.x%)	xx	(xx.x%)	xx	(xx.x%)
Mineral and Electrolyte Analyses								
Related	xx	(xx.x%)	xx	(xx.x%)	xx	(xx.x%)	xx	(xx.x%)
Bronchitis								
Related	xx	(xx.x%)	xx	(xx.x%)	xx	(xx.x%)	xx	(xx.x%)
Upper respiratory tract infection								
Related	xx	(xx.x%)	xx	(xx.x%)	xx	(xx.x%)	xx	(xx.x%)
Leukocytoses NEC								
Related	xx	(xx.x%)	xx	(xx.x%)	xx	(xx.x%)	xx	(xx.x%)
.								
.								

N's are the number of participants enrolled.
n's are the number of participants reporting one or more AEs within a specific system organ class.
Incidence is calculated by n divided by the number enrolled x 100.
AE records included in the table have been coded into MedDRA codes by SCHARP clinical staff.

HVTNxxx/HPTNxxx:
Closed DSMB Report for DSMB meeting on [Date].
Data Cutoff date:[Date].

Table 13A. Distribution of Safety Laboratory Values, by Treatment Assignment

	Total	A	B	C
ALT				
Infusion #1 (baseline)				
N	xxx	xxx	xxx	xxx
Median (IQR)	xxx (xxx – xxx)	xxx (xxx – xxx)	xxx (xxx – xxx)	xxx (xxx – xxx)
Min, Max	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx
Median change from baseline (IQR)	xxx (xxx – xxx)	xxx (xxx – xxx)	xxx (xxx – xxx)	xxx (xxx – xxx)
Infusion #2				
N	xxx	xxx	xxx	xxx
Median (IQR)	xxx (xxx – xxx)	xxx (xxx – xxx)	xxx (xxx – xxx)	xxx (xxx – xxx)
Min, Max	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx
Median change from baseline (IQR)	xxx (xxx – xxx)	xxx (xxx – xxx)	xxx (xxx – xxx)	xxx (xxx – xxx)
….				
Infusion #10				
N	xxx	xxx	xxx	xxx
Median (IQR)	xxx (xxx – xxx)	xxx (xxx – xxx)	xxx (xxx – xxx)	xxx (xxx – xxx)
Min, Max	xxx, xxx	xxx, xxx	xxx, xxx	xxx, xxx
Median change from baseline (IQR)	xxx (xxx – xxx)	xxx (xxx – xxx)	xxx (xxx – xxx)	xxx (xxx – xxx)
Hemoglobin				
.				
.				
.				

Table 13B. Safety Laboratory Values Meeting Grade 1 AE Criteria or Above, by Treatment Assignment

	Total	A	B	C
ALT				
Infusion #1	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Infusion #2	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
…	…	…	…	…
Infusion #10	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Hemoglobin				
Infusion #1	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Infusion #2	…	…	…	…
…	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Infusion #10	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Platelets				
Infusion #1	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Infusion #2	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
…	…	…	…	…
Infusion #10	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)

Figure 6. Boxplot for ALT by Infusion Visit and Treatment Assignment
Figure 7. Boxplot for Hemoglobin by Infusion Visit and Treatment Assignment
Figure 8. Boxplot for Platelets by Infusion Visit and Treatment Assignment
Figure 9. Boxplot for WBC by Infusion Visit and Treatment Assignment
Figure 10. Boxplot for Neutrophil Count by Infusion Visit and Treatment Assignment
Figure 11. Boxplot for Lymphocyte Count by Infusion Visit and Treatment Assignment
Figure 12. Boxplot for Creatinine by Infusion Visit and Treatment Assignment

Graphical presentation of Safety Lab distributions by infusion visit and treatment assignment.

Figure 13. Confirmation/Adjudication Process for HIV Infections

The process of adjudicating HIV infections is outlined in three testing algorithms (Routine, Recent Exposure and Redraw), starting from the time that the initial positive specimen is drawn through the time that the site is notified of a HIV infection.

Table 14. Pregnancy Listing

Trt.	Publication ID	LMP Date	Pregnancy outcome date	Date Last Inf. Prior to Outcome	Pregnancy Outcome	Time from Prior Inf. To LMP	# Inf. Prior to LMP	#Inf. Prior to Outcome	Total # Inf.	Comments
A	XXX-XXXX	dd-MMM-yyyy	dd-MMM-yyyy	dd-MMM-yyyy	dd-MMM-yyyy	text	text	X	XX	
	XXX-XXXX	dd-MMM-yyyy	dd-MMM-yyyy	dd-MMM-yyyy	dd-MMM-yyyy	text	text	X	XX	
.	XXX-XXXX	dd-MMM-yyyy	dd-MMM-yyyy	dd-MMM-yyyy	dd-MMM-yyyy	text	text	X	XX	
.	.									
B	XXX-XXXX	dd-MMM-yyyy	dd-MMM-yyyy	dd-MMM-yyyy	dd-MMM-yyyy	text	text	X	XX	
	XXX-XXXX	dd-MMM-yyyy	dd-MMM-yyyy	dd-MMM-yyyy	dd-MMM-yyyy	text	text	X	XX	
.	XXX-XXXX	dd-MMM-yyyy	dd-MMM-yyyy	dd-MMM-yyyy	dd-MMM-yyyy	text	text	X	XX	
.	.									
C	XXX-XXXX	dd-MMM-yyyy	dd-MMM-yyyy	dd-MMM-yyyy	dd-MMM-yyyy	text	text	X	XX	
	XXX-XXXX	dd-MMM-yyyy	dd-MMM-yyyy	dd-MMM-yyyy	dd-MMM-yyyy	text	text	X	XX	
	XXX-XXXX	dd-MMM-yyyy	dd-MMM-yyyy	dd-MMM-yyyy	dd-MMM-yyyy	text	text	X	XX	

Table 15. HIV Adjudication Timeline

Initial Positive Sample Draw Date	Days from Initial Positive Draw Date to Initial Positive Test Date	Days from Initial Positive Test Date to Confirmation Draw Date	Days from Confirmation Draw Date to Confirmation Test Date	Days from Confirmation Test Date to Atlas Portal Post Date	Days from Atlas Post Date to Adjudication Date	Days from Adjudication Date to Site Notification Date	Total Days Since Initial Positive Sample Draw Date
dd-MMM-yyyy	xxx	xxx	xxx	xxx	xxx	xxx	xxx
dd-MMM-yyyy	xxx	xxx	xxx	xxx	xxx	xxx	xxx
.							
.							
dd-MMM-yyyy	xxx	xxx	xxx	xxx	xxx	xxx	xxx
Median (Min, Max)	**xxx (xxx, xxx)**	**xxx (xxx, xxx)**	**xxx (xxx, xxx)**	**xxx (xxx, xxx)**	**xxx (xxx, xxx)**	**xxx (xxx, xxx)**	**xxx (xxx, xxx)**

HVTNxxx/HPTNxxx:
Closed DSMB Report for DSMB meeting on [Date].
Data Cutoff date:[Date].

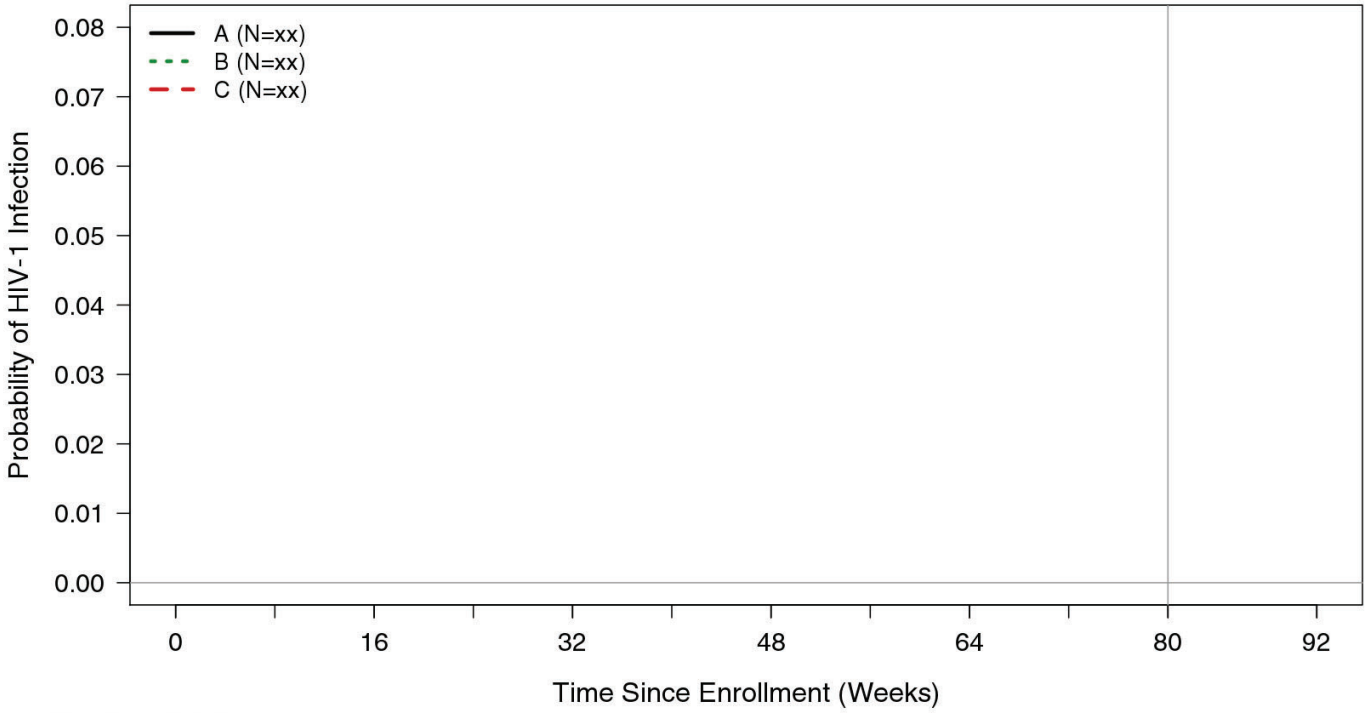
Table 16. HIV Infections

Infection Classification[1]	Trt Group	Publication ID	Initial Positive Sample Draw Date	Initial Positive Sample Draw Visit Number	Initial Positive Sample Draw Study Week	Initial Positive Sample Draw Study Day	Confirmatory Sample Draw	Enrollment Sample RNA Positive	Number of Infusions Received
Pre-Trial	A	xxx-xxxx	dd-MMM-yyyy	xxx	xxx	xxx	dd-MMM-yyyy	text	xxx
		xxx-xxxx	dd-MMM-yyyy	xxx	xxx	xxx	dd-MMM-yyyy	text	xxx
.			.				.		
	B	xxx-xxxx	dd-MMM-yyyy	xxx	xxx	xxx	dd-MMM-yyyy	text	xxx
		xxx-xxxx	dd-MMM-yyyy	xxx	xxx	xxx	dd-MMM-yyyy	text	xxx
.									
.									
	C	xxx-xxxx	dd-MMM-yyyy	xxx	xxx	xxx	dd-MMM-yyyy	text	xxx
		xxx-xxxx	dd-MMM-yyyy	xxx	xxx	xxx	dd-MMM-yyyy	text	xxx
.									
.									
MITT	A	xxx-xxxx	dd-MMM-yyyy	xxx	xxx	xxx	dd-MMM-yyyy	text	xxx
		xxx-xxxx	dd-MMM-yyyy	xxx	xxx	xxx	dd-MMM-yyyy	text	xxx
.			.				.		
	B	xxx-xxxx	dd-MMM-yyyy	xxx	xxx	xxx	dd-MMM-yyyy	text	xxx
		xxx-xxxx	dd-MMM-yyyy	xxx	xxx	xxx	dd-MMM-yyyy	text	xxx
.									
.									
	C	xxx-xxxx	dd-MMM-yyyy	xxx	xxx	xxx	dd-MMM-yyyy	text	xxx
		xxx-xxxx	dd-MMM-yyyy	xxx	xxx	xxx	dd-MMM-yyyy	text	xxx
.									
.									

[1]Infections are categorized as either 'Pre-Trial' or 'MITT'. Infections are 'Pre-Trial' if the enrollment sample tested HIV-positive. Pre-Trial infections will be excluded from analysis of the study endpoint as indicated in the protocol.

HVTNxxx/HPTNxxx:
Closed DSMB Report for DSMB meeting on [Date].
Data Cutoff date:[Date].

Figure 14. Cumulative HIV Incidence Among All MITT Participants by Treatment Arm



Number at risk

A	xx	xx	xx	xx	xx	xx	xx
B	xx	xx	xx	xx	xx	xx	xx
C	xx	xx	xx	xx	xx	xx	xx

Cumulative number of HIV-1 infections

A	xx	xx	xx	xx	xx	xx	xx
B	xx	xx	xx	xx	xx	xx	xx
C	xx	xx	xx	xx	xx	xx	xx

Table 17. ART initiation information for HIV infections

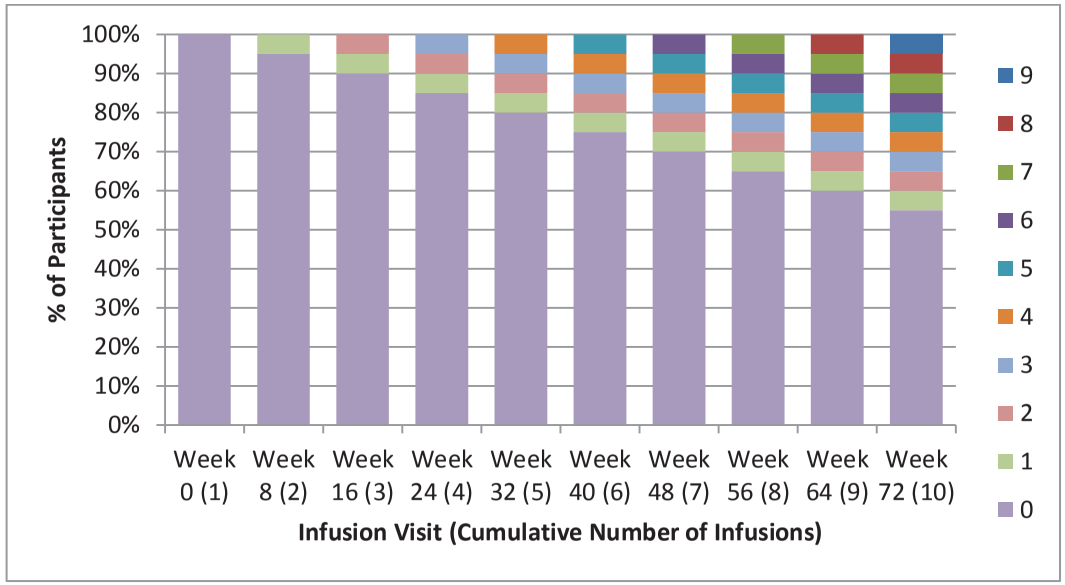
Infection Classification[1]	Trt Group	Publication ID	Post-dx ART initiation week	Excluded from primary analysis	Reason for ART initiation
Pre-Trial	A	xxx-xxxx	dd-MMM-yyyy	text	text
		xxx-xxxx	dd-MMM-yyyy	text	text
.			.		
	B	xxx-xxxx	dd-MMM-yyyy	text	text
		xxx-xxxx	dd-MMM-yyyy	text	text
.					
.					
	C	xxx-xxxx	dd-MMM-yyyy	text	text
		xxx-xxxx	dd-MMM-yyyy	text	text
.					
.					
MITT	A	xxx-xxxx	dd-MMM-yyyy	text	text
		xxx-xxxx	dd-MMM-yyyy	text	text
.			.		
	B	xxx-xxxx	dd-MMM-yyyy	text	text
		xxx-xxxx	dd-MMM-yyyy	text	text
.					
.					
	C	xxx-xxxx	dd-MMM-yyyy	text	text
		xxx-xxxx	dd-MMM-yyyy	text	text
.					
.					

[1]Infections are categorized as either 'Pre-Trial' or 'MITT'. Infections are 'Pre-Trial' if the enrollment sample tested HIV-positive. Pre-Trial infections will be excluded from analysis of the study endpoint as indicated in the protocol.

Figure 15. Viral Load Over Time Among All Infected MITT Participants

Longitudinal pre-ART viral load measurements are presented by treatment group for MITT infected participants. Individual participant trajectories are indicated by solid black lines, while mean pre-ART viral load measures within a treatment group are plotted using a dashed red line. Means are only estimated for weeks with at least three participants with pre-ART viral load data.

Figure 16. Cumulative Number of Infusions Missed by Infusion Visit for All Infected MITT Participants



HVTNxxx/HPTNxxx:
Closed DSMB Report for DSMB meeting on [Date].
Data Cutoff date:[Date].

Table 18a. Visit Retention for All MITT HIV-1 Infected Participants by Treatment Assignment

	Total	A	B	C
Participants Enrolled In Schedule 2	xxx	xxx	xxx	xxx
Week 2 Post Diagnosis				
Terminated	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Not Expected (not in window)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Expected (in visit window)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Attended visit	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Missed visit	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Not yet attended (still in window)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Week 4 Post Diagnosis				
Terminated	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Not Expected (not in window)				
Expected (in visit window)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Attended visit	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Missed visit	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Not yet attended (still in window)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Week 6 Post Diagnosis				
Terminated	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Not Expected (not in window)				
Expected (in visit window)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Attended visit	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Missed visit	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
.				
.				
Week 24 Post Diagnosis				
Terminated	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Not Expected (not in window)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Expected (in visit window)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)

HVTNxxx/HPTNxxx:
Closed DSMB Report for DSMB meeting on [Date].
Data Cutoff date:[Date].

Table 18b. Visit Retention for All Pre-Trial HIV-1 Infected Participants and All HIV-2 Infected Participants by Treatment Assignment

	Total	A	B	C
Participants Enrolled In Schedule 3	xxx	xxx	xxx	xxx
Week 2 Post Diagnosis				
Terminated	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Not Expected (not in window)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Expected (in visit window)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Attended visit	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Missed visit	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Not yet attended (still in window)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Week 4 Post Diagnosis				
Terminated	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Not Expected (not in window or did not receive prev. infusion)				
Expected (in visit window and received previous infusion)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Attended visit	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Missed visit	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Not yet attended (still in window)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Week 24 Post Diagnosis				
Terminated	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Not Expected (not in window)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Expected (in visit window)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)

Figure 17. Cumulative Enrollment

Line plot of the observed and expected accrual for all sites combined.

Appendix B

The CASI behavioral risk survey administered at the enrollment visit in HVTN 704/HPTN 085 and at South African sites in HVTN 703/HPTN 081 is included below. The survey is used for constructing baseline covariates potentially predictive of the primary endpoint considered for inclusion in the superlearner HIV-1 risk predictor described in Section 8.6.

AMP Study

0%

Collection: LOGIN
Contains: PTID, SCHEDULE, VISIT, VISITCHK

AMP Study

Question: PTID
Required

Site Staff: Please answer the following questions.Please enter a valid Participant ID in the following format: 111-1-1111-1

Question: SCHEDULE
Required

Scale Summary		
Code	Label	Show-If
1	Schedule 1	
2	Schedule 2 (HIV Infected)	
3	Schedule 3 (HIV Infected at Enrollment)	
4	Schedule 4	

Which study Schedule is the participant currently in?

- ◯ Schedule 1
- ◯ Schedule 2 (HIV Infected)
- ◯ Schedule 3 (HIV Infected at Enrollment)
- ◯ Schedule 4

Question: VISIT
Required

Scale Summary		
Code	Label	Show-If
02.0	Visit 02.0 (Enrollment/Infusion #1)	
04.0	Visit 04.0 (Infusion #2)	
07.0	Visit 07.0 (Infusion #3)	
09.0	Visit 09.0 (Infusion #4)	
11.0	Visit 11.0 (Infusion #5)	
13.0	Visit 13.0 (Infusion #6)	
15.0	Visit 15.0 (Infusion #7)	
17.0	Visit 17.0 (Infusion #8)	
19.0	Visit 19.0 (Infusion #9)	
21.0	Visit 21.0 (Infusion #10)	
26.0	Visit 26.0 (End Visit)	

35.0	Visit 35.0	
48.0	Visit 48.0	
72.0	Visit 72.0	
74.0	Visit 74.0	
76.0	Visit 76.0	
78.0	Visit 78.0	

What is the visit code for this visit?

Please select the visit code from the drop down menu.

-- Select One --

Question: VISITCHK
Required

Please confirm the visit code by entering it here:

Please enter a "0" first if the visit is before 10.0 - for example, "07.0"

Auto Page Break

Click "next" to select the appropriate language.

Page Break

Question: LANG_SELECT
Required

Scale Summary		
Code	Label	Show-If
1033	English	
1077	Zulu	(Error!)
1076	Xhosa	(Error!)
1132	Sotho	(Error!)
1074	Setswana	*Never Shown*
1078	Shona	*Never Shown*
1073	Dholuo	(Error!)
1116	Chichewa	*Never Shown*
1046	Portuguese	*Never Shown*
1089	Swahili	*Never Shown*
1115	Sepedi	(Error!)

1. Language choice

- ○ English
- ○ Zulu
- ○ Xhosa
- ○ Sotho
- ○ Setswana
- ○ Shona
- ○ Dholuo
- ○ Chichewa
- ○ Portuguese
- ○ Swahili
- ○ Sepedi

Page Break

Collection: STAFF_QUESTIONS
Contains: COMPLETEDBY

Question: COMPLETEDBY
Required

Scale Summary		
Code	Label	Show-If
1	Participant is completing questionnaire	
2	Interviewer is administering questionnaire	

2. Is this questionnaire being completed by the participant directly or is an interviewer from the site staff reading the questionnaire to the participant and entering participant's responses?

- ◯ Participant is completing questionnaire
- ◯ Interviewer is administering questionnaire

Page Break

Collection: TOTAL_NUM_PARTNERS
Contains: VAS, SEX_BEHAVIOR, VAGINA, RECEP_VAGINAL, RECEP_ANAL, PENIS, IVAS, IVASW, INSERTIVE_VAGINAL, IVASM, INS_ANAL, MSP

Many people are taking part in this research study. We ask the same questions of all participants. However, some questions may not apply to you.

Please answer these questions honestly. We make no judgments about how you have sex or the number of times or with whom. We do not judge about alcohol or drug use.

Your answers to these questions will help us understand the type of behaviors our participants are doing while in this study.

Page Break

The first set of questions is about your sexual relationships with men, women, and transgender people in the last months. By men we mean persons who were considered male at birth and currently identify as male. By women we mean persons who were considered female at birth and currently identify as female. By transgender we mean persons whose gender identity or expression differs from their biological sex assigned at birth.

A transgender woman is a person who is considered male at birth and who now identifies primarily as female. A transgender woman may have a vagina and/or penis. A transgender man is a person who is considered female at birth and who now identifies primarily as male. A transgender man may have a penis and/or a vagina.

By sex, we are talking about VAGINAL sex (when a penis is put into the vagina) or ANAL sex (when a penis is put into the anus or butt). For some questions, we will be asking about sex without a condom. By this we mean that a condom was not used the whole time the penis was inserted, or the condom broke, tore, spilled or slipped off. A condom can be either a male or female condom.

Page Break

Question: VAS
Required

Scale Summary		
Code	Label	Show-If
1		
99	Prefer not to answer	

3. In the last months, how many people did you have vaginal or anal sex with (with or without a condom)?

- ○ people
- ○ Prefer not to answer

Auto Page Break

Jump-To: JMP1
Description:
Jump-To-Item: PPT_RISK_BEHAVIOR
Jump-If: (VAS.TEXT = 0) or (VAS = 99:[Prefer not to answer])

Collection: SEX_BEHAVIOR
Contains: VS, AS, VASC, VAS7, VASC7
Show if: (VAS.TEXT >= 1)

Question: VS
Required

Scale Summary		
Code	Label	Show-If
1		
99	Prefer not to answer	

4. Of these people, how many did you have vaginal sex with (with or without a condom) in the last months?

- ○ people
- ○ Prefer not to answer

Question: AS
Required

Scale Summary		
Code	Label	Show-If
1		
99	Prefer not to answer	

5. Of these people, how many did you have anal sex with (with or without a condom) in the last months?

- ○ people
- ○ Prefer not to answer

Question: VASC
Required

Scale Summary		
Code	Label	Show-If
1	Never	
2	Sometimes	
3	Always	
99	Prefer not to answer	

6. In general, in the last months, how often did you use a condom during vaginal or anal sex?

- ○ Never
- ○ Sometimes
- ○ Always
- ○ Prefer not to answer

Page Break

Question: VAS7
Required
Show if: (VAS ≠ 99:[Prefer not to answer]) and (VAS.TEXT > 0)

Scale Summary		
Code	Label	Show-If
1		
99	Prefer not to answer	

7. In **the last 7 days**, how many times have you had vaginal or anal sex (with or without a condom)?

- ○ # of times
- ○ Prefer not to answer

Auto Page Break

Question: VASC7
Required
Show if: (VAS7 ≠ 99:[Prefer not to answer]) and (VAS7.TEXT > 0)

Scale Summary		
Code	Label	Show-If
1	Never	
2	Sometimes	
3	Always	
99	Prefer not to answer	

8. In general, in **the last 7 days**, how often did you use a condom during vaginal or anal sex?

- ◯ Never
- ◯ Sometimes
- ◯ Always
- ◯ Prefer not to answer

Page Break

Question: VAGINA
Required

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

9. Do you have a vagina?

- ◯ Yes
- ◯ No
- ◯ Prefer not to answer

Page Break

Collection: RECEP_VAGINAL
Contains: VSM, VSMNC, VSTW, VSTWNC, VSTM, VSTMNC
Show if: (VS.TEXT > 0) and (VAGINA = 1:[Yes])

The next set of questions ask about the people you have had RECEPTIVE vaginal sex with in the last months. By receptive vaginal sex, we mean when a penis is put into your vagina

Page Break

Question: VSM
Required

Scale Summary		
Code	Label	Show-If
1		
99	Prefer to not answer	

10. In the last months, how many men did you have vaginal sex with (with or without a condom)? (By men, we mean persons who are considered male at birth and currently identify as male.)

- ○ # of men
- ○ Prefer to not answer

Auto Page Break

Question: VSMNC
Required
Show if: (VSM.TEXT >= 1)

Scale Summary		
Code	Label	Show-If
1		
2	Prefer not to answer	

11. With how many **men** did you have **vaginal sex** without a condom?

- ◯ # of men
- ◯ Prefer not to answer

Page Break

Question: VSTW
Required

Scale Summary		
Code	Label	Show-If
1		
99	Prefer not to answer	

12. In the last months, how many **transgender women** did you have vaginal sex with (with or without a condom)? (By **transgender women**, we mean persons who are considered male at birth and now identify primarily as female.)

- ○ # of transgender women
- ○ Prefer not to answer

Auto Page Break

Question: VSTWNC
Required
Show if: (VSTW.TEXT >= 1)

Scale Summary		
Code	Label	Show-If
1		
99	Prefer not to answer	

13. With how many **transgender women** did you have **vaginal sex** without a condom?

- ◯ # of transgender women
- ◯ Prefer not to answer

Page Break

Question: VSTM
Required

Scale Summary		
Code	Label	Show-If
1		
99	Prefer not to answer	

14. In the last months, how many **transgender men** did you have vaginal sex with (with or without a condom)? (By **transgender men**, we mean persons who are considered female at birth and now identify primarily as male.)

- ○ # of transgender men
- ○ Prefer not to answer

Auto Page Break

Question: VSTMNC
Required
Show if: (VSTM.TEXT >= 1)

Scale Summary		
Code	Label	Show-If
1		
99	Prefer not to answer	

15. With how many **transgender men** did you have **vaginal sex** without a condom?

- ◯ # of transgender men
- ◯ Prefer not to answer

Page Break

Collection: RECEP_ANAL
Contains: RASM, RASMNC, RASTW, RASTWNC, RASTM, RASTMNC
Show if: (AS.TEXT > 0)

The next set of questions asks about the people you have had RECEPTIVE anal sex with in the last months. By receptive anal sex, we mean when a penis is put into your anus or butt.

Page Break

Question: RASM
Required

Scale Summary		
Code	Label	Show-If
1		
99	Prefer not to answer	

16. In the last months, how many **men** did you have **receptive anal sex** with (with or without a condom)? (By **men**, we mean persons who are considered male at birth and currently identify as male.)

- ○ # of men
- ○ Prefer not to answer

Auto Page Break

Question: RASMNC
Required
Show if: (RASM.TEXT > 0)

Scale Summary		
Code	Label	Show-If
1		
99	Prefer not to answer	

17. With how many **men** did you have **receptive anal sex** without a condom?

- ◯ # of men
- ◯ Prefer not to answer

Page Break

Question: RASTW
Required

Scale Summary		
Code	Label	Show-If
1		
99	Prefer not to answer	

18. In the last months, how many **transgender women** did you have **receptive anal sex** with (with or without a condom)? (By **transgender women**, we mean persons who are considered male at birth and now identify primarily as female.)

- ◯ # of transgender women
- ◯ Prefer not to answer

Auto Page Break

Question: RASTWNC
Required
Show if: (RASTW.TEXT > 0)

Scale Summary		
Code	Label	Show-If
1		
99	Prefer not to answer	

19. With how many **transgender women** did you have **receptive anal sex** without a condom?

- ○ # of transgender women
- ○ Prefer not to answer

Page Break

Question: RASTM
Required

Scale Summary		
Code	Label	Show-If
1		
99	Prefer not to answer	

20. In the last months, how many **transgender men** did you have **receptive anal sex** with (with or without a condom)? (By **transgender men**, we mean persons who are considered female at birth and now identify primarily as male.)

- ○ # of transgender men
- ○ Prefer not to answer

Auto Page Break

Question: RASTMNC
Required
Show if: (RASTM.TEXT > 0)

Scale Summary		
Code	Label	Show-If
1		
99	Prefer not to answer	

21. With how many **transgender men** did you have **receptive anal sex** without a condom?

- ○ # of transgender men
- ○ Prefer not to answer

Page Break

Question: PENIS
Required

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

22. Do you have a penis?

- ◯ Yes
- ◯ No
- ◯ Prefer not to answer

Page Break

The next set of questions ask you about the people you have **vaginal and/or anal INSERTIVE** sex with. By insertive sex, we mean that **you** put **your** penis into someone else's vagina, anus, or butt.

Page Break

Question: IVAS
Required
Show if: (PENIS = 1:[Yes]) and (VAS.TEXT >= 1)

Scale Summary		
Code	Label	Show-If
1		
99	Prefer not to answer	

23. In the last months, how many people did you have **insertive vaginal or anal sex** with (with or without a condom)?

- ○ # of people
- ○ Prefer not to answer

Page Break

Question: IVASW
Required
Show if: (IVAS.TEXT >= 1) and (PENIS = 1:[Yes])

Scale Summary		
Code	Label	Show-If
1		
99	Prefer not to answer	

24. How many of these people were **women**? (By women, we mean persons who are considered female at birth and currently identify as female.)

- ○ # of women
- ○ Prefer not to answer

Auto Page Break

Collection: INSERTIVE_VAGINAL
Contains: IVSW, IVSWNC
Show if: (IVASW.TEXT >= 1) and (PENIS = 1:[Yes])

Question: IVSW
Required

Scale Summary		
Code	Label	Show-If
1		
99	Prefer not to answer	

25. Of these **women**, how many did you have **insertive vaginal sex** with (with or without a condom)?

- ○ # of women
- ○ Prefer not to answer

Auto Page Break

Question: IVSWNC
Required
Show if: (IVSW.TEXT > 0)

Scale Summary		
Code	Label	Show-If
1		
99	Prefer not to answer	

26. With how many of these **women** did you have **insertive vaginal sex** without a condom?

- ○ # of women
- ○ Prefer not to answer

Page Break

Question: IVASM
Required
Show if: (IVAS.TEXT >= 1) and (PENIS = 1:[Yes])

Scale Summary		
Code	Label	Show-If
1		
99	Prefer not to answer	

27. How many of these people were **men**? (By men, we mean persons who are considered male at birth and currently identify as male.)

- ○ # of men
- ○ Prefer not to answer

Collection: INS_ANAL
Contains: IASM, IASMNC, IVASTW, IASTW, IASTWNC, IVASTM, IASTM, IASTMNC
Show if: (AS.TEXT > 0) and (PENIS = 1:[Yes])

Question: IASM
Required
Show if: (AS ≠ 99:[Prefer not to answer]) and (AS.TEXT > 0) and (IVASM ≠ 99:[Prefer not to answer]) and (IVASM.TEXT > 0)

Scale Summary		
Code	Label	Show-If
1		
99	Prefer not to answer	

28. Of these **men**, how many did you have **insertive anal sex** with (with or without a condom)?

- ○ # of men
- ○ Prefer not to answer

Auto Page Break

Question: IASMNC
Required
Show if: (IASM.TEXT > 0)

Scale Summary		
Code	Label	Show-If
1		
99	Prefer not to answer	

29. With how many of these **men** did you have **insertive anal sex** without a condom?

- ◯ # of men
- ◯ Prefer not to answer

Page Break

Question: IVASTW
Required
Show if: (IVAS ≠ 99:[Prefer not to answer]) and (IVAS.TEXT > 0)

Scale Summary		
Code	Label	Show-If
1		
99	Prefer not to answer	

30. How many of these people were **transgender women**? (By transgender women, we mean persons who are considered male at birth and now identify primarily as female.)

- ○ # of transgender women
- ○ Prefer not to answer

Question: IASTW
Required
Show if: (AS.TEXT > 0) and (IVASTW.TEXT > 0) and (IVASTW ≠ 99:[Prefer not to answer]) and (AS ≠ 99:[Prefer not to answer])

Scale Summary		
Code	Label	Show-If
1		
99	Prefer not to answer	

31. Of these **transgender women**, how many did you have **insertive anal sex** with (with or without a condom)?

- ○ # of transgender women
- ○ Prefer not to answer

Auto Page Break

Question: IASTWNC
Required
Show if: (IASTW.TEXT > 0)

Scale Summary		
Code	Label	Show-If
1		
99	Prefer not to answer	

32. With how many of these **transgender women** did you have **insertive anal sex** without a condom?

- ○ # of transgender women
- ○ Prefer not to answer

Page Break

Question: IVASTM
Required
Show if: (IVAS ≠ 99:[Prefer not to answer]) and (IVAS.TEXT > 0)

Scale Summary		
Code	Label	Show-If
1		
99	Prefer not to answer	

33. How many of these people were **transgender men**? (By transgender men, we mean persons who are considered female at birth and now identify primarily as male.)

- ○ # of transgender men
- ○ Prefer not to answer

Question: IASTM
Required
Show if: (AS ≠ 99:[Prefer not to answer]) and (AS.TEXT > 0) and (IVASTM ≠ 99:[Prefer not to answer]) and (IVASTM ≠ 99:[Prefer not to answer]) and (IVASTM.TEXT > 0)

Scale Summary		
Code	Label	Show-If
1		
99	Prefer not to answer	

34. Of these **transgender men**, how many did you have **insertive anal sex** with (with or without a condom)?

- ○ # of transgender men
- ○ Prefer not to answer

Auto Page Break

Question: IASTMNC
Required
Show if: (IASTM.TEXT > 0)

Scale Summary		
Code	Label	Show-If
1		
99	Prefer not to answer	

35. With how many of these **transgender men** did you have **insertive anal sex** without a condom?

- ○ # of transgender men
- ○ Prefer not to answer

Page Break

The next set of questions ask about your main partner. By main partner, we mean someone who you lived with or saw a lot, or to whom you felt a special emotional commitment, and with whom you had vaginal or anal sex.

Page Break

Question: MSP
Required
Show if: (VAS.TEXT >= 1)

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

36. Of the persons who you had **vaginal or anal sex** with, is/are any of them your main sexual partner(s)?

- ◯ Yes
- ◯ No
- ◯ Prefer not to answer

Page Break

Collection: MAIN_PARTNERS
Contains: MSPCH, MSPNUM, MSPC, MSPID, MSPO, MSPEX, MSPHIV, MSPDR, MSPSTD, MSPWORRIED, OSP
Show if: (MSP = 1:[Yes])

Question: MSPCH
Required
Show if: (MSP = 1:[Yes])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

37. Have you changed your main sex partner in the last months?

- ◯ Yes
- ◯ No
- ◯ Prefer not to answer

Auto Page Break

Question: MSPNUM
Required
Show if: (MSPCH = 1:[Yes])

Scale Summary		
Code	Label	Show-If
1		
99	Prefer not to answer	

38. How many main sex partners have you had in the last months?

- ◯ # of main sex partners
- ◯ Prefer not to answer

Page Break

Question: MSPC
Required
Show if: (MSP = 1:[Yes])

Scale Summary		
Code	Label	Show-If
1	Never	
2	Sometimes	
3	Always	
99	Prefer not to answer	

39. How often did you use condoms when you had vaginal or anal sex with your main partner(s) in the last months?

- ◯ Never
- ◯ Sometimes
- ◯ Always
- ◯ Prefer not to answer

Page Break

Question: MSPID
Required
Show if: (MSP = 1:[Yes])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
3	Don't know	
99	Prefer not to answer	

40. Do any of your main partner(s) inject drugs to get high?

- ◯ Yes
- ◯ No
- ◯ Don't know
- ◯ Prefer not to answer

Question: MSPO
Required
Show if: (MSP = 1:[Yes])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
3	Don't know	
99	Prefer not to answer	

41. Have any of your main partner(s) had sex with someone else besides you during the same time period?

- ◯ Yes
- ◯ No
- ◯ Don't know
- ◯ Prefer not to answer

Auto Page Break

Question: MSPEX
Required
Show if: (MSPO = 1:[Yes])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
3	Don't know	
99	Prefer not to answer	

42. Did any of your main partner(s) have vaginal or anal sex with another person in exchange for money, drugs, goods, or services?

- ◯ Yes
- ◯ No
- ◯ Don't know
- ◯ Prefer not to answer

Page Break

Question: MSPHIV
Required
Show if: (MSP = 1:[Yes])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
3	Don't know	
99	Prefer not to answer	

43. Are any of your main partner(s) HIV-infected?

- ◯ Yes
- ◯ No
- ◯ Don't know
- ◯ Prefer not to answer

Question: MSPDR
Required
Show if: (MSP = 1:[Yes])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
3	Don't know	
99	Prefer not to answer	

44. Were any of your main partner(s) ever drunk or high on drugs while you were having sex with them?

- ◯ Yes
- ◯ No
- ◯ Don't know
- ◯ Prefer not to answer

Question: MSPSTD
Required
Show if: (MSP = 1:[Yes])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
3	Don't know	
99	Prefer not to answer	

45. Have any of your main partner(s) been diagnosed with or treated for a sexually transmitted infection the last months?

- ◯ Yes
- ◯ No
- ◯ Don't know
- ◯ Prefer not to answer

Page Break

Question: MSPWORRIED
Required
Show if: (MSPHIV = 2:[No]) or (MSPHIV = 3:[Don't know])

Scale Summary		
Code	Label	Show-If
1	Very worried	
2	Somewhat worried	
3	Not at all worried	
99	Prefer not to answer	

46. How worried are you that your main partner(s) may become infected with HIV in **the next year**?

- ◯ Very worried
- ◯ Somewhat worried
- ◯ Not at all worried
- ◯ Prefer not to answer

Page Break

Question: OSP
Required
Show if: (MSP = 1:[Yes])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

47. Are there any other people, not including your main partner(s), that you recently had sex with?

- ◯ Yes
- ◯ No
- ◯ Prefer not to answer

Page Break

Collection: OTHER_PARTNERS
Contains: OSPID, OSPSO, OSPEX, OSPHIV, OSPHIVNC, OSPDR, OSPSTD, OSPWORRIED
Show if: (OSP = 1:[Yes])

The next set of questions ask you about the other people you have had sex with recently.

Question: OSPID
Required
Show if: (OSP = 1:[Yes])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
3	Don't know	
99	Prefer not to answer	

48. During the last months, did you have vaginal or anal sex with someone who injected drugs to get high?

- ◯ Yes
- ◯ No
- ◯ Don't know
- ◯ Prefer not to answer

Question: OSPSO
Required
Show if: (OSP = 1:[Yes])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
3	Don't know	
99	Prefer not to answer	

49. During the last months, did you have vaginal or anal sex with someone who was having sex with someone else besides you during the same time period?

- ◯ Yes
- ◯ No
- ◯ Don't know
- ◯ Prefer not to answer

Auto Page Break

Question: OSPEX
Required
Show if: (OSPSO = 1:[Yes])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
3	Don't know	
99	Prefer not to answer	

50. Did any of these persons have vaginal or anal sex with another person in exchange for money, drugs, goods, or services?

- ◯ Yes
- ◯ No
- ◯ Don't know
- ◯ Prefer not to answer

Page Break

Question: OSPHIV
Required
Show if: (OSP = 1:[Yes])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
3	Don't know	
99	Prefer not to answer	

51. During the last months, did you have vaginal or anal sex with someone who was HIV-infected?

- ◯ Yes
- ◯ No
- ◯ Don't know
- ◯ Prefer not to answer

Auto Page Break

Question: OSPHIVNC
Required
Show if: (OSPHIV = 1:[Yes])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
3	Don't know	
99	Prefer not to answer	

52. Did you have **vaginal or anal sex** without a condom with any HIV-infected persons?

- ◯ Yes
- ◯ No
- ◯ Don't know
- ◯ Prefer not to answer

Page Break

Question: OSPDR
Required
Show if: (OSP = 1:[Yes])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
3	Don't know	
99	Prefer not to answer	

53. During the last months, did you have vaginal or anal sex with someone who was drunk or high on drugs while you were having sex with them?

- ◯ Yes
- ◯ No
- ◯ Don't know
- ◯ Prefer not to answer

Page Break

Question: OSPSTD
Required
Show if: (OSP = 1:[Yes])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
3	Don't know	
99	Prefer not to answer	

54. During the last months, did you have vaginal or anal sex with someone who has recently been diagnosed with, or treated for one or more sexually transmitted infections?

- ◯ Yes
- ◯ No
- ◯ Don't know
- ◯ Prefer not to answer

Question: OSPWORRIED
Required
Show if: (OSPHIV = 2:[No]) or (OSPHIV = 3:[Don't know])

Scale Summary		
Code	Label	Show-If
1	Very worried	
2	Somewhat worried	
3	Not at all worried	
99	Prefer not to answer	

55. How worried are you that one or more of your sex partners may become infected with HIV in **the next year**?

- ◯ Very worried
- ◯ Somewhat worried
- ◯ Not at all worried
- ◯ Prefer not to answer

Page Break

Collection: PPT_RISK_BEHAVIOR
Contains: ALCOH, ALCOHNUM, ALCOHB, VASDRUNK, IDUSE, IDNEEDLESHARE, MDKS, MS2HR, CRCO, CRCOS2HR, PRCO, PRCOS2HR, AMPMETH, AMPMETS2HR, METMAN, METMANS2HR, HERMED, HERMEDS2HR, MDMA, MDMAS2HR, WHO, WHOS2HR, POP, POPS2HR, OTHDRUG, OTHDRUG_FREQ, OTHDRUGS2HR, CIGVAPE, VASEX, HIVINFYR

The next set of questions ask about some other behaviors.

Question: ALCOH
Required

Scale Summary		
Code	Label	Show-If
1	Never	
2	Monthly or less	
3	2-4 times a month	
4	2-3 times a week	
5	4 or more times a week	
99	Prefer not to answer	

56. During the last months, how often did you have a drink containing alcohol?

- ◯ Never
- ◯ Monthly or less
- ◯ 2-4 times a month
- ◯ 2-3 times a week
- ◯ 4 or more times a week
- ◯ Prefer not to answer

Auto Page Break

Question: ALCOHNUM
Required
Show if: (ALCOH ≠ 1:[Never]) and (ALCOH ≠ 99:[Prefer not to answer])

Scale Summary		
Code	Label	Show-If
1	1 or 2	
2	3 or 4	
3	5 or 6	
4	7 to 9	
5	10 or more	
99	Prefer not to answer	

57. During the last months, on a typical day when you were drinking, how many standard drinks containing alcohol did you have?

- ◯ 1 or 2
- ◯ 3 or 4
- ◯ 5 or 6
- ◯ 7 to 9
- ◯ 10 or more
- ◯ Prefer not to answer

Question: ALCOHB
Required
Show if: (ALCOH ≠ 1:[Never]) and (ALCOH ≠ 99:[Prefer not to answer])

Scale Summary		
Code	Label	Show-If
1	Never	
2	Less than monthly	
3	Monthly	
4	Weekly	
5	Daily or almost daily	
99	Prefer not to answer	

58. During the last months, how often did you have 6 or more drinks on one occasion?

- ◯ Never
- ◯ Less than monthly
- ◯ Monthly
- ◯ Weekly
- ◯ Daily or almost daily
- ◯ Prefer not to answer

Question: VASDRUNK
Required
Show if: (VAS ≠ 99:[Prefer not to answer]) and (VAS.TEXT ≠ 0) and (ALCOH ≠ 99:[Prefer not to answer]) and (ALCOH ≠ 1:[Never])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

59. During the last months, did you have vaginal or anal sex while you were drunk?

- ◯ Yes
- ◯ No
- ◯ Prefer not to answer

Page Break

Question: IDUSE
Required

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

60. During the last months, did you inject any drugs to get high?

- ◯ Yes
- ◯ No
- ◯ Prefer not to answer

Auto Page Break

Question: IDNEEDLESHARE
Required
Show if: (IDUSE = 1:[Yes])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

61. Did you share a needle with others?

- ◯ Yes
- ◯ No
- ◯ Prefer not to answer

Page Break

Question: MDKS
Required

Scale Summary		
Code	Label	Show-If
1	Never	
2	Once per week or less	
3	2-3 times a week	
4	4-6 times a week	
5	Every day	
99	Prefer not to answer	

62. During the last months, how often did you use Marijuana, dagga, K2, spice?

- ◯ Never
- ◯ Once per week or less
- ◯ 2-3 times a week
- ◯ 4-6 times a week
- ◯ Every day
- ◯ Prefer not to answer

Page Break

Question: MS2HR
Required
Show if: (VAS.TEXT > 0) and (MDKS ≠ 1:[Never]) and (MDKS ≠ 99:[Prefer not to answer])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

63. During the last months, did you have vaginal or anal sex within 2 hours of you using marijuana?

- ◯ Yes
- ◯ No
- ◯ Prefer not to answer

Page Break

Question: CRCO
Required

Scale Summary		
Code	Label	Show-If
1	Never	
2	Once per week or less	
3	2-3 times a week	
4	4-6 times a week	
5	Every day	
99	Prefer not to answer	

64. During the last months, how often did you use crack cocaine?

- ◯ Never
- ◯ Once per week or less
- ◯ 2-3 times a week
- ◯ 4-6 times a week
- ◯ Every day
- ◯ Prefer not to answer

Page Break

Question: CRCOS2HR
Required
Show if: (VAS.TEXT > 0) and (CRCO ≠ 1:[Never]) and (CRCO ≠ 99:[Prefer not to answer])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

65. During the last months, did you have vaginal or anal sex within 2 hours of you using crack cocaine?

- ◯ Yes
- ◯ No
- ◯ Prefer not to answer

Page Break

Question: PRCO
Required

Scale Summary		
Code	Label	Show-If
1	Never	
2	Once per week or less	
3	2-3 times a week	
4	4-6 times a week	
5	Every day	
99	Prefer not to answer	

66. During the last months, how often did you use powder cocaine?

- ◯ Never
- ◯ Once per week or less
- ◯ 2-3 times a week
- ◯ 4-6 times a week
- ◯ Every day
- ◯ Prefer not to answer

Page Break

Question: PRCOS2HR
Required
Show if: (VAS.TEXT > 0) and (PRCO ≠ 1:[Never]) and (PRCO ≠ 99:[Prefer not to answer])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

67. During the last months, did you have vaginal or anal sex within 2 hours of you using powder cocaine?

- ◯ Yes
- ◯ No
- ◯ Prefer not to answer

Page Break

Question: AMPMETH
Required

Scale Summary		
Code	Label	Show-If
1	Never	
2	Once per week or less	
3	2-3 times a week	
4	4-6 times a week	
5	Every day	
99	Prefer not to answer	

68. During the last months, how often did you use amphetamine/methamphetamine, crystal meth, Khat/Cat, or tik?

- ◯ Never
- ◯ Once per week or less
- ◯ 2-3 times a week
- ◯ 4-6 times a week
- ◯ Every day
- ◯ Prefer not to answer

Page Break

Question: AMPMETS2HR
Required
Show if: (VAS.TEXT > 0) and (AMPMETH ≠ 1:[Never]) and (AMPMETH ≠ 99:[Prefer not to answer])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

69. During the last months, did you have vaginal or anal sex within 2 hours of you using amphetamine/methamphetamine, crystal meth, Khat/Cat, or tik?

- ◯ Yes
- ◯ No
- ◯ Prefer not to answer

Page Break

Question: METMAN
Required

Scale Summary		
Code	Label	Show-If
1	Never	
2	Once per week or less	
3	2-3 times a week	
4	4-6 times a week	
5	Every day	
99	Prefer not to answer	

70. During the last months, how often did you use methaqualone or mandrax?

- ◯ Never
- ◯ Once per week or less
- ◯ 2-3 times a week
- ◯ 4-6 times a week
- ◯ Every day
- ◯ Prefer not to answer

Page Break

Question: METMANS2HR
Required
Show if: (VAS.TEXT > 0) and (METMAN ≠ 1:[Never]) and (METMAN ≠ 99:[Prefer not to answer])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

71. During the last months, did you have vaginal or anal sex within 2 hours of you using methaqualone or mandrax?

- ◯ Yes
- ◯ No
- ◯ Prefer not to answer

Page Break

Question: HERMED
Required

Scale Summary		
Code	Label	Show-If
1	Never	
2	Once per week or less	
3	2-3 times a week	
4	4-6 times a week	
5	Every day	
99	Prefer not to answer	

72. During the last months, how often did you use heroin, prescription pain killers/medications?

- ◯ Never
- ◯ Once per week or less
- ◯ 2-3 times a week
- ◯ 4-6 times a week
- ◯ Every day
- ◯ Prefer not to answer

Page Break

Question: HERMEDS2HR
Required
Show if: (VAS.TEXT > 0) and (HERMED ≠ 1:[Never]) and (HERMED ≠ 99:[Prefer not to answer])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

73. During the last months, did you have vaginal or anal sex within 2 hours of you using heroin, prescription pain killers/medications?

- ◯ Yes
- ◯ No
- ◯ Prefer not to answer

Page Break

Question: MDMA
Required

Scale Summary		
Code	Label	Show-If
1	Never	
2	Once per week or less	
3	2-3 times a week	
4	4-6 times a week	
5	Every day	
99	Prefer not to answer	

74. During the last months, how often did you use MDMA or Ecstacy?

- ◯ Never
- ◯ Once per week or less
- ◯ 2-3 times a week
- ◯ 4-6 times a week
- ◯ Every day
- ◯ Prefer not to answer

Page Break

Question: MDMAS2HR
Required
Show if: (VAS.TEXT > 0) and (MDMA ≠ 1:[Never]) and (MDMA ≠ 99:[Prefer not to answer])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

75. During the last months, did you have vaginal or anal sex within 2 hours of you using MDMA or Ecstacy?

- ◯ Yes
- ◯ No
- ◯ Prefer not to answer

Page Break

Question: WHO
Required

Scale Summary		
Code	Label	Show-If
1	Never	
2	Once per week or less	
3	2-3 times a week	
4	4-6 times a week	
5	Every day	
99	Prefer not to answer	

76. During the last months, how often did you use whoonga/wunga or nyaope?

- ◯ Never
- ◯ Once per week or less
- ◯ 2-3 times a week
- ◯ 4-6 times a week
- ◯ Every day
- ◯ Prefer not to answer

Page Break

Question: WHOS2HR
Required
Show if: (VAS.TEXT > 0) and (WHO ≠ 1:[Never]) and (WHO ≠ 99:[Prefer not to answer])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

77. During the last months, did you have vaginal or anal sex within 2 hours of you using Whoonga/wunga or nyaope?

- ◯ Yes
- ◯ No
- ◯ Prefer not to answer

Page Break

Question: POP
Required

Scale Summary		
Code	Label	Show-If
1	Never	
2	Once per week or less	
3	2-3 times a week	
4	4-6 times a week	
5	Every day	
99	Prefer not to answer	

78. During the last months, how often did you use poppers?

- ◯ Never
- ◯ Once per week or less
- ◯ 2-3 times a week
- ◯ 4-6 times a week
- ◯ Every day
- ◯ Prefer not to answer

Page Break

Question: POPS2HR
Required
Show if: (VAS.TEXT > 0) and (POP ≠ 1:[Never]) and (POP ≠ 99:[Prefer not to answer])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

79. During the last months, did you have vaginal or anal sex within 2 hours of you using Poppers?

- ◯ Yes
- ◯ No
- ◯ Prefer not to answer

Page Break

Question: OTHDRUG
Required

Scale Summary		
Code	Label	Show-If
1	Yes	
2	Not applicable - No other drugs used	
99	Prefer not to answer	

80. During the last months, have you used any other drugs? If yes, please specify.

- ○ Yes
- ○ Not applicable - No other drugs used
- ○ Prefer not to answer

Page Break

Question: OTHDRUG_FREQ
Required
Show if: (OTHDRUG = 1:[Yes])

Scale Summary		
Code	Label	Show-If
2	Once per week or less	
3	2-3 times a week	
4	4-6 times a week	
5	Every day	
99	Prefer not to answer	

81. During the last months, how often did you use ?

- ◯ Once per week or less
- ◯ 2-3 times a week
- ◯ 4-6 times a week
- ◯ Every day
- ◯ Prefer not to answer

Page Break

Question: OTHDRUGS2HR
Required
Show if: (VAS.TEXT > 0) and (OTHDRUG_FREQ ≠ 99:[Prefer not to answer]) and (OTHDRUG_FREQ was-answered)

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

82. During the last months, did you have vaginal or anal sex within 2 hours of you using ?

- ○ Yes
- ○ No
- ○ Prefer not to answer

Page Break

Question: CIGVAPE
Required

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

83. Do you currently smoke cigarettes or e-cigs (Vape)?

- ◯ Yes
- ◯ No
- ◯ Prefer not to answer

Page Break

Question: VASEX
Required
Show if: (VAS.TEXT > 0)

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

84. In the last months, have you given and/or received money, gifts, drugs, goods, shelter, or services in exchange for vaginal or anal sex?

- ◯ Yes
- ◯ No
- ◯ Prefer not to answer

Question: HIVINFYR
Required
Show if: (SCHEDULE = 1:[Schedule 1]) or (SCHEDULE = 4:[Schedule 4])

Scale Summary		
Code	Label	Show-If
1	Not at all likely	
2	Somewhat unlikely	
3	Neutral/No opinion	
4	Somewhat likely	
5	Extremely Likely	
99	Prefer not to answer	

85. How likely do you think it is that you may become infected with HIV in **the next year**?

- ◯ Not at all likely
- ◯ Somewhat unlikely
- ◯ Neutral/No opinion
- ◯ Somewhat likely
- ◯ Extremely Likely
- ◯ Prefer not to answer

Collection: STUDY_PRODUCT
Contains: ANTIPLAC, HIGHLOW, INVINFUSION
Show if: (SCHEDULE = 1:[Schedule 1]) or (SCHEDULE = 4:[Schedule 4])

Question: ANTIPLAC
Required
Show if: (VISIT is-any-of 09.0:[Visit 09.0 (Infusion #4)] or 15.0:[Visit 15.0 (Infusion #7)] or 21.0:[Visit 21.0 (Infusion #10)] or 26.0:[Visit 26.0 (End Visit)] or 72.0:[Visit 72.0] or 74.0:[Visit 74.0] or 76.0:[Visit 76.0] or 78.0:[Visit 78.0])

Scale Summary		
Code	Label	Show-If
1	VRC01	
2	Placebo	
3	Don't know	
99	Prefer not to answer	

86. Do you think you received the VRC01 antibody or placebo in this study?

- ◯ VRC01
- ◯ Placebo
- ◯ Don't know
- ◯ Prefer not to answer

Auto Page Break

Question: HIGHLOW
Required
Show if: (ANTIPLAC = 1:[VRC01])

Scale Summary		
Code	Label	Show-If
1	High Dose	
2	Low Dose	
3	Unsure	
99	Prefer not to answer	

87. Do you think you received the high dose, low dose, or are you unsure?

- ◯ High Dose
- ◯ Low Dose
- ◯ Unsure
- ◯ Prefer not to answer

Question: INVINFUSION
Required
Show if: (VISIT = 02.0:[Visit 02.0 (Enrollment/Infusion #1)])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

88. Have you, a family member, or close friend ever had an IV infusion?

- ◯ Yes
- ◯ No
- ◯ Prefer not to answer

Appendix C

The abbreviated CASI behavioral risk survey administered at the enrollment visit at sites outside of South Africa in HVTN 703/HPTN 081 is included below. The survey is used for constructing baseline covariates potentially predictive of the primary endpoint considered for inclusion in the superlearner HIV-1 risk predictor described in Section 8.6.

AMP Study

0%

Collection: LOGIN
Contains: PTID, SCHEDULE, VISIT, VISITCHK

AMP Study

Question: PTID
Required

Site Staff: Please answer the following questions. Please enter a valid Participant ID in the following format: 111-1-1111-1

Question: SCHEDULE
Required

Scale Summary		
Code	Label	Show-If
1	Schedule 1	
2	Schedule 2 (HIV Infected)	
3	Schedule 3 (HIV Infected at Enrollment)	
4	Schedule 4	

Which study Schedule is the participant currently in?

- ◯ Schedule 1
- ◯ Schedule 2 (HIV Infected)
- ◯ Schedule 3 (HIV Infected at Enrollment)
- ◯ Schedule 4

Question: VISIT
Required

Scale Summary		
Code	Label	Show-If
02.0	Visit 02.0 (Enrollment/Infusion #1)	
04.0	Visit 04.0 (Infusion #2)	
07.0	Visit 07.0 (Infusion #3)	
09.0	Visit 09.0 (Infusion #4)	
11.0	Visit 11.0 (Infusion #5)	
13.0	Visit 13.0 (Infusion #6)	
15.0	Visit 15.0 (Infusion #7)	
17.0	Visit 17.0 (Infusion #8)	
19.0	Visit 19.0 (Infusion #9)	
21.0	Visit 21.0 (Infusion #10)	
26.0	Visit 26.0 (End Visit)	

35.0	Visit 35.0	
48.0	Visit 48.0	
72.0	Visit 72.0	
74.0	Visit 74.0	
76.0	Visit 76.0	
78.0	Visit 78.0	

What is the visit code for this visit?

Please select the visit code from the drop down menu.

-- Select One --

Question: VISITCHK
Required

Please confirm the visit code by entering it here:

Please enter a "0" first if the visit is before 10.0 - for example, "07.0"

Click “next” to select the appropriate language.

Question: LANG_SELECT
Required

Scale Summary		
Code	Label	Show-If
1033	English	
1077	Zulu	*Never Shown*
1076	Xhosa	*Never Shown*
1132	Sotho	*Never Shown*
1074	Setswana	(Error!)
1078	Shona	(Error!)
1073	Dholuo	*Never Shown*
1116	Chichewa	*Never Shown*
1046	Portuguese	*Never Shown*
1089	Swahili	(Error!)

1. Language choice

- ○ English
- ○ Zulu
- ○ Xhosa
- ○ Sotho
- ○ Setswana
- ○ Shona
- ○ Dholuo
- ○ Chichewa
- ○ Portuguese
- ○ Swahili

Collection: STAFF_QUESTIONS
Contains: COMPLETEDBY

Question: COMPLETEDBY
Required

Scale Summary		
Code	Label	Show-If

1	Participant is completing questionnaire	
2	Interviewer is administering questionnaire	

2. Is this questionnaire being completed by the participant directly or is an interviewer from the site staff reading the questionnaire to the participant and entering participant's responses?

- ◯ Participant is completing questionnaire
- ◯ Interviewer is administering questionnaire

Collection: TOTAL_NUM_PARTNERS
Contains: SEXNUM, NCNUM, SEX_BEHAVIOR, MSP

Many people are taking part in this research study. We ask the same questions of all participants. However, some questions may not apply to you.

Please answer these questions honestly. We make no judgments about how you have sex or the number of times or with whom. We do not judge about alcohol or drug use.

Your answers to these questions will help us understand participants' behaviors so that we may assess effectiveness of current HIV prevention methods.

The first set of questions is about your sexual relationships with men, in the last months. By men we mean persons who are considered male at birth and currently identify as male.

By sex, we are talking about VAGINAL sex (when a penis is put into the vagina). For some questions, we will be asking about sex without a condom. By this we mean that a condom was not used the whole time the penis was inserted, or the condom broke, tore, spilled or slipped off. A condom can be either a male or female condom.

Question: SEXNUM
Required

Scale Summary		
Code	Label	Show-If
1		
99	Prefer not to answer	

3. In the last months, how many men did you have vaginal sex with (with or without a condom)?

- ◯ # of men ____
- ◯ Prefer not to answer

Jump-To: JMP1
Description:
Jump-To-Item: PPT_RISK_BEHAVIOR
Jump-If: (SEXNUM.TEXT = 0) or (SEXNUM = 99:[Prefer not to answer])

Question: NCNUM
Required
Show if: (SEXNUM.TEXT > 0)

Scale Summary		
Code	Label	Show-If
1		
99	Prefer not to answer	

4. With how many men did you have vaginal sex without a condom?

- ◯ # of men ____
- ◯ Prefer not to answer

Collection: SEX_BEHAVIOR
Contains: CONDFREQ, SXTIMES7D, CONDFREQ7D

Show if: (SEXNUM.TEXT > 0)

Question: CONDFREQ
Required

Scale Summary		
Code	Label	Show-If
1	Never	
2	Sometimes	
3	Always	
99	Prefer not to answer	

5. In general, in the last months, how often did you use a condom during vaginal sex?

- ○ Never
- ○ Sometimes
- ○ Always
- ○ Prefer not to answer

Question: SXTIMES7D
Required
Show if: (SEXNUM ≠ 99:[Prefer not to answer]) and (SEXNUM.TEXT > 0)

Scale Summary		
Code	Label	Show-If
1		
99	Prefer not to answer	

6. In **the last 7 days**, how many times have you had vaginal sex (with or without a condom)?

- ○ # of times [ ]
- ○ Prefer not to answer

Question: CONDFREQ7D
Required
Show if: (SXTIMES7D ≠ 99:[Prefer not to answer]) and (SXTIMES7D.TEXT > 0)

Scale Summary		
Code	Label	Show-If
1	Never	
2	Sometimes	
3	Always	
99	Prefer not to answer	

7. In general, in **the last 7 days**, how often did you use a condom during vaginal sex?

- ○ Never
- ○ Sometimes
- ○ Always
- ○ Prefer not to answer

The next set of questions asks about your main partner. By main partner, we mean someone who you lived with or saw a lot, or to whom you felt a special commitment, and with whom you had vaginal sex.

Question: MSP
Required
Show if: (SEXNUM.TEXT >= 1)

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

8. Of the persons who you had vaginal sex with, is/are any of them your main sexual partner(s)?

- ◯ Yes
- ◯ No
- ◯ Prefer not to answer

Collection: MAIN_PARTNERS
Contains: MSPCH, MSPNUM, MSPC, MSPID, MSPO, MSPEX, MSPHIV, MSPDR, MSPSTD, MSPWORRIED, OSP
Show if: (MSP = 1:[Yes])

Question: MSPCH
Required
Show if: (MSP = 1:[Yes])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

9. Have you changed your main sex partner in the last months?

- ◯ Yes
- ◯ No
- ◯ Prefer not to answer

Question: MSPNUM
Required
Show if: (MSPCH = 1:[Yes])

Scale Summary		
Code	Label	Show-If
1		
99	Prefer not to answer	

10. How many main sex partners have you had in the last months?

- ◯ # of main sex partners
- ◯ Prefer not to answer

Question: MSPC
Required
Show if: (MSP = 1:[Yes])

Scale Summary		
Code	Label	Show-If
1	Never	
2	Sometimes	
3	Always	
99	Prefer not to answer	

11. How often did you use condoms when you had vaginal sex with your main partner(s) in the last months?

- ◯ Never
- ◯ Sometimes
- ◯ Always
- ◯ Prefer not to answer

Question: MSPID
Required
Show if: (MSP = 1:[Yes])

Scale Summary		

Code	Label	Show-If
1	Yes	
2	No	
3	Don't know	
99	Prefer not to answer	

12. Do any of your main partner(s) inject drugs to get high?

- ◯ Yes
- ◯ No
- ◯ Don't know
- ◯ Prefer not to answer

Question: MSPO
Required
Show if: (MSP = 1:[Yes])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
3	Don't know	
99	Prefer not to answer	

13. Have any of your main partner(s) had sex with someone else besides you during the same time period?

- ◯ Yes
- ◯ No
- ◯ Don't know
- ◯ Prefer not to answer

Question: MSPEX
Required
Show if: (MSPO = 1:[Yes])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
3	Don't know	
99	Prefer not to answer	

14. Did any of your main partner(s) have vaginal sex with another person in exchange for money, drugs, goods, or services?

- ◯ Yes
- ◯ No
- ◯ Don't know
- ◯ Prefer not to answer

Question: MSPHIV
Required
Show if: (MSP = 1:[Yes])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
3	Don't know	
99	Prefer not to answer	

15. Are any of your main partner(s) HIV-infected?

- ◯ Yes
- ◯ No
- ◯ Don't know
- ◯ Prefer not to answer

Question: MSPDR
Required
Show if: (MSP = 1:[Yes])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
3	Don't know	
99	Prefer not to answer	

16. Were any of your main partner(s) ever drunk or high on drugs while you were having sex with them?

- ◯ Yes
- ◯ No
- ◯ Don't know
- ◯ Prefer not to answer

Question: MSPSTD
Required
Show if: (MSP = 1:[Yes])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
3	Don't know	
99	Prefer not to answer	

17. Have any of your main partner(s) been diagnosed with or treated for a sexually transmitted infection the last months?

- ◯ Yes
- ◯ No
- ◯ Don't know
- ◯ Prefer not to answer

Question: MSPWORRIED
Required
Show if: (MSPHIV = 2:[No]) or (MSPHIV = 3:[Don't know])

Scale Summary		
Code	Label	Show-If
1	Very worried	
2	Somewhat worried	
3	Not at all worried	
99	Prefer not to answer	

18. How worried are you that your main partner(s) may become infected with HIV in **the next year**?

- ◯ Very worried
- ◯ Somewhat worried
- ◯ Not at all worried
- ◯ Prefer not to answer

Question: OSP
Required
Show if: (MSP = 1:[Yes])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

19. Are there any other people, not including your main partner(s), that you recently had sex with?

- ◯ Yes
- ◯ No
- ◯ Prefer not to answer

Collection: OTHER_PARTNERS
Contains: OSPID, OSPSO, OSPEX, OSPHIV, OSPHIVNC, OSPDR, OSPSTD, OSPWORRIED
Show if: (OSP = 1:[Yes])

The next set of questions ask you about the other people you have had sex with recently.

Question: OSPID
Required
Show if: (OSP = 1:[Yes])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
3	Don't know	
99	Prefer not to answer	

20. During the last months, did you have sex with someone who injected drugs to get high?

- ◯ Yes
- ◯ No
- ◯ Don't know
- ◯ Prefer not to answer

Question: OSPSO
Required
Show if: (OSP = 1:[Yes])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
3	Don't know	
99	Prefer not to answer	

21. During the last months, did you have sex with someone who was having sex with someone else besides you during the same time period?

- ◯ Yes
- ◯ No
- ◯ Don't know
- ◯ Prefer not to answer

Question: OSPEX
Required

Show if: (OSPSO = 1:[Yes])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
3	Don't know	
99	Prefer not to answer	

22. Did any of these persons have sex with another person in exchange for money, drugs, goods, or services?

- ◯ Yes
- ◯ No
- ◯ Don't know
- ◯ Prefer not to answer

Question: OSPHIV
Required
Show if: (OSP = 1:[Yes])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
3	Don't know	
99	Prefer not to answer	

23. During the last months, did you have sex with someone who was HIV-infected?

- ◯ Yes
- ◯ No
- ◯ Don't know
- ◯ Prefer not to answer

Question: OSPHIVNC
Required
Show if: (OSPHIV = 1:[Yes])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
3	Don't know	
99	Prefer not to answer	

24. Did you have sex without a condom with any HIV-infected persons?

- ◯ Yes
- ◯ No
- ◯ Don't know
- ◯ Prefer not to answer

Question: OSPDR
Required
Show if: (OSP = 1:[Yes])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
3	Don't know	
99	Prefer not to answer	

25. During the last months, did you have sex with someone who was drunk or high on drugs while you were having sex with them?

- ◯ Yes
- ◯ No
- ◯ Don't know
- ◯ Prefer not to answer

Question: OSPSTD
Required
Show if: (OSP = 1:[Yes])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
3	Don't know	
99	Prefer not to answer	

26. During the last months, did you have sex with someone who has recently been diagnosed with, or treated for one or more sexually transmitted infections?

- ◯ Yes
- ◯ No
- ◯ Don't know
- ◯ Prefer not to answer

Question: OSPWORRIED
Required
Show if: (OSPHIV = 2:[No]) or (OSPHIV = 3:[Don't know])

Scale Summary		
Code	Label	Show-If
1	Very worried	
2	Somewhat worried	
3	Not at all worried	
99	Prefer not to answer	

27. How worried are you that one or more of your sex partners may become infected with HIV in **the next year**?

- ◯ Very worried
- ◯ Somewhat worried
- ◯ Not at all worried
- ◯ Prefer not to answer

Collection: PPT_RISK_BEHAVIOR
Contains: ALCOH, ALCOHNUM, ALCOHB, VASDRUNK, IDUSE, IDNEEDLESHARE, MDKS, MS2HR, CRCO, CRCOS2HR, PRCO, PRCOS2HR, AMPMETH, AMPMETS2HR, METMAN, METMANS2HR, HERMED, HERMEDS2HR, MDMA, MDMAS2HR, WHO, WHOS2HR, POP, POPS2HR, OTHDRUG, OTHDRUG_FREQ, OTHDRUGS2HR, CIGVAPE, VASEX, HIVINFYR

The next set of questions ask about some other behaviors.

Question: ALCOH
Required

Scale Summary		
Code	Label	Show-If
1	Never	
2	Monthly or less	
3	2-4 times a month	

4	2-3 times a week	
5	4 or more times a week	
99	Prefer not to answer	

28. During the last months, how often did you have a drink containing alcohol?

- ◯ Never
- ◯ Monthly or less
- ◯ 2-4 times a month
- ◯ 2-3 times a week
- ◯ 4 or more times a week
- ◯ Prefer not to answer

Question: ALCOHNUM
Required
Show if: (ALCOH ≠ 1:[Never]) and (ALCOH ≠ 99:[Prefer not to answer])

Scale Summary		
Code	Label	Show-If
1	1 or 2	
2	3 or 4	
3	5 or 6	
4	7 to 9	
5	10 or more	
99	Prefer not to answer	

29. During the last months, on a typical day when you were drinking, how many standard drinks containing alcohol did you have?

- ◯ 1 or 2
- ◯ 3 or 4
- ◯ 5 or 6
- ◯ 7 to 9
- ◯ 10 or more
- ◯ Prefer not to answer

Question: ALCOHB
Required
Show if: (ALCOH ≠ 1:[Never]) and (ALCOH ≠ 99:[Prefer not to answer])

Scale Summary		
Code	Label	Show-If
1	Never	
2	Less than monthly	
3	Monthly	
4	Weekly	
5	Daily or almost daily	
99	Prefer not to answer	

30. During the last months, how often did you have 6 or more drinks on one occasion?

- ◯ Never
- ◯ Less than monthly
- ◯ Monthly
- ◯ Weekly
- ◯ Daily or almost daily
- ◯ Prefer not to answer

Question: VASDRUNK
Required

Show if: (SEXNUM.TEXT > 0) and (ALCOH ≠ 99:[Prefer not to answer]) and (ALCOH ≠ 1:[Never])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

31. During the last months, did you have sex while you were drunk?

- ◯ Yes
- ◯ No
- ◯ Prefer not to answer

Question: IDUSE
Required

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

32. During the last months, did you inject any drugs to get high?

- ◯ Yes
- ◯ No
- ◯ Prefer not to answer

Question: IDNEEDLESHARE
Required
Show if: (IDUSE = 1:[Yes])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

33. Did you share a needle with others?

- ◯ Yes
- ◯ No
- ◯ Prefer not to answer

Question: MDKS
Required

Scale Summary		
Code	Label	Show-If
1	Never	
2	Once per week or less	
3	2-3 times a week	
4	4-6 times a week	
5	Every day	
99	Prefer not to answer	

34. During the last months, how often did you use Marijuana, dagga, K2, spice?

- ◯ Never
- ◯ Once per week or less
- ◯ 2-3 times a week
- ◯ 4-6 times a week
- ◯ Every day

- ◯ Prefer not to answer

Question: MS2HR
Required
Show if: (SEXNUM.TEXT > 0) and (MDKS ≠ 1:[Never]) and (MDKS ≠ 99:[Prefer not to answer])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

35. During the last months, did you have sex within 2 hours of you using marijuana?

- ◯ Yes
- ◯ No
- ◯ Prefer not to answer

Question: CRCO
Required

Scale Summary		
Code	Label	Show-If
1	Never	
2	Once per week or less	
3	2-3 times a week	
4	4-6 times a week	
5	Every day	
99	Prefer not to answer	

36. During the last months, how often did you use crack cocaine?

- ◯ Never
- ◯ Once per week or less
- ◯ 2-3 times a week
- ◯ 4-6 times a week
- ◯ Every day
- ◯ Prefer not to answer

Question: CRCOS2HR
Required
Show if: (SEXNUM.TEXT > 0) and (CRCO ≠ 1:[Never]) and (CRCO ≠ 99:[Prefer not to answer])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

37. During the last months, did you have sex within 2 hours of you using crack cocaine?

- ◯ Yes
- ◯ No
- ◯ Prefer not to answer

Question: PRCO
Required

Scale Summary		
Code	Label	Show-If
1	Never	
2	Once per week or less	
3	2-3 times a week	

4	4-6 times a week	
5	Every day	
99	Prefer not to answer	

38. During the last months, how often did you use powder cocaine?

- ◯ Never
- ◯ Once per week or less
- ◯ 2-3 times a week
- ◯ 4-6 times a week
- ◯ Every day
- ◯ Prefer not to answer

Question: PRCOS2HR
Required
Show if: (SEXNUM.TEXT > 0) and (PRCO ≠ 1:[Never]) and (PRCO ≠ 99:[Prefer not to answer])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

39. During the last months, did you have sex within 2 hours of you using powder cocaine?

- ◯ Yes
- ◯ No
- ◯ Prefer not to answer

Question: AMPMETH
Required

Scale Summary		
Code	Label	Show-If
1	Never	
2	Once per week or less	
3	2-3 times a week	
4	4-6 times a week	
5	Every day	
99	Prefer not to answer	

40. During the last months, how often did you use amphetamine/methamphetamine, crystal meth, Khat/Cat, or tik?

- ◯ Never
- ◯ Once per week or less
- ◯ 2-3 times a week
- ◯ 4-6 times a week
- ◯ Every day
- ◯ Prefer not to answer

Question: AMPMETS2HR
Required
Show if: (SEXNUM.TEXT > 0) and (AMPMETH ≠ 1:[Never]) and (AMPMETH ≠ 99:[Prefer not to answer])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

41. During the last months, did you have sex within 2 hours of you using

amphetamine/methamphetamine, crystal meth, Khat/Cat, or tik?

- ◯ Yes
- ◯ No
- ◯ Prefer not to answer

Question: METMAN
Required

Scale Summary		
Code	Label	Show-If
1	Never	
2	Once per week or less	
3	2-3 times a week	
4	4-6 times a week	
5	Every day	
99	Prefer not to answer	

42. During the last months, how often did you use methaqualone or mandrax?

- ◯ Never
- ◯ Once per week or less
- ◯ 2-3 times a week
- ◯ 4-6 times a week
- ◯ Every day
- ◯ Prefer not to answer

Question: METMANS2HR
Required
Show if: (SEXNUM.TEXT > 0) and (METMAN ≠ 1:[Never]) and (METMAN ≠ 99:[Prefer not to answer])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

43. During the last months, did you have sex within 2 hours of you using methaqualone or mandrax?

- ◯ Yes
- ◯ No
- ◯ Prefer not to answer

Question: HERMED
Required

Scale Summary		
Code	Label	Show-If
1	Never	
2	Once per week or less	
3	2-3 times a week	
4	4-6 times a week	
5	Every day	
99	Prefer not to answer	

44. During the last months, how often did you use heroin, prescription pain killers/medications?

- ◯ Never
- ◯ Once per week or less
- ◯ 2-3 times a week
- ◯ 4-6 times a week

- ◯ Every day
- ◯ Prefer not to answer

Question: HERMEDS2HR
Required
Show if: (SEXNUM.TEXT > 0) and (HERMED ≠ 1:[Never]) and (HERMED ≠ 99:[Prefer not to answer])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

45. During the last months, did you have sex within 2 hours of you using heroin, prescription pain killers/medications?
    - ◯ Yes
    - ◯ No
    - ◯ Prefer not to answer

Question: MDMA
Required

Scale Summary		
Code	Label	Show-If
1	Never	
2	Once per week or less	
3	2-3 times a week	
4	4-6 times a week	
5	Every day	
99	Prefer not to answer	

46. During the last months, how often did you use MDMA or Ecstacy?
    - ◯ Never
    - ◯ Once per week or less
    - ◯ 2-3 times a week
    - ◯ 4-6 times a week
    - ◯ Every day
    - ◯ Prefer not to answer

Question: MDMAS2HR
Required
Show if: (SEXNUM.TEXT > 0) and (MDMA ≠ 1:[Never]) and (MDMA ≠ 99:[Prefer not to answer])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

47. During the last months, did you have sex within 2 hours of you using MDMA or Ecstacy?
    - ◯ Yes
    - ◯ No
    - ◯ Prefer not to answer

Question: WHO
Required

Scale Summary		
Code	Label	Show-If

1	Never	
2	Once per week or less	
3	2-3 times a week	
4	4-6 times a week	
5	Every day	
99	Prefer not to answer	

48. During the last months, how often did you use whoonga/wunga or nyaope?

- ◯ Never
- ◯ Once per week or less
- ◯ 2-3 times a week
- ◯ 4-6 times a week
- ◯ Every day
- ◯ Prefer not to answer

Question: WHOS2HR
Required
Show if: (SEXNUM.TEXT > 0) and (WHO ≠ 1:[Never]) and (WHO ≠ 99:[Prefer not to answer])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

49. During the last months, did you have sex within 2 hours of you using Whoonga/wunga or nyaope?

- ◯ Yes
- ◯ No
- ◯ Prefer not to answer

Question: POP
Required

Scale Summary		
Code	Label	Show-If
1	Never	
2	Once per week or less	
3	2-3 times a week	
4	4-6 times a week	
5	Every day	
99	Prefer not to answer	

50. During the last months, how often did you use poppers?

- ◯ Never
- ◯ Once per week or less
- ◯ 2-3 times a week
- ◯ 4-6 times a week
- ◯ Every day
- ◯ Prefer not to answer

Question: POPS2HR
Required
Show if: (SEXNUM.TEXT > 0) and (POP ≠ 1:[Never]) and (POP ≠ 99:[Prefer not to answer])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	

99	Prefer not to answer	

51. During the last months, did you have sex within 2 hours of you using Poppers?

- ◯ Yes
- ◯ No
- ◯ Prefer not to answer

Question: OTHDRUG
Required

Scale Summary		
Code	Label	Show-If
1	Yes	
2	Not applicable - No other drugs used	
99	Prefer not to answer	

52. During the last months, have you used any other drugs? If yes, please specify.

- ◯ Yes
- ◯ Not applicable - No other drugs used
- ◯ Prefer not to answer

Question: OTHDRUG_FREQ
Required
Show if: (OTHDRUG = 1:[Yes])

Scale Summary		
Code	Label	Show-If
2	Once per week or less	
3	2-3 times a week	
4	4-6 times a week	
5	Every day	
99	Prefer not to answer	

53. During the last months, how often did you use ?

- ◯ Once per week or less
- ◯ 2-3 times a week
- ◯ 4-6 times a week
- ◯ Every day
- ◯ Prefer not to answer

Question: OTHDRUGS2HR
Required
Show if: (SEXNUM.TEXT > 0) and (OTHDRUG_FREQ ≠ 99:[Prefer not to answer]) and (OTHDRUG_FREQ was-answered)

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

54. During the last months, did you have sex within 2 hours of you using ?

- ◯ Yes
- ◯ No
- ◯ Prefer not to answer

Question: CIGVAPE
Required

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

55. Do you currently smoke cigarettes or e-cigs (Vape)?

- ◯ Yes
- ◯ No
- ◯ Prefer not to answer

Question: VASEX
Required
Show if: (SEXNUM.TEXT > 0)

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

56. In the last months, have you given and/or received money, gifts, drugs, goods, shelter, or services in exchange for sex?

- ◯ Yes
- ◯ No
- ◯ Prefer not to answer

Question: HIVINFYR
Required
Show if: (SCHEDULE = 1:[Schedule 1]) or (SCHEDULE = 4:[Schedule 4])

Scale Summary		
Code	Label	Show-If
1	Not at all likely	
2	Somewhat unlikely	
3	Neutral/No opinion	
4	Somewhat likely	
5	Extremely Likely	
99	Prefer not to answer	

57. How likely do you think it is that you may become infected with HIV in **the next year**?

- ◯ Not at all likely
- ◯ Somewhat unlikely
- ◯ Neutral/No opinion
- ◯ Somewhat likely
- ◯ Extremely Likely
- ◯ Prefer not to answer

Collection: STUDY_PRODUCT
Contains: ANTIPLAC, HIGHLOW, INVINFUSION
Show if: (SCHEDULE = 1:[Schedule 1]) or (SCHEDULE = 4:[Schedule 4])

Question: ANTIPLAC
Required
Show if: (VISIT is-any-of 09.0:[Visit 09.0 (Infusion #4)] or 15.0:[Visit 15.0 (Infusion #7)] or 21.0:[Visit 21.0 (Infusion #10)] or 26.0:[Visit 26.0 (End Visit)] or 72.0:[Visit 72.0] or 74.0:[Visit 74.0] or 76.0:[Visit 76.0] or 78.0:[Visit 78.0])

Scale Summary		
Code	Label	Show-If

1	VRC01	
2	Placebo	
3	Don't know	
99	Prefer not to answer	

58. Do you think you received the VRC01 antibody or placebo in this study?

- ◯ VRC01
- ◯ Placebo
- ◯ Don't know
- ◯ Prefer not to answer

Question: HIGHLOW
Required
Show if: (ANTIPLAC = 1:[VRC01])

Scale Summary		
Code	Label	Show-If
1	High Dose	
2	Low Dose	
3	Unsure	
99	Prefer not to answer	

59. Do you think you received the high dose, low dose, or are you unsure?

- ◯ High Dose
- ◯ Low Dose
- ◯ Unsure
- ◯ Prefer not to answer

Question: INVINFUSION
Required
Show if: (VISIT = 02.0:[Visit 02.0 (Enrollment/Infusion #1)])

Scale Summary		
Code	Label	Show-If
1	Yes	
2	No	
99	Prefer not to answer	

60. Have you, a family member, or close friend ever had an IV infusion?

- ◯ Yes
- ◯ No
- ◯ Prefer not to answer

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