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IPM 032

A FOLLOW-ON, OPEN-LABEL TRIAL TO ASSESS CONTINUED SAFETY OF AND ADHERENCE TO THE DAPIVIRINE (25 mg) VAGINAL RING-004 IN HEALTHY, HIV-NEGATIVE WOMEN

- **Statistical Analysis Plan v1.0 dated 29 March 2019**
- **SAP Appendix 13.1 – 13.7**

- **Virology Addendum Analysis v1.0 dated 24 May 2021**
- **Virology Addendum SAP, Appendix 1, Tables and Listings Shells, v1.0 dated 24 May 2021**

INTERNATIONAL PARTNERSHIP FOR MICROBICIDES

STATISTICAL ANALYSIS PLAN

A FOLLOW-ON, OPEN-LABEL TRIAL TO ASSESS CONTINUED SAFETY OF AND ADHERENCE TO THE DAPIVIRINE (25 mg) VAGINAL RING-004 IN HEALTHY, HIV-NEGATIVE WOMEN

IPM 032

(Based on: Protocol Version 2.0, Amendment 2.0, dated 16 January 2017)

Version 1.0

International Partnership for Microbicides
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APPROVAL SIGNATURE PAGE

IPM 032 – Statistical Analysis Plan

A FOLLOW-ON, OPEN-LABEL TRIAL TO ASSESS CONTINUED SAFETY OF AND ADHERENCE TO THE DAPIVIRINE (25 mg) VAGINAL RING-004 IN HEALTHY, HIV-NEGATIVE WOMEN

I have read the above referenced Statistical Analysis Plan and approve its contents.

_____ _____

Annaléne Nel, MBChB PhD
Executive Vice President, Chief Medical Officer
International Partnership for Microbicides

Date

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Roland Klopper, MCom
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Date

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Date

Abbreviations

AE	Adverse Event
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
ATC	Anatomical Therapeutic Chemical
BMI	Body Mass Index
CRF	Case Report Form
CSR	Clinical Study Report
DAIDS	Division of Acquired Immunodeficiency Syndrome
DSMB	Data and Safety Monitoring Board
EMA	European Medicines Agency
HIV	Human Immunodeficiency Virus
ICH	International Conference on Harmonisation
IP	Investigational Product
IPM	International Partnership for Microbicides
IRE	Immediately Reportable Event
ITT	Intent-to-Treat
MedDRA	Medical Dictionary for Regulatory Activities
m-ITT	Modified Intent-to-Treat
NRTI	Nucleoside Reverse Transcriptase Inhibitor
NNRTI	Non-nucleoside Reverse Transcriptase Inhibitor
PCR	Polymerase Chain Reaction
PI	Protease Inhibitor
PID	Participant Identification Number
PK	Pharmacokinetic
PP	Per-Protocol
PT	Preferred Term
QM&C	Quality Management and Compliance
RAM	Resistance Associated Mutation
RBC	Red Blood Cells
RNA	Ribonucleic Acid
RPR	Rapid Plasma Reagin
SAE	Serious Adverse Event

SAP	Statistical Analysis Plan
SD	Standard Deviation
SOC	System Organ Class
STI	Sexually Transmitted Infection
TEAE	Treatment Emergent Adverse Event
TPHA	Treponema Pallidum Haemagglutination Test
TPPA	Treponema Pallidum Particle Agglutination Assay
WBC	White Blood Cells
WHO DDE	World Health Organization Drug Dictionary Enhanced

Table of Contents

1. INTRODUCTION

This document serves as the Statistical Analysis Plan (SAP) for the protocol pre-specified primary, secondary and exploratory endpoints for IPM 032, the Phase IIIb follow-on trial to IPM 027. Specifically, this document describes the statistical methods that will be used to analyse the final data from IPM 032 to support the completion of the Clinical Study Report (CSR). The planned analyses described in this SAP will form the basis for the assessment of safety and adherence to the use of the Dapivirine Vaginal Ring-004, as determined in the follow-on trial, and will be included in regulatory submissions and/or future manuscripts. Also, exploratory analyses not necessarily identified in this SAP may be performed.

Table shells, example figures, and listing shells that will accompany the analysis are provided in Appendices 1, 2, and 3, respectively. The appendices are viewed as supporting material of the analysis and will not require signature approval if formatting changes are made.

This document is based on the current version of the IPM 032 trial protocol, Version 2.0, Amendment 2.0, which was approved on 16 January 2017. However, due to changes in the global donor environment, not all planned changes from protocol Version 2.0, Amendment 1.0 (dated 22 October 2015) were implemented. The sections in protocol Version 2.0, Amendment 2.0 that have been implemented are detailed in Appendix 6.

This analysis plan refers to Case Report Forms (CRFs) Version 1.0, dated 16 May 2016, and additional CRFs for capturing screen failure information (Version 2.0, dated 23 May 2016). The following CRFs were updated during the trial:

- Contraceptive/menstrual/obstetric history (CMO) CRF, end of trial inventory (ETI) CRF, menses information and pregnancy test results (PTR) CRF, pregnancy outcome 1 (PO1) CRF, ring insertion/removal (RL) log CRF, and HIV seroconversion evaluation (SERCON) CRF (Version 1.0, dated 16 May 2016, and Version 2.0, dated 27 April 2017 used starting 16 October 2017).

The following CRFs were developed during the course of the trial and implemented as indicated:

- Narrative log (NARR) CRF, returned ring log (RRL) CRF, seroconversion – HIV RNA PCR testing (SER PCR) CRF, and screening and enrollment (SEL) log CRF (Version 1.0, dated 27 April 2017 implemented starting 16 October 2017); participant transfer (PTRAN) CRF (Version 1.0, dated 28 June 2017, implemented

starting 20 July 2017); and participant receipt (PREC) CRF (Version 1.0, dated 28 June 2017, implemented starting 15 August 2017).

2. TRIAL OBJECTIVES

2.1 Primary Objectives

The primary trial objectives are:

- To assess the safety profile of the 25 mg Dapivirine Vaginal Ring-004, when inserted at monthly intervals, in an open-label trial.
- To assess adherence to the use of the 25 mg Dapivirine Vaginal Ring-004 inserted at monthly intervals, in an open-label trial.

2.2 Secondary Objectives

The secondary trial objectives are:

- To assess the incidence of HIV-1 seroconversion.
- To assess the frequency of HIV-1 drug resistance in women who acquire HIV-1 infection.

2.3 Exploratory Objectives

The exploratory trial objectives are:

- To assess the feasibility of 3-monthly follow-up visits, as a possible schedule for post-licensure vaginal ring clinical follow-up.
- To explore the correlation between drug concentrations and results from the visual inspection of the returned vaginal rings by research staff between the monthly and 3-monthly research centre follow-up schedules.
- To determine the proportion of participants electing to undergo HIV rapid tests at the research centres between scheduled 3-monthly visits.
- To characterize the IPM 027 participants who decline enrollment into IPM 032 (Decliner Population) [***Not implemented.***]
- To explore self-reported acceptability of and adherence to the 25 mg Dapivirine Vaginal Ring-004.

Note: Objectives indicated as “Not implemented” above, are not addressed in this analysis plan.

2.4 Assessment of Objectives

Consistent with the primary objectives, the **primary endpoints** are:

Safety

- All Adverse Events (AEs) assessed by the investigator to be related to the Dapivirine Vaginal Ring-004.

- All Grade 3 and 4 AEs.
- All Serious Adverse Events (SAEs).

Adherence

Residual amounts of dapivirine in returned rings and/or dapivirine concentrations in plasma and/or dapivirine concentrations in vaginal fluid.

The primary endpoints will be assessed through:

Safety

All product-related AEs, Grade 3 or 4 AEs, SAEs, physical examination, gynaecological assessments, including pelvic/speculum examination, laboratory tests and other indicated investigations.

Adherence

- Determined dapivirine residual amounts in returned used vaginal rings and/or
- Measured concentrations of dapivirine in plasma [***Not implemented***] and/or
- Measured concentrations of dapivirine in vaginal fluids [***Not implemented.***]

Consistent with the secondary objectives, the **secondary endpoints** are:

- The HIV-1 seroconversion rate per 100 woman-years of product use at the end of the vaginal ring use period.
- HIV-1 drug resistance mutations among participants who acquire HIV-1 infection.

The secondary endpoints will be assessed through:

- Rapid and specialised laboratory testing according to a pre-specified HIV testing algorithm.
- Viral genotype resistance testing methods which include sensitive methods to detect low frequency drug-resistant variants (only population genotyping will be done.)

Consistent with the exploratory objectives, the **exploratory endpoints** include:

- Feasibility of a 3-monthly clinical follow-up schedule.
- Dapivirine residual amounts in returned used vaginal rings and/or dapivirine concentrations in plasma and/or vaginal fluid in correlation with results from the visual inspection of the returned used vaginal rings by research staff.
- Proportion of participants opting for HIV rapid tests at the research centre between scheduled 3-monthly research centre follow-up visits.
- The proportion of women who report the use of the vaginal ring as acceptable.
- Participant self-reported patterns of ring use.

The exploratory endpoints will be assessed through:

- Participant report of feasibility regarding a 3-monthly clinical follow-up schedule (Participant Questionnaire).
- Number of women opting not to receive two additional rings at the 3-monthly visits.
- Proportion of returned rings (used and unused) during the 3-monthly clinical follow-up schedule.
- Dapivirine residual amounts in returned used vaginal rings and/or dapivirine concentrations in blood and/or vaginal fluid.
- Visual inspection of the returned used vaginal rings by research centre staff.
- Number of participants undergoing HIV rapid tests at the research centre between scheduled 3-monthly research centre follow-up visits.
- Qualitative data regarding ring acceptability and self-reported patterns of ring use.

Note: Although collected and stored, blood and vaginal fluid samples were not analysed for dapivirine, as dapivirine concentrations were found in the Phase III program to have limited value as adherence measures. There is currently no biomarker to indicate whether the ring was used at the time of an HIV risk event; the best measure of ring use during the prescribed 1-month use period is dapivirine ring residual levels in used rings.

3 TRIAL DESIGN

3.1 General Design and Plan

IPM 032 is a Phase IIIb, multi-centre follow-on open-label trial to evaluate the continued adherence to and safety of the Dapivirine Vaginal Ring-004 inserted at monthly intervals in healthy, HIV-negative women who have participated in the IPM 027 Phase III Dapivirine Vaginal Ring-004 trial. All women who have participated in IPM 027 and are HIV-negative at screening for IPM 032, will be eligible. It was estimated that approximately 1400 participants will be enrolled.

All participants will attend a research centre follow-up visit one month after enrollment. Following this visit, at the investigator's discretion, a participant can continue on a 3-monthly visit schedule. Monthly visits may however be extended up to the first three months of participation. Once the 3-monthly trial visit schedule commences, three rings will be dispensed to the participant. One ring will be self-inserted at the research centre and two additional rings will be dispensed for the participant to take home, or dispensing will take place as arranged with the participant.

Each participant will engage in the screening process for up to 45 days prior to enrollment and will use the Dapivirine Vaginal Ring-004 for a period of up to 12 months. IPM will have the option to extend this trial period. Accrual was expected to take place over approximately 6 months; participants enrolled more than 6 months after the onset of the study site's accrual period may have a shortened follow-up period.

Each participant will have an exit visit 1 to 2 months after ring discontinuation, to assess safety and identify HIV-1 seroconversions after product discontinuation.

3.2 Sample Size

This is an open-label, follow-on trial to IPM 027 to evaluate the safety of and adherence to the Dapivirine Vaginal Ring-004, inserted at monthly intervals in healthy, HIV-negative women who have participated in the IPM 027 trial. No formal sample size or power calculations have thus been performed. It was expected that approximately 70% of the participants enrolled in IPM 027 will participate in this trial. Therefore, a total sample size of approximately 1400 HIV-negative women was anticipated.

3.3 Randomisation

This is an open-label, follow-on trial. No randomisation will be done.

3.4 Blinding

This is an open-label study. No blinding will be performed.

4 SEQUENCE OF PLANNED ANALYSES

4.1 Safety Monitoring

Safety data from the trial were to be evaluated by an independent Data and Safety Monitoring Board (DSMB). The first scheduled meeting was to take place approximately six months after all research centres had been activated; subsequent meetings were held at approximately annual intervals for the duration of IPM 032. Based on the review of the data, the DSMB was required to provide recommendations about continuation, pausing, termination or other modifications to the trial, including changes to the information provided to participants for obtaining their informed consent. An IPM 032 DSMB charter was developed to describe the roles and responsibilities of the DSMB, its composition, data to be provided to the DSMB, the process for disseminating trial data to the DSMB, and the communication plan between the DSMB and IPM.

4.2 Interim Analyses

No interim analysis was planned for this trial. However, the Sponsor reviewed the treatment emergent safety data at regular intervals during the conduct of the trial.

Note: Although no formal interim analysis was planned or conducted for IPM 032, two summary reports of available data as of 30 April 2018 and 08 November 2018, respectively, were prepared and submitted to the European Medicines Agency (EMA), in response to requests by EMA during their review of the Dapivirine Vaginal Ring Article 58 application.

4.3 Final Analysis and Reporting

This SAP will be approved before final database lock. All final and planned analyses identified in the protocol and in this SAP will be performed only after the database has been locked. A review of the data will be performed prior to database lock for data quality purposes and for classification of protocol deviations as minor or major.

5 ANALYSIS POPULATIONS

Four analysis populations have been defined for this trial: a Safety population, Modified Intent-to-treat (m-ITT) population, Virology population and a Per-protocol (PP) or Protocol-adherent population. The number of participants valid for each population, and when appropriate, the reasons for excluding trial participants from these populations, will be presented overall and by research centre using relevant summary statistics.

5.1 Safety Population

The safety population will include all participants who were enrolled, and received and inserted at least one Dapivirine Vaginal Ring

5.2 Modified Intent-to-Treat (m-ITT) Population

Some participants recently infected with HIV-1 may not yet have detectable levels of HIV-1 antibodies at the enrollment visit, and therefore, HIV-infected women who are assumed to be HIV-negative may be enrolled in the trial. To accommodate this situation, an m-ITT population will be determined and used for the analysis of HIV-1 seroconversion rate. This population will exclude all participants who are included in the safety population but who were found to have been HIV-1 infected at the enrollment visit (*i.e.* women who have seroconverted after enrollment but were retrospectively found to be HIV-1 RNA positive at enrollment).

Virology Population

The virology population includes all participants in the m-ITT population, with the exception of those participants who seroconverted after the last product use visit (LPUV). That is, women who were still HIV-1 RNA negative at LPUV, and who became infected after discontinuation of ring use, will be excluded. Genotypic analyses from the small numbers of participants with infection at enrolment, or with no detectable HIV-1 RNA at the LPUV but with seroconversion at the Exit visit, will be described separately.

5.3 Per-Protocol (PP) Population

The PP (or protocol-adherent) population is a subset of the m-ITT population, *i.e.* all trial participants who are confirmed as HIV-1 negative at the enrollment visit, with no major protocol deviations, as defined in Section 7.2.

6 GENERAL STATISTICAL CONSIDERATIONS

6.1 Analysis Software

Statistical analyses will be conducted by an external statistical service provider (Clindata Research Innovation) and reviewed by the International Partnership for Microbicides (IPM). The analyses will be performed using SAS® for Windows (version 9.3 or higher, SAS Institute Inc., Cary, North Carolina, USA).

6.2 Methods for Handling Missing Data

While every effort will be made to minimise the amount of missing data, some degree of missing data, primarily associated with missed visits, is expected. The amount of missing data will be explored and incorporated into the analyses, where appropriate. For the analysis of adherence to monthly ring use, patterns of missing data may be informative. Depending on the proportion of participants who discontinue early, an analysis of time to discontinuation may be conducted. Such an analysis would allow investigation of the covariates associated with early discontinuation. Patterns of missing data may also provide further insight into participants' preference for monthly or 3-monthly follow-up visits to research centres.

6.3 Multiple Comparisons and Multiplicity

The primary safety analysis is a descriptive analysis of the proportion of participants experiencing AEs. The primary adherence analysis is also descriptive in nature. As a result, no adjustments are required for multiplicity.

6.4 Multicentre Trials

Differences in participant safety and adherence to the dapivirine vaginal ring across research centres will be explored graphically and descriptively. The safety and adherence analyses will be summarised overall and for each research centre separately.

6.5 Planned Subgroups, Interactions, and Covariates

The analysis of the HIV-1 seroconversion rate will be based on the m-ITT population, and the primary virology analysis of drug resistance will be based on the virology population. It is expected that women with pre-existing conditions (*e.g.* women with STIs at Screening) will be treated and evaluated before or at enrolment into the trial, therefore no baseline adjustments are planned prospectively; however, all data will be reviewed to assess any potentially relevant baseline imbalances between research centres.

Unless specified otherwise, statistical models will include research centre as main effect. Kaplan-Meier survival curves will be produced overall and by research centre, if possible.

The following subgroup analysis will be performed for the primary safety endpoint (AEs related to Investigational Product (IP), Grade 3 and 4 AEs and SAEs):

1. Participants in the age group < 25 years, and ≥ 25 years

The following subgroup analysis will be performed for the primary adherence endpoint (residual amounts of dapivirine in returned rings):

1. Participant age at baseline (< 25 *versus* ≥ 25 years)
2. Marital status at baseline (married *versus* not married)
3. Has a main sex partner at baseline (yes *versus* no)
4. Presence of genital symptoms/Sexually Transmitted Infections (STIs) at baseline (yes *versus* no)

6.6 Data Presentations

Descriptive statistics will be presented overall and by research centre.

For continuous variables, the descriptive statistics will include, but not be limited to, mean and standard deviation (SD) (when appropriate), quartiles, range, and number of observations. For categorical variables, descriptive statistics may include frequencies, relative frequencies, and the number of observations.

Derived data where it is known in advance the result will be an integer (*e.g*. study day) will be presented with no decimal places. Means, medians and quartiles will be displayed to one more decimal place than the source data, dispersion statistics (*e.g*. standard deviation) will have two more decimal places, and the minimum and maximum will be displayed to the same number of decimal places as reported in the raw data. Percentages will be presented to one decimal place (excluding 0 and 100%). When appropriate, 95% confidence intervals will be presented.

The subsequent sections discuss the planned analyses beyond the listings and simple descriptive analyses.

Baseline is defined as the last available measurement before the first insertion of the IP. All visit dates will be calculated from the enrollment visit as baseline date.

Missing or partial dates will be imputed for AEs or concomitant medication dates. No other date imputations will be performed. For AEs or concomitant medication start dates, the following conventions will be applied:

2. If only the month and year are known, then the 15th of the month will be used (*i.e.* “15” will be imputed as the day of the month) unless the month and the year equal the month and the year of the first insertion of the ring. In such cases, the same day as the day of first ring insertion will be used (to ensure that the AE or concomitant medication is considered as treatment-emergent)
3. If only the year is known, then the first day of January will be used (*i.e.* “01JAN” will be imputed as the day and month) unless the year equals the year of first ring insertion, in which case the date will be imputed with the date of first ring insertion.

For concomitant medication end dates, the following conventions will be applied:

4. If only the month and the year are known, then the last day of the month will be used
5. If only the year is known, then the last day of December (*i.e.* "31DEC") or the date of trial completion/discontinuation will be used (whichever comes first).

In instances where the date of IP initiation, *i.e.* the start date of ring use, is missing or unknown, the missing date will be imputed with the date of the enrollment visit.

In accordance with the protocol, each scheduled visit has a window period of ± 7 days. If the participant does not return to the research centre for a scheduled visit prior to the start of the trial window of the next visit, the visit will be considered missed. If a participant presents for a visit outside the window for a scheduled trial visit, but prior to the start of the window for the next visit, it will be treated as a late visit. Missed visits and late visits will be documented as protocol deviations (refer to Section 7.2). Data recorded at late visits will be analysed as pertaining to the scheduled visit. Unscheduled visits may be performed at any time during the trial. If an unscheduled visit takes place within any given window period and any repeat observations are made within the given window period, the repeat values will be captured as pertaining to the unscheduled visit. Data from scheduled and unscheduled visits will be shown in the participant listings, and listings will be appropriately labelled when data arise from unscheduled visits. Data from scheduled visits will be presented in the summary tables.

Visit Schedule A will consist of participants who attend Trial Month Visits 1, 4, 7, 10, 13, and 16/Exit; Visit Schedule B will consist of participants who attend Trial Month Visits 1, 2, 5, 8, 11, 14, and 17/Exit; and Visit Schedule C will consist of participants who attend Trial Month Visits 1, 2, 3, 6, 9, 12, and 15/Exit.

Tables, figures, and listings of trial results will accompany the text of the CSR. Listings of all clinical data recorded in the CRFs will be provided, except for those CRFs which are used for administrative purposes, such as the Participant Encounter Form (PEN) and the End of Trial Inventory (ETI). Listings will be sorted by research centre and participant identification number (PID), and key variables such as visit date and/or trial visit number will be presented in each listing.

7 TRIAL PARTICIPANTS

All participants who provide informed consent for this trial will be accounted for, in accordance with ICH guideline E3 (*Structure and Content of Clinical Study Reports*)[2].

7.1 Disposition of Trial Participants

The number and percentage of trial participants who were screened, enrolled, received IP, permanently discontinued IP, permanently discontinued the trial, and who completed the trial will be presented, overall and by Visit Schedule (A, B or C).

For those participants who were prematurely discontinued from the trial, the time to permanent discontinuation of IP and the time to permanent discontinuation from the trial will be calculated, and presented together with Kaplan-Meier curves overall and, if appropriate, by research centre, and baseline covariates where appropriate (refer to Section 6.5; subgroups 1 to 4). Two separate probability curves will be presented;

- All reasons for premature discontinuation combined; and
- All reasons for premature discontinuation excluding seroconversion.

For participants that do not discontinue prematurely, the time to event duration will be censored as follows:

- For time to premature discontinuation of IP, the event date will be censored at the date of last known IP use
- For time to premature discontinuation from the trial, the event date will be censored at the date of last contact

For all participants the time to discontinuation from the trial (scheduled or premature) will be calculated and presented together with Kaplan-Meier curves overall and if appropriate by research centre, and baseline covariates where appropriate.

The time to an event will be calculated as follows:

- Time to event (days) = (Date of IP discontinuation/trial discontinuation/Censoring Date – Date of first ring use) + 1

A listing reflecting each participant's screening date, enrollment date, and scheduled and unscheduled visit dates, as documented in the PEN CRF, will be provided.

7.2 Protocol Deviations

All recorded protocol deviations will be listed and summarised overall and by research centre.

The IPM Clinical Trial Physician(s) (one or more IPM physicians assigned to continually monitor trial data during the course of the trial) will establish protocol deviation criteria for the trial, in conjunction with the IPM Head of Quality Management and Compliance (QM&C), the Head of Biometrics and other clinical team members, as appropriate. The final list of protocol deviation criteria will be approved by the IPM Chief Medical Officer. Before database lock and statistical analysis, all reported protocol deviations will be reviewed by the IPM Clinical Trial Physician(s), Head of QM&C and Head of Biometrics, in conjunction with the trial statistician (from Clindata Research Innovation), to determine the impact of each deviation on the analysis, and to compile a final list of major protocol deviations for purposes of defining the PP analysis population. The final list will be signed off by the IPM Chief Medical Officer.

Major protocol deviations that will result in exclusion of a participant from the PP analysis will include:

- Inappropriate enrollment into the trial (*e.g.* participant met an exclusion criterion, or participant failed to meet all inclusion criteria) as documented in the Deviations Log (DL) CRF. A major deviation will exclude the participant completely from the population.
- IP-related deviations (*e.g.* IP was incorrectly withheld from participants, participants incorrectly resumed IP use, or inappropriate IP was dispensed to a participant). The data of such participants will be censored at the date of the last negative HIV-1 test result prior to the occurrence of the deviation.
- The participant demonstrated non-adherence to IP use, evident from any missed 3-monthly research centre visits. The data of such participants will be censored at the date of the last negative HIV-1 test result prior to the first missed 3-monthly visit.
- Any other major protocol deviation identified during review of the data that may impact the integrity of the data. The decision whether the participant should be excluded entirely from the population or whether the data of the participant should be censored will be made during the review of the protocol deviations.

The number of participants with minor and major protocol deviations will be presented using appropriate summary statistics, overall and by research centre.

7.3 Adherence to Ring Regimen

The data collected in IPM 032 allows for both objective and subjective assessments of adherence to ring use by the participants in this trial.

Dapivirine residual levels in returned used rings are used as objective, quantitative measure of adherence to ring use in this trial.

Subjective adherence measures include self-reported ring use as collected on the Accidental Expulsion/Removal Log (EXP) CRF. Missed clinical trial visits are also used as an indicator of non-adherence to prescribed product use.

7.3.1 Dapivirine Ring Residual Levels in Used Rings

A comprehensive description of the planned analysis of dapivirine ring residual levels is provided in Section 9.2.

7.3.2 Self-reported Adherence

A comprehensive description of the planned analysis of self-reported adherence to the ring regimen is provided in Section 9.4.4.

8 EVALUATION OF DEMOGRAPHIC AND BASELINE CHARACTERISTICS

Unless otherwise specified, baseline characteristics, including medical history (MED), contraceptive/menstrual/obstetric history (CMO), and gynaecological history (GHXL) obtained

at the Screening and Enrollment visits, will be summarised descriptively, overall and by research centre, using appropriate summary statistics as described in Section 6.6.

8.1 Baseline Demographics

The following baseline demographic characteristics will be listed and summarised: age, race, height, weight and body mass index (BMI), education level, relationship status, current residential status with main sex partner, information on vaginal sex once a week or more, usual number of vaginal sex acts, genital STIs at baseline, number of male sex partners at baseline, partner knowledge of ring use and whether the participant has children or not. Age and BMI will be derived as described in Table 1 below.

Table 1 Derived and Computed Demographic Variables

Variable Name	Description	Computation Methods, Notes, or Equation(s)
Age	Age (years)	INT((date of enrollment – date of birth)/365.25)
BMI	Body Mass Index (kg/m^2)	(Participant body weight in kg)/ (Participant height in m)^2

Qualitative demographic characteristics (nominal or ordinal categories) will be summarised using absolute and relative frequencies. Quantitative demographic characteristics (continuous) will be summarised using the appropriate summary statistics, namely number of participants, mean, SD, quartiles, and range.

The demographic characteristics will be summarised by research centre, IPM 027 treatment arm, seroconversion status and overall. An additional table will be created to summarise the demographic characteristics by research centre, overall and IPM 032 enrollment status (IPM 027 participants enrolled into IPM 032 vs not enrolled in IPM 032).

All demographic and baseline characteristics will be presented in participant listings.

8.2 Baseline Medical History

Medical history will be collected during the Screening visit and Trial Visit 0 (pre-enrollment). Medical history will be presented in tabular form using appropriate descriptive statistics. All medical history will be listed.

8.3 Baseline Screening Assessments

Laboratory assessments conducted at baseline, including cytology, syphilis testing (Rapid Plasma Reagin [RPR]; confirmatory Treponema Pallidum Haemagglutination Test/Treponema Pallidum Particle Agglutination Assay [TPHA/TPPA]), haematology, biochemistry, urinalysis, urine pregnancy tests, and HIV rapid tests will be presented for all participants. General physical examination and pelvic examination results will be presented at the Screening visit for all participants.

Obstetrics and gynaecological history will be collected during the Screening visit, and gynaecological conditions will be coded using Version 19.0 of the Medical Dictionary for Regulatory Activities (MedDRA). Obstetrics and gynaecological history will be presented in tabular form with absolute and relative frequencies, and gynaecological conditions will be classified using System Organ Class (SOC) and Preferred Term (PT).

8.4 Prior Therapies and Medications

Prior medication is defined as any medication that started and ended before the first insertion of IP. Medications will be coded using the World Health Organization Drug Dictionary Enhanced (WHO DDE) (version June 2017). A table summarising the number and percentage of participants using drugs, by Anatomical Therapeutic Chemical (ATC) level 2 classification and preferred name, will be presented.

9 EVALUATION OF TRIAL ENDPOINTS

9.1 Primary Endpoint 1 – Safety

The analysis of AEs will be mainly descriptive in nature. That is, the number and percentage of participants experiencing AEs will be presented per SOC and PT, overall and by research centre. The proportion of participants experiencing the following will be determined and summarized:

- AEs considered by the Investigator as related to IP
- Grade 3 or 4 AEs
- SAEs

For these three endpoints, and for the most frequently reported AEs (*i.e*. AEs occurring in at least 5% of participants overall) the proportion and the corresponding 95% confidence interval will be presented for the overall counts. The confidence interval will be determined using Fisher's exact test.

Separate tabulations will be created for AEs of special interest (selected urogenital AEs and STIs). For this purpose, PTs may be grouped into categories of interest (refer to Appendix 5).

9.2 Primary Endpoint 2 – Adherence

Dapivirine residual levels in used rings will be determined for all participants receiving IP, as a measure of adherence to ring use. The data will be listed, summarised and presented graphically, as described below.

Dapivirine Residual Levels in Used Rings

All used vaginal rings that are returned to the research centres at each trial visit are collected and shipped at regular, pre-defined intervals to an analytical laboratory,

where the rings are analysed to determine the residual amounts of dapivirine in the rings.

For this trial, a reported ring residual level of > 23.5 mg dapivirine will be used as an indication of non-adherence to ring use over the 30-day period (± 7 days) that a woman was to keep the ring *in situ*. Based on the data from the Phase III program, the cut-off value of > 23.5 mg for dapivirine ring residual levels was shown to be a good measure of non-adherence to ring use, indicating no or very little ring use.

The following summaries and graphical presentations will be produced for these data:

- A summary of ring residual levels at each trial visit and at the time of seroconversion, the time of first HIV-1 RNA positive as well as the time of last HIV-1 RNA negative will be presented with standard descriptive statistics – presented overall, by IPM 027 treatment arm, and by research centre. Corresponding box plots will be prepared.
- A descriptive summary of the ring residual levels by trial visit and by category of residual amount (< 20 mg, 20 – 21 mg, > 21 – 22 mg, > 22 – 23.5 mg, and > 23.5 mg). This summary will be prepared overall, by IPM 027 treatment arm and by research centre, with corresponding bar charts.
- A summary relating the ring residual levels to time intervals (in days) between consecutive ring replacements (< 23 days, 23 – 37 days, > 37 – 84 days, and > 84 days). Corresponding box plots will be prepared.

Note: All summaries and graphical presentations will be produced for both uncorrected dapivirine ring residual levels (as reported by the analytical laboratory) and residual levels corrected for manufacturing and assay variability, unless otherwise specified.

The aforementioned graphical presentations will be repeated for the ring residuals from the IPM 027 and IPM 032 trials, and will be based only on the participants from IPM 027 who enrolled in IPM 032. However, only the uncorrected ring residual levels will be used.

In addition, a listing will be produced for those trial participants who HIV-1 seroconverted, with HIV-1 infection estimated to have occurred on IP, listing the date of the last negative HIV RNA PCR test, the date of the first positive HIV RNA PCR test, the number of days in-between, the time to first positive HIV-1 RNA, the corresponding corrected and uncorrected dapivirine ring residual levels, and the appearance and colour of the rings.

A summary table, listing and scatter plot of the residual levels of dapivirine in the last three rings returned by these participants prior to HIV-1 seroconversion will be produced and compared visually with the average ring residual levels of those participants who remained HIV-negative over the duration of the trial. If possible, the

summary table and plot will also be produced by categories of the appearance and colour of these rings.

Finally, a summary table, listing and scatter plot of the residual levels of dapivirine in the last two rings prior to the first positive HIV-1 RNA will be produced and compared visually with the average ring residual levels of those participants who remained HIV-negative over the duration of the trial.

9.3 Secondary Endpoints

9.3.1 Secondary Endpoint 1: HIV-1 seroconversion rate per 100 person-years of product use

Consistent with secondary objective 1, secondary endpoint 1 is the HIV-1 seroconversion rate per 100 person-years of product use at the end of the vaginal ring use period.

Assessments

Trial participants will be tested for HIV-1 infection at all trial visits until the last product use visit, and at the exit visit, 1-2 months after ring discontinuation. HIV-1 seroconversion will be determined per the HIV testing algorithm presented in the IPM 032 protocol (Appendix B) and assessed by the Principal investigator or dedicated sub-investigator at the research centre and the IPM clinical physician to confirm HIV-1 seroconversion and estimated point of infection[5]. The HSMC was established to act in advisory capacity as IPM 032 secondary endpoints did not require independent evaluation of HIV-1 seroconversions and/or HIV-1 trial endpoints. The HSMC was consulted on an ad hoc basis, *e.g.* regarding inconclusive or atypical HIV test results. The point of HIV-1 infection was estimated by performing reverse sequential HIV Ribonucleic Acid (RNA) Polymerase Chain Reaction (PCR) testing (on stored samples collected at each visit) until a negative test result is achieved.

Statistical methods

Participants who are not diagnosed with HIV-1 using seroconversion testing at the end of the trial participation period will be censored at the last HIV-1 test date, at or prior to the last product use visit.

If HIV-1 is detected at the Exit visit, HIV-1 RNA PCR testing will be performed on stored samples in reverse sequential order to estimate the time point of HIV-1 infection.

- If HIV-1 infection is detected at or prior to the last product use visit, the participant will be included in the analysis as an HIV-1 seroconverter.
- If the time of infection is determined to be after completion of product use, the participant will be censored on the last HIV-1 test date at or prior to the last product use visit.

This analysis (Analysis 1) will be performed on the m-ITT population, as well as on the PP population.

Three additional analyses of HIV-1 seroconversion rate will be performed:

- Analysis 2: In instances where it cannot be ruled out that HIV-1 infection may have occurred during IP use due to atypical/inconclusive HIV RNA PCR test results or extended periods of non-product use, such participants will be considered as HIV-1 infected on product in this analysis.
- Analysis 3: All confirmed HIV-1 seroconverters determined to have been HIV-1 infected after enrollment will be considered as infected on product, even in instances where HIV-1 seroconversion and estimated point of infection was determined to be after the last product use visit.
- Analysis 4 (HIV-1 infection rate): Similar to Analysis 1, but based on time to first positive HIV-1 RNA.

All additional analyses will be performed on the m-ITT population.

For the number of participants included in the m-ITT analysis in IPM 032, matching placebo participants will be resampled with replacement from the IPM 027 trial, based on research center, age and STI prevalence at screening. These factors were selected because of their strong association with HIV incidence.

Age categories (18-24, and ≥ 25 years) will be used to ensure that a sufficient number of participants are represented in each combination of categories of age, center and STI prevalence at screening (Yes/No). This resampling will be repeated 10 000 times; by ordering the 10 000 incidence rates and taking the 250th and 9750th value, a 95% confidence interval can be established. The placebo ring data of the complete double-blind period of IPM 027 will be used for this simulation.

The incidence of HIV-1 seroconversions, the incidence density rate of HIV-1 seroconversion (*i.e.* HIV-1 seroconversion rate per 100 person-years of product use at the end of the ring use period) as well as a 95% confidence interval for the HIV-1 seroconversion rate per 100 person-years (based on the normal approximation of the Poisson distribution) may be presented for the simulated placebo and treatment arm, overall and for each research centre. Similarly, the incidence of HIV-1 seroconversions, the incidence density rate and 95% CI will be presented by visit schedule (A, B or C) and overall. The 95% CI will be calculated using the formula below:

95% confidence interval = $[(n/PY) \pm 1.96 \times ([n/PY] / PY)^{½}] \times 100$

where:

n = number of HIV-1 seroconversions

PY = total number of person-years of product use

Kaplan-Meier curves, of time to HIV-1 seroconversion will be presented, overall and by research centre using PROC LIFETEST in SAS®.

The time to event will be calculated as follows:

> Time to event (days) = (Date of seroconversion/Censoring Date – Date of first ring use) + 1

Individual participant profiles for participants that seroconverted (listings and/or graphical presentations) may be produced, including potential prognostic factors (age, marital status, number of male partners, presence of STIs at baseline, number of sex acts, condom use during last round of vaginal sex, anal sex since last visit), occurrence of urogenital AEs, dapivirine ring residual levels over time, colour and appearance of returned rings, the estimated point of HIV-1 infection, and point of HIV-1 seroconversion.

9.3.2 Secondary Endpoint 2: HIV-1 drug resistance mutations among participants who acquire HIV-1

Consistent with the secondary objective to evaluate HIV-1 drug resistance mutations among participants who acquire HIV-1 in the trial, secondary endpoint 2 is the proportion of HIV-1 seroconverters with drug resistant mutations.

Assessments

HIV viral genotyping will be performed on all HIV-1 seroconverters.

Statistical methods

The analysis of HIV-1 drug resistance will be primarily descriptive in nature, and will depend on the pattern of resistance-associated mutations (RAMs) observed in the HIV-1 seroconverters. The Stanford NNRTI Resistance Mutation Scores of Drug Resistance Mutations in HIV-1 (database version 8.4 - dated 2017-06-16) is provided in Appendix 4.

The number of RAMs observed will be listed by participant, and a frequency tabulation of individual RAMs associated with the various classes of antiretrovirals (Protease Inhibitors [PIs], Nucleoside Reverse Transcriptase Inhibitors [NRTIs] and Non-nucleoside Reverse Transcriptase Inhibitors [NNRTIs]) will be produced. The proportion of HIV-1 seroconverters with at least one HIV-1 drug resistant mutation will be presented overall, and by research centre, if possible, with corresponding 95% confidence intervals (using the Fisher's exact test).

If the data allows, the following frequency tabulations will be created:

- The number (and percentage) of participants who had a resistance test performed (pre-seroconversion, at seroconversion and at the Exit visit.)

- Reasons why a resistance test was not performed (if available in the database.)
- The number (and percentage) of participants with each individual mutation by class (NNRTI, NRTI, major PI.)
- The number (and percentage) of participants with 0, 1, 2, and $\geq$ 3 mutations by class (NNRTI, NRTI, major PI.)
- The number (and percentage) of participants with different mutational patterns (including single mutations), by class (NNRTI, NRTI, major PI.)
- Additional mutations (*e.g.* those selected by dapivirine in vitro but not included in the Stanford HIV database set) will be described.

In addition, for each NNRTI drug, the resistance mutation scores for NNRTIs efavirenz, etravirine, nevirapine and rilpivirine, will be calculated according to the Stanford database version 8.4, dated 2017-06-16 (see Appendix 4), per genotype by summing the individual scores associated with individual mutations (and the additional scores for combinations of mutations where applicable.) Based on the resistance mutation score, virus from participants will be classified as susceptible, potential low-level resistant, low-level resistant, intermediate resistant or high-level resistant for each NNRTI drug, based on the following cut-offs:

NNRTI resistance mutation score	**Level of resistance**
<10	Susceptible
10 - <15	Potential low-level resistant
15 - < 30	Low-level resistant
30 - < 60	Intermediate resistant
≥ 60	High-level resistant

For each approved NNRTI drug (efavirenz, etravirine, nevirapine and rilpivirine), descriptive statistics will be presented on the total NNRTI resistance mutation score and a frequency tabulation will be presented on the resistance level.

Note: Only results at time of HIV-1 seroconversion will be included in tabulations. Listings of all individual data will be created and will include all participant resistance assessments.

These analyses will be performed overall, by HIV-1 RNA level at HIV-1 seroconversion (≥ 2000 copies/mL , < 2000 copies/mL), treatment schedule (A, B or C) and by HIV-1 subtype (C, other).

There will be an additional analysis to determine the number and timing of samples analysed prior to and after HIV-1 seroconversion. Any changes of genotype between the prior- and after- HIV-1 seroconversion samples will be described.

Finally, the primary analysis will be repeated for the Virology Population, for all samples analysed at any time during the period of the first positive HIV-1 RNA visit and the Exit visit. This is to ensure that all mutations are accounted for.

9.4 Exploratory Endpoints

9.4.1 Exploratory Endpoint 1: Participant report of feasibility of 3-monthly clinical follow-up schedule

Consistent with exploratory objective 1, exploratory endpoint 1 is the participant report of feasibility regarding a 3-monthly clinical follow-up schedule (Participant Questionnaire).

Assessments

Participants will complete a Participant Questionnaire at all trial visits until the last product use visit. In particular, the following items will be captured:

Participant Questionnaire Part A (month 1, 2 and 3):

Item 1: As per investigator decision are you coming to the research centre next month or in three months for your next visit?

Item 2: Will you take your extra rings with you today or will you come back to the research centre each month to pick up your new ring?

Item 3: What are your reasons for leaving the rings at the research centre today?

Participant Questionnaire Part B (month 2 and 3):

Item 10: If you were not in a study, would you prefer to come to the health care clinic / provider for new rings each month, or every three months?

Item 11: If you were not in a study, would you prefer to come to the health care clinic / provider for an HIV test each month, or every three months?

Participant Questionnaire (3 month follow-up):

Item 1: Will you take your extra rings with you today or will you come back to the research centre each month to pick up your new ring?

Item 2: What are your reasons for leaving the rings at the research centre today?

Item 16: If you were not in a study, would you prefer to come to the health care clinic / provider for new rings each month, or every three months?

Item 17: If you were not in a study, would you prefer to come to the health care clinic / provider for an HIV test each month, or every three months?

Participant Questionnaire (last product use visit):

Item 1: When you were doing your three monthly visits, did you take your extra rings with you or did you come back to the research centre each month to pick up your new ring?

Item 2: What were your reasons for leaving the rings at the research centre?

Item 16: If you were not in a study, would you prefer to come to the health care clinic / provider for new rings each month, or every three months?

Item 17: If you were not in a study, would you prefer to come to the health care clinic / provider for an HIV test each month, or every three months?

At all trial visits and the last product use visit, the RL CRF will be completed, indicating the rings dispensed at each trial visit (items 1 and 2) and the used / unused rings returned at each trial visit (items 7 and 8).

Statistical methods

The analysis of feasibility of the 3-monthly clinical follow-up schedule will be primarily descriptive in nature, and will include absolute and relative frequencies for each trial visit for Participant Questionnaire items listed above, overall and by Visit Schedule (A, B or C). In particular, the number and percentage of women opting not to receive two additional rings at the 3-monthly clinical follow-up schedule will be reported.

The proportion of returned rings (used and unused) during the 3-monthly clinical follow-up schedule will also be reported. This will be calculated as the number of used/unused rings returned divided by the number of rings dispensed.

9.4.2 Exploratory Endpoint 2: Correlation between dapivirine residual amounts in returned used vaginal rings and/or drug concentrations, and results from visual inspection of returned vaginal rings

Consistent with exploratory objective 2, exploratory endpoint 2 is the dapivirine ring residual levels in returned used vaginal rings and/or dapivirine concentrations in plasma and/or vaginal fluid (not assayed) in correlation with results from the visual inspection of the returned used vaginal rings by research staff.

Assessments

At all trial visits and the last product use visit, the RL CRF will be completed, indicating the rings dispensed at each trial visit (items 1 and 2) and the appearance of used/unused rings returned at each trial visit (items 7, 8 and 9).

Residual levels of dapivirine in used rings will be determined for all participants receiving IP at each trial visit.

Statistical methods

The correlation between the amount of corrected residual dapivirine in the used vaginal rings and the corresponding results from the visual inspection of the returned used vaginal rings, will be explored descriptively by producing summary statistics and

a corresponding scatter plot of the dapivirine levels for each category of appearance and colour of the returned ring.

9.4.3 Exploratory Endpoint 3: Proportion of participants opting for HIV rapid tests at the research centre between scheduled 3-monthly visits

Consistent with exploratory objective 3, exploratory endpoint 3 is the proportion of participants opting for HIV rapid tests at the research centre between scheduled 3-monthly research centre follow-up visits.

Assessments

Trial participants will have HIV rapid tests performed at the research centre at all trial visits until the last product use visit, and at the exit visit, 1-2 months after ring discontinuation, and as needed.

Statistical methods

The proportion of participants undergoing HIV rapid tests at the research centre between scheduled 3-monthly follow up visits will be calculated as the number of participants with at least one HIV rapid test performed at an unscheduled visit divided by the total number of participants with at least one HIV rapid test performed at any visit.

9.4.4 Exploratory Endpoint 4: Self-reported acceptability and adherence to vaginal ring use

Consistent with exploratory objective 4, exploratory endpoints 4 and 5 are the proportion of participants who respond positively to questions on ring acceptability at the last product use visit, and participant self-reported patterns of ring use, respectively.

Assessments – Self-reported acceptability

Participant questionnaires will be administered at every trial visit after enrollment, until the last product use visit.

Statistical methods – Self-reported acceptability

The proportion of participants among all trial participants who respond positively (*i.e.* Yes) to the following two questions at the last product use visit:

- “Do you think it is possible for women to use the ring as requested (*i.e*. without removing it)?”
- “Do you think women in your community would want to use this ring if it were available?”

A participant will be classified as having found the vaginal ring acceptable if she responds positively to the first question, about keeping the ring inserted as prescribed. Community acceptability will be demonstrated by positive responses to the second question. For each question, the proportion of participants who responded positively,

and the corresponding Fisher's exact 95% confidence interval, will be calculated and presented.

Summary tables with descriptive statistics will be presented for the socio-demographic variables and psycho-social variables collected in the participant questionnaires.

Note: Additional explanatory analyses will utilise the qualitative data from focus group discussions and individual interviews; these analyses will be performed separately from the analyses described in this analysis plan, and will be discussed in the Clinical Study Report.

Assessments – Self-reported adherence

Information on rings dispensed and returned are recorded at each trial visit on the RL CRF. Participant self-reports of accidental ring expulsions and removals are recorded on the EXP CRF.

Statistical methods – Self-reported adherence

Self-reported adherence to the ring regimen will be calculated per visit, and presented descriptively overall and by research centre. The adherence rate per visit will be calculated as:

- 100 x (number of days that the participant reportedly wore the ring / the total number of days that the participant was expected to wear the ring).

The number of days that the participant reportedly wore the ring is based on data captured in the Ring Insertion/Removal Log (RL) CRF and the EXP CRF at the scheduled visit and any preceding unscheduled visit between the current and the previous scheduled visit. The total number of days that the participant was expected to wear the ring is a calendar month (30 days) from the insertion date.

The self-reported adherence rates will be presented in the following categories:

- ≥ 90%
- ≥ 80% to < 90%
- < 80%.

Summary tables with descriptive statistics will be presented for accidental ring expulsions and removals by the participant for reasons other than instructed by the research centre staff.

10 EVALUATION OF SAFETY PARAMETERS

10.1 Adverse Events

An AE is defined as any untoward medical occurrence in a clinical trial participant. An AE can therefore be any unfavourable and unintended sign (including an abnormal

laboratory assessment finding), symptom or disease temporally associated with the participation in this trial, whether or not considered related to the IP. All AEs will be coded using MedDRA (Version 19.0).

10.1.1 Treatment Emergent Adverse Events (TEAEs)

TEAEs are defined as AEs which occurred/worsened after the first insertion of the IP, up to six weeks after last ring use.

10.1.2 Product-related Adverse Events

Product-relatedness is reported as “Related” or “Not Related”. While every effort is made to ensure that this field is not missing through data reviews and queries, if the relationship with the IP is missing on the CRF, it will be assumed that the AE was “Related” to the IP.

Summary Tables

A summary table of TEAEs will be presented, indicating the frequency and proportion of participants with:

- At least one TEAE
- At least one serious TEAE
- At least one Division of Acquired Immunodeficiency Syndrome (DAIDS) Grade 3 or 4 TEAE
- At least one product-related TEAE
- At least one serious product-related TEAE
- A TEAE leading to death
- A TEAE leading to premature (permanent) IP discontinuation
- A TEAE leading to temporary IP discontinuation
- A TEAE leading to trial discontinuation.

If meaningful, the same summary tables may be produced for non-TEAEs.

The definitions and location of data elements to be used to define each measure are described in Table 2 below.

Table 2 Definition and Data Sources of AEs

Measure	Statistic	Data Sources*
Participants with at least one TEAE	Frequency	A participant reported with an AE in the AE CRF Source: AE
Participants with at least one serious TEAE	Frequency	A participant reported as having an SAE per the AE CRF Source: AE

Measure	Statistic	Data Sources*
Participants with at least one DAIDS Grade 3 or 4 TEAE	Frequency	A participant reported as having a DAIDS Grade 3 or 4 AE Source: AE
Participants with at least one product-related TEAE	Frequency	A participant reported as having a "related" event, per the AE CRF Source: AE
Participants with at least one serious product-related TEAE	Frequency	A participant reported as having a "related" SAE, per the AE CRF Source: AE
Participants with a TEAE leading to death	Frequency	A participant reported as having an AE with the reported outcome "fatal" per the AE CRF Source: AE
Participants with a TEAE leading to premature (permanent) IP discontinuation	Frequency	A participant reported as having an AE with an action taken of "drug withdrawn" per the AE CRF Source: AE
Participants with a TEA leading to temporary IP discontinuation	Frequency	A participant reported as having an AE with an action taken of "drug interrupted" per the AE CRF Source: AE
Participants with a TEAE leading to trial discontinuation	Frequency	A participant reported as having a Trial Completion status of "Participant discontinued from the trial early" and a reason of "Adverse event/intercurrent illness" per the TC CRF Source: TC

* Percentages will use the total number of enrolled participants as denominator.

A by-participant listing of all TEAEs will include the variables in Table 3 below.

Table 3 AE Variables

Variable	Data Type	Data Sources
SAE	Dichotomous	Yes/No Source: AE
Outcome	Nominal	Fatal, Not recovered/not resolved, Recovering/resolving, Resolved/recovered w/sequelae, Recovered/resolved, Unknown Source: AE
Severity	Ordinal	Grade 1 Mild, Grade 2 Moderate, Grade 3 Severe, Grade 4 Potentially life-threatening, Grade 5 Death Source: AE
Relationship	Ordinal	Related, Not related Source: AE
Action	Nominal, DDMMMYY	Dose not changed, Drug interrupted, Drug withdrawn, N/A Date interrupted, date reintroduced, date withdrawn

Variable	Data Type	Data Sources
		Source: AE
Other action	Nominal	None, Treatment medication, Non-drug therapy, Other Source: AE
SOC	Nominal	System Organ Class Source: AE
PT	Nominal	Preferred Term Source: AE
AE Term (Verbatim)	Nominal	Reported Event Source: AE

The incidence of TEAEs will be presented by SOC and PT, overall, IPM 027 treatment arm and by research centre.

The incidence of the following TEAEs by severity will be presented by SOC and PT, overall, IPM 027 treatment arm and by research centre:

- TEAEs
- Serious TEAEs
- Product-related TEAEs
- Serious product-related TEAEs
- Social harms reported as TEAEs (refer to Section 10.9).

In addition, for IPM 027 participants who directly enrolled in the IPM 032 trial from the open-label treatment period of IPM 027, a subgroup display of Overall TEAEs, TEAEs by worst severity and Product-related TEAEs will be presented.

Maximum severity will be assumed for an AE with missing severity.

A by-participant listing of all deaths, SAEs, non-TEAEs, permanent IP discontinuations and premature trial discontinuations will be presented in Appendix 16 of the CSR. These by-participant listings will include variables described in the summary of TEAEs in addition to the following variables:

Table 4 Additional AE Variables

Variable	Data Type	Data Sources
AE start date	DDMMMYY	Start date Source: AE
Outcome date	DDMMMYY	Outcome date Source: AE
Trial day	Continuous	Trial day = (Start Date of AE – Date of First Use of IP) + 1 Source: Calculated from AE (*AESTDAT*) and ENR

Variable	Data Type	Data Sources
		(*TCDAT*)
Duration (days)	Continuous	Duration (days) = *AEENDAT – AESTDAT +1* Source: Calculated from AE Duration will only be calculated if both the start and stop dates are available, or if the start date is known and the AE is ongoing at trial end; in such cases, the duration will be reported as "> (Trial Termination Date – Start Date of AE) + 1"

10.2 Clinical Laboratory Evaluation

Collection of blood and urine specimens for haematology (including full blood counts, differential and platelet count), biochemistry (including creatinine, Aspartate Aminotransferase [AST] and Alanine Aminotransferase [ALT]) and urinalysis tests (urine dipstick analysis and urine microscopy if clinically indicated) is conducted at Screening or any other trial visit if clinically indicated. For the South African research centres, clinical laboratory assessments are performed by a central laboratory, and for the Uganda research centre, by the research centre's certified laboratory. In accordance, reference ranges are provided by the central laboratory and local laboratory, respectively.

Listings of all clinical laboratory data for each participant will be provided. Laboratory test results will be categorised by DAIDS Grade, and clinical significance. Specific haematology, biochemistry, urinalysis, and microscopy parameters assessed during the trial are listed below.

Table 5 Haematology, Biochemistry, Urinalysis and Microscopy Parameters

Haematology (continuous)[1]	Biochemistry (continuous)[1]	Urinalysis (continuous)
Erythrocytes Haemoglobin Haematocrit Platelets Leukocytes Neutrophils Lymphocytes Monocytes Eosinophils Basophils	Electrolytes Sodium Potassium Chloride Calcium Phosphate Liver Function Bilirubin Alkaline phosphatase ALT AST Renal Function Urea	N/A **Urinalysis (categorical)** Protein Glucose **Microscopy (categorical)** White blood cells (WBC) Red blood cells (RBC)

[1] Graded according to the DAIDS table[1] (Grades 1-4).

Haematology (continuous)[1]	Biochemistry (continuous)[1]	Urinalysis (continuous)
	Creatinine	

Data sources: Haematology and biochemistry reported in HAE and CHEM CRFs; urinalysis and microscopy reported in UTR CRF.

Additionally, a listing of all abnormal clinical laboratory data will be provided.

10.3 Pelvic examinations

10.3.1 Assessments

Pelvic examinations will be performed at Screening and the last product use visit, or at any visit if clinically indicated.

10.3.2 Summary Tables

A summary of pelvic examinations will be presented for the all scheduled trial visits, overall, IPM 027 treatment arm and by research centre in tabular form. By-participant listings will also be provided. The summary tables and listings will include the variables in Table 6 below.

Table 6 Pelvic Examination Variables

Variable	Data Type	Data Sources
Presence of Vulvar findings	Categorical	Source: PEL Indicator variable for: Vulvar erythema, vulvar edema, vulvar rash, vulvar tenderness, Bartholin's or Skene's gland abnormality
Presence of Vaginal findings	Categorical	Source: PEL Indicator variable for: Vaginal erythema, vaginal edema, vaginal masses, vaginal abrasions or lacerations, vaginal tenderness, vaginal discharge
Presence of Cervical findings	Categorical	Source: PEL Indicator variable for: Cervical erythema, cervical edema and/or friability, cervical masses, cervical motion tenderness, cervical discharge
General/other findings	Categorical	Source: PEL Indicator variable for: Odour, uterine masses, adnexal masses, uterine tenderness, adnexal tenderness, condyloma, abnormal genital tract bleeding, other
Presence of Vulvar Lesions findings	Categorical	Source: PEL Indicator variable for: Ulcer, blister, pustule, peeling, ecchymosis, other lesions
Presence of Vaginal Lesions findings	Categorical	Source: PEL Indicator variable for: Ulcer, blister, pustule, peeling, ecchymosis, other lesions
Presence of Cervical Lesions findings	Categorical	Source: PEL Indicator variable for: Ulcer, blister, pustule, peeling, ecchymosis, other lesions
Cervical ectopy	Categorical	Source: PEL

10.4 Cervical cytology

10.4.1 Assessments

A cervical cytology sample will be collected at Screening (if not done in the previous year or if the result was abnormal at the last point of testing) and as needed.

10.4.2 Summary Tables

A summary of the cervical cytology results will be presented overall, IPM 027 treatment arm and by research centre, for the Screening visit. By-participant listings will also be provided for all visits. The summary tables and listings will include the following variables:

Table 7 Cervical Cytology Variables

Variable	Data Type	Data Sources
Cervical cytology result	Categorical	Source: CR Indicator variable for: Negative for intraepithelial lesion or cancer (malignancy), ASCUS, SIL-low grade (LSIL), ASC-H, SIL-high grade (HSIL), AGC, AGC-favor neoplastic, cancer, other findings

10.5 STI assessments

10.5.1 Assessments

Cervicovaginal samples will be collected for STI testing (Trichomonas, Gonorrhoea, and Chlamydia) at Screening and at the last product use visit, or any other trial visit as clinically indicated. At Screening, blood will be collected for Syphilis (RPR) testing. TPHA/TPPA testing will be performed if the RPR is reactive.

10.5.2 Summary Tables

STI results will be presented for the Screening and last product use visits, overall, IPM 027 treatment arm and by research centre. Variables that will be summarised in the tables and listings include:

Table 8 STI Variables

Variable	Data Type	Data Sources
Trichomonas rapid Test	Dichotomous	Source: STI
Gonorrhoea	Dichotomous	Source: STI
Chlamydia	Dichotomous	Source: STI
Syphilis RPR screening test	Dichotomous	Source: STI
Syphilis RPR titre	Discrete	Source: STI
Syphilis confirmatory test TPHA/TPPA	Categorical	Source: STI
Blood present during collection of cervico-vaginal samples	Dichotomous	Source: STI

10.6 Immediately Reportable Events

In addition to SAEs, the following events are considered immediately reportable events (IREs):

1) Pregnancy
2) HIV-1 seroconversion
3) Any non-serious AE leading to permanent discontinuation of the IP

10.6.1 Assessments

Urine pregnancy tests will be conducted at all scheduled trial visits, except for the Exit visit, and can be performed additionally at unscheduled visits as needed. Serum pregnancy tests will be performed at the Investigator's discretion. A negative serum test after a positive urine test would overrule the positive urine test.

HIV rapid tests will be performed at the research centre at all trial visits until the last product use visit, and at the exit visit, 1-2 months after ring discontinuation, and as needed. HIV RNA PCR samples will be collected at the Screening and Enrollment visits and at all trial visits, but will only be analysed if there is reason to believe that the participant is HIV-positive.

All AEs (serious and non-serious) are monitored throughout the trial; analysis of AEs is discussed in Section 10.1.

10.6.2 Summary Tables

Results from pregnancy tests will be presented in tabular form overall, by IPM 027 treatment arm and by research centre for each trial visit and will include appropriate statistics. A table including the following summaries will be included:

- Proportion of pregnancies
- Pregnancy incidence rates by contraceptive method (DMPA, norethisterone, oral contraception, etc.)
- Pregnancy incidence rates by outcome (full term live birth, premature term live birth, etc.).
- Pregnancy incidence rates per 100 person-years
- Frequencies of congenital anomalies

By-participant listings will be provided for each participant.

Table 9 Pregnancy Tests

Variable	Data Type	Data Sources
Type of test (urine or serum)	Dichotomous	Source: PHTR

Pregnancy Test	Dichotomous	Source: PHTR

Results from HIV tests will be presented in tabular form overall, by IPM 027 treatment arm and by research centre for each trial visit and will include appropriate statistics. By-participant listings will be provided for each participant, including whether the participant HIV-1 seroconverted (confirmed), the date of seroconversion, the time to seroconversion, and whether HIV-1 infection occurred while using IP.

Table 10 HIV Tests

Variable	Data Type	Data Sources
HIV Test Result (Test #1)	Dichotomous	Source: PHTR
HIV Test Result (Test #2)	Dichotomous	Source: PHTR
HIV Test Result (Test #3)	Dichotomous	Source: PHTR
HIV-1 Western Blot	Nominal	Source: SER
Repeat HIV-1 Western Blot	Nominal	Source: SER
HIV-2 Western Blot	Nominal	Source: SER
Repeat HIV-2 Western Blot	Nominal	Source: SER
RNA PCR Testing	Nominal	Source: electronic lab data *Only tested for HIV-1 seroconverters

10.7 Concomitant Medications

Concomitant medication is defined as any medication taken in conjunction with the IP, *i.e.* medication that either:

1) Started after the first insertion of the IP, or
2) Started before the first insertion of the IP, but ended on or after the first insertion of the IP. This includes medication indicated as “Ongoing” at the end of the trial.

Concomitant medications will be coded using the WHO DDE (version June 2017); a table displaying the frequency and proportion of participants using medications during the trial overall, by research centre, and by ATC level 2 and preferred name, will be presented. Concomitant medication will also be presented in the form of listings which will contain information for each medication used.

Table 11 Concomitant Medication Variables

Variable	Data Type	Data Sources
Drug Name	Text	Verbatim; Source: CM, *CMTRT_1-3*
ATC category	Text	Verbatim; Source: CM, *ATCCode1-3*
Indication	Text	Verbatim; Source: CM, *CMINDC_1-3*
Dose/Unit	Text	Verbatim; Source: CM, *CMDOSE_1-3*
Route	Text	Verbatim; Source: CM, *CMRTE_1-3*
Frequency	Text	Verbatim; Source: CM, *CMDSFQ_1-3*

Start date	DDMMMYY	Source: CM, *CMSTDT_1-3*
Stop date	DDMMMYY	Source: CM, *CMENDT_1-3*
Ongoing at last visit	Dichotomous	Source: CM, *CMONGO_1-3*

10.8 Physical Examination Findings and Vital Signs

A physical examination will be conducted at Screening and at the last product use visit. At these visits, vital signs will be recorded and body systems will be evaluated for abnormal/normal findings, with the exception of Height, which will only be measured at Screening. For vital signs, the observed data and the absolute change from baseline (Screening) will be summarised overall and by research centre using appropriate descriptive statistics, as described in Section 6.6. Listings of all vital signs data will be provided.

Data from physical examination findings will be listed only.

Variables that will be summarised in the listings include:

Table 12 Physical Examination and Vital Signs Parameters

Variable	Data Type	Data Sources
Height	Continuous	Source: PX (Screening)
Weight	Continuous	Source: PX
BMI	Continuous	Derived: weight(kg)/height(m)^2, rounded to 1 decimal
Temperature	Continuous; Dichotomous	Source: PX
Pulse	Continuous; Dichotomous	Source: PX
Respiratory rate	Continuous; Dichotomous	Source: PX
Blood pressure	Continuous; Dichotomous	Source: PX
General Examination of Body Systems: General appearance, gastrointestinal/abdomen, neck, lymph nodes, cardiovascular/heart, respiratory/lungs, musculoskeletal/extremities, neurological, skin, eyes, ear/nose/throat, and other (1-3).	Nominal	Source: PX

10.9 Social Harms

During each HIV counselling session, participants will be asked questions to assess the occurrence of social harms related to trial participation. Participants who experience social harms related to trial participation will be counselled accordingly and

provided with assistance to mitigate the circumstances, if possible. This will be recorded in the source documents and applicable CRFs.

By-participant listings of all social harms data will be provided as well as summary tables of such occurrences. Social harms that were reported as AEs, as well as all occurrences of sexual assault (whether associated with physical injury or not), will be summarised by SOC and PT, and by severity (refer to Section 10.1).

11 CHANGES IN THE PROTOCOL-PLANNED ANALYSES

There are no changes to the protocol-planned analyses.

12 REFERENCES

1. Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events, Version 1.0 December, 2004; Clarification 1 August 2009.
2. ICH (1996). International Conference on Harmonisation. Guideline E3 Structure and Content of Clinical Trial Reports.
3. ICH (1998). International Conference on Harmonisation. Guideline E9 Statistical Principles for Clinical Trials.
4. IPM 032 Protocol: *A FOLLOW-ON, OPEN-LABEL TRIAL TO ASSESS CONTINUED SAFETY OF AND ADHERENCE TO THE DAPIVIRINE (25 mg) VAGINAL RING-004 IN HEALTHY, HIV-NEGATIVE WOMEN* Version 2.0, Amendment 1.0; 22 October 2015.
5. IPM 032 Protocol: *A FOLLOW-ON, OPEN-LABEL TRIAL TO ASSESS CONTINUED SAFETY OF AND ADHERENCE TO THE DAPIVIRINE (25 mg) VAGINAL RING-004 IN HEALTHY, HIV-NEGATIVE WOMEN* Version 2.0, Amendment 2.0; 16 January 2016.

13 APPENDICES

13.1 Appendix 1 – Table Shells
13.2 Appendix 2 – Figure Shells
13.3 Appendix 3 – Individual Participant Listing Shells
13.4 Appendix 4 – Stanford HIV-1 Drug Resistance (database version 8.4 – dated 2017-06-16)
13.5 Appendix 5 – Adverse events of special interest
13.6 Appendix 6 – Implemented Sections of IPM 032 Protocol V2.0 Amendment 2.0, dated 16 January 2016
13.7 Appendix 7 – Protocol deviation criteria

13 APPENDICES

TABLE OF CONTENTS

IPM 032

TABLES – VERSION 1.0, 26 MAR 2020

14.1	**Demographic Data**
14.1.1	**Disposition**
14.1.1.1	Disposition of Participants by Visit Schedule
14.1.1.2	Analysis Population Assignment
14.1.1.3	Protocol Deviations
14.1.2	**Demographics**
14.1.2.1	Demographics at Screening by IPM 027 Treatment Arm
14.1.2.2	Demographics at Screening by Enrolled Status (from IPM 027)
14.1.3	**Baseline Characteristics**
14.1.3.1	Medical History at Screening
14.1.3.2	Contraceptive/ Menstrual/ Obstetric History at Screening
14.1.3.3	Gynaecological History at Screening
14.1.3.4	Prior Medication
14.2	**Efficacy Data**
14.3	**Safety Data**
14.3.1	**Display of Adverse Events**
14.3.1.1	Overall Summary of Treatment Emergent Adverse Events
14.3.1.2	Treatment Emergent Adverse Events by System Organ Class and Preferred Term
14.3.1.3	Product-Related Treatment Emergent Adverse Events by System Organ Class and Preferred Term
14.3.1.4	Grade 3 or 4 Treatment Emergent Adverse Events by System Organ Class and Preferred Term
14.3.1.5	Serious Treatment Emergent Adverse Events by Primary System Organ Class and Preferred Term
14.3.1.6	Urogenital Treatment Emergent Adverse Events Primary System Organ Class and Preferred Term
14.3.1.7	Treatment Emergent Adverse Events by Worst Severity, Primary System Organ Class and Preferred Term
14.3.1.8	Serious Treatment Emergent Adverse Events by Worst Severity, Primary System Organ Class and Preferred Term
14.3.1.9	Product-Related Treatment Emergent Adverse Events by Worst Severity, Primary System Organ Class and Preferred Term
14.3.1.10	Serious Product-Related Treatment Emergent Adverse Events by Worst Severity, Primary System Organ Class and Preferred Term
14.3.1.11	Social Harms Reported as Treatment Emergent Adverse Events by Worst Severity, Primary System Organ Class and Preferred Term
14.3.2	**Listings of Deaths, Other Serious and Significant Adverse Events**
14.3.3	**Narratives of Deaths, Other Serious and Certain Other Significant Adverse Events**
14.3.4	**Abnormal Laboratory Value Listing (Each Patient)**
14.3.5	**Extent Of Exposure, Dosage Information, And Compliance**
14.3.5.1	Adherence, Overall Summary of Dapivirine Residual Levels (mg) in Used Rings
14.3.5.2	Adherence, Summary of Dapivirine Residual Levels (mg) in Used Rings by Category
14.3.5.3	Adherence, Summary Relating Ring Residual Levels (mg) to Time Intervals Between Consecutive Ring Replacements
14.3.5.4	Residual Levels of Dapivirine (mg) in the Last Three Rings Returned by Participants Who Seroconverted, Prior to HIV-1 Seroconversion
14.3.5.5	Self-Reported Adherence to Dapivirine Ring
14.3.5.6	Self-Reported Acceptability to Dapivirine Ring
14.3.5.7	Accidental Expulsion/ Removal

Table 14.1.1.1
Disposition of Participants by Visit Schedule
All Participants

	Statistic	Schedule A	Schedule B	Schedule C	Unknown	All Schedules
Screened participants	N					X
Screen failures	n (%)[a]					X (X.X)
Reasons for ineligibility						
Incl /	n (%)[b]					X (X.X)
Excl /	n (%)[b]					X (X.X)
Incl and excl	n (%)[b]					X (X.X)
Participants enrolled	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Participants who received IP	n (%)[c]	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Permanently discontinued IP	n (%)[c]	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Permanently discontinued trial	n (%)[c]	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Completed trial	n (%)[c]	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Reason for discontinuing trial						
Non-compliance	n (%)[d]	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Lost to follow-up	n (%)[d]	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Adverse event/intercurrent illness	n (%)[d]	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Inappropriate enrolment	n (%)[d]	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)
HIV-1 seroconversion	n (%)[d]	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Pregnancy	n (%)[d]	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Sponsor terminated the trial	n (%)[d]	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Death	n (%)[d]	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Other	n (%)[d]	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Participant withdrew consent	n (%)[d]	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Relocation	n (%)[e]	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Employment/work	n (%)[e]	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Family/partner pressure	n (%)[e]	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Other	n (%)[e]	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)

Excl = Exclusion; HIV-1 = Human immunodeficiency virus type 1; Incl = Inclusion; IP = Investigational product
Percentages are calculated out of the number of participants (per visit schedule) [a] Screened [b] Screen failed [c] In the safety population [d] Non-completed [e] Withdrew consent
Visit Schedule A = Participants attended trial month visit 1, 4, 7, 10, 13 and 16/Exit
Visit Schedule B = Participants attended trial month visit 1, 2, 5, 8, 11, 14 and 17/Exit
Visit Schedule C = Participants attended trial month visit 1, 2, 3, 6, 9, 12 and 15/Exit

Table 14.1.1.2
Analysis Population Assignment
Safety Population

	Statistic	Centre 01	Centre 02	…	Centre 08	All Centres
Safety population	N	XXX	XXX	…	XXX	XXX
m-ITT population	n (%)[a]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Virology population	n (%)[a]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
PP population	n (%)[a]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)

m-ITT = Modified intent-to-treat; PP = Per-protocol
[a] Percentages are calculated out of the participants in the safety population per centre
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07; Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Table 14.1.1.3
Protocol Deviations
Safety Population

Subgroup: All IPM 032 participants

	Statistic	Centre 01 (N=XXX)	Centre 02 (N=XXX)	…	Centre 08 (N=XXX)	All Centres (N=XXX)
Participants with no reported protocol deviations	n (%)[a]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Participants with reported protocol deviations*	n (%)[a]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Minor deviations	n (%)[b]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Major deviations	n (%)[b]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
No classification	n (%)[b]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Deviation criteria*						
Inappropiate enrollment (failed to meet eligibility criteria)	n (%)[b]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Missed visit	n (%)[b]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Visit completed outside of permissible window	n (%)[b]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Informed consent process deviations	n (%)[b]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Investigational product deviations	n (%)[b]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Safety reporting deviations	n (%)[b]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Failure to discontinueinvestigational product	n (%)[b]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Inappropriate treatment/management of medical conditions and follow-up of AEs	n (%)[b]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Mishandled laboratory samples	n (%)[b]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Missing or incorrectly timed trial procedures	n (%)[b]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Conduct of additional non-trial related procedures	n (%)[b]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Participant non-adherence to trial requirements	n (%)[b]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Failure to discontinue participants who meet the trial discontinuation criteria	n (%)[b]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Other	n (%)[b]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)

Programmer's Note: Please repeat this table for the following subgroups: Seroconverted prior to product use; Seroconverted on product use; Seroconverted after product use; No seroconversion

AE = Adverse event
Percentages are calculated out of the number of participants (per centre) [a] In the safety population [b] Reported a protocol deviation
* More than one protocol deviation may have been reported for a participant; Where a subject reports more than one deviation per coded term they will only be counted once for the worst classification
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07; Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Table 14.1.2.1
Demographics at Screening by IPM 027 Treatment Arm
Safety Population

Subgroup: All IPM 032 participants

		Centre 01				All Centres	
Parameter (unit)	Statistic	IPM 027 Dapivirine (N=XXX)	IPM 027 Placebo (N=XXX)	IPM 032 Overall (N=XXX)	…	IPM 027 Placebo (N=XXX)	IPM 032 Overall (N=XXX)
Age (years)	n	XXX	XXX	XXX		XXX	XXX
	Mean	XX.X	XX.X	XX.X		XX.X	XX.X
	(q1,med,q3)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)		(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)
	SD	XX.XX	XX.XX	XX.XX		XX.XX	XX.XX
	(Min, Max)	(XX, XX)	(XX, XX)	(XX, XX)		(XX, XX)	(XX, XX)
Race							
Coloured	n (%)[a]	X (X.X)	X (X.X)	X (X.X)		X (X.X)	X (X.X)
Black	n (%)[a]	X (X.X)	X (X.X)	X (X.X)		X (X.X)	X (X.X)
Indian	n (%)[a]	X (X.X)	X (X.X)	X (X.X)		X (X.X)	X (X.X)
Etc.	n (%)[a]	X (X.X)	X (X.X)	X (X.X)		X (X.X)	X (X.X)
Height (cm)	n	XXX	XXX	XXX		XXX	XXX
	Mean	XX.X	XX.X	XX.X		XX.X	XX.X
	(q1,med,q3)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)		(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)
	SD	XX.XX	XX.XX	XX.XX		XX.XX	XX.XX
	(Min, Max)	(XX, XX)	(XX, XX)	(XX, XX)		(XX, XX)	(XX, XX)
Weight (kg)	n	XXX	XXX	XXX		XXX	XXX
	Mean	XX.X	XX.X	XX.X		XX.X	XX.X
	(q1,med,q3)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)		(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)
	SD	XX.XX	XX.XX	XX.XX		XX.XX	XX.XX
	(Min, Max)	(XX, XX)	(XX, XX)	(XX, XX)		(XX, XX)	(XX, XX)
BMI (kg/m^2)	n	XXX	XXX	XXX		XXX	XXX
	Mean	XX.X	XX.X	XX.X		XX.X	XX.X
	(q1,med,q3)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)		(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)
	SD	XX.XX	XX.XX	XX.XX		XX.XX	XX.XX
	(Min, Max)	(XX, XX)	(XX, XX)	(XX, XX)		(XX, XX)	(XX, XX)

Programmer's Note: Please repeat this table for the following subgroups: Seroconverted prior to product use; Seroconverted on product use; Seroconverted after product use; No seroconversion

Percentages are calculated out of the number of participants (per centre and IPM 027 treatment) [a] In the safety population [b] With main partner
Age = INT((Enrollment Date – Date of Birth)/365.25)); Body Mass Index (BMI) = (body weight in kg)/(body height in m)^2
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Table 14.1.2.1
Demographics at Screening by IPM 027 Treatment Arm
Safety Population

Subgroup: All IPM 032 participants

		Centre 01				All Centres	
Parameter (unit)	Statistic	IPM 027 Dapivirine (N=XXX)	IPM 027 Placebo (N=XXX)	IPM 032 Overall (N=XXX)	…	IPM 027 Placebo (N=XXX)	IPM 032 Overall (N=XXX)
Education							
Primary school	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Secondary school	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Tertiary education	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Marital status							
Married	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Single	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Separated	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Divorced	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Widowed	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
With main partner							
Yes	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
No	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Co-residential status w/ main Partner (past year)							
Lived together all the time	n (%)[b]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Lived together none of the time	n (%)[b]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Lived together some of the time	n (%)[b]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Current co-residential status w/ main partner							
Yes	n (%)[b]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
No	n (%)[b]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)

Programmer's Note: Please repeat this table for the following subgroups: Seroconverted prior to product use; Seroconverted on product use; Seroconverted after product use; No seroconversion

Percentages are calculated out of the number of participants (per centre and IPM 027 treatment) [a] In the safety population [b] With main partner
Age = INT((Enrollment Date – Date of Birth)/365.25)); Body Mass Index (BMI) = (body weight in kg)/(body height in m)^2
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Table 14.1.2.1
Demographics at Screening by IPM 027 Treatment Arm
Safety Population

Subgroup: All IPM 032 participants

		Centre 01				All Centres	
Parameter (unit)	Statistic	IPM 027 Dapivirine (N=XXX)	IPM 027 Placebo (N=XXX)	IPM 032 Overall (N=XXX)	…	IPM 027 Placebo (N=XXX)	IPM 032 Overall (N=XXX)
Genital STIs at baseline							
Yes	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
No	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Vaginal sex once a week or more in the past month							
Yes	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
No	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Usual number of vaginal sex acts	n	XXX	XXX	XXX	…	XXX	XXX
	Mean	XX.X	XX.X	XX.X	…	XX.X	XX.X
	(q1,med,q3)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	…	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)
	SD	XX.XX	XX.XX	XX.XX	…	XX.XX	XX.XX
	(Min, Max)	(XX, XX)	(XX, XX)	(XX, XX)	…	(XX, XX)	(XX, XX)
No. of male sex partners at baseline							
0-1	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
2 or more	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Partner knowledge of ring use							
Yes	n (%)[b]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
No	n (%)[b]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Has children							
Yes	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
No	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)

Programmer's Note: Please repeat this table for the following subgroups: Seroconverted prior to product use; Seroconverted on product use; Seroconverted after product use; No seroconversion

Percentages are calculated out of the number of participants (per centre and IPM 027 treatment) [a] In the safety population [b] With main partner
Age = INT((Enrollment Date – Date of Birth)/365.25)); Body Mass Index (BMI) = (body weight in kg)/(body height in m)^2
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Table 14.1.2.2
Demographics at Screening by Enrolled Status (from IPM 027)
Safety Population

Subgroup: All IPM 032 participants

		Centre 01				All Centres	
Parameter (unit)	Statistic	Directly Enrolled In IPM 032 (N=XXX)	Did Not Directly Enroll in IPM 032 (N=XXX)	IPM 032 Overall (N=XXX)	…	Did Not Directly Enroll in IPM 032 (N=XXX)	IPM 032 Overall (N=XXX)
Age (years)	n	XXX	XXX	XXX	…	XXX	XXX
	Mean	XX.X	XX.X	XX.X	…	XX.X	XX.X
	(q1,med,q3)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	…	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)
	SD	XX.XX	XX.XX	XX.XX	…	XX.XX	XX.XX
	(Min, Max)	(XX, XX)	(XX, XX)	(XX, XX)	…	(XX, XX)	(XX, XX)
Race							
Coloured	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Black	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Indian	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Etc.	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Height (cm)	n	XXX	XXX	XXX	…	XXX	XXX
	Mean	XX.X	XX.X	XX.X	…	XX.X	XX.X
	(q1,med,q3)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	…	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)
	SD	XX.XX	XX.XX	XX.XX	…	XX.XX	XX.XX
	(Min, Max)	(XX, XX)	(XX, XX)	(XX, XX)	…	(XX, XX)	(XX, XX)
Weight (kg)	n	XXX	XXX	XXX	…	XXX	XXX
	Mean	XX.X	XX.X	XX.X	…	XX.X	XX.X
	(q1,med,q3)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	…	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)
	SD	XX.XX	XX.XX	XX.XX	…	XX.XX	XX.XX
	(Min, Max)	(XX, XX)	(XX, XX)	(XX, XX)	…	(XX, XX)	(XX, XX)
BMI (kg/m^2)	n	XXX	XXX	XXX	…	XXX	XXX
	Mean	XX.X	XX.X	XX.X	…	XX.X	XX.X
	(q1,med,q3)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	…	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)
	SD	XX.XX	XX.XX	XX.XX	…	XX.XX	XX.XX
	(Min, Max)	(XX, XX)	(XX, XX)	(XX, XX)	…	(XX, XX)	(XX, XX)

Programmer's Note: Please repeat this table for the following subgroups: Seroconverted prior to product use; Seroconverted on product use; Seroconverted after product use; No seroconversion

Percentages are calculated out of the number of participants (per centre and enrolled status) [a] In the safety population [b] With main partner
Age = INT((Enrollment Date – Date of Birth)/365.25)); Body Mass Index (BMI) = (body weight in kg)/(body height in m)^2
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Table 14.1.2.2
Demographics at Screening by Enrolled Status (from IPM 027)
Safety Population

Subgroup: All IPM 032 participants

		Centre 01				All Centres	
Parameter (unit)	Statistic	Directly Enrolled In IPM 032 (N=XXX)	Did Not Directly Enroll in IPM 032 (N=XXX)	IPM 032 Overall (N=XXX)	…	Did Not Directly Enroll in IPM 032 (N=XXX)	IPM 032 Overall (N=XXX)
Education							
Primary school	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Secondary school	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Tertiary education	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Marital status							
Married	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Single	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Separated	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Divorced	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Widowed	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
With main partner							
Yes	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
No	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Co-residential status w/ main partner							
Lived together all the time	n (%)[b]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Lived together none of the time	n (%)[b]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Lived together some of the time	n (%)[b]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Current co-residential status w/ main partner							
Yes	n (%)[b]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
No	n (%)[b]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)

Programmer's Note: Please repeat this table for the following subgroups: Seroconverted prior to product use; Seroconverted on product use; Seroconverted after product use; No seroconversion

Percentages are calculated out of the number of participants (per centre and enrolled status) [a] In the safety population [b] With main partner
Age = INT((Enrollment Date – Date of Birth)/365.25)); Body Mass Index (BMI) = (body weight in kg)/(body height in m)^2
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Table 14.1.2.2
Demographics at Screening by Enrolled Status (from IPM 027)
Safety Population

Subgroup: All IPM 032 participants

		Centre 01				All Centres	
Parameter (unit)	Statistic	Directly Enrolled In IPM 032 (N=XXX)	Did Not Directly Enroll in IPM 032 (N=XXX)	IPM 032 Overall (N=XXX)	…	Did Not Directly Enroll in IPM 032 (N=XXX)	IPM 032 Overall (N=XXX)
Genital STIs at baseline							
Yes	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
No	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Vaginal sex once a week or more in the past month							
Yes	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
No	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Usual number of vaginal sex acts	n	XXX	XXX	XXX	…	XXX	XXX
	Mean	XX.X	XX.X	XX.X	…	XX.X	XX.X
	(q1,med,q3)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	…	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)
	SD	XX.XX	XX.XX	XX.XX	…	XX.XX	XX.XX
	(Min, Max)	(XX, XX)	(XX, XX)	(XX, XX)	…	(XX, XX)	(XX, XX)
No. of male sex partners							
0-1	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
2 or more	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Partner knowledge of ring use							
Yes	n (%)[b]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
No	n (%)[b]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Has children							
Yes	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
No	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)

Programmer's Note: Please repeat this table for the following subgroups: Seroconverted prior to product use; Seroconverted on product use; Seroconverted after product use; No seroconversion

Percentages are calculated out of the number of participants (per centre and enrolled status) [a] In the safety population [b] With main partner
Age = INT((Enrollment Date – Date of Birth)/365.25)); Body Mass Index (BMI) = (body weight in kg)/(body height in m)^2
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Table 14.1.3.1
Medical History at Screening
Safety Population

	Statistic	Centre 01 (N=XXX)	Centre 02 (N=XXX)	…	Centre 08 (N=XXX)	All Centres (N=XXX)
Participants with no reported medical history	n (%)[a]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Participants with reported medical history*	n (%)[a]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)

[a] Percentages are calculated out of the number of participants in the safety population per centre
* More than one diagnosis/condition may be reported by a participant
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Table 14.1.3.2
Contraceptive/ Menstrual/ Obstetric History at Screening
Safety Population

	Statistic	Centre 01 (N=XXX)	Centre 02 (N=XXX)	…	Centre 08 (N=XXX)	All Centres (N=XXX)
Participants using any contraceptives*	n (%)[a]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Oral contraceptive regimen	n (%)[b]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Transdermal contraceptive patch	n (%)[b]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Subcutaneous implant	n (%)[b]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
IUD	n (%)[b]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Surgical sterilisation	n (%)[b]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Other	n (%)[b]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Menstrual bleeding						
Regular cycle	n (%)[a]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Irregular cycle	n (%)[a]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Amenorrhoeic	n (%)[a]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Duration of menstrual cycle	n	XXX	XXX	…	XXX	XXX
	Mean	XX.X	XX.X	…	XX.X	XX.X
	(q1,med,q3)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	…	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)
	SD	XX.XX	XX.XX	…	XX.XX	XX.XX
	(Min, Max)	(XX, XX)	(XX, XX)	…	(XX, XX)	(XX, XX)
Menstrual flow						
Light	n (%)[c]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Moderate	n (%)[c]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Heavy	n (%)[c]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)

IUD = Intrauterine device
Percentages are calculated out of the number of participants (per centre) [a] In the safety population [b] Using contraceptives [c] Reported having menses [d] With a parity score > 0
* More than one contraceptive may apply to a participant
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Table 14.1.3.2
Contraceptive/ Menstrual/ Obstetric History at Screening
Safety Population

	Statistic	Centre 01 (N=XXX)	Centre 02 (N=XXX)	…	Centre 08 (N=XXX)	All Centres (N=XXX)
History of dysmenorrhea						
Yes	n (%)[c]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
No	n (%)[c]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Gravidity						
0	n (%)[a]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
1-3	n (%)[a]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
4+	n (%)[a]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Parity						
0	n (%)[a]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
1-3	n (%)[a]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
4+	n (%)[a]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Vaginal deliveries						
0	n (%)[d]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
1-3	n (%)[d]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
4+	n (%)[d]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Cesarean sections						
0	n (%)[d]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
1-3	n (%)[d]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
4+	n (%)[d]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)

IUD = Intrauterine device
Percentages are calculated out of the number of participants (per centre) [a] In the safety population [b] Using contraceptives [c] Reported having menses [d] With a parity score > 0
* More than one contraceptive may apply to a participant
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Table 14.1.3.3
Gynaecological History at Screening
Safety Population

	Statistic	Centre 01 (N=XXX)	Centre 02 (N=XXX)	…	Centre 08 (N=XXX)	All Centres (N=XXX)
Participants with reported gynaecological history*	n (%)[a]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
MedDRA System Organ Class 1	n (%)[b]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
MedDRA Preferred Term 1	n (%)[b]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
MedDRA Preferred Term 2	n (%)[b]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)

Programmers Note: Please repeat for each system organ class and preferred term

Percentages are calculated out of the number of participants (per centre) [a] In the safety population [b] With gynaecological data
* More than one diagnosis/condition may be reported by a participant
Gynaecological conditions were coded using MedDRA Version 19.0
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Table 14.1.3.4
Prior Medication
Safety Population

	Statistic	Centre 01 (N=XXX)	Centre 02 (N=XXX)	…	Centre 08 (N=XXX)	All Centres (N=XXX)
Partticipants with reported prior medication	n (%)[a]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
WHO Drug Name	n (%)[b]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Preferred name 1	n (%)[b]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
Preferred name 2	n (%)[b]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
…						

Programmers Note: Please repeat for each drug name class and preferred term

Percentages are calculated out of the number of participants (per centre) [a] In the safety population [b] Reported prior medication
Prior medication is defined as any medication that started and ended before the first insertion of the investigational product (IP)
Medications were coded using WHO DDE (version June 2017)
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Table 14.3.1.1
Overall Summary of Treatment Emergent Adverse Events
Safety Population

Subgroup: All IPM 032 participants

		Centre 01				All Centres		
	Statistic	IPM 027 Dapivirine (N=XXX)	IPM 027 Placebo (N=XXX)	IPM 032 Overall (N=XXX)	…	IPM 027 Dapivirine (N=XXX)	IPM 027 Placebo (N=XXX)	IPM 032 Overall (N=XXX)
At least one TEAE	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
At least one serious TEAE	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
At least one DAIDS Grade 3 or 4 TEAE	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
At least one product-related TEAE	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
At least one serious product-related TEAE	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
TEAEs leading to death	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
TEAEs leading to permanent IP discontinuation	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
TEAEs leading to temporary IP discontinuation	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
TEAEs leading to trial discontinuation	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
Urogenital TEAEs	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
Social harms reported as TEAEs	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
Non TEAEs	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)

Programmers Note: Please repeat table for the following subgroup: IPM 027 participants who directly enrolled in IPM 032 (Note that the number of participants in the headers (N=XXX) should reflect the number of participants in each subgroup)

IP = Investigational product; TEAE = Treatment emergent adverse event
Deaths are not included in summary
[a] Percentages are calculated out of the number of participants in the safety population per centre and IPM 027 treatment
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Table 14.3.1.2
Treatment Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

Subgroup: All IPM 032 participants

		Centre 01			…	All Centres		
MedDRA System Organ Class MedDRA Preferred Term	Statistic	IPM 027 Dapivirine (N=XXX)	IPM 027 Placebo (N=XXX)	IPM 032 Overall (N=XXX)	…	IPM 027 Dapivirine (N=XXX)	IPM 027 Placebo (N=XXX)	IPM 032 Overall (N=XXX)
Any TEAE	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
	95% CI[b]	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X		XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
MedDRA System Organ Class 1	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
MedDRA Preferred Term 1	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
MedDRA Preferred Term 2	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
…								

Programmers Notes:
- Please repeat for each primary system organ class and preferred term
- Please repeat table for the following subgroup: IPM 027 participants who directly enrolled in IPM 032 (Note that the number of participants in the headers (N=XXX) should reflect the number of participants in each subgroup)

CI = Confidence interval; TEAE = Treatment emergent adverse event
[a] Percentages are calculated out of the number of participants in the safety population per centre and IPM 027 treatment
[b] 95% CI are calculated using Fisher's exact test
System organ class and preferred term were coded using MedDRA (Version 19.0)
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Table 14.3.1.3
Product-Related Treatment Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

Subgroup: All IPM 032 participants

		Centre 01			…	All Centres		
MedDRA System Organ Class MedDRA Preferred Term	Statistic	IPM 027 Dapivirine (N=XXX)	IPM 027 Placebo (N=XXX)	IPM 032 Overall (N=XXX)	…	IPM 027 Dapivirine (N=XXX)	IPM 027 Placebo (N=XXX)	IPM 032 Overall (N=XXX)
Any IP related TEAE	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
	95% CI[b]	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X		XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
MedDRA System Organ Class 1	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
MedDRA Preferred Term 1	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
MedDRA Preferred Term 2	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
…								

Programmers Notes:
- Please repeat for each primary system organ class and preferred term
- Please repeat table for the following Subgroups: Age < 25 years; Age ≥ 25 years and IPM 027 participants who directly enrolled in IPM 032 (Note that the number of participants in the headers (N=XXX) should reflect the number of participants in each subgroup)

CI = Confidence interval; IP = Investigational product; TEAE = Treatment emergent adverse event
[a] Percentages are calculated out of the number of participants in the safety population per centre and IPM 027 treatment
[b] 95% CI are calculated using Fisher's exact test
System organ class and preferred term were coded using MedDRA (Version 19.0)
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Table 14.3.1.4
Grade 3 or 4 Treatment Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

Subgroup: All IPM 032 participants

		Centre 01			…	All Centres		
MedDRA System Organ Class MedDRA Preferred Term	Statistic	IPM 027 Dapivirine (N=XXX)	IPM 027 Placebo (N=XXX)	IPM 032 Overall (N=XXX)	…	IPM 027 Dapivirine (N=XXX)	IPM 027 Placebo (N=XXX)	IPM 032 Overall (N=XXX)
Any Grade 3 or Grade 4 TEAE	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
	95% CI[b]	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X		XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
MedDRA System Organ Class 1	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
MedDRA Preferred Term 1	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
MedDRA Preferred Term 2	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
…								

Programmers Notes:
- Please repeat for each primary system organ class and preferred term
- Please repeat table for the following Subgroups: Age < 25 years; Age ≥ 25 years (Note that the number of participants in the headers (N=XXX) should reflect the number of participants in each subgroup)

CI = Confidence interval; TEAE = Treatment emergent adverse event
[a] Percentages are calculated out of the number of participants in the safety population per centre and IPM 027 treatment
[b] 95% CI are calculated using Fisher's exact test
System organ class and preferred term were coded using MedDRA (Version 19.0)
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Table 14.3.1.5
Serious Treatment Emergent Adverse Events by Primary System Organ Class and Preferred Term
Safety Population

Subgroup: All IPM 032 participants

		Centre 01				All Centres		
MedDRA System Organ Class MedDRA Preferred Term	Statistic	IPM 027 Dapivirine (N=XXX)	IPM 027 Placebo (N=XXX)	IPM 032 Overall (N=XXX)	…	IPM 027 Dapivirine (N=XXX)	IPM 027 Placebo (N=XXX)	IPM 032 Overall (N=XXX)
Any serious TEAE	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
	95% CI[b]	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	…	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
MedDRA System Organ Class 1	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
MedDRA Preferred Term 1	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
MedDRA Preferred Term 2	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
…								

Programmers Notes:
- Please repeat for each primary system organ class and preferred term
- Please repeat table for the following Subgroups: Age < 25 years; Age ≥ 25 years and IPM 027 participants who directly enrolled in IPM 032 (Note that the number of participants in the headers (N=XXX) should reflect the number of participants in each subgroup)

CI = Confidence interval; TEAE = Treatment emergent adverse event
[a] Percentages are calculated out of the number of participants in the safety population per centre and IPM 027 treatment
[b] 95% CI are calculated using Fisher's exact test
System organ class and preferred term were coded using MedDRA (Version 19.0)
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Table 14.3.1.6
Urogenital Treatment Emergent Adverse Events by Primary System Organ Class and Preferred Term
Safety Population

		Centre 01				All Centres		
MedDRA System Organ Class MedDRA Preferred Term	Statistic	IPM 027 Dapivirine (N=XXX)	IPM 027 Placebo (N=XXX)	IPM 032 Overall (N=XXX)	…	IPM 027 Dapivirine (N=XXX)	IPM 027 Placebo (N=XXX)	IPM 032 Overall (N=XXX)
Any urogenital TEAE	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
	95% CI[b]	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X	…	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X
MedDRA System Organ Class 1	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
MedDRA Preferred Term 1	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
MedDRA Preferred Term 2	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
…								

Programmers Note: Please repeat for each primary system organ class and preferred term

TEAE = Treatment emergent adverse event
[a] Percentages are calculated out of the number of participants in the safety population per centre and IPM 027 treatment
[b] 95% CI are calculated using Fisher's exact test
System organ class and preferred term were coded using MedDRA (Version 19.0)
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Table 14.3.1.7
Treatment Emergent Adverse Events by Worst Severity, Primary System Organ Class and Preferred Term
Safety Population

Subgroup: All IPM 032 participants

	Centre 01						…	All Centres							
	IPM 027 Dapivirine (N=XXX)		IPM 027 Placebo (N=XXX)		IPM 032 Overall (N=XXX)		…	IPM 027 Dapivirine (N=XXX)		…	IPM 032 Overall (N=XXX)			
MedDRA System Organ Class MedDRA Preferred Term	Grade 1 n (%)[a]	… Grade 5 n (%)[a]	Grade 1 n (%)[a]	… Grade 5 n (%)[a]	Grade 1 n (%)[a]	… Grade 5 n (%)[a]	…	Grade 1 n (%)[a]	… Grade 5 n (%)[a]	…	Grade 1 n (%)[a]	… Grade 5 n (%)[a]			
MedDRA System Organ Class 1	X (X.X)	… X (X.X)	X (X.X)	… X (X.X)	X (X.X)	… X (X.X)	…	X (X.X)	… X (X.X)	…	X (X.X)	… X (X.X)			
MedDRA Preferred Term 1	X (X.X)	… X (X.X)	X (X.X)	… X (X.X)	X (X.X)	… X (X.X)	…	X (X.X)	… X (X.X)	…	X (X.X)	… X (X.X)			
MedDRA Preferred Term 2	X (X.X)	… X (X.X)	X (X.X)	… X (X.X)	X (X.X)	… X (X.X)	…	X (X.X)	… X (X.X)	…	X (X.X)	… X (X.X)			
…															

Programmers Notes:
- Please repeat for each primary system organ class and preferred term
- Please repeat the table for the following subgroup: IPM 027 participants who directly enrolled in IPM 032 (Note that the number of participants in the headers (N=XXX) should reflect the number of participants in each subgroup)

[a] Percentages are calculated out of the number of participants in the safety population per centre and IPM 027 treatment
Severity Grade: 1 = Mild; 2 = Moderate; 3 = Severe; 4 = Potentially life-threatening; 5 = Death
Where a subject reports more than one adverse event per SOC and preferred term they will only be counted once for the worst severity
A missing severity grade is assumed to be 4
System organ class and preferred term were coded using MedDRA (Version 19.0).
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Table 14.3.1.8
Serious Treatment Emergent Adverse Events by Worst Severity, Primary System Organ Class and Preferred Term
Safety Population

Subgroup: All IPM 032 participants

	Centre 01						…	All Centres							
	IPM 027 Dapivirine (N=XXX)		IPM 027 Placebo (N=XXX)		IPM 032 Overall (N=XXX)		…	IPM 027 Dapivirine (N=XXX)		…	IPM 032 Overall (N=XXX)			
MedDRA System Organ Class MedDRA Preferred Term	Grade 1 n (%)[a]	… Grade 5 n (%)[a]	Grade 1 n (%)[a]	… Grade 5 n (%)[a]	Grade 1 n (%)[a]	… Grade 5 n (%)[a]	…	Grade 1 n (%)[a]	… Grade 5 n (%)[a]	…	Grade 1 n (%)[a]	… Grade 5 n (%)[a]			
MedDRA System Organ Class 1	X (X.X)	… X (X.X)	X (X.X)	… X (X.X)	X (X.X)	… X (X.X)	…	X (X.X)	… X (X.X)	…	X (X.X)	… X (X.X)			
MedDRA Preferred Term 1	X (X.X)	… X (X.X)	X (X.X)	… X (X.X)	X (X.X)	… X (X.X)	…	X (X.X)	… X (X.X)	…	X (X.X)	… X (X.X)			
MedDRA Preferred Term 2	X (X.X)	… X (X.X)	X (X.X)	… X (X.X)	X (X.X)	… X (X.X)	…	X (X.X)	… X (X.X)	…	X (X.X)	… X (X.X)			
…															

Programmers Notes:
- Please repeat for each primary system organ class and preferred term
- Please repeat the table for the following subgroup: IPM 027 participants who directly enrolled in IPM 032 (Note that the number of participants in the headers (N=XXX) should reflect the number of participants in each subgroup)

[a] Percentages are calculated out of the number of participants in the safety population per centre and IPM 027 treatment
Severity Grade: 1 = Mild; 2 = Moderate; 3 = Severe; 4 = Potentially life-threatening; 5 = Death
Where a subject reports more than one adverse event per SOC and preferred term they will only be counted once for the worst severity
A missing severity grade is assumed to be 4
System organ class and preferred term were coded using MedDRA (Version 19.0)
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Table 14.3.1.9
Product-Related Treatment Emergent Adverse Events by Worst Severity, Primary System Organ Class and Preferred Term
Safety Population

Subgroup: All IPM 032 participants

	Centre 01						…	All Centres							
	IPM 027 Dapivirine (N=XXX)		IPM 027 Placebo (N=XXX)		IPM 032 Overall (N=XXX)		…	IPM 027 Dapivirine (N=XXX)		…	IPM 032 Overall (N=XXX)			
MedDRA System Organ Class MedDRA Preferred Term	Grade 1 n (%)[a]	… Grade 5 n (%)[a]	Grade 1 n (%)[a]	… Grade 5 n (%)[a]	Grade 1 n (%)[a]	… Grade 5 n (%)[a]	…	Grade 1 n (%)[a]	… Grade 5 n (%)[a]	…	Grade 1 n (%)[a]	… Grade 5 n (%)[a]			
MedDRA System Organ Class 1	X (X.X)	… X (X.X)	X (X.X)	… X (X.X)	X (X.X)	… X (X.X)	…	X (X.X)	… X (X.X)	…	X (X.X)	… X (X.X)			
MedDRA Preferred Term 1	X (X.X)	… X (X.X)	X (X.X)	… X (X.X)	X (X.X)	… X (X.X)	…	X (X.X)	… X (X.X)	…	X (X.X)	… X (X.X)			
MedDRA Preferred Term 2	X (X.X)	… X (X.X)	X (X.X)	… X (X.X)	X (X.X)	… X (X.X)	…	X (X.X)	… X (X.X)	…	X (X.X)	… X (X.X)			
…															

Programmers Notes:
- Please repeat for each primary system organ class and preferred term
- Please repeat the table for the following subgroup: IPM 027 participants who directly enrolled in IPM 032 (Note that the number of participants in the headers (N=XXX) should reflect the number of participants in each subgroup)

[a] Percentages are calculated out of the number of participants in the safety population per centre and IPM 027 treatment
Severity Grade: 1 = Mild; 2 = Moderate; 3 = Severe; 4 = Potentially life-threatening; 5 = Death
Where a subject reports more than one adverse event per SOC and preferred term they will only be counted once for the worst severity
A missing severity grade is assumed to be 4
System organ class and preferred term were coded using MedDRA (Version 19.0)
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Table 14.3.1.10
Serious Product-Related Treatment Emergent Adverse Events by Worst Severity, Primary System Organ Class and Preferred Term
Safety Population

Subgroup: All IPM 032 participants

	Centre 01						…	All Centres							
	IPM 027 Dapivirine (N=XXX)		IPM 027 Placebo (N=XXX)		IPM 032 Overall (N=XXX)		…	IPM 027 Dapivirine (N=XXX)		…	IPM 032 Overall (N=XXX)			
MedDRA System Organ Class MedDRA Preferred Term	Grade 1 n (%)[a]	… Grade 5 n (%)[a]	Grade 1 n (%)[a]	… Grade 5 n (%)[a]	Grade 1 n (%)[a]	… Grade 5 n (%)[a]	…	Grade 1 n (%)[a]	… Grade 5 n (%)[a]	…	Grade 1 n (%)[a]	… Grade 5 n (%)[a]			
MedDRA System Organ Class 1	X (X.X)	… X (X.X)	X (X.X)	… X (X.X)	X (X.X)	… X (X.X)	…	X (X.X)	… X (X.X)	…	X (X.X)	… X (X.X)			
MedDRA Preferred Term 1	X (X.X)	… X (X.X)	X (X.X)	… X (X.X)	X (X.X)	… X (X.X)	…	X (X.X)	… X (X.X)	…	X (X.X)	… X (X.X)			
MedDRA Preferred Term 2	X (X.X)	… X (X.X)	X (X.X)	… X (X.X)	X (X.X)	… X (X.X)	…	X (X.X)	… X (X.X)	…	X (X.X)	… X (X.X)			
…															

Programmers Notes:
- Please repeat for each primary system organ class and preferred term
- Please repeat the table for the following subgroup: IPM 027 participants who directly enrolled in IPM 032 (Note that the number of participants in the headers (N=XXX) should reflect the number of participants in each subgroup)

[a] Percentages are calculated out of the number of participants in the safety population per centre and IPM 027 treatment
Severity Grade: 1 = Mild; 2 = Moderate; 3 = Severe; 4 = Potentially life-threatening; 5 = Death
Where a subject reports more than one adverse event per SOC and preferred term they will only be counted once for the worst severity
A missing severity grade is assumed to be 4
System organ class and preferred term were coded using MedDRA (Version 19.0)
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Table 14.3.1.11
Social Harms Reported as Treatment Emergent Adverse Events by Worst Severity, Primary System Organ Class and Preferred Term
Safety Population

Subgroup: All IPM 032 participants

	Centre 01						…	All Centres							
	IPM 027 Dapivirine (N=XXX)		IPM 027 Placebo (N=XXX)		IPM 032 Overall (N=XXX)		…	IPM 027 Dapivirine (N=XXX)		…	IPM 032 Overall (N=XXX)			
MedDRA System Organ Class MedDRA Preferred Term	Grade 1 n (%)[a]	… Grade 5 n (%)[a]	Grade 1 n (%)[a]	… Grade 5 n (%)[a]	Grade 1 n (%)[a]	… Grade 5 n (%)[a]	…	Grade 1 n (%)[a]	… Grade 5 n (%)[a]	…	Grade 1 n (%)[a]	… Grade 5 n (%)[a]			
MedDRA System Organ Class 1	X (X.X)	… X (X.X)	X (X.X)	… X (X.X)	X (X.X)	… X (X.X)	…	X (X.X)	… X (X.X)	…	X (X.X)	… X (X.X)			
MedDRA Preferred Term 1	X (X.X)	… X (X.X)	X (X.X)	… X (X.X)	X (X.X)	… X (X.X)	…	X (X.X)	… X (X.X)	…	X (X.X)	… X (X.X)			
MedDRA Preferred Term 2	X (X.X)	… X (X.X)	X (X.X)	… X (X.X)	X (X.X)	… X (X.X)	…	X (X.X)	… X (X.X)	…	X (X.X)	… X (X.X)			
…															

Programmers Notes:
- Please repeat for each primary system organ class and preferred term
- Please repeat the table for the following subgroup: IPM 027 participants who directly enrolled in IPM 032 (Note that the number of participants in the headers (N=XXX) should reflect the number of participants in each subgroup)

[a] Percentages are calculated out of the number of participants in the safety population per centre and IPM 027 treatment
Severity Grade: 1 = Mild; 2 = Moderate; 3 = Severe; 4 = Potentially life-threatening; 5 = Death
Where a subject reports more than one adverse event per SOC and preferred term they will only be counted once for the worst severity
A missing severity grade is assumed to be 4
System organ class and preferred term were coded using MedDRA (Version 19.0)
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Table 14.3.5.1
Adherence, Overall Summary of Dapivirine Residual Levels (mg) in Used Rings
Safety Population

Subgroup: All IPM 032 participants

Month Ring Used	Trial	n	Mean	Q1	Median	Q3	SD	Min	Max	95% CI[b]
Enrolment / Trial Month X	IPM 032 / IPM 027	XXX	XX.X	XX.X	XX.X	XX.X	XX.XX	XX	XX	XX.X, XX.X
		XXX	XX.X	XX.X	XX.X	XX.X	XX.XX	XX	XX	XX.X, XX.X

Programmers Note: Please repeat table for the following Subgroups: Martital status: Married; Martital status: Unmarried; Age < 25 years; Age ≥ 25 years; Main sex partner: Yes; Main sex partner: No; Presence of genital symptoms/STIs: Yes; Presence of genital symptoms/STIs: No (Note that the number of participants (n) should reflect the number of participants in each subgroup)

CI = Confidence interval
[b] 95% CI for the mean
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NC

Table 14.3.5.2
Adherence, Summary of Dapivirine Residual Levels (mg) in Used Rings by Category
Safety Population

Month Ring Used	Trial	All Rings	0 - < 20 mg n (%)[a]	20 - ≤ 21 mg n (%)[a]	> 21 - ≤ 22 mg n (%)[a]	> 22 - ≤ 23.5 mg n (%)[a]	> 23.5 mg n (%)[a]
Enrolment / Trial Month X	IPM 032 / IPM 027	XXX	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)

[a] Percentages are calculated out of the total number of rings per trial month
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Table 14.3.5.3
Adherence, Summary Relating Ring Residual Levels (mg) to Time Intervals Between Consecutive Ring Replacements
Safety Population

Month Ring Used	Time Interval Between Consecutive Ring Replacements for Residual Levels in Ring	n	Mean	Q1	Median	Q3	SD	Min	Max
Enrolment / Trial Month X	< 23 days	XXX	XX.X	XX.X	XX.X	XX.X	XX.XX	XX	XX
	23 – 37 days	XXX	XX.X	XX.X	XX.X	XX.X	XX.XX	XX	XX
	> 37 – 84 days	XXX	XX.X	XX.X	XX.X	XX.X	XX.XX	XX	XX
	> 84 days	XXX	XX.X	XX.X	XX.X	XX.X	XX.XX	XX	XX

Table 14.3.5.4
Residual Levels of Dapivirine (mg) in the Last Three Rings Returned by Participants Who Seroconverted, Prior to HIV-1 Seroconversion
Safety Population

Appearance Colour	Statistic	HIV + (N=XXX)	HIV – (N=XXX)
Used			
White to off-white	n, r	XXX, XXX	XXX, XXX
	Mean	XX.X	XX.X
	(q1,med,q3)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)
	SD	XX.XX	XX.XX
	(Min, Max)	(XX, XX)	(XX, XX)
Slight yellow to yellow	n, r	XXX, XXX	XXX, XXX
	Mean	XX.X	XX.X
	(q1,med,q3)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)
	SD	XX.XX	XX.XX
	(Min, Max)	(XX, XX)	(XX, XX)
Tan	n, r	XXX, XXX	XXX, XXX
	Mean	XX.X	XX.X
	(q1,med,q3)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)
	SD	XX.XX	XX.XX
	(Min, Max)	(XX, XX)	(XX, XX)
Brown	n, r	XXX, XXX	XXX, XXX
	Mean	XX.X	XX.X
	(q1,med,q3)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)
	SD	XX.XX	XX.XX
	(Min, Max)	(XX, XX)	(XX, XX)
Other	n, r	XXX, XXX	XXX, XXX
	Mean	XX.X	XX.X
	(q1,med,q3)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)
	SD	XX.XX	XX.XX
	(Min, Max)	(XX, XX)	(XX, XX)

Programmers Note: Please repeat for the following appearance categories: Unused; Not sure

n = Number of participants; r = Number of rings
HIV-1 = Human immunodeficiency virus type 1; HIV+ = Participants who HIV-1 seroconverted during trial duration; HIV- = Participants who remained HIV- for the duration of the trial
Only the residual levels of dapivirine in the last three rings returned by participants who HIV-1 seroconverted, prior to HIV-1 seroconversion, are included. All residual levels are used for participants that remained HIV- for the duration of the trial.

Table 14.3.5.5
Self-Reported Adherence to Dapivirine Ring
Safety Population

		Centre 01				All Centres		
Month Ring Used	Analysis Category	IPM 027 Dapivirine n (%)[a]	IPM 027 Placebo n (%)[a]	IPM 032 Overall n (%)[a]	…	IPM 027 Dapivirine n (%)[a]	IPM 027 Placebo n (%)[a]	IPM 032 Overall n (%)[a]
Trial month X / Exit visit	n	XXX	XXX	XXX	…	XXX	XXX	XXX
	< 80%	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
	≥ 80% - < 90%	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
	≥ 90%	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)

[a] Percentages are calculated out of the number of participants in the safety population per centre and IPM 027 treatment with available data
Adherence rate per was calculated as 100 x (number of days that the participant reportedly wore the ring/the total number of days that the participant was expected to wear the ring)
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Table 14.3.5.6
Self-Reported Acceptability of Dapivirine Ring
Safety Population

LPUV Question	Statistic	IPM 032 Overall (N=XXX)
Participants who responded positively to the following		
Do you think it is possible for women to use the ring as requested (i.e. without removing it)?	n (%)[a]	X (X.X)
	95% CI[b]	XX, XX
Do you think women in your community would want to use this ring if it were available?	n (%)[a]	X (X.X)
	95% CI[b]	XX, XX

CI = Confidence interval; LPUV = Last product use visit
[a] Percentages are calculated out of the number of participants in the safety population
[b] 95% CI calculated using Fisher's exact test
A participant will be classified as having found the vaginal ring acceptable if she responds positively to the first question, about keeping the ring inserted as prescribed. Community acceptability will be demonstrated by positive responses to the second question

Table 14.3.5.7
Accidental Ring Expulsion/ Removal
Safety Population

Visit	Reason Ring Was Removed / Came Out	Statistic	IPM 032 Overall (N=XXX)
Trial Month X	Participants who had an accidental ring removal/expulsion	n (%)[a]	X (X.X)
	Participants who had no accidental ring removals/expulsions	n (%)[a]	X (X.X)
	…		

[a] Percentages are calculated out of the number of participants in the safety population

Table 14.3.6.1
Vital Signs
Safety Population

Parameter (unit) Visit	Statistic	Centre 01 IPM 027 Dapivirine (N=XXX)	Centre 01 IPM 027 Placebo (N=XXX)	Centre 01 IPM 032 Overall (N=XXX)	…	All Centres IPM 027 Dapivirine (N=XXX)	All Centres IPM 027 Placebo (N=XXX)	All Centres IPM 032 Overall (N=XXX)
Parameter (unit)								
Baseline	n	XXX	XXX	XXX	…	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X	…	XX.X	XX.X	XX.X
	(q1,med,q3)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	…	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)
	SD	XX.XX	XX.XX	XX.XX	…	XX.XX	XX.XX	XX.XX
	(Min, Max)	(XX, XX)	(XX, XX)	(XX, XX)	…	(XX, XX)	(XX, XX)	(XX, XX)
					…			
LPUV	n	XXX	XXX	XXX	…	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X	…	XX.X	XX.X	XX.X
	(q1,med,q3)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	…	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)
	SD	XX.XX	XX.XX	XX.XX	…	XX.XX	XX.XX	XX.XX
	(Min, Max)	(XX, XX)	(XX, XX)	(XX, XX)	…	(XX, XX)	(XX, XX)	(XX, XX)
					…			
Change from baseline to LPUV	n	XXX	XXX	XXX	…	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X	…	XX.X	XX.X	XX.X
	(q1,med,q3)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	…	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)
	SD	XX.XX	XX.XX	XX.XX	…	XX.XX	XX.XX	XX.XX
	(Min, Max)	(XX, XX)	(XX, XX)	(XX, XX)	…	(XX, XX)	(XX, XX)	(XX, XX)
	95% CI[a]	XX, XX	XX, XX	XX, XX		XX, XX	XX, XX	XX, XX

Programmers Notes:
- Please repeat for each measured parameter
- 95% CIs are calculated for Change from Baseline only

CI = Confidence interval; LPUV = Last product use visit
[a] 95% CI for the mean
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Table 14.3.7.1
Pelvic/ Speculum Examinations
Safety Population

Visit	Findings Indicator	Statistic	Centre 01 IPM 027 Dapivirine (N=XXX)	Centre 01 IPM 027 Placebo (N=XXX)	Centre 01 IPM 032 Overall (N=XXX)	…	All Centres IPM 027 Dapivirine (N=XXX)	All Centres IPM 027 Placebo (N=XXX)	All Centres IPM 032 Overall (N=XXX)
Trial Month X	Presence of vulvar findings	N	XXX	XXX	XXX	…	XXX	XXX	XXX
	Vulvar erythema								
	Vulvar edema	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
	Vulvar rash	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
	Etc.	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
		n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
		n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)

Programmers Notes:
- Please repeat for the presence of Cervical findings, General/other findings, Vulvar Lesions findings, Vaginal Lesions findings, Cervical Lesions findings, and Cervical ectop
- Please repeat table for all available visits

LPUV = Last product use visit
[a] Percentages are calculated out of the number of participants in the safety population per centre and IPM 027 treatment
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Table 14.3.7.2
Cervical Cytology at Baseline
Safety Population

		Centre 01			…	All Centres		
Findings	Statistic	IPM 027 Dapivirine (N=XXX)	IPM 027 Placebo (N=XXX)	IPM 032 Overall (N=XXX)		IPM 027 Dapivirine (N=XXX)	IPM 027 Placebo (N=XXX)	IPM 032 Overall (N=XXX)
Negative for intraepithelial lesion or cancer (malignancy)	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
ASCUS	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
SIL-low grade	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
ASC-H	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
SIL-high grade	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
AGC	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
AGC-favor neoplastic	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
Cancer	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
Other findings	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)

[a] Percentages are calculated out of the number of participants in the safety population per centre and IPM 027 treatment
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Table 14.3.7.3
Sexually Transmitted Infections
Safety Population

Visit Test	Statistic	Centre 01 IPM 027 Dapivirine (N=XXX)	Centre 01 IPM 027 Placebo (N=XXX)	Centre 01 IPM 032 Overall (N=XXX)	…	All Centres IPM 027 Dapivirine (N=XXX)	All Centres IPM 027 Placebo (N=XXX)	All Centres IPM 032 Overall (N=XXX)
Screening	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
Any STI*	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
Chlamydia positive	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
Syphilis RPR	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
Gonorrhoea positive	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
Trichomonas positive	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
Blood present during collection of cervico-vaginal samples	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
	n (%)[a]				…			
					…			
LPUV	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
Any STI*	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
Chlamydia positive	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
Syphilis confirmatory test	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
TPHA/TPPA	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
Gonorrhoea positive	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
Trichomonas positive	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
Blood present during collection of cervico-vaginal samples	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)

LPUV = Last product use visit
[a] Percentages are calculated out of the number of participants in the safety population per centre and IPM 027 treatment
* Includes Chlamydia, Gonorrhoea, Syphilis and Trichomonas
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Table 14.3.7.4
Immediately Reportable Events
Safety Population

Event	Statistic	Centre 01 IPM 027 Dapivirine (N=XXX)	Centre 01 IPM 027 Placebo (N=XXX)	Centre 01 IPM 032 Overall (N=XXX)	…	All Centres IPM 027 Dapivirine (N=XXX)	All Centres IPM 027 Placebo (N=XXX)	All Centres IPM 032 Overall (N=XXX)
Number of participants confirmed pregnant								
Number op participants confirmed pregnant	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
Total number of person-years	PY	XXX	XXX	XXX	…	XXX	XXX	XXX
Pregnancy incidence rate (per 100 person-years)		XX.X	XX.X	XX.X		XX.X	XX.X	XX.X
Number of confirmed pregnancies	n	XXX	XXX	XXX	…	XXX	XXX	XXX
Pregnancy report								
Number of confirmed pregnancies	n	XXX	XXX	XXX	…	XXX	XXX	XXX
Contraceptive method at the time of positive pregnancy test								
Oral contraceptive	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
Transdermal contraceptive patch	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
Long acting injectable progestins	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
Etc.								
Pregnancy outcome								
Full term live birth (≥ 37 weeks)	n (%)[b]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
Premature term live birth (< 37 weeks)	n (%)[b]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
Stillbirth/intrauterine fetal demise (≥ 20 weeks)	n (%)[b]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
Etc.								
HIV-1 Seroconverters	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)

HIV-1 = Human immunodeficiency virus type 1
PY = (Date of last ring removal – Date of first ring insertion + 1)/365.25
Percentages are calculated out of the number of participants (per centre and IPM 027 treatment) [a] In the safety population [b] Total pregnancy outcomes
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Table 14.3.7.5

Analysis 1, HIV-1 Seroconversion Rate per 100 Person-Years of Product Use

Population: m-ITT

	Statistic	IPM 027 Dapivirine (N=XXX)	IPM 027 Placebo (N=XXX)	IPM 032 Overall (N=XXX)
Number of confirmed HIV-1 seroconversions on IP	n (%)[a]	X (X.X)	X (X.X)	X (X.X)
Total number of person-years	PY	XXX	XXX	XXX
Seroconversion rate (per 100 person-years)	n/PY	XX.X	XX.X	XX.X
95% CI for seroconversion-rate (per 100 person-years)	95% CI[b]	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X

Programmers Note: Please repeat the table for the PP population

CI = Confidence interval; HIV-1 = Human immunodeficiency virus type 1; IP = Investigational product

[a] Percentages are calculated out of the number of participants in the applicable population per IPM 027 treatment

[b] 95% CI calculated as [(n/PY) ± 1.96 x ([n/PY] / PY)½] x 100; where n = number of HIV seroconversions and PY = total number of person-years of product use calculated as PY = (Date of last ring removal – Date of first ring insertion + 1)/365.25

Table 14.3.7.6
Analysis 2, HIV-1 Seroconversion Rate per 100 Person-Years of Product Use
m-ITT

	Statistic	IPM 027 Dapivirine (N=XXX)	IPM 027 Placebo (N=XXX)	IPM 032 Overall (N=XXX)
Number of confirmed HIV-1 seroconversions on IP	n (%)[a]	X (X.X)	X (X.X)	X (X.X)
Total number of person-years	PY	XXX	XXX	XXX
Seroconversion rate (per 100 person-years)	n/PY	XX.X	XX.X	XX.X
95% CI for seroconversion-rate (per 100 person-years)	95% CI[b]	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X

CI = Confidence interval; HIV-1 = Human immunodeficiency virus type 1; IP = Investigational product
[a] Percentages are calculated out of the number of participants in the m-ITT population per IPM 027 treatment
[b] 95% CI calculated as [(n/PY) ± 1.96 x ([n/PY] / PY)½] x 100; where n = number of HIV seroconversions and PY = total number of person-years of product use calculated as PY = (Date of last ring removal – Date of first ring insertion + 1)/365.25
In instances where it cannot be ruled out that HIV-1 infection may have occurred during IP use in case the HIV RNA test has detectable levels at the next visit after ring use, such participants will be considered as being seroconverted

Table 14.3.7.7
Analysis 3, HIV-1 Seroconversion Rate per 100 Person-Years of Product Use
m-ITT

	Statistic	IPM 027 Dapivirine (N=XXX)	IPM 027 Placebo (N=XXX)	IPM 032 Overall (N=XXX)
Number of confirmed HIV-1 seroconversions on IP	n (%)[a]	X (X.X)	X (X.X)	X (X.X)
Total number of person-years	PY	XXX	XXX	XXX
Seroconversion rate (per 100 person-years)	n/PY	XX.X	XX.X	XX.X
95% CI for seroconversion-rate (per 100 person-years)	95% CI[b]	XX.X, XX.X	XX.X, XX.X	XX.X, XX.X

CI = Confidence interval; HIV-1 = Human immunodeficiency virus type 1; IP = Investigational product
[a] Percentages are calculated out of the number of participants in the m-ITT population per IPM 027 treatment
[b] 95% CI calculated as [(n/PY) ± 1.96 x ([n/PY] / PY)½] x 100; where n = number of HIV-1 seroconversions and PY = total number of person-years of product use calculated as PY = (Date of last ring removal – Date of first ring insertion + 1)/365.25
All confirmed HIV-1 seroconverters determined to have been HIV-1 infected after enrollment will be considered as infected on product, even instances where HIV-1 seroconversion and estimated point of infection was determined to be after the last product use visit

Table 14.3.7.8
Analysis 4, HIV-1 Infection Rate per 100 Person-Years of Product Use
m-ITT Population

	Statistic	IPM 027 Dapivirine (N=XXX)	IPM 027 Placebo (N=XXX)	IPM 032 Overall (N=XXX)
Number of confirmed HIV-1 infections on IP	n (%)[a]	X (X.X)	X (X.X)	X (X.X)
Total number of person-years	PY	XXX	XXX	XXX
Infection rate (per 100 person-years)	n/PY	XX.X	XX.X	XX.X
95% CI for infection-rate (per 100 person-years)	95% CI[b]	(XX.X, XX.X)	(XX.X, XX.X)	(XX.X, XX.X)

HIV-1 = Human immunodeficiency virus type 1; IP = Investigational product
[a] Percentages are calculated out of the number of participants in the m-ITT population per IPM 027 treatment
[b] 95% CI calculated as [(n/PY) ± 1.96 x ([n/PY] / PY)½] x 100; where n = number of HIV-1 infections and PY = total number of person-years of product use calculated as PY = (Date of last ring removal – Date of first ring insertion + 1)/365.25
Similar to Analysis 1, but based on time to first positive HIV-1 RNA

Table 14.3.7.9
Overview of Number of Participants in the Trial
Safety Population

	Statistic	IPM 027 Dapivirine (N=XXX)	IPM 027 Placebo (N=XXX)	IPM 032 Overall (N=XXX)
Participants in the safety population	N	XXX	XXX	XXX
Participants in the m-ITT population	n (%)[a]	X (X.X)	X (X.X)	X (X.X)
Participants in the virology population	n (%)[a]	X (X.X)	X (X.X)	X (X.X)
Participants without HIV-1 seroconversion	n (%)[a]	X (X.X)	X (X.X)	X (X.X)
Participants with HIV-1 seroconversion	n (%)[a]	X (X.X)	X (X.X)	X (X.X)
Participants with HIV-1 seroconversion prior to IP	n (%)[a]	X (X.X)	X (X.X)	X (X.X)
Participants with HIV-1 seroconversion on IP	n (%)[a]	X (X.X)	X (X.X)	X (X.X)
Participants with HIV-1 seroconversion after IP (LPUV)	n (%)[a]	X (X.X)	X (X.X)	X (X.X)
Participants with HIV-1 seroconversion – not prior/on/after IP	n (%)[a]	X (X.X)	X (X.X)	X (X.X)

HIV-1 = Human immunodeficiency virus type 1;IP = Investigational product; LPUV = Last product use visit
[a] Percentages are calculated out of the number of participants in the safety population per IPM 027 treatment
Seroconversion prior to IP: Participant was already HIV-infected at Enrollment before commencing Dapivirine Vaginal Ring-004 use, based on reverse sequential HIV RNA PCR testing;
Seroconversion on IP: HIV seroconverted participant was determined to have been HIV-1 infected while on IP, as evaluated by the Principal Investigator/designee once the HIV-1 point of infection had been estimated based on reverse sequential HIV RNA PCR testing;
Seroconversion after IP: Participant became HIV-1 infected after the Last Product Use Visit;
Seroconversion – not prior/on/after IP: One participant discontinued ring use for 5 months (as she was not planning on continuing in the trial) before seroconverting, and one had a plasma HIV-1 ribonucleic acid (RNA) concentration below the limit of detection at the Last Product Use Visit (and a re-test of the same sample was negative)

Table 14.3.7.10.2
Reverse Transcriptase Inhibitor and Protease Inhibitor Resistance-Associated Mutations Observed at Any Timepoint
Virology Population

Subgroup: All IPM 032 participants

	Statistic	IPM 027 Dapivirine (N=XXX)	IPM 027 Placebo (N=XXX)	IPM 032 Overall (N=XXX)
Participants who HIV-1 seroconverted on IP	n (%)[a]	X (X.X)	X (X.X)	X (X.X)
Participants who had a resistance test performed	n (%)[a]	X (X.X)	X (X.X)	X (X.X)
Participants with a successful resistance test result	n (%)[a]	X (X.X)	X (X.X)	X (X.X)
Participants with HIV-1 drug resistance-associated mutations	n (%)[a]	X (X.X)	X (X.X)	X (X.X)
NNRTI mutations[c]				
A98G	n (%)[b]	X (X.X)	X (X.X)	X (X.X)
E138A	n (%)[b]	X (X.X)	X (X.X)	X (X.X)
…	…	…	…	…
NRTI mutations[c]				
E44D	n (%)[b]	X (X.X)	X (X.X)	X (X.X)
…	…	…	…	…
Major PI mutations[c]				
L33F	n (%)[b]	X (X.X)	X (X.X)	X (X.X)
M46L	n (%)[b]	X (X.X)	X (X.X)	X (X.X)
…	…	…	…	…

Programmers Notes:

- *Please repeat table for the following subgroups: HIV-1 RNA level:* HIV-1 RNA level: ≥ 2000 copies/mL, < *2000 copies/mL); HIV-1 subtype (C / Other); Schedule A, B or C*
- ***Table 14.7.10.2** will be similar to Table 14.7.10.1 but the heading and analysis will be based on Any Timepoint*

HIV-1 = Human immunodeficiency virus type 1; NNRTI = Non-nucleoside reverse transcriptase inhibitor ; NRTI = Nucleoside reverse transcriptase inhibitor; PI = Protease inhibitor
Percentages are calculated out of the number of participants (per IPM 027 treatment) [a] In the virology population [b] Successful results
[c] Resistance-associated mutations of interest not present in the data set are not included in the table
Resistance-associated mutations were defined using the Stanford HIV database algorithm Version 8.

Table 14.3.7.11
Data Overview of HIV-1 Seroconversion Timing Relative To HIV-1 RNA Detection and Treatment
Virology Population

	Statistic	IPM 027 Dapivirine (N=XXX)	IPM 027 Placebo (N=XXX)	IPM 032 Overall (N=XXX)
First positive HIV-1 RNA Timing				
At time of seroconversion	n (%)[a]	X (X.X)	X (X.X)	X (X.X)
Mutations detected before seroconversion	n (%)[b]	X (X.X)	X (X.X)	X (X.X)
Mutations detected at seroconversion	n (%)[b]	X (X.X)	X (X.X)	X (X.X)
Mutations detected after seroconversion	n (%)[b]	X (X.X)	X (X.X)	X (X.X)
Before seroconversion	n (%)[a]	X (X.X)	X (X.X)	X (X.X)
Mutations detected before seroconversion	n (%)[b]	X (X.X)	X (X.X)	X (X.X)
Mutations detected at seroconversion	n (%)[b]	X (X.X)	X (X.X)	X (X.X)
Mutations detected after seroconversion	n (%)[b]	X (X.X)	X (X.X)	X (X.X)
Average days	Mean	XX.X	XX.X	XX.X
Minimum and maximum days	(Min,Max)	(XX, XX)	(XX, XX)	(XX, XX)
IP use stopped				
At time of seroconversion	n (%)[a]	X (X.X)	X (X.X)	X (X.X)
After seroconversion	n (%)[a]	X (X.X)	X (X.X)	X (X.X)
Before seroconversion	n (%)[a]	X (X.X)	X (X.X)	X (X.X)

Programmers Note: In case the date of last investigational product exposure (i.e. last ring removal) is missing, it is imputed with the last ring insertion date.

HIV-1 = Human immunodeficiency virus type 1
Percentages are calculated out of the number of participants (per IPM 027 treatment) [a] In the virology population [b] At the applicable visit

Table 14.3.7.12
Overview of HIV-1 RNA and Genotyping Information Availability
Virology Population

	Statistic	IPM 027 Dapivirine (N=XXX)	IPM 027 Placebo (N=XXX)	IPM 032 Overall (N=XXX)
HIV-1 RNA for participants with HIV-1 seroconversion				
Participants with assessment prior to seroconversion	n (%)[a]	X (X.X)	X (X.X)	X (X.X)
No HIV-1 RNA detected in any sample	n (%)[b]	X (X.X)	X (X.X)	X (X.X)
HIV-1 RNA detected in at least 1 sample	n (%)[b]	X (X.X)	X (X.X)	X (X.X)
Participants with assessment at time of seroconversion	n (%)[a]	X (X.X)	X (X.X)	X (X.X)
Participants with assessment after seroconversion (on IP)	n (%)[a]	X (X.X)	X (X.X)	X (X.X)
Participants with assessment after seroconversion (after IP)	n (%)[a]	X (X.X)	X (X.X)	X (X.X)
Participants without assessment at time of seroconversion	n (%)[a]	X (X.X)	X (X.X)	X (X.X)
Population-based sequencing				
Participants with assessment prior to seroconversion	n (%)[a]	X (X.X)	X (X.X)	X (X.X)
Plasma HIV-1 RNA ≥2000 cop/mL	n (%)[b]	X (X.X)	X (X.X)	X (X.X)
Plasma HIV-1 RNA <2000 cop/mL, ≥200 cop/mL	n (%)[b]	X (X.X)	X (X.X)	X (X.X)
Participants with assessment at time of seroconversion	n (%)[a]	X (X.X)	X (X.X)	X (X.X)
Plasma HIV-1 RNA ≥2000 cop/mL	n (%)[b]	X (X.X)	X (X.X)	X (X.X)
Plasma HIV-1 RNA <2000 cop/mL, ≥200 cop/mL	n (%)[b]	X (X.X)	X (X.X)	X (X.X)
Participants with assessment after seroconversion (on IP)	n (%)[a]	X (X.X)	X (X.X)	X (X.X)
Plasma HIV-1 RNA ≥2000 cop/mL	n (%)[b]	X (X.X)	X (X.X)	X (X.X)
Plasma HIV-1 RNA <2000 cop/mL, ≥200 cop/mL	n (%)[b]	X (X.X)	X (X.X)	X (X.X)
Participants with assessment after seroconversion (after IP)	n (%)[a]	X (X.X)	X (X.X)	X (X.X)
Plasma HIV-1 RNA ≥2000 cop/mL	n (%)[b]	X (X.X)	X (X.X)	X (X.X)
Plasma HIV-1 RNA <2000 cop/mL, ≥200 cop/mL	n (%)[b]	X (X.X)	X (X.X)	X (X.X)

HIV-1 = Human immunodeficiency virus type 1
Percentages are calculated out of the number of participants (per IPM 027 treatment) [a] In the virology population [b] With data [c] With a population-based sequencing assessment

Table 14.3.7.12
Overview of HIV-1 RNA and Genotyping Information Availability
Virology Population

	Statistic	IPM 027 Dapivirine (N=XXX)	IPM 027 Placebo (N=XXX)	IPM 032 Overall (N=XXX)
Population-based sequencing				
Participants without assessment at time of seroconversion	n (%)[a]	X (X.X)	X (X.X)	X (X.X)
HIV-1 Subtype				
A1	n (%)[c]	X (X.X)	X (X.X)	X (X.X)
C	n (%)[c]	X (X.X)	X (X.X)	X (X.X)
Etc.	n (%)[c]	X (X.X)	X (X.X)	X (X.X)

HIV-1 = Human immunodeficiency virus type 1
Percentages are calculated out of the number of the number of participants (per IPM 027 treatment) [a] In the virology population [b] With [c] With a population-based sequencing assessment

Table 14.3.7.13.1
Summary of Mutational Patterns of Resistance-Associated Mutations at Seroconversion Timepoint
Virology Population

Subgroup: All IPM 032 participants

Resistance-Associated Mutation Combination	Statistic	IPM 027 Dapivirine (N=XXX)	IPM 027 Placebo (N=XXX)	IPM 032 Overall (N=XXX)
Number of successful assessments	n (%)[a]	X (X.X)	X (X.X)	X (X.X)
NNRTI mutations				
None	n (%)[a]	X (X.X)	X (X.X)	X (X.X)
Any	n (%)[b]	X (X.X)	X (X.X)	X (X.X)
One	n (%)[b]	X (X.X)	X (X.X)	X (X.X)
Two	n (%)[b]	X (X.X)	X (X.X)	X (X.X)
Three	n (%)[b]	X (X.X)	X (X.X)	X (X.X)
…	…	…	…	…
Average	Mean	XX.X	XX.X	XX.X
NRTI mutations				
None	n (%)[a]	X (X.X)	X (X.X)	X (X.X)
Any	n (%)[b]	X (X.X)	X (X.X)	X (X.X)
One	n (%)[b]	X (X.X)	X (X.X)	X (X.X)
Two	n (%)[b]	X (X.X)	X (X.X)	X (X.X)
Three	n (%)[b]	X (X.X)	X (X.X)	X (X.X)
…	…	…	…	…
Average	Mean	XX.X	XX.X	XX.X
Major PI mutations				
None	n (%)[a]	X (X.X)	X (X.X)	X (X.X)
Any	n (%)[b]	X (X.X)	X (X.X)	X (X.X)
One	n (%)[b]	X (X.X)	X (X.X)	X (X.X)
Two	n (%)[b]	X (X.X)	X (X.X)	X (X.X)
Three	n (%)[b]	X (X.X)	X (X.X)	X (X.X)
…	…	…	…	…
Average	Mean	XX.X	XX.X	XX.X

Programmers Notes:
Please repeat table for the following subgroups: HIV-1 RNA level: HIV-1 RNA level: ≥2000 copies/mL, *<2000 copies/mL); HIV-1 subtype (C / Other) and Schedule A, B or C*

- ***Table14.3.7.13.2*** *will be similar to Table14.3.7.13.1 but the heading and analysis will be based on Any Timepoint*

HIV-1 = Human immunodeficiency virus type 1; NNRTI = Non-nucleoside reverse transcriptase inhibitor ; NRTI = Nucleoside reverse transcriptase inhibitor; PI = Protease inhibitor
Percentages are calculated out of the number of participants (per IPM 027 treatment) [a] In the virology population [b] Reported HIV-1 drug resistance-associated mutation
Resistance-associated mutations were defined using the Stanford HIV database algorithm Version 8.4

Table 14.3.7.14.1
Summary of Mutational Patterns of Resistance-Associated Mutations at Seroconversion Timepoint
Virology Population

Subgroup: All IPM 032 participants

Mutation Score Classification	Statistic	IPM 027 Dapivirine (N=XXX)	IPM 027 Placebo (N=XXX)	IPM 032 Overall (N=XXX)
Resistance categorization score	N	XX	XX	XX
Susceptible				
Potential low-level resistant	n (%)[a]	X (X.X)	X (X.X)	X (X.X)
Low-level resistant	n (%)[a]	X (X.X)	X (X.X)	X (X.X)
Intermediate resistant	n (%)[a]	X (X.X)	X (X.X)	X (X.X)
High-level resistant	n (%)[a]	X (X.X)	X (X.X)	X (X.X)

Programmers Note:
Please repeat table for the following subgroups: HIV-1 RNA level: HIV-1 RNA level: ≥ 2000 copies/mL, < *2000 copies/mL); HIV-1 subtype (C / Other); Schedule A, B or C*

- ***Table14.3.14.2*** *will be similar to Table14.3.14.1 but the analysis and header will be based on Any Timepoint*

HIV-1 = Human immunodeficiency virus type 1; NNRTI = Non-nucleoside reverse transcriptase inhibitor; NRTI = Nucleoside reverse transcriptase inhibitor; PI = Protease inhibitor
Percentages are calculated out of the number of (per IPM 027 treatment) [a] Participants in the virology population [b] Successful assessments
Resistance-associated mutations were defined using the Stanford HIV database algorithm Version 8.4

Table 14.3.7.15
Timing Profile
Safety Population

Subgroup: All IPM 032 participants

		IPM 027			IPM 032		
	Statistic	IPM 027 Dapivirine (N=XXX)	IPM 027 Placebo (N=XXX)	IPM 027 Overall (N=XXX)	IPM 027 Dapivirine (N=XXX)	IPM 027 Placebo (N=XXX)	IPM 032 Overall (N=XXX)
Time on randomized IP	n	XXX	XXX	XXX			
	Mean	XX.X	XX.X	XX.X			
	(q1,med,q3)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)			
	SD	XX.XX	XX.XX	XX.XX			
	(Min, Max)	(XX, XX)	(XX, XX)	(XX, XX)			
Time on open-label IP	n	XXX					
	Mean	XX.X					
	(q1,med,q3)	(XX.X,XX.X,XX.X)					
	SD	XX.XX					
	(Min, Max)	(XX, XX)					
Total time on IP	n	XXX	XXX	XXX	XXX	XXX	XXX
	Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	(q1,med,q3)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)
	SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
	(Min, Max)	(XX, XX)	(XX, XX)	(XX, XX)	(XX, XX)	(XX, XX)	(XX, XX)

Programmers Note: Please repeat the table for the following subgroup: IPM 027 participants who directly enrolled in IPM 032. Note that the category 'Time off IP between IPM 027 and IPM 032' can be omitted for that subgroup.

HIV-1 = Human immunodeficiency virus type 1; IP = Investigational product

Table 14.3.7.15
Timing Profile
Safety Population

Subgroup: All IPM 032 participants

		IPM 027			IPM 032		
	Statistic	IPM 027 Dapivirine (N=XXX)	IPM 027 Placebo (N=XXX)	IPM 027 Overall (N=XXX)	IPM 027 Dapivirine (N=XXX)	IPM 027 Placebo (N=XXX)	IPM 032 Overall (N=XXX)
Time off IP between IPM 027 and IPM 032	n				XXX	XXX	XXX
	Mean				XX.X	XX.X	XX.X
	(q1,med,q3)				(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)
	SD				XX.XX	XX.XX	XX.XX
	(Min, Max)				(XX, XX)	(XX, XX)	(XX, XX)
Time to first positive HIV-1 RNA	n				XXX	XXX	XXX
	Mean				XX.X	XX.X	XX.X
	(q1,med,q3)				(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)
	SD				XX.XX	XX.XX	XX.XX
	(Min, Max)				(XX, XX)	(XX, XX)	(XX, XX)
Time to seroconversion	n				XXX	XXX	XXX
	Mean				XX.X	XX.X	XX.X
	(q1,med,q3)				(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)
	SD				XX.XX	XX.XX	XX.XX
	(Min, Max)				(XX, XX)	(XX, XX)	(XX, XX)

Programmers Note: Please repeat the table for the following subgroup: IPM 027 participants who directly enrolled in IPM 032. Note that the category 'Time off IP between IPM 027 and IPM 032' can be omitted for that subgroup.

HIV-1 = Human immunodeficiency virus type 1; IP = Investigational product

Table 14.3.7.16
Pregnancy Test Results
Safety Population

Subgroup: All IPM 032 participants

			Centre 01			…	All Centres		
Visit	Pregnancy Result	Statistic	IPM 027 Dapivirine (N=XXX)	IPM 027 Placebo (N=XXX)	IPM 032 Overall (N=XXX)	…	IPM 027 Dapivirine (N=XXX)	IPM 027 Placebo (N=XXX)	IPM 032 Overall (N=XXX)
Trial Month X / LPUV / All visits	Positive /	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)	X (X.X)
	Negative	n (%)[a]	X (X.X)	X (X.X)	X (X.X)		X (X.X)	X (X.X)	X (X.X)

[a] Percentages are calculated out of the number of participants in the safety population per centre and IPM027 treatment
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Table 14.3.8.1
Concomitant Medication
Safety Population

	Statistic	Centre 01 (N=XXX)	Centre 02 (N=XXX)	…	Centre 08 (N=XXX)	All Centres (N=XXX)
Participants with a reported concomitant medication	n (%)[a]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
ATC Level 2						
Preferred name	n (%)[b]	X (X.X)	X (X.X)	…	X (X.X)	X (X.X)
…						

Percentages are calculated out of the number of participants (by centre) [a] In the safety population [b] Reported concomitant medication
Concomitant medication is defined as any medication taken in conjunction with the investigational product (IP). This includes any medication that started after the first insertion of the IP, or started before the first insertion of the IP but ended on/after the first insertion of the IP.
Medications were coded using WHO DDE (version June 2017)
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Table 14.6.1
Participant Report, Feasibility of 3-Monthly Clinical Follow-Up Schedule
Safety Population

Visit Question of Interest Response	Statistic	Schedule A (N=XXX)	Schedule B (N=XXX)	Schedule C (N=XXX)	All Schedules (N=XXX)
Trial Month X					
Number of used/unused rings returned	m	XXX	XXX	XXX	XXX
Number of rings dispensed	M	XXX	XXX	XXX	XXX
The proportion of returned rings (used and unused) during the 3-monthly clinical follow-up schedule will also be reported	m/M	XX.X	XX.X	XX.X	XX.X
As per investigator decision are you coming to the research centre next month or in three months for your next visit?					
Next month	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
In three months	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Will you take your extra rings with you today or will you come back to the research centre each month to pick up your new ring?					
Will take them all	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Will leave them at the research centre to collect monthly	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
What are your reasons for leaving the rings at the research centre today?					
Do not want anyone to see the rings	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Do not have a private place to store unused rings	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Etc.	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
If you were not in a study, would you prefer to come to the health care clinic / provider for new rings each month, or every three months?					
Each month	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Every three months	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Don't mind	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Depends	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
If you were not in a study, would you prefer to come to the health care clinic / provider for an HIV test each month, or every three months?					
Each month	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Every three months	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Don't mind	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Depends	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)

[a] Percentages are calculated out of the number of participants in the safety population per visit schedule
Visit Schedule A = Participants attended trial month visit 1, 4, 7, 10, 13 and 16/Exit
Visit Schedule B = Participants attended trial month visit 1, 2, 5, 8, 11, 14 and 17/Exit
Visit Schedule C = Participants attended trial month visit 1, 2, 3, 6, 9, 12 and 15/Exit

Table 14.6.1
Participant Report, Feasibility of 3-Monthly Clinical Follow-Up Schedule
Safety Population

Visit Question of Interest Response	Statistic	Schedule A (N=XXX)	Schedule B (N=XXX)	Schedule C (N=XXX)	All Schedules (N=XXX)
Trial Month X					
Will you take your extra rings with you today or will you come back to the research centre each month to pick up your new ring?					
Will take them all	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Will leave them at the research centre to collect monthly	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
What are your reasons for leaving the rings at the research centre today?					
Do not want anyone to see the rings	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Do not have a private place to store unused rings	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Etc.	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
If you were not in a study, would you prefer to come to the health care clinic / provider for new rings each month, or every three months?					
Each month	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Every three months	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Don't mind	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Depends	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
If you were not in a study, would you prefer to come to the health care clinic / provider for an HIV test each month, or every three months?					
Each month	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Every three months	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Don't mind	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Depends	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)

[a] Percentages are calculated out of the number of participants in the safety population per visit schedule
Visit Schedule A = Participants attended trial month visit 1, 4, 7, 10, 13 and 16/Exit
Visit Schedule B = Participants attended trial month visit 1, 2, 5, 8, 11, 14 and 17/Exit
Visit Schedule C = Participants attended trial month visit 1, 2, 3, 6, 9, 12 and 15/Exit

Table 14.6.1
Participant Report, Feasibility of 3-Monthly Clinical Follow-Up Schedule
Safety Population

Visit Question of Interest Response	Statistic	Schedule A (N=XXX)	Schedule B (N=XXX)	Schedule C (N=XXX)	All Schedules (N=XXX)
Trial Month X					
When you were doing your three monthly visits, did you take your extra rings with you or did you come back to the research centre each month to pick up your new ring?					
Always took them	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Always left them at the research centre to collect monthly	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Sometimes took them, sometimes left them at the research centre	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
What were your reasons for leaving the rings at the research centre?					
Did not want anyone to see the rings	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Did not have a private place to store the unused rings	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Etc.	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
If you were not in a study, would you prefer to come to the health care clinic / provider for new rings each month, or every three months?					
Each month	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Every three months	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Don't mind	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Depends	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
If you were not in a study, would you prefer to come to the health care clinic / provider for an HIV test each month, or every three months?					
Each month	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Every three months	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Don't mind	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)
Depends	n (%)[a]	X (X.X)	X (X.X)	X (X.X)	X (X.X)

[a] Percentages are calculated out of the number of participants in the safety population per visit schedule
Visit Schedule A = Participants attended trial month visit 1, 4, 7, 10, 13 and 16/Exit
Visit Schedule B = Participants attended trial month visit 1, 2, 5, 8, 11, 14 and 17/Exit
Visit Schedule C = Participants attended trial month visit 1, 2, 3, 6, 9, 12 and 15/Exir

Table 14.6.2
Correlation Between Dapivirine Residual Levels (mg) and Results From Visual Inspection of Returned Vaginal Rings
Safety Population

Month Ring Used	Appearance	Statistic	White to Off-White	Slight Yellow to Yellow	Tan	Brown	Other
Trial month X / Exit visit	Used	n	XXX	XXX	XXX	XXX	XXX
		Mean	XX.X	XX.X	XX.X	XX.X	XX.X
		(q1,med,q3)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)
		SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
		(Min, Max)	(XX, XX)	(XX, XX)	(XX, XX)	(XX, XX)	(XX, XX)
	Unused	n	XXX	XXX	XXX	XXX	XXX
		Mean	XX.X	XX.X	XX.X	XX.X	XX.X
		(q1,med,q3)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)
		SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
		(Min, Max)	(XX, XX)	(XX, XX)	(XX, XX)	(XX, XX)	(XX, XX)
	Not sure	n	XXX	XXX	XXX	XXX	XXX
		Mean	XX.X	XX.X	XX.X	XX.X	XX.X
		(q1,med,q3)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)	(XX.X,XX.X,XX.X)
		SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
		(Min, Max)	(XX, XX)	(XX, XX)	(XX, XX)	(XX, XX)	(XX, XX)

Table 14.6.3
Proportion of Participants Opting for HIV Rapid Tests at the Research Centre Between Scheduled 3-Monthly Visits
Safety Population

	Statistic	IPM 032 Overall (N=XXX)
Number of participants with at least one HIV rapid test performed at an unscheduled visit	n (%)[a]	X (X.X)
Total number of participants with at least one HIV rapid test performed at any visit	n (%)[a]	X (X.X)
Proportion of participants undergoing HIV rapid tests at the research centre between scheduled 3-monthly follow up visits	p (%)	X.X (XX.X)

[a] Percentages are calculated out of the number of participants in the safety population
p = (Number of participants with at least one HIV rapid test performed at an unscheduled visit) / (total number of participants with at least one HIV rapid test performed at any visit)

Table 14.6.4
Social Harms Report
Safety Population

	Statistic	IPM 032 Overall (N=XXX)
Participants who reported any social harm	n (%)[a] m	X (X.X) X
Responses by participants		
Has a similar event happened before?		
Yes	n (%)[b] m	X (X.X) X
No	n (%)[b] m	X (X.X) X
Not reported	n (%)[b] m	X (X.X) X
Due to trial involvement?		
Yes	n (%)[b] m	X (X.X) X
No	n (%)[b] m	X (X.X) X
Not sure	n (%)[b] m	X (X.X) X
Not reported	n (%)[b] m	X (X.X) X
Is the situation resolved?		
Yes	n (%)[b] m	X (X.X) X
No	n (%)[b] m	X (X.X) X
Not sure	n (%)[b] m	X (X.X) X
Not reported	n (%)[b] m	X (X.X) X
Impact on quality of life		
Minor disturbance	n (%)[b] m	X (X.X) X
Moderate disturbance	n (%)[b] m	X (X.X) X
Major disturbance	n (%)[b] m	X (X.X) X
Responses by research centre		
Type of social harm	n (%)[b] m	X (X.X) X
Physical	n (%)[b] m	X (X.X) X
Emotional	n (%)[b] m	X (X.X) X
Financial	n (%)[b] m	X (X.X) X
Not reported	n (%)[b] m	X (X.X) X

Percentages are calculated out of the number of participants [a] In the safety population [b] Reported social harm

Table 14.6.4
Social Harms Report
Safety Population

	Statistic	IPM 032 Overall (N=XXX)
Actions taken by participant		
None	n (%)[b] m	X (X.X) X
Sought support services	n (%)[b] m	X (X.X) X
Sought counseling	n (%)[b] m	X (X.X) X
Sought medical care	n (%)[b] m	X (X.X) X
Other	n (%)[b] m	X (X.X) X
Not reported	n (%)[b] m	X (X.X) X
Actions taken by research centre		
None	n (%)[b] m	X (X.X) X
Referred to support services	n (%)[b] m	X (X.X) X
Referred for counseling	n (%)[b] m	X (X.X) X
Medical care	n (%)[b] m	X (X.X) X
Other	n (%)[b] m	X (X.X) X
Not reported	n (%)[b] m	X (X.X) X
Resolution status	n (%)[b] m	X (X.X) X
Resolved	n (%)[b] m	X (X.X) X
Unresolved	n (%)[b] m	X (X.X) X
Ongoing at participant's last visit		

Percentages are calculated out of the number of [a] Participants in the safety population [b] Social harms reported

Table 14.6.5
Participant Questionnaire – Part A (Month 1, 2, and 3)
Safety Population

Trial Month 1

	Statistic	IPM 032 Overall (N=XXX)
Investigator decision on next visit		
Next month	n (%)[a]	X (X.X)
In three months time	n (%)[a]	X (X.X)
Decision on extra rings		
Will take them all	n (%)[a]	X (X.X)
Will leave them at the research centre to collect monthly	n (%)[a]	X (X.X)
Reasons for leaving the rings at research centre today		
Do not want anyone to see the rings	n (%)[b]	X (X.X)
Do not have a private place to keep the unused rings at home	n (%)[b]	X (X.X)
Do not have a private place to keep the used rings at home	n (%)[b]	X (X.X)
Do not have an appropriate storage place to keep the rings (used/unused) at home	n (%)[b]	X (X.X)
Do not have a private place to insert the rings at home	n (%)[b]	X (X.X)
Worried I might lose the ring(s)	n (%)[b]	X (X.X)
Feel I might forget to insert a new ring if I don't come each month	n (%)[b]	X (X.X)
Like coming to the research centre for HIV tests each month	n (%)[b]	X (X.X)
Like coming to the research centre monthly for social reasons	n (%)[b]	X (X.X)
Other	n (%)[b]	X (X.X)
Main partner knowledge of the vaginal ring and study participation		
With main partner	n (%)[a]	X (X.X)
He knows about the study and the ring	n (%)[c]	X (X.X)
He only knows that I am in the study	n (%)[c]	X (X.X)
He only knows that I am wearing a ring	n (%)[c]	X (X.X)
He doesn't know about the study or the ring	n (%)[c]	X (X.X)
Don't know	n (%)[c]	X (X.X)

Programmers Notes:
- Please add in 'Chose not to answer' where applicable
- Please repeat the table for Trial Month 2 and Trial Month 3

Percentages are calculated out of number of participants [a] In the safety population [b] Left rings at the research centre [c] With main partner

Table 14.6.5
Participant Questionnaire – Part A (Month 1, 2, and 3)
Safety Population

Trial Month 1

	Statistic	IPM 032 Overall (N=XXX)
View on the information sheet		
The sheet is good as it is	n (%)[a]	X (X.X)
The sheet is hard to understand	n (%)[a]	X (X.X)
The sheet needs more information	n (%)[a]	X (X.X)
The sheet needs to be changed	n (%)[a]	X (X.X)
Did not read the instruction sheet	n (%)[a]	X (X.X)
Can't remember (the instruction sheet)		

Programmers Notes:
- Please add in 'Chose not to answer' where applicable
- Please repeat the table for Trial Month 2 and Trial Month 3

Percentages are calculated out of number of participants [a] In the safety population [b] Left rings at the research centre [c] With main partner

Table 14.6.6
Participant Questionnaire – Part B (Month 2 and 3 only)
Safety Population

Trial Month 2

	Statistic	IPM 032 Overall (N=XXX)
Ring removed/expelled since last scheduled visit?		
Yes	n (%)[a]	X (X.X)
No	n (%)[a]	X (X.X)
Reason why the ring was removed/expelled		
Took it out because it was uncomfortable/painful	n (%)[b]	X (X.X)
Took it out to clean the ring	n (%)[b]	X (X.X)
Took it out because on menses	n (%)[b]	X (X.X)
Took it out because of real/perceived side effects	n (%)[b]	X (X.X)
Took it out because partner requested it	n (%)[b]	X (X.X)
Took it out for sex	n (%)[b]	X (X.X)
Took it out so that partner did not find out about it	n (%)[b]	X (X.X)
Accidentally came out	n (%)[b]	X (X.X)
Other	n (%)[b]	X (X.X)
When the ring was removed/expelled did you clean the ring before reinsertion?		
Yes	n (%)[b]	X (X.X)
No	n (%)[b]	X (X.X)
What did you use to clean the ring when it was removed/expelled?		
Water only	n (%)[c]	X (X.X)
Soap only	n (%)[c]	X (X.X)
Water and soap	n (%)[c]	X (X.X)
Disinfectant	n (%)[c]	X (X.X)
Herbal products	n (%)[c]	X (X.X)
Traditional medicine	n (%)[c]	X (X.X)
Bubble bath	n (%)[c]	X (X.X)
Bath salts	n (%)[c]	X (X.X)
Dishwashing liquid	n (%)[c]	X (X.X)
Other	n (%)[c]	X (X.X)

Programmers Notes:
- Please add in 'Chose not to answer' where applicable
- Please repeat the table for Trial Month 3

Percentages are calculated out of the number of participants [a] In the safety population [b] Whose ring was expelled/removed since last visit [c] Cleaned ring before reinsertion

Table 14.6.6
Participant Questionnaire – Part B (Month 2 and 3 only)
Safety Population

Trial Month 2

	Statistic	IPM 032 Overall (N=XXX)
Since your last scheduled visit, was it easy or difficult to remove your ring?		
Easy to remove	n (%)[b]	X (X.X)
Difficult to remove	n (%)[b]	X (X.X)
Sometimes easy, sometimes difficult to remove	n (%)[b]	X (X.X)
Neither easy nor difficult to remove	n (%)[b]	X (X.X)
N/A, I did not remove my own ring	n (%)[b]	X (X.X)
Since your last scheduled visit, was it easy or difficult to insert a new ring?		
Easy to insert	n (%)[b]	X (X.X)
Difficult to insert	n (%)[b]	X (X.X)
Sometimes easy, sometimes difficult to insert	n (%)[b]	X (X.X)
Neither easy nor difficult to insert	n (%)[b]	X (X.X)
N/A, I did not insert my own ring	n (%)[b]	X (X.X)
Blood sample preferences		
It is fine to have a blood sample taken at every visit	n (%)[a]	X (X.X)
Prefer to have blood sample taken less often	n (%)[a]	X (X.X)
Vaginal fluid sample preferences		
It is fine to have a vaginal fluid sample taken at every visit	n (%)[a]	X (X.X)
Prefer to have vaginal fluid sample taken less often	n (%)[a]	X (X.X)
Experienced any of the following in the study		
Length of time spent at the research centre for the study visits was too long	n (%)[a]	X (X.X)
Transport to the research centre for scheduled visits was a problem	n (%)[a]	X (X.X)
I was treated well when coming to the research centre for regular visits	n (%)[a]	X (X.X)
Partner is happy about participation (if he is aware of participation)	n (%)[a]	X (X.X)
My neighbors, family, or friends know about my participation in this study	n (%)[a]	X (X.X)
My neighbors, family, or friends (as above) are happy about my participation in this study (if they are aware of participation)	n (%)[a]	X (X.X)
Other	n (%)[a]	X (X.X)

Programmers Notes:
- Please add in 'Chose not to answer' where applicable
- Please repeat the table for Trial Month 3

Percentages are calculated out of the number of participants [a] In the safety population [b] Cleaned ring before reinsertion

Table 14.6.6
Participant Questionnaire – Part B (Month 2 and 3 only)
Safety Population

Trial Month 2

	Statistic	IPM 032 Overall (N=XXX)
Preference if not in the DREAM study: Prefer to come to the health care clinic/provider for new rings each month or every three months		
Each month	n (%)[a]	X (X.X)
Every three months	n (%)[a]	X (X.X)
Don't mind	n (%)[a]	X (X.X)
Depends	n (%)[a]	X (X.X)
Preference if not in the DREAM study: Prefer to come to the health care clinic/provider for HIV tests each month or every three months		
Each month	n (%)[a]	X (X.X)
Every three months	n (%)[a]	X (X.X)
Don't mind	n (%)[a]	X (X.X)
Depends	n (%)[a]	X (X.X)

Programmers Notes:
- Please add in 'Chose not to answer' where applicable
- Please repeat the table for Trial Month 3

Percentages are calculated out of the number of participants [a] In the safety population [b] Whose ring was expelled/removed since last visit [c] Cleaned ring before reinsertion

Table 14.6.7
Participant Questionnaire – Part C (Month 1, 2, and 3)
Safety Population

Trial Month 1

	Statistic	IPM 032 Overall (N=XXX)
Currently have a main sex partner		
Yes	n (%)[a]	X (X.X)
No	n (%)[a]	X (X.X)
Currently live with main partner		
Yes	n (%)[b]	X (X.X)
No	n (%)[b]	X (X.X)
Other partners in the past three months		
0	n (%)[a]	X (X.X)
1	n (%)[a]	X (X.X)
2 or more	n (%)[a]	X (X.X)
Number of sex acts over the past month	Mean (q1,med,q3) SD (Min, Max)	XX.X (XX.X,XX.X,XX.X) XX.XX (XX, XX)
Use of a male condom over the past month		
Always	n (%)[a]	X (X.X)
Sometimes	n (%)[a]	X (X.X)
Often	n (%)[a]	X (X.X)
Never	n (%)[a]	X (X.X)

Programmers Notes:
- Please add in 'Chose not to answer' where applicable
- Please repeat the table for Trial Month 2 and Trial Month 3

Percentages are calculated out of the number of participants [a] In the safety population [b] Has main partner [c] Used a condom [d] Had a menstrual bleeding/spotting in past three months
[e] Inserted fingers into vagina

Table 14.6.7
Participant Questionnaire – Part C (Month 1, 2, and 3)
Safety Population

Trial Month 1

	Statistic	IPM 032 Overall (N=XXX)
Use of a female condom over the past month		
Always	n (%)[a]	X (X.X)
Sometimes	n (%)[a]	X (X.X)
Often	n (%)[a]	X (X.X)
Never	n (%)[a]	X (X.X)
Used a condom during last round of vaginal sex		
No	n (%)[a]	X (X.X)
Yes	n (%)[a]	X (X.X)
Male condom		
Female condom		
Had anal sex during the last year		
No	n (%)[a]	X (X.X)
Yes	n (%)[a]	X (X.X)
Used a condom	n (%)[a]	X (X.X)
Did not use a condom	n (%)[a]	X (X.X)
Level of being worried about getting infected with HIV in the next year		
Very worried	n (%)[a]	X (X.X)
A little worried	n (%)[a]	X (X.X)
Not worried at all	n (%)[a]	X (X.X)
Had menstrual bleeding/spotting in the past 3 months		
Yes	n (%)[a]	X (X.X)
No	n (%)[a]	X (X.X)

Programmers Notes:
- Please add in 'Chose not to answer' where applicable
- Please repeat the table for Trial Month 2 and Trial Month 3

Percentages are calculated out of the number of participants [a] In the safety population [b] Has main partner [c] Used a condom [d] Had a menstrual bleeding/spotting in past three months
[e] Inserted fingers into vagina

Table 14.6.7
Participant Questionnaire – Part C (Month 1, 2, and 3)
Safety Population

Trial Month 1

	Statistic	IPM 032 Overall (N=XXX)
Products used in the past 3 months to control menstrual bleeding/spotting		
Tissue, toilet paper, paper, cloth or cotton wool put inside the vagina	n (%)[d]	X (X.X)
Tissue, toilet paper, paper, cloth or cotton wool put inside the underwear/clothing	n (%)[d]	X (X.X)
Tampon	n (%)[d]	X (X.X)
Sanitary pad	n (%)[d]	X (X.X)
Menstrual cup	n (%)[d]	X (X.X)
Water without soap (inside the vagina)	n (%)[d]	X (X.X)
Water with soap (inside the vagina)	n (%)[d]	X (X.X)
Nothing was used	n (%)[d]	X (X.X)
Other	n (%)[d]	X (X.X)
Inserted fingers into vagina since last schedule visit		
Yes	n (%)[a]	X (X.X)
No	n (%)[a]	X (X.X)
Reason for inserting fingers into vagina	n (%)[d]	X (X.X)
Check the position of the ring	n (%)[d]	X (X.X)
Insert/remove the ring	n (%)[d]	X (X.X)
Cleaning	n (%)[d]	X (X.X)
Sexual pleasure	n (%)[d]	X (X.X)
Insert a product for the management of menses	n (%)[d]	X (X.X)
Other	n (%)[d]	X (X.X)

Programmers Notes:
- Please add in 'Chose not to answer' where applicable
- Please repeat the table for Trial Month 2 and Trial Month 3

Percentages are calculated out of the number of participants [a] In the safety population [b] Has main partner [c] Used a condom [d] Had a menstrual bleeding/spotting in past three months [e] Inserted fingers into vagina

Table 14.6.8
Participant Questionnaire – 3 Month Follow-Up
Safety Population

Trial Month X

	Statistic	IPM 032 Overall (N=XXX)
Decision to take the rings today or leave them at the research centre to collect monthly	n (%)[a]	X (X.X)
Will take them all	n (%)[a]	X (X.X)
Will leave them at the research centre to collect monthly		
Reasons for leaving the rings at research centre today		
Do not want anyone to see the rings	n (%)[b]	X (X.X)
Do not have a private place to keep the unused rings at home	n (%)[b]	X (X.X)
Do not have a private place to keep the used rings at home	n (%)[b]	X (X.X)
Do not have an appropriate storage place to keep the rings (used/unused) at home	n (%)[b]	X (X.X)
Do not have a private place to insert the rings at home	n (%)[b]	X (X.X)
Worried I might lose the ring(s)	n (%)[b]	X (X.X)
Feel I might forget to insert a new ring if I don't come each month	n (%)[b]	X (X.X)
Like coming to the research centre for HIV tests each month	n (%)[b]	X (X.X)
Like coming to the research centre monthly for social reasons	n (%)[b]	X (X.X)
Other	n (%)[b]	X (X.X)
Additional HIV test when returned to the research centre to collect the ring		
Yes	n (%)[b]	X (X.X)
No	n (%)[b]	X (X.X)
N/A	n (%)[b]	X (X.X)
Main partner knowledge of the vaginal ring and study participation		
He knows about the study and the ring	n (%)[c]	X (X.X)
He only knows that I am in the study	n (%)[c]	X (X.X)
He only knows that I am wearing a ring	n (%)[c]	X (X.X)
He doesn't know about the study or the ring	n (%)[c]	X (X.X)
Don't know	n (%)[c]	X (X.X)

Programmers Notes:
- Please add in 'Chose not to answer' where applicable
- Please repeat the table for all available Trial Months

Percentages are calculated out of the number of participants [a] In the safety population [b] Left rings at the research centre [c] With main partner [d] Took rings
[e] Used a condom [f] Had anal sex since last visit [g] Had a menstrual bleeding/spotting since last visit [h] Had ring expelled/removed since last visit
[i] Cleaned ring before reinsertion [j] Inserted fingers into vagina

Table 14.6.8
Participant Questionnaire – 3 Month Follow-Up
Safety Population

Trial Month X

	Statistic	IPM 032 Overall (N=XXX)
View on the information sheet		
The sheet is good as it is	n (%)[a]	X (X.X)
The sheet is hard to understand	n (%)[a]	X (X.X)
The sheet needs more information	n (%)[a]	X (X.X)
The sheet needs to be changed	n (%)[a]	X (X.X)
Did not read the instruction sheet	n (%)[a]	X (X.X)
Can't remember (the instruction sheet)	n (%)[a]	X (X.X)
Since your last scheduled visit, was it easy or difficult to remove your ring?		
Easy to remove	n (%)[h]	X (X.X)
Difficult to remove	n (%)[h]	X (X.X)
Sometimes easy, sometimes difficult to remove	n (%)[h]	X (X.X)
Neither easy nor difficult to remove	n (%)[h]	X (X.X)
N/A, I did not remove my own ring	n (%)[h]	X (X.X)
Since your last scheduled visit, was it easy or difficult to insert a new ring?		
Easy to insert	n (%)[h]	X (X.X)
Difficult to insert	n (%)[h]	X (X.X)
Sometimes easy, sometimes difficult to insert	n (%)[h]	X (X.X)
Neither easy nor difficult to insert	n (%)[h]	X (X.X)
N/A, I did not insert my own ring	n (%)[h]	X (X.X)

Programmers Notes:
- Please add in 'Chose not to answer' where applicable
- Please repeat the table for all available Trial Months

Percentages are calculated out of the number of participants [a] In the safety population [b] Left rings at the research centre [c] With main partner [d] Took rings
[e] Used a condom [f] Had anal sex since last visit [g] Had a menstrual bleeding/spotting since last visit [h] Had ring expelled/removed since last visit
[i] Cleaned ring before reinsertion [j] Inserted fingers into vagina

Table 14.6.8
Participant Questionnaire – 3 Month Follow-Up
Safety Population

Trial Month X

	Statistic	IPM 032 Overall (N=XXX)
Experience with the bag given to put the used rings in		
The bag was easy to open and close	n (%)[a]	X (X.X)
The bag was hard to open and close	n (%)[a]	X (X.X)
The bag was sometimes lost	n (%)[a]	X (X.X)
The bag was sometimes used for something else	n (%)[a]	X (X.X)
The bag was fine	n (%)[a]	X (X.X)
I did not like having to keep the empty bag(s)	n (%)[a]	X (X.X)
I did not like having the used ring(s) in the house	n (%)[a]	X (X.X)
I did not like carrying the used ring(s) to the research centre	n (%)[a]	X (X.X)
Someone found the ring bag(s) (with or without rings),	n (%)[a]	X (X.X)
I did not like the look of the bag	n (%)[a]	X (X.X)
It was difficult to bring the bags back to the clinic	n (%)[a]	X (X.X)
Other	n (%)[a]	X (X.X)
Not applicable, I did not use the bags or return a ring since the last visit	n (%)[a]	X (X.X)
Place of storage of the unused ring(s) before insertion	n (%)[d]	X (X.X)
In bag/handbag	n (%)[d]	X (X.X)
In a shared cupboard/drawer in the house	n (%)[d]	X (X.X)
In a personal cupboard/drawer in my room/in the house	n (%)[d]	X (X.X)
In a locked place that no-one else could access	n (%)[d]	X (X.X)
At someone else's house	n (%)[d]	X (X.X)
Other	n (%)[d]	X (X.X)
Not applicable, I did not have any extra unused rings since the last visit	n (%)[d]	X (X.X)

Programmers Notes:
- Please add in 'Chose not to answer' where applicable
- Please repeat the table for all available Trial Months

Percentages are calculated out of the number of participants [a] In the safety population [b] Left rings at the research centre [c] With main partner [d] Took rings
[e] Used a condom [f] Had anal sex since last visit [g] Had a menstrual bleeding/spotting since last visit [h] Had ring expelled/removed since last visit
[i] Cleaned ring before reinsertion [j] Inserted fingers into vagina

Table 14.6.8
Participant Questionnaire – 3 Month Follow-Up
Safety Population

Trial Month X

	Statistic	IPM 032 Overall (N=XXX)
Experience when storing the unused ring(s)		
There were no problems storing the unused ring(s)	n (%)[d]	X (X.X)
I was concerned that someone might find the unused ring	n (%)[d]	X (X.X)
I sometimes forgot where I had stored the unused ring(s)/lost the unused ring(s)	n (%)[d]	X (X.X)
The ring(s) accidentally got thrown away	n (%)[d]	X (X.X)
I did not like storing the unused rings	n (%)[d]	X (X.X)
Someone found the ring(s) and that was problematic	n (%)[d]	X (X.X)
Someone found the ring(s) but it was not problematic	n (%)[d]	X (X.X)
Other	n (%)[d]	X (X.X)
Not applicable, I did not have any extra unused rings since the last visit	n (%)[d]	X (X.X)
Place of storage of the used ring(s) after removal		
I returned the used ring(s) to the research centre straight away	n (%)[h]	X (X.X)
In a bag/handbag	n (%)[h]	X (X.X)
In a shared cupboard/drawer in the house	n (%)[h]	X (X.X)
In a personal cupboard/drawer in my room/in the house	n (%)[h]	X (X.X)
In a locked place that no-one else could access	n (%)[h]	X (X.X)
At someone else's house	n (%)[h]	X (X.X)
Other	n (%)[h]	X (X.X)
Not applicable, I did not store any extra used rings since the last visit	n (%)[h]	X (X.X)
Experience when storing the used ring		
There were no problems storing the used ring	n (%)[h]	X (X.X)
I was concerned that someone might find the used ring	n (%)[h]	X (X.X)
I sometimes forgot where I had stored the used ring(s)/lost the used ring(s)	n (%)[h]	X (X.X)
The ring accidentally got thrown away	n (%)[h]	X (X.X)
I did not like storing the used rings	n (%)[h]	X (X.X)
Someone found the ring(s) and that was problematic	n (%)[h]	X (X.X)
Someone found the ring(s) but it was not problematic	n (%)[h]	X (X.X)
Other	n (%)[h]	X (X.X)
Not applicable, I did not store any extra used rings since the last visit	n (%)[h]	X (X.X)
Programmers Notes:		
- Please add in 'Chose not to answer' where applicable		
- Please repeat the table for all available Trial Months		

Percentages are calculated out of the number of participants [a] In the safety population [b] Left rings at the research centre [c] With main partner [d] Took rings
[e] Used a condom [f] Had anal sex since last visit [g] Had a menstrual bleeding/spotting since last visit [h] Had ring expelled/removed since last visit
[i] Cleaned ring before reinsertion [j] Inserted fingers into vagina

Table 14.6.8
Participant Questionnaire – 3 Month Follow-Up
Safety Population

Trial Month X

	Statistic	IPM 032 Overall (N=XXX)
Blood sample preferences		
It is fine to have a blood sample taken at every visit	n (%)[a]	X (X.X)
Prefer to have blood sample taken less often	n (%)[a]	X (X.X)
Vaginal fluid sample preferences		
It is fine to have a vaginal fluid sample taken at every visit	n (%)[a]	X (X.X)
Prefer to have vaginal fluid sample taken less often	n (%)[a]	X (X.X)
Experienced any of the following in the study		
Length of time spent at the research centre for the study visits was too long	n (%)[a]	X (X.X)
Length of time spent at the research centre to pick up rings was too long	n (%)[a]	X (X.X)
Transport to the research centre for scheduled visits was a problem	n (%)[a]	X (X.X)
I was treated well when coming to the research centre for regular visits	n (%)[a]	X (X.X)
I was treated well when I came to the research centre to pick up rings	n (%)[a]	X (X.X)
Transport to pick up rings was a problem	n (%)[a]	X (X.X)
Partner is happy about participation (if he is aware of participation)	n (%)[a]	X (X.X)
My neighbors, family, or friends know about my participation in this study	n (%)[a]	X (X.X)
My neighbors, family, or friends (as above) are happy about my participation in this study (if they are aware of participation)	n (%)[a]	X (X.X)
Other	n (%)[a]	X (X.X)
Preference if not in the DREAM study: Prefer to come to the health care clinic/provider for new rings each month or every three months		
Each month	n (%)[a]	X (X.X)
Every three months	n (%)[a]	X (X.X)
Don’t mind	n (%)[a]	X (X.X)
Depends	n (%)[a]	X (X.X)

Programmers Notes:
- Please add in ‘Chose not to answer’ where applicable
- Please repeat the table for all available Trial Months

Percentages are calculated out of the number of participants [a] In the safety population [b] Who left their rings at the research centre [c] With main partner [d] Who took their rings
[e] Who used a condom [f] Who had anal sex since last visit [g] Who had a menstrual bleeding/spotting since last visit [h] Who had ring expelled/removed since last visit
[i] Who cleaned ring before reinsertion [j] Who inserted fingers into their vaginas

Table 14.6.8
Participant Questionnaire – 3 Month Follow-Up
Safety Population

Trial Month X

	Statistic	IPM 032 Overall (N=XXX)
Preference if not in the DREAM study: Prefer to come to the health care clinic/provider for HIV tests each month or every three months		
Each month	n (%)[a]	X (X.X)
Every three months	n (%)[a]	X (X.X)
Don't mind	n (%)[a]	X (X.X)
Depends	n (%)[a]	X (X.X)
Currently have a main sex partner		
Yes	n (%)[a]	X (X.X)
No	n (%)[a]	X (X.X)
Currently live with main partner		
Yes	n (%)[b]	X (X.X)
No	n (%)[b]	X (X.X)
Other partners since last scheduled visit		
0 - 1	n (%)[a]	X (X.X)
>= 2	n (%)[a]	X (X.X)
Number of sex acts over the past month	Mean (q1,med,q3) SD (Min, Max)	XX.X (XX.X,XX.X,XX.X) XX.XX (XX, XX)
Use of a male condom over the past month		
Always	n (%)[a]	X (X.X)
Sometimes	n (%)[a]	X (X.X)
Often	n (%)[a]	X (X.X)
Never	n (%)[a]	X (X.X)

Programmers Notes:
- Please add in 'Chose not to answer' where applicable
- Please repeat the table for all available Trial Months

Percentages are calculated out of the number of participants [a] In the safety population [b] Who left their rings at the research centre [c] With main partner [d] Who took their rings
[e] Who used a condom [f] Who had anal sex since last visit [g] Who had a menstrual bleeding/spotting since last visit [h] Who had ring expelled/removed since last visit
[i] Who cleaned ring before reinsertion [j] Who inserted fingers into their vaginas

Table 14.6.8
Participant Questionnaire – 3 Month Follow-Up
Safety Population

Trial Month X

	Statistic	IPM 032 Overall (N=XXX)
Use of a female condom over the past month		
Always	n (%)[a]	X (X.X)
Sometimes	n (%)[a]	X (X.X)
Often	n (%)[a]	X (X.X)
Never	n (%)[a]	X (X.X)
Used a condom during last round of vaginal sex		
No	n (%)[a]	X (X.X)
Yes	n (%)[a]	X (X.X)
Male condom	n (%)[e]	X (X.X)
Female condom	n (%)[e]	X (X.X)
Had anal sex since last scheduled visit		
No	n (%)[a]	X (X.X)
Yes	n (%)[a]	X (X.X)
Used a condom	n (%)[f]	X (X.X)
Did not use a condom	n (%)[f]	X (X.X)
Level of being worried about getting infected with HIV in the next year		
Very worried	n (%)[a]	X (X.X)
A little worried	n (%)[a]	X (X.X)
Not worried at all	n (%)[a]	X (X.X)
Had menstrual bleeding/spotting since last scheduled visit		
Yes	n (%)[a]	X (X.X)
No	n (%)[a]	X (X.X)

Programmers Notes:
- Please add in 'Chose not to answer' where applicable
- Please repeat the table for all available Trial Months

Percentages are calculated out of the number of participants [a] In the safety population [b] Left rings at the research centre [c] With main partner [d] Took rings
[e] Used a condom [f] Had anal sex since last visit [g] Had a menstrual bleeding/spotting since last visit [h] Had ring expelled/removed since last visit
[i] Cleaned ring before reinsertion [j] Inserted fingers into vagina

Table 14.6.8
Participant Questionnaire – 3 Month Follow-Up
Safety Population

Trial Month X

	Statistic	IPM 032 Overall (N=XXX)
Products used in the past 3 months to control menstrual bleeding/spotting		
Tissue, toilet paper, paper, cloth or cotton wool put inside the vagina	n (%)[g]	X (X.X)
Tissue, toilet paper, paper, cloth or cotton wool put inside the underwear/clothing	n (%)[g]	X (X.X)
Tampon	n (%)[g]	X (X.X)
Sanitary pad	n (%)[g]	X (X.X)
Menstrual cup	n (%)[g]	X (X.X)
Water without soap (inside the vagina)	n (%)[g]	X (X.X)
Water with soap (inside the vagina)	n (%)[g]	X (X.X)
Nothing was used	n (%)[g]	X (X.X)
Other	n (%)[g]	X (X.X)
Ring removed/expelled since last scheduled visit?		
Yes	n (%)[a]	X (X.X)
No	n (%)[a]	X (X.X)
Reason why the ring was removed/expelled		
Took it out because it was uncomfortable/painful	n (%)[h]	X (X.X)
Took it out to clean the ring	n (%)[h]	X (X.X)
Took it out because on menses	n (%)[h]	X (X.X)
Took it out because of real/perceived side effects	n (%)[h]	X (X.X)
Took it out because partner requested it	n (%)[h]	X (X.X)
Took it out for sex	n (%)[h]	X (X.X)
Took it out so that partner did not find out about it	n (%)[h]	X (X.X)
Accidentally came out	n (%)[h]	X (X.X)
Other	n (%)[h]	X (X.X)
When the ring was removed/expelled did you clean the ring before reinsertion?		
Yes	n (%)[h]	X (X.X)
No	n (%)[h]	X (X.X)

Programmers Notes:
- Please add in 'Chose not to answer' where applicable
- Please repeat the table for all available Trial Months

Percentages are calculated out of the number of participants [a] In the safety population [b] Left rings at the research centre [c] With main partner [d] Took rings
[e] Used a condom [f] Had anal sex since last visit [g] Had a menstrual bleeding/spotting since last visit [h] Had ring expelled/removed since last visit
[i] Cleaned ring before reinsertion [j] Inserted fingers into vagina

Table 14.6.8
Participant Questionnaire – 3 Month Follow-Up
Safety Population

Trial Month X

	Statistic	IPM 032 Overall (N=XXX)
What did you use to clean the ring when it was removed/expelled?		
Water only	n (%)[i]	X (X.X)
Soap only	n (%)[i]	X (X.X)
Water and soap	n (%)[i]	X (X.X)
Disinfectant		
Water and soap	n (%)[i]	X (X.X)
Disinfectant	n (%)[i]	X (X.X)
Herbal products	n (%)[i]	X (X.X)
Traditional medicine	n (%)[i]	X (X.X)
Bubble bath	n (%)[i]	X (X.X)
Bath salts	n (%)[i]	X (X.X)
Dishwashing liquid	n (%)[i]	X (X.X)
Other	n (%)[i]	X (X.X)
Inserted fingers into vagina since last schedule visit		
Yes	n (%)[a]	X (X.X)
No	n (%)[a]	X (X.X)
Reason for inserting fingers into vagina	n (%)[j]	X (X.X)
Check the position of the ring	n (%)[j]	X (X.X)
Insert/remove the ring	n (%)[j]	X (X.X)
Cleaning	n (%)[j]	X (X.X)
Sexual pleasure	n (%)[j]	X (X.X)
Insert a product for the management of menses	n (%)[j]	X (X.X)
Other	n (%)[j]	X (X.X)

Programmers Notes:
- Please add in 'Chose not to answer' where applicable
- Please repeat the table for all available Trial Months

Percentages are calculated out of the number of participants [a] In the safety population [b] Left rings at the research centre [c] With main partner [d] Took rings
[e] Used a condom [f] Had anal sex since last visit [g] Had a menstrual bleeding/spotting since last visit [h] Had ring expelled/removed since last visit
[i] Cleaned ring before reinsertion [j] Inserted fingers into vagina

Table 14.6.9
Participant Questionnaire – Last Product Use Visit
Safety Population

Trial Month X

	Statistic	IPM 032 Overall (N=XXX)
Decision on extra rings, during three monthly visits		
Always took them	n (%)[a]	X (X.X)
Always left them at the research centre to collect monthly	n (%)[a]	X (X.X)
Sometimes took them, sometimes left them at the research centre	n (%)[a]	X (X.X)
Initially leave them at the research centre then later start taking them	n (%)[b]	X (X.X)
Initially take them, then start leaving them at the research centre	n (%)[b]	X (X.X)
It varied	n (%)[b]	X (X.X)
Reasons for leaving the rings at research centre		
Did not want anyone to see the rings	n (%)[c]	X (X.X)
Did not have a private place to keep the unused rings at home	n (%)[c]	X (X.X)
Did not have a private place to keep the used rings at home	n (%)[c]	X (X.X)
Did not have an appropriate storage place to keep the rings (used/unused) at home	n (%)[c]	X (X.X)
Did not have a private place to insert the rings at home	n (%)[c]	X (X.X)
Worried I might lose the ring(s)	n (%)[c]	X (X.X)
Felt I might forget to insert a new ring if I don't come each month	n (%)[c]	X (X.X)
Liked coming to the research centre for HIV tests each month	n (%)[c]	X (X.X)
Liked coming to the research centre monthly for social reasons	n (%)[c]	X (X.X)
Other	n (%)[c]	X (X.X)
Main partner knowledge of the vaginal ring and study participation		
He knows about the study and the ring	n (%)[d]	X (X.X)
He only knows that I am in a study	n (%)[d]	X (X.X)
He only knows that I am wearing a ring	n (%)[d]	X (X.X)
He doesn't know about the study or the ring	n (%)[d]	X (X.X)
Don't know	n (%)[d]	X (X.X)

Programmers Note: Please add in 'Chose not to answer' where applicable

Percentages are calculated out of the number of participants [a] In the safety population [b] Sometimes took/sometimes left the rings [c] Left rings at the research centre
[d] With main partner [e] Took rings [f] Used a condom [g] Had anal sex since last visit [h] Had a menstrual bleeding/spotting since last visit
[i] Had ring expelled/removed since last visit [j] Cleaned ring before reinsertion [k] Inserted fingers into vagina

Table 14.6.9
Participant Questionnaire – Last Product Use Visit
Safety Population

Trial Month X

	Statistic	IPM 032 Overall (N=XXX)
View on the information sheet		
The sheet is good as it is	n (%)[a]	X (X.X)
The sheet is hard to understand	n (%)[a]	X (X.X)
The sheet needs more information	n (%)[a]	X (X.X)
The sheet needs to be changed	n (%)[a]	X (X.X)
Did not read the instruction sheet	n (%)[a]	X (X.X)
Can't remember (the instruction sheet)	n (%)[a]	X (X.X)
Over the duration of the study, was it easy or difficult to remove your ring?		
Easy to remove	n (%)[a]	X (X.X)
Difficult to remove	n (%)[a]	X (X.X)
Sometimes easy, sometimes difficult to remove	n (%)[a]	X (X.X)
Got easier to remove over time with practice	n (%)[a]	X (X.X)
Neither easy nor difficult to remove	n (%)[a]	X (X.X)
Over the duration of the study, was it easy or difficult to insert a new ring?		
Easy to insert	n (%)[a]	X (X.X)
Difficult to insert	n (%)[a]	X (X.X)
Sometimes easy, sometimes difficult to insert	n (%)[a]	X (X.X)
Got easier to insert over time with practice	n (%)[a]	X (X.X)
Neither easy nor difficult to insert	n (%)[a]	X (X.X)

Programmers Note: Please add in 'Chose not to answer' where applicable

Percentages are calculated out of the number of participants [a] In the safety population [b] Sometimes took/sometimes left the rings [c] Left rings at the research centre
[d] With main partner [e] Took rings [f] Used a condom [g] Had anal sex since last visit [h] Had a menstrual bleeding/spotting since last visit
[i] Had ring expelled/removed since last visit [j] Cleaned ring before reinsertion [k] Inserted fingers into vagina

Table 14.6.9
Participant Questionnaire – Last Product Use Visit
Safety Population

Trial Month X

	Statistic	IPM 032 Overall (N=XXX)
Experience with the bag given to put the used rings in		
The bag was easy to open and close	n (%)[a]	X (X.X)
The bag was hard to open and close	n (%)[a]	X (X.X)
The bag was sometimes lost	n (%)[a]	X (X.X)
The bag was sometimes used for something else	n (%)[a]	X (X.X)
The bag was fine	n (%)[a]	X (X.X)
I did not like having to keep the empty bag(s)	n (%)[a]	X (X.X)
I did not like having the used ring(s) in the house	n (%)[a]	X (X.X)
I did not like carrying the used ring(s) to the research centre	n (%)[a]	X (X.X)
Someone found the ring bag(s) (with or without rings),	n (%)[a]	X (X.X)
I did not like the look of the bag	n (%)[a]	X (X.X)
It was difficult to bring the bags back to the clinic	n (%)[a]	X (X.X)
Other	n (%)[a]	X (X.X)
Not applicable, I did not use the bags or return a ring since the last visit	n (%)[a]	X (X.X)
Place of storage of the unused ring(s) before insertion	n (%)[e]	X (X.X)
In bag/handbag	n (%)[e]	X (X.X)
In a shared cupboard/drawer in the house	n (%)[e]	X (X.X)
In a personal cupboard/drawer in my room/in the house	n (%)[e]	X (X.X)
In a locked place that no-one else could access	n (%)[e]	X (X.X)
At someone else's house	n (%)[e]	X (X.X)
Other	n (%)[e]	X (X.X)
Not applicable, I did not ever take any extra unused rings home	n (%)[e]	X (X.X)

Programmers Note: Please add in 'Chose not to answer' where applicable

Percentages are calculated out of the number of participants [a] In the safety population [b] Sometimes took/sometimes left the rings [c] Left rings at the research centre
[d] With main partner [e] Took rings [f] Used a condom [g] Had anal sex since last visit [h] Had a menstrual bleeding/spotting since last visit
[i] Had ring expelled/removed since last visit [j] Cleaned ring before reinsertion [k] Inserted fingers into vagina

Table 14.6.9
Participant Questionnaire – Last Product Use Visit
Safety Population

Trial Month X

	Statistic	IPM 032 Overall (N=XXX)
Experience when storing the unused ring(s)		
There were no problems storing the unused ring(s)	n (%)[e]	X (X.X)
I was concerned that someone might find the unused ring	n (%)[e]	X (X.X)
I sometimes forgot where I had stored the unused ring(s)/lost the unused ring(s)	n (%)[e]	X (X.X)
The ring(s) accidentally got thrown away	n (%)[e]	X (X.X)
I did not like storing the unused rings	n (%)[e]	X (X.X)
Someone found the ring(s) and that was problematic	n (%)[e]	X (X.X)
Someone found the ring(s) but it was not problematic	n (%)[e]	X (X.X)
Other	n (%)[e]	X (X.X)
Not applicable, I did not ever take any extra unused rings home	n (%)[e]	X (X.X)
Place of storage of the used ring(s) after removal		
I returned the used ring(s) to the research centre straight away	n (%)[a]	X (X.X)
In a bag/handbag	n (%)[a]	X (X.X)
In a shared cupboard/drawer in the house	n (%)[a]	X (X.X)
In a personal cupboard/drawer in my room/in the house	n (%)[a]	X (X.X)
In a locked place that no-one else could access	n (%)[a]	X (X.X)
At someone else's house	n (%)[a]	X (X.X)
Other	n (%)[a]	X (X.X)
Not applicable, I did not store any extra used rings since the last visit	n (%)[a]	X (X.X)
Experience when storing the used ring		
There were no problems storing the used ring	n (%)[a]	X (X.X)
I was concerned that someone might find the used ring	n (%)[a]	X (X.X)
I sometimes forgot where I had stored the used ring(s)/lost the used ring(s)	n (%)[a]	X (X.X)
The ring accidentally got thrown away	n (%)[a]	X (X.X)
I did not like storing the used rings	n (%)[a]	X (X.X)
Someone found the ring(s) and that was problematic	n (%)[a]	X (X.X)
Someone found the ring(s) but it was not problematic	n (%)[a]	X (X.X)
Other	n (%)[a]	X (X.X)
Not applicable, I did not ever have/store any extra used rings at home	n (%)[a]	X (X.X)

Programmers Note: Please add in 'Chose not to answer' where applicable

Percentages are calculated out of the number of participants [a] In the safety population [b] Sometimes took/sometimes left the rings [c] Left rings at the research centre
[d] With main partner [e] Took rings [f] Used a condom [g] Had anal sex since last visit [h] Had a menstrual bleeding/spotting since last visit
[i] Had ring expelled/removed since last visit [j] Cleaned ring before reinsertion [k] Inserted fingers into vagina

Table 14.6.9
Participant Questionnaire – Last Product Use Visit
Safety Population

Trial Month X

	Statistic	IPM 032 Overall (N=XXX)
Blood sample preferences		
It is fine to have a blood sample taken at every visit	n (%)[a]	X (X.X)
Prefer to have blood sample taken less often	n (%)[a]	X (X.X)
Vaginal fluid sample preferences		
It is fine to have a vaginal fluid sample taken at every visit	n (%)[a]	X (X.X)
Prefer to have vaginal fluid sample taken less often	n (%)[a]	X (X.X)
Experienced any of the following in the study		
In general, the length of time spent at the research centre for the study visits was too long	n (%)[a]	X (X.X)
In general, the length of time spent at the research centre to pick up rings was too long	n (%)[a]	X (X.X)
Transport to the research centre for scheduled visits was a problem	n (%)[a]	X (X.X)
I was treated well when coming to the research centre for regular visits	n (%)[a]	X (X.X)
I was treated well when I came to the research centre to pick up rings	n (%)[a]	X (X.X)
Transport to pick up rings was a problem	n (%)[a]	X (X.X)
Partner is happy about participation (if he is aware of participation)	n (%)[a]	X (X.X)
My neighbors, family, or friends know about my participation in this study	n (%)[a]	X (X.X)
My neighbors, family, or friends (as above) are happy about my participation in this study (if they are aware of participation)	n (%)[a]	X (X.X)
Other	n (%)[a]	X (X.X)
Participant experience of study		
Participant really didn't like participating in this study	n (%)[a]	X (X.X)
Participating in this study was alright/okay	n (%)[a]	X (X.X)
Participant really liked participating in this study	n (%)[a]	X (X.X)
Other	n (%)[a]	X (X.X)

Programmers Note: Please add in 'Chose not to answer' where applicable

Percentages are calculated out of the number of participants [a] In the safety population [b] Sometimes took/sometimes left the rings [c] Left rings at the research centre
[d] With main partner [e] Took rings [f] Used a condom [g] Had anal sex since last visit [h] Had a menstrual bleeding/spotting since last visit
[i] Had ring expelled/removed since last visit [j] Cleaned ring before reinsertion [k] Inserted fingers into vagina

Table 14.6.9
Participant Questionnaire – Last Product Use Visit
Safety Population

Trial Month X

	Statistic	IPM 032 Overall (N=XXX)
Preference if not in the DREAM study: Prefer to come to the health care clinic/provider for new rings each month or every three months		
Each month	n (%)[a]	X (X.X)
Every three months	n (%)[a]	X (X.X)
Don't mind	n (%)[a]	X (X.X)
Depends	n (%)[a]	X (X.X)
Preference if not in the DREAM study: Prefer to come to the health care clinic/provider for HIV tests each month or every three months		
Each month	n (%)[a]	X (X.X)
Every three months	n (%)[a]	X (X.X)
Don't mind	n (%)[a]	X (X.X)
Depends	n (%)[a]	X (X.X)
Currently have a main sex partner		
Yes	n (%)[a]	X (X.X)
No	n (%)[a]	X (X.X)
Currently live with main partner		
Yes	n (%)[d]	X (X.X)
No	n (%)[d]	X (X.X)
Other partners since last scheduled visit		
0 – 1	n (%)[a]	X (X.X)
>= 2	n (%)[a]	X (X.X)
Number of sex acts over the past month	Mean (q1,med,q3) SD (Min, Max)	XX.X (XX.X,XX.X,XX.X) XX.XX (XX, XX)

Programmers Note: Please add in 'Chose not to answer' where applicable

Percentages are calculated out of the number of participants [a] In the safety population [b] Sometimes took/sometimes left the rings [c] Left rings at the research centre
[d] With main partner [e] Took rings [f] Used a condom [g] Had anal sex since last visit [h] Had a menstrual bleeding/spotting since last visit
[i] Had ring expelled/removed since last visit [j] Cleaned ring before reinsertion [k] Inserted fingers into vagina

Table 14.6.9
Participant Questionnaire – Last Product Use Visit
Safety Population

Trial Month X

	Statistic	IPM 032 Overall (N=XXX)
Use of a male condom over the past month		
Always	n (%)[a]	X (X.X)
Sometimes	n (%)[a]	X (X.X)
Often	n (%)[a]	X (X.X)
Never	n (%)[a]	X (X.X)
Use of a female condom over the past month		
Always	n (%)[a]	X (X.X)
Sometimes	n (%)[a]	X (X.X)
Often	n (%)[a]	X (X.X)
Never	n (%)[a]	X (X.X)
Used a condom during last round of vaginal sex		
No	n (%)[a]	X (X.X)
Yes	n (%)[a]	X (X.X)
Male condom	n (%)[f]	X (X.X)
Female condom	n (%)[f]	X (X.X)
Had anal sex since last scheduled visit		
No	n (%)[a]	X (X.X)
Yes	n (%)[a]	X (X.X)
Used a condom	n (%)[g]	X (X.X)
Did not use a condom	n (%)[g]	X (X.X)
Had menstrual bleeding/spotting since last scheduled visit		
Yes	n (%)[a]	X (X.X)
No	n (%)[a]	X (X.X)

Programmers Note: Please add in 'Chose not to answer' where applicable

Percentages are calculated out of the number of participants [a] In the safety population [b] Sometimes took/sometimes left the rings [c] Left rings at the research centre
[d] With main partner [e] Took rings [f] Used a condom [g] Had anal sex since last visit [h] Had a menstrual bleeding/spotting since last visit
[i] Had ring expelled/removed since last visit [j] Cleaned ring before reinsertion [k] Inserted fingers into vagina

Table 14.6.9
Participant Questionnaire – Last Product Use Visit
Safety Population

Trial Month X

	Statistic	IPM 032 Overall (N=XXX)
Products used in the past 3 months to control menstrual bleeding/spotting		
Tissue, toilet paper, paper, cloth or cotton wool put inside the vagina	n (%)[h]	X (X.X)
Tissue, toilet paper, paper, cloth or cotton wool put inside the underwear/clothing	n (%)[h]	X (X.X)
Tampon	n (%)[h]	X (X.X)
Sanitary pad	n (%)[h]	X (X.X)
Menstrual cup	n (%)[h]	X (X.X)
Water without soap (inside the vagina)	n (%)[h]	X (X.X)
Water with soap (inside the vagina)	n (%)[h]	X (X.X)
Nothing was used	n (%)[h]	X (X.X)
Other	n (%)[h]	X (X.X)
Ring removed/expelled since last scheduled visit?		
Yes	n (%)[a]	X (X.X)
No	n (%)[a]	X (X.X)
Reason why the ring was removed/expelled		
Took it out because it was uncomfortable/painful	n (%)[i]	X (X.X)
Took it out to clean the ring	n (%)[i]	X (X.X)
Took it out because on menses	n (%)[i]	X (X.X)
Took it out because of real/perceived side effects	n (%)[i]	X (X.X)
Took it out because partner requested it	n (%)[i]	X (X.X)
Took it out for sex	n (%)[i]	X (X.X)
Took it out so that partner did not find out about it	n (%)[i]	X (X.X)
Accidentally came out	n (%)[i]	X (X.X)
Other	n (%)[i]	X (X.X)
When the ring was removed/expelled did you clean the ring before reinsertion?		
Yes	n (%)[i]	X (X.X)
No	n (%)[i]	X (X.X)

Programmers Note: Please add in 'Chose not to answer' where applicable

Percentages are calculated out of the number of participants [a] In the safety population [b] Sometimes took/sometimes left the rings [c] Left rings at the research centre
[d] With main partner [e] Took rings [f] Used a condom [g] Had anal sex since last visit [h] Had a menstrual bleeding/spotting since last visit
[i] Had ring expelled/removed since last visit [j] Cleaned ring before reinsertion [k] Inserted fingers into vagina

Table 14.6.9
Participant Questionnaire – Last Product Use Visit
Safety Population

Trial Month X

	Statistic	IPM 032 Overall (N=XXX)
What did you use to clean the ring when it was removed/expelled?		
Water only	n (%)[j]	X (X.X)
Soap only	n (%)[j]	X (X.X)
Water and soap	n (%)[j]	X (X.X)
Disinfectant	n (%)[j]	X (X.X)
Water and soap	n (%)[j]	X (X.X)
Disinfectant	n (%)[j]	X (X.X)
Herbal products	n (%)[j]	X (X.X)
Traditional medicine	n (%)[j]	X (X.X)
Bubble bath	n (%)[j]	X (X.X)
Bath salts	n (%)[j]	X (X.X)
Dishwashing liquid	n (%)[j]	X (X.X)
Other	n (%)[j]	X (X.X)
Level of being worried about getting infected with HIV in the next year		
Very worried	n (%)[a]	X (X.X)
A little worried	n (%)[a]	X (X.X)
Not worried at all	n (%)[a]	X (X.X)
Inserted fingers into vagina since last schedule visit		
Yes	n (%)[a]	X (X.X)
No	n (%)[a]	X (X.X)
Reason for inserting fingers into vagina	n (%)[k]	X (X.X)
Check the position of the ring	n (%)[k]	X (X.X)
Insert/remove the ring	n (%)[k]	X (X.X)
Cleaning	n (%)[k]	X (X.X)
Sexual pleasure	n (%)[k]	X (X.X)
Insert a product for the management of menses	n (%)[k]	X (X.X)
Other	n (%)[k]	X (X.X)

Programmers Note: Please add in 'Chose not to answer' where applicable

Percentages are calculated out of the number of participants [a] In the safety population [b] Sometimes took/sometimes left the rings [c] Left rings at the research centre
[d] With main partner [e] Took rings [f] Used a condom [g] Had anal sex since last visit [h] Had a menstrual bleeding/spotting since last visit
[i] Had ring expelled/removed since last visit [j] Cleaned ring before reinsertion [k] Inserted fingers into vagina

Table 14.6.9
Participant Questionnaire – Last Product Use Visit
Safety Population

Trial Month X

	Statistic	IPM 032 Overall (N=XXX)
Participant views on are the following good ways to ensure ring use: Adherence		
Test blood to see how much medicine is in the blood		
Yes	n (%)[a]	X (X.X)
No	n (%)[a]	X (X.X)
Test used ring to see how much medicine is still in the ring		
Yes	n (%)[a]	X (X.X)
No	n (%)[a]	X (X.X)
Ask the woman if she has been using the ring		
Yes	n (%)[a]	X (X.X)
No	n (%)[a]	X (X.X)
Other		
Yes	n (%)[a]	X (X.X)
No	n (%)[a]	X (X.X)
Would more women use the ring properly if they knew the blood tests/used rings would show staff who was using the ring as intended and who was not?		
Yes	n (%)[a]	X (X.X)
No	n (%)[a]	X (X.X)
Don't know	n (%)[a]	X (X.X)
Is it possible for women to use the ring as requested?		
Yes	n (%)[a]	X (X.X)
No	n (%)[a]	X (X.X)
Don't know	n (%)[a]	X (X.X)

Programmers Note: Please add in 'Chose not to answer' where applicable

Percentages are calculated out of the number of participants [a] In the safety population [b] Sometimes took/sometimes left the rings [c] Left rings at the research centre
[d] With main partner [e] Took rings [f] Used a condom [g] Had anal sex since last visit [h] Had a menstrual bleeding/spotting since last visit
[i] Had ring expelled/removed since last visit [j] Cleaned ring before reinsertion [k] Inserted fingers into vagina

Table 14.6.9
Participant Questionnaire – Last Product Use Visit
Safety Population

Trial Month X

	Statistic	IPM 032 Overall (N=XXX)
Most likely reason(s) for women to remove the ring	n (%)[a]	X (X.X)
Partner request	n (%)[a]	X (X.X)
Fear of partner feeling it	n (%)[a]	X (X.X)
Influence of others (not partner)	n (%)[a]	X (X.X)
Wants a break from having the ring inside	n (%)[a]	X (X.X)
Menses	n (%)[a]	X (X.X)
Side effects	n (%)[a]	X (X.X)
Discomfort/pain	n (%)[a]	X (X.X)
Belief that ring doesn't work	n (%)[a]	X (X.X)
Other	n (%)[a]	X (X.X)
All women can use the ring without taking it out		
Strongly agree	n (%)[a]	X (X.X)
Somewhat agree	n (%)[a]	X (X.X)
Strongly disagree	n (%)[a]	X (X.X)
Women would need a break from using the ring every few months		
Strongly agree	n (%)[a]	X (X.X)
Somewhat agree	n (%)[a]	X (X.X)
Strongly disagree	n (%)[a]	X (X.X)
Would women in the community want to wear the ring if it were available?		
Yes	n (%)[a]	X (X.X)
No	n (%)[a]	X (X.X)
If the ring is made available to the public, where would most women want to get it from?		
A clinic	n (%)[a]	X (X.X)
Pharmacy	n (%)[a]	X (X.X)
Private doctor	n (%)[a]	X (X.X)
Other	n (%)[a]	X (X.X)
They wouldn't want to use it	n (%)[a]	X (X.X)

Programmers Note: Please add in 'Chose not to answer' where applicable

Percentages are calculated out of the number of participants [a] In the safety population [b] Sometimes took/sometimes left the rings [c] Left rings at the research centre
[d] With main partner [e] Took rings [f] Used a condom [g] Had anal sex since last visit [h] Had a menstrual bleeding/spotting since last visit
[i] Had ring expelled/removed since last visit [j] Cleaned ring before reinsertion [k] Inserted fingers into vagina

Table 14.6.9
Participant Questionnaire – Last Product Use Visit
Safety Population

Trial Month X

	Statistic	IPM 032 Overall (N=XXX)
Willingness to pay for the ring, if it was to be made available to the public		
It should be free	n (%)[a]	X (X.X)
Would pay	n (%)[a]	X (X.X)
Spend South African Rand on ring	Mean	XX.X
	(q1,med,q3)	(XX.X,XX.X,XX.X)
	SD	XX.XX
	(Min, Max)	(XX, XX)
Spend Ugandan Shilling on ring	Mean	XX.X
	(q1,med,q3)	(XX.X,XX.X,XX.X)
	SD	XX.XX
	(Min, Max)	(XX, XX)
Where should the ring be marketed/advertised if it was to be made available to the public?		
By qualified healthcare providers	n (%)[a]	X (X.X)
The local clinic/hospital notice boards	n (%)[a]	X (X.X)
Pamphlets in clinics only	n (%)[a]	X (X.X)
Pamphlets in pharmacies/private doctor	n (%)[a]	X (X.X)
Pamphlets in public places	n (%)[a]	X (X.X)
Television and/or radio	n (%)[a]	X (X.X)
Billboards	n (%)[a]	X (X.X)
Other place	n (%)[a]	X (X.X)

Programmers Note: Please add in 'Chose not to answer' where applicable

Percentages are calculated out of the number of participants [a] In the safety population [b] Sometimes took/sometimes left the rings [c] Left rings at the research centre
[d] With main partner [e] Took rings [f] Used a condom [g] Had anal sex since last visit [h] Had a menstrual bleeding/spotting since last visit
[i] Had ring expelled/removed since last visit [j] Cleaned ring before reinsertion [k] Inserted fingers into vagina

Table 14.6.10
Participant Questionnaire – Vaginal Practices
Safety Population

Trial Month X

Product Used	Applied using			Removed Ring?		Reason for using product					
	Hands	Cloth	Other	No	Yes	General Cleaning	Clean During Menses	Clean Before Sex	Clean After Sex	…	Other
External cleaning											
Water only	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)
Soap only	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)
Soap and Water	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)
Disinfectant/ detergent	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)
Traditional products	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)
Other	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)
Internal cleaning											
Water only	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)
Soap only	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)
Soap and Water	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)
Disinfectant/ detergent	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)
Traditional products	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)
Gels	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)
Other	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)
Vaginal steaming											
Traditional products	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)
Commercial products	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)
Other	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)

Programmmers Note: Please repeat the table for all available Trial Months

Percentages are calculated out of the number of participants in the safety population

Table 14.6.10
Participant Questionnaire – Vaginal Practices
Safety Population

Trial Month X

Product Used	Applied using			Removed Ring?		Reason for using product					
	Hands	Cloth	Other	No	Yes	General Cleaning	Clean During Menses	Clean Before Sex	Clean After Sex	…	Other
Inserted into vagina											
Tampon	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)
Cloth	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)
Paper	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)
Cotton wool	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)
Snuff/Kuber	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)
Zambuk	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)
Talc	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)
Other commercial products	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)
Traditional products	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)
Other	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)
External application of products											
Commercial cream	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)
Talc	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)
Intimate sprays	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)
Traditional products	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)
Other	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	X (X.X)	…	X (X.X)

Programmmers Note: Please repeat the table for all available Trial Months

Percentages are calculated out of the number of participants in the safety population

IPM 032

FIGURE SHELLS – VERSION 1.0, 26 MAR 2020

Number	Listing Heading
14.1	**Demographics**
14.1.1.1	**Disposition of Participants**
14.1.1.1.1	Time to Trial Discontinuation
14.1.1.1.2	Time to (Premature) Permanent Investigational Product Discontinuation
14.3	**Safety Data**
14.3.5.1	**Adherence – Dapivirine Residual Levels in Used Rings**
14.3.5.1.1	Dapivirine Ring Residual Levels (mg)
14.3.5.1.2	Dapivirine Ring Residual Levels (mg) By Trial Visit and Category of Residual Amount
14.3.5.1.3	Relating The Dapivirine Ring Residual Levels (mg) To The Time Intervals Between Consecutive Ring Replacements
14.3.5.1.4	Residual Levels of Dapivirine (mg) in The Last Three Returned Rings Prior To HIV Seroconversion VS Average Ring Residual Levels
14.3.5.1.8	Corrected Residual Levels of Dapivirine in The Last Three Returned Rings Prior To HIV Seroconversion VS Average Ring Residual Levels of HIV- Participants
14.3.7	**Other Safety Data**
14.3.7.7	Time to HIV-1 Seroconversion – m-ITT population
14.3.7.8	Time to HIV-1 Seroconversion – PP population
14.6	**Other Data**
14.6.4	Correlation Between Dapivirine Residual Amounts (mg) in Returned Used Vaginal Rings and Results From Visual Inspection of Returned Vaginal Rings

Figure 14.1.1.1.1
Kaplan-Meier Curves, Time to Trial Discontinuity
Safety Population

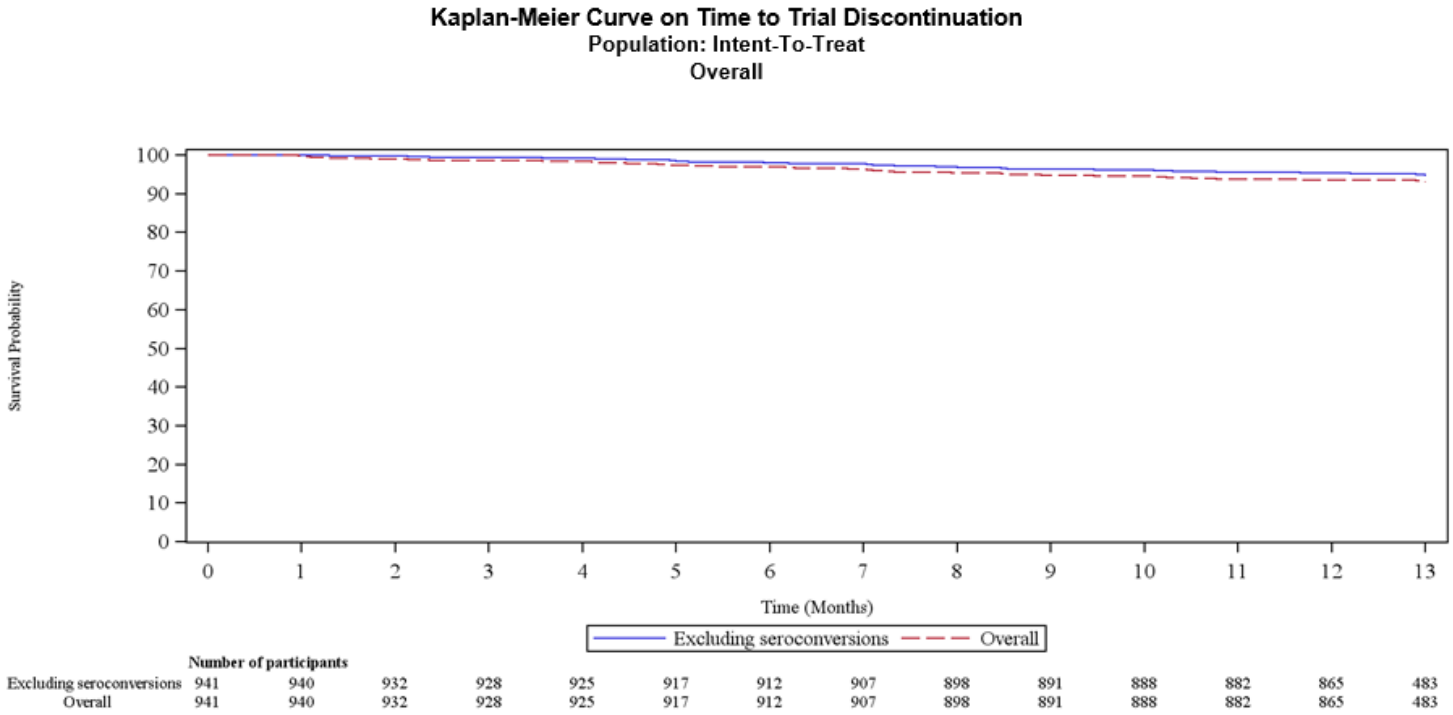
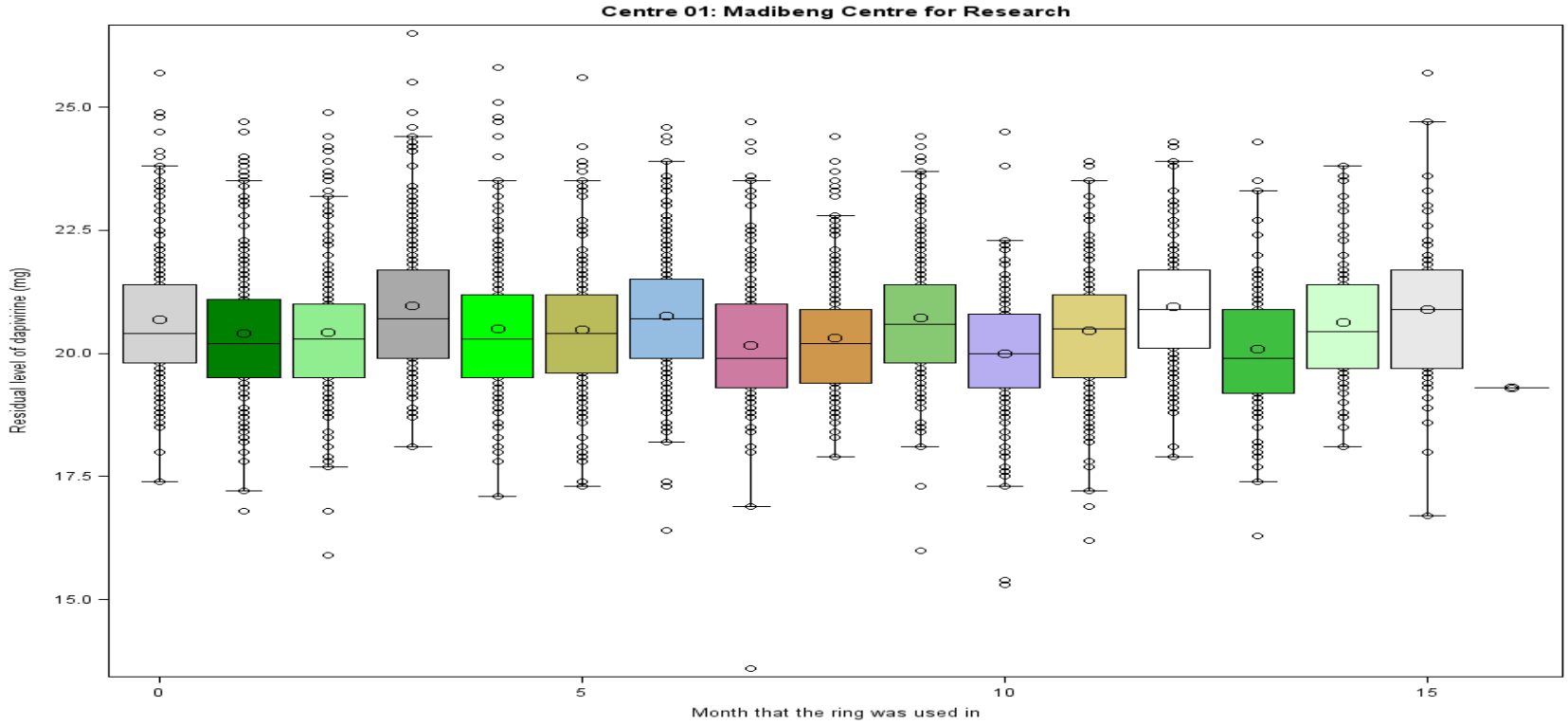


Figure 14.1.1.1.2
Kaplan-Meier Curves, Time to (Premature) Permanent Investigational Product Discontinuation
Safety Population

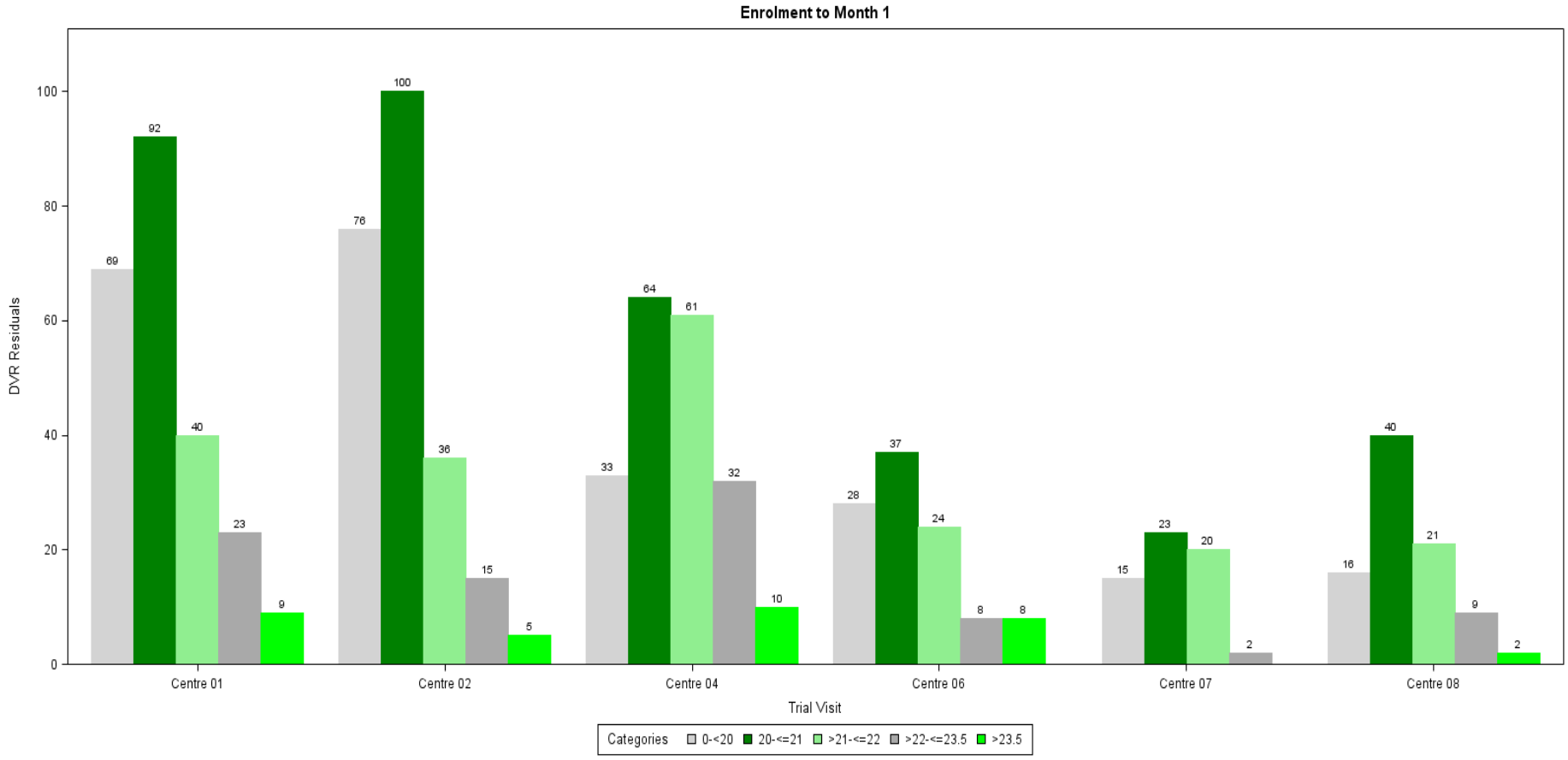
Programmers Note: Figure wil resemble F14.1.1.1 with time to permanent IP data.

Figure 14.3.5.1.1
Dapivirine Ring Residual Levels (mg)
Safety Population



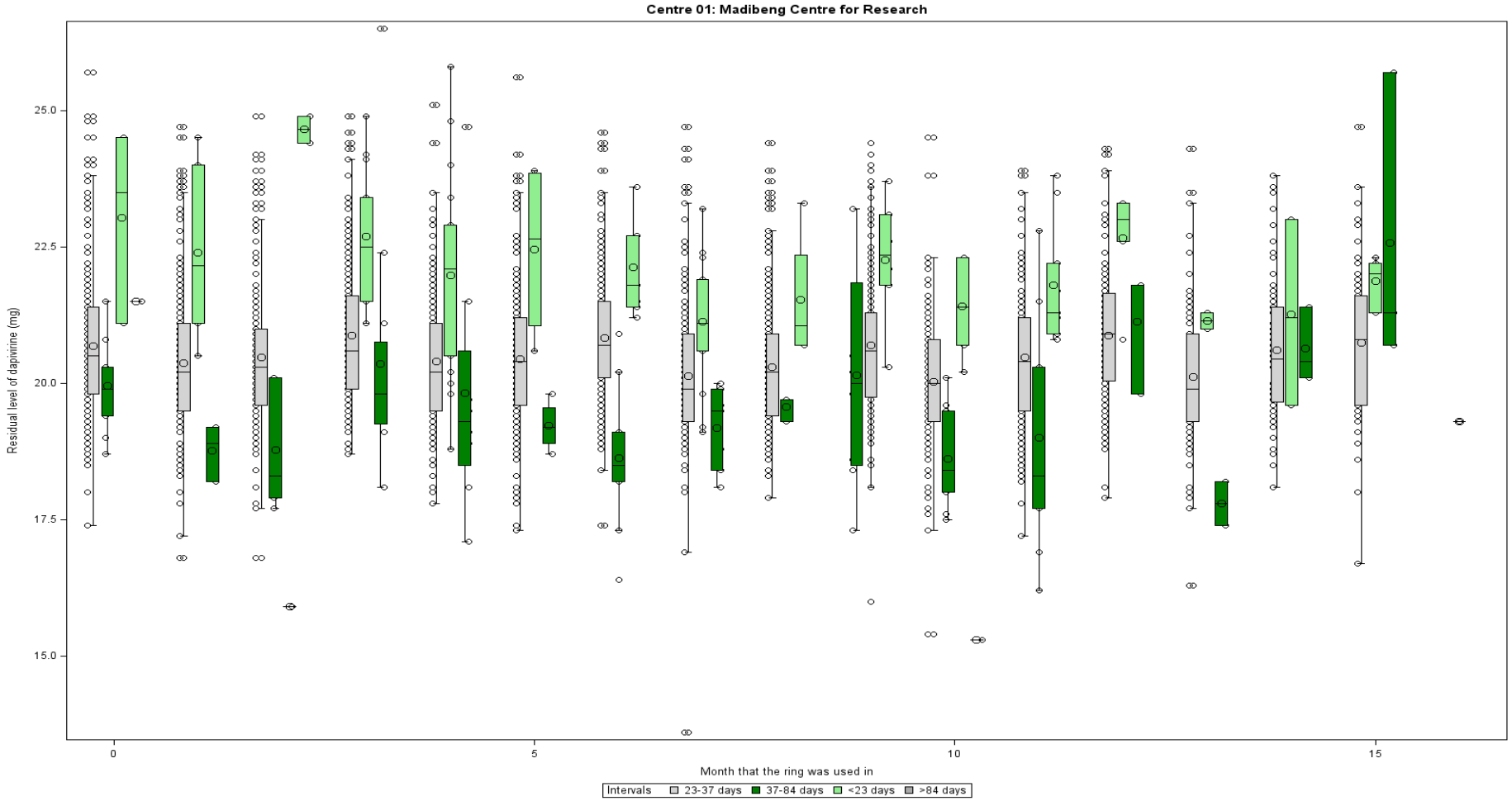
Programmers Note: Please repeat for all centres.

Figure 14.3.5.1.2
Dapivirine Ring Residual Levels (mg) By Trial Visit and Category of Residual Amount
Safety Population



Programmers Note: Please repeat for all trial months.

Figure 14.3.5.1.3
Relating The Dapivirine Ring Residual Levels (mg) To The Time Intervals Between Consecutive Ring Replacements
Safety Population



Programmers Note: Please repeat for all centres.

Figure 14.3.5.1.4
Residual Levels of Dapivirine (mg) in The Last Three Returned Rings Prior To HIV Seroconversion VS Average Ring Residual Levels
Safety Population

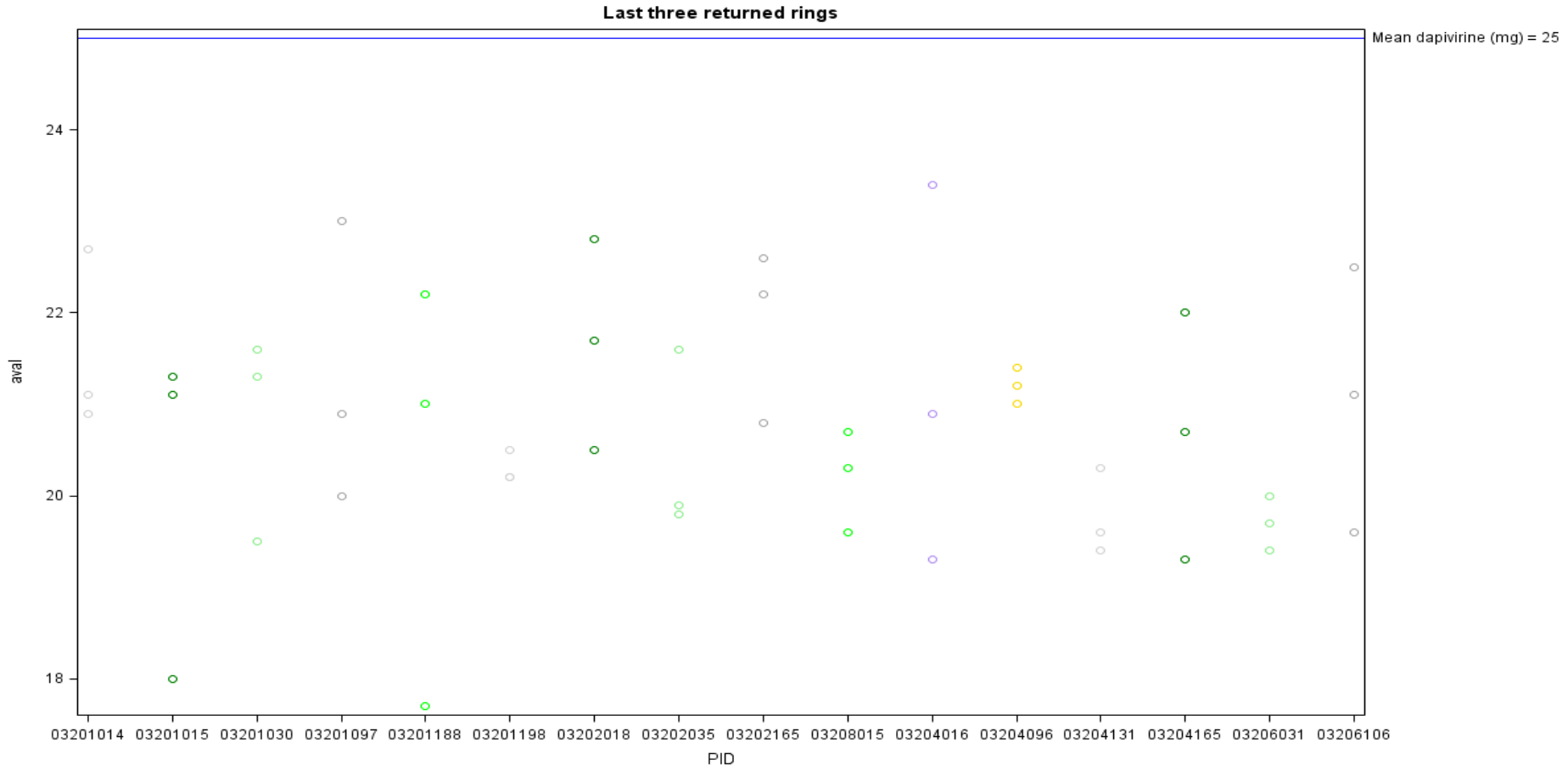


Figure 14.3.5.1.5
Residual Levels of Dapivirine (mg) in The Last Two Returned Rings Prior To HIV Seroconversion VS Average Ring Residual Levels
Safety Population

Programmers Note: Figure wil resemble F14.5.1.4 using data from last two rings of those who seroconverted.

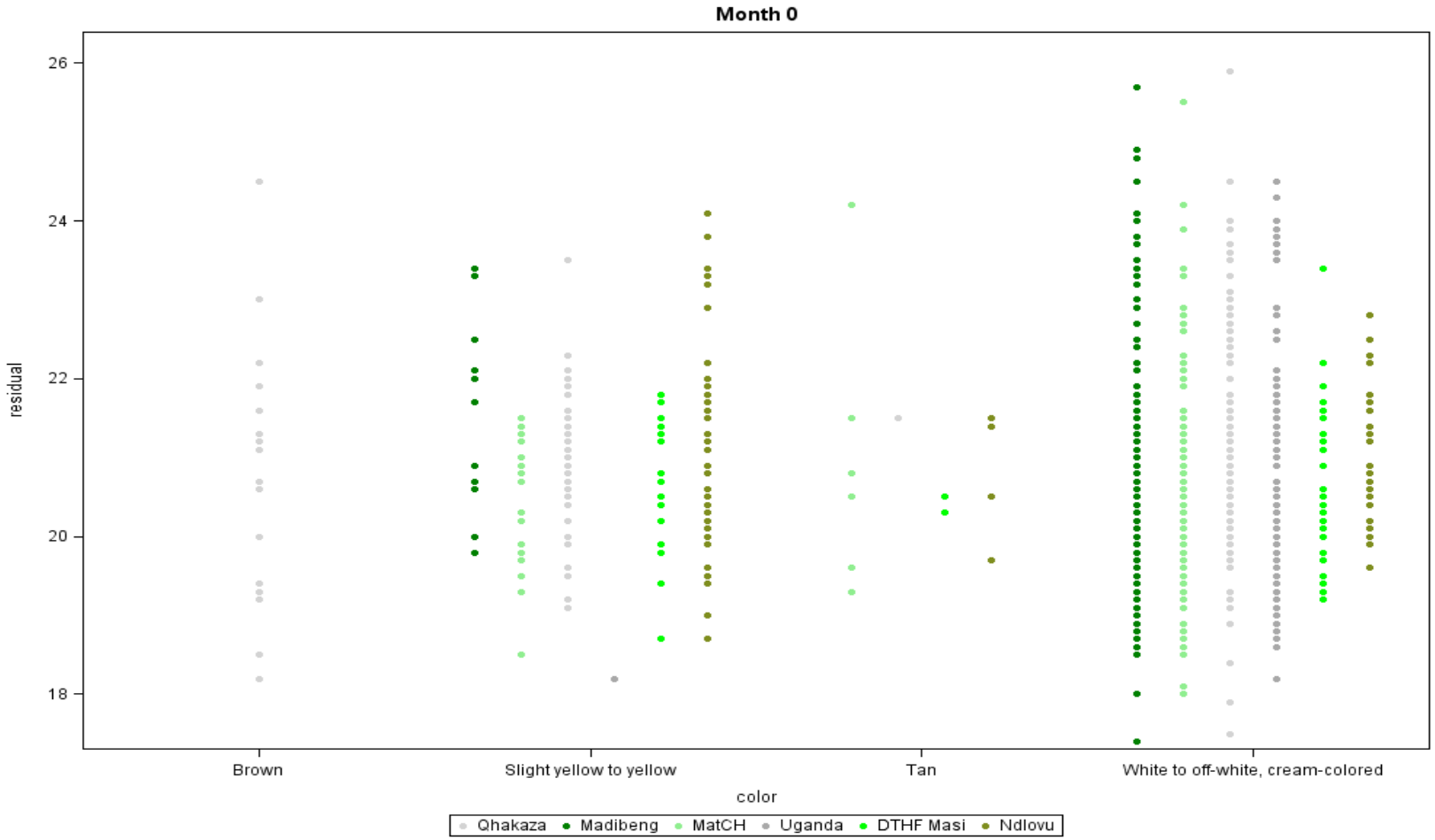
Figure 14.3.7.7
Time to HIV-1 Seoconversion
m-ITT Population

Programmers Note: Figure wil resemble F14.1.1.1.

Figure 14.3.7.8
Time to HIV-1 Seroconversion
PP Population

Programmers Note: Figure wil resemble F14.1.1.1.

Figure 14.6.4
Correlation Between Dapivirine Residual Leverl (mg) in Returned Used Vaginal Rings and Results From Visual Inspection of Returned Vaginal Rings
Safety Population



IPM 032

LIST OF PARTICIPANT LISTINGS – VERSION 1.0, 26 MAR 2020

Number	Listing Heading
16.2.1	**Discontinued Participants**
16.2.1.1	Enrollment
16.2.1.2	Screen Failures
16.2.1.3	Participant Disposition: Participant Visits
16.2.1.4	Missed Visits
16.2.2	**Protocol Deviations**
16.2.2.1	Protocol Deviations
16.2.3	**Participants Excluded from Efficacy Analysis**
16.2.3.1	Analysis Populations
16.2.4	**Demographic Data**
16.2.4.1	Demographics at Screening
16.2.4.2	Demographics at Screening
16.2.4.3	Medical History at Screening
16.2.4.4	Contraceptive/ Menstrual/ Obstetric History at Screening
16.2.4.5	Gynaecological History at Screening
16.2.4.6	Prior Medication
16.2.4.7	Concomitant Medication
16.2.5	**Compliance and/ or Drug Concentration Data**
16.2.5.1	Adherence to Investigational Product
16.2.5.2	Self-Reported Acceptability and Adherence to Investigational Product
16.2.5.3	Returned Ring Log
16.2.5.4	Ring Insertion/ Removal
16.2.5.5	Accidental Expulsion/ Removal
16.2.5.6	Participant Questionnaire – Part A (Month 1, 2 and 3)
16.2.5.7	Participant Questionnaire – Part B (Month 2 and 3 Only)
16.2.5.8	Participant Questionnaire – Part C (Month 1, 2 and 3)
16.2.5.9	Participant Questionnaire – 3 Month Follow-up
16.2.5.10	Participant Questionnaire – LPUV
16.2.5.11	Feasibility of a 3-Monthly Clinical Follow-Up Schedule
16.2.5.12	Participant Questionnaire – Vaginal Practices
16.2.5.13	Dapivirine Concentration Sample Collection
16.2.5.14	Dapivirine Concentration in the Last Three Returned Rings Prior to HIV-1 Seroconversion
16.2.5.15	Dapivirine Concentration in the Last Two Returned Rings Prior to First Positive HIV RNA PCR Test
16.2.6	**Individual Efficacy Response Data**
16.2.7	**Adverse Events Listings**
16.2.7.1	Treatment Emergent Adverse Events
16.2.7.2	Product-Related Treatment Emergent Adverse Events
16.2.7.3	Treatment Emergent Adverse Events Leading to Temporary Product Discontinuation
16.2.7.4	Treatment Emergent Adverse Events Leading to Permanent Product Discontinuation
16.2.7.5	Treatment Emergent Adverse Events Leading to Premature Trial Discontinuation
16.2.7.6	Serious Treatment Emergent Adverse Events
16.2.7.7	Grade 3 or 4 Treatment Emergent Adverse Events
16.2.7.8	Treatment Emergent Adverse Events Leading to Death

Number	Listing Heading
16.2.7.9	Urogenital Treatment Emergent Adverse Events
16.2.7.10	Social Harms Reported as Treatment Emergent Adverse Events
16.2.7.11	Non-Treatment Emergent Adverse Events
16.2.8	**Listings of Individual Laboratory Measurements and Other Safety Data**
16.2.8.1	Haematology Results
16.2.8.2	Biochemistry Results
16.2.8.3	Urinalysis and Microscopy Results
16.2.8.4	Abnormal Clinical Laboratory Data
16.2.8.5	Vital Signs
16.2.8.6	Physical Examination
16.2.8.7	Menses Information and Pregnancy Test Results
16.2.8.8	Sexually Transmitted Infections
16.2.8.9	HIV-1 Seroconversion
16.2.8.10	HIV-1 Seroconversion: Genotype Testing
16.2.8.11	HIV-1 Seroconversion on Investigational Product
16.2.8.12	Participants with Drug Resistance Mutations
16.2.8.13	HIV-1 NNRTI Drug Susceptibility: Stanford Interpretation of Genotype
16.2.8.14	Population-Based Sequencing: Mutations per Region
16.2.8.15	Population-Based Genotyping Amongst Participants who HIV-1 Seroconverted
16.2.8.16	Pelvic/ Speculum Examinations
16.2.8.17	Cervical Cytology Results
16.2.8.18.1	Social Harms Report
16.2.8.18.2	Social Harms Follow-up Report
16.2.8.19	Timing Profile
16.2.9	**PK Listings**
16.2.10	**PD Listings**

Listing 16.2.1.1
Enrollment
Safety Population

Centre Participant ID	Visit Schedule	Date of Signed Consent	Consent Version No. and Date	Met All INCL Criteria	Met No EXCL Criteria
Centre XXX					
XXXXXXXX	A / B / C	ddMMMyyyy	XX-ddMMMyyyy	Yes / No	Yes / No

Programmers Notes:
- Populate IPM027 Exit Date with whichever is later, LPUV or Exit Visit.
- Please note that the incl/excl criteria is that of the DVR-naïve cohort; see p.12/13 of the protocol for the incl/excl criteria of the participants who were previously exposed to the DVR

AE = Adverse event; EXCL = Exclusion criteria; INCL = Inclusion criteria; LPUV = Last product use visit
Visit Schedule A = Participants attended trial month visit 1, 4, 7, 10, 13 and 16/Exit
Visit Schedule B = Participants attended trial month visit 1, 2, 5, 8, 11, 14 and 17/Exit
Visit Schedule C = Participants attended trial month visit 1, 2, 3, 6, 9, 12 and 15/Exit
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.1.1
Enrollment
Safety Population

Centre Participant ID	Visit Schedule	INCL No. Not Met	EXCL No. Met
Centre XX			
XXXXXXXX	A /	1. Previously enrolled in the IPM 027 trial /	1. Investigational product use permanently discontinued in response to an AE (where the AE was considered related to investigational product) or safety-related concern while taking part in the IPM 027 trial /
	B /	2. Available for all visits and consent to follow all procedures scheduled for the trial /	2. Currently pregnant, intending to become pregnant, or currently breast-feeding /
	C	3. Using an effective method of contraception at the Enrolment Visit, and intending to use an effective contraceptive method for the duration of trial participation, unless post-menopausal with no history of menses for one year prior to screening /	3. Known drug abuse or alcohol dependence in the 12 months prior to screening /
		4. HIV-negative as determined by the HIV algorithm applied at Screening/Pre-Enrolment /	4. Participated in another research trial (other than IPM 027) using drugs, medical devices, microbicides or oral pre-exposure prophylaxis agents within 30 days prior to screening /
		5. Willing to refrain from participation in another research trial using drugs, vaccines, medical devices and microbicides for the duration of the IPM 032 trial /	5. Any new illness or condition(s), chronic condition(s) or abnormal laboratory finding(s) that, in the opinion of the investigator, might put the participant at risk, or interfere with the trial objectives or the participant's adherence to trial requirements
		6. Willing to provide adequate locator information for trial retention purposes and be reachable per local standard procedures (e.g. by home visit or telephone; or via family or close neighbour contacts); confidentiality to be maintained	

Programmers Notes:
- Populate IPM027 Exit Date with whichever is later, LPUV or Exit Visit.
- Please note that the incl/excl criteria is that of the the participants who were previously exposed to the DVR; see p. 13/14 of the protocol for the incl/excl criteria of the DVR naïve cohort

AE = Adverse event; EXCL = Exclusion criteria; INCL = Inclusion criteria; LPUV = Last product use visit
Visit Schedule A = Participants attended trial month visit 1, 4, 7, 10, 13 and 16/Exit
Visit Schedule B = Participants attended trial month visit 1, 2, 5, 8, 11, 14 and 17/Exit
Visit Schedule C = Participants attended trial month visit 1, 2, 3, 6, 9, 12 and 15/Exit
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.1.1
Enrollment
Safety Population

Centre Participant ID	Visit Schedule	IPM027 LPUV and IPM032 Screening / Enrollment Visits Combined	IPM027 Exit Date	IPM027 Participant ID	Comments
Centre XX XXXXXXXX	A / B / C	Yes / No	ddMMMyyyy	XXXXXXX / None	

Programmers Notes:
- Populate IPM027 Exit Date with whichever is later, LPUV or Exit Visit.
- Please note that the incl/excl criteria is that of the the participants who were previously exposed to the DVR; see p. 13/14 of the protocol for the incl/excl criteria of the DVR naïve cohort

AE = Adverse event; EXCL = Exclusion criteria; INCL = Inclusion criteria; LPUV = Last product use visit
Visit Schedule A = Participants attended trial month visit 1, 4, 7, 10, 13 and 16/Exit
Visit Schedule B = Participants attended trial month visit 1, 2, 5, 8, 11, 14 and 17/Exit
Visit Schedule C = Participants attended trial month visit 1, 2, 3, 6, 9, 12 and 15/Exit
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.1.2
Screen Failures
All Participants

Centre Screening ID	Screen Failure Date	Date of Signed Consent	Consent Version No. and Date	Reason(s) for Ineligibility	Incl Criteria Not Met
Centre XX XXXXXXXX	ddMMMyyyy	ddMMMyyyy	XX-ddMMMyyyy	INCL not met / EXCL met / Other: Xxxxxxxx	1. Previously enrolled in the IPM 027 trial / 2. Available for all visits and consent to follow all procedures scheduled for the trial / 3. Using an effective method of contraception at the Enrolment Visit, and intending to use an effective contraceptive method for the duration of trial participation, unless post-menopausal with no history of menses for one year prior to screening / 4. HIV-negative as determined by the HIV algorithm applied at Screening/Pre-Enrolment / 5. Willing to refrain from participation in another research trial using drugs, vaccines, medical devices and microbicides for the duration of the IPM 032 trial / 6. Willing to provide adequate locator information for trial retention purposes and be reachable per local standard procedures (e.g. by home visit or telephone; or via family or close neighbour contacts); confidentiality to be maintained

Programmers Notes:
- Please capture multiple responses, separated with a ';'
- Please note that the incl/excl criteria is that of the the participants who were previously exposed to the DVR; see p. 13/14 of the protocol for the incl/excl criteria of the DVR naïve cohort

AE = Adverse; Excl = Exclusion; Incl = Inclusion
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.1.2
Screen Failures
All Participants

Centre Screening ID	Screen Failure Date	Excl Criteria Met	IPM 027 PID	Comment
Centre XX				
XXXXXXXX	ddMMMyyyy	1. Investigational product use permanently discontinued in response to an AE (where the AE was considered related to investigational product) or safety-related concern while taking part in the IPM 027 trial / 2. Currently pregnant, intending to become pregnant, or currently breast-feeding / 3. Known drug abuse or alcohol dependence in the 12 months prior to screening / 4. Participated in another research trial (other than IPM 027) using drugs, medical devices, microbicides or oral pre-exposure prophylaxis agents within 30 days prior to screening / 5. Any new illness or condition(s), chronic condition(s) or abnormal laboratory finding(s) that, in the opinion of the investigator, might put the participant at risk, or interfere with the trial objectives or the participant's adherence to trial requirements	XXXXXXXXX	

Programmers Notes:
- Please capture multiple responses, separated with a ';'
- Please note that the incl/excl criteria is that of the the participants who were previously exposed to the DVR; see p. 13/14 of the protocol for the incl/excl criteria of the DVR naïve cohort

AE = Adverse; Excl = Exclusion; Incl = Inclusion
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.1.3
Participant Disposition: Participant Visits
Safety Population

Centre Participant ID	Visit Date	Visit	Enrollment Date	Type of Visit	Reason(s) for Unscheduled Visit	Completion Date	Completion Status
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	ddMMMyyyy	Scheduled / Unscheduled / LPUV / Exit visit	Intends to withdraw / Blood draw or additional testing / HIV testing / Suspected/confirmed pregnancy / Report social harm / Return/collect study product / Treatment/follow-up of AE or medical condition / Other: XXXXXX	ddMMMyyyy	Completed the trial / Discontinued early

Programmers Note: Please capture multiple responses, separated with a ';'

AE = Adverse event; LPUV = Last product use visit
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.1.3
Participant Disposition: Participant Visits
Safety Population

Centre Participant ID	Visit Date	Visit	Enrollment Date	Type of Visit	Reasons for Early Completion	Comments
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	ddMMMyyyy	Scheduled / Unscheduled / LPUV / Exit visit	Participant withdrew consent: Relocation / Participant withdrew consent: Employment/work / Participant withdrew consent: Family/partner pressure / Participant withdrew consent: Other / Non-compliance: Xxxxxxxxx / Lost to follow-up / Adverse event/intercurrent illness: Xxxxxxx / Inappropriate enrollment / HIV seroconversion / Pregnancy / Sponsor terminated the trial / Death / Other	

Programmers Note: Please capture multiple responses, separated with a ';'

AE = Adverse event; LPUV = Last product use visit
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.1.4
Missed Visits
Safety Population

Centre Participant ID	Visit	Reason for Missed Visits	Comments
Centre XX			
XXXXXXXX	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Unable to contact participant / Unable to attend schedule appointment(s) within a permitted window: Participant found new employment / Unable to attend schedule appointment(s) within a permitted window: Participant relocated / Unable to attend schedule appointment(s) within a permitted window: Other: Xxxxxxxxxxxxxxxxxx / Participant refused visit / Participant admitted to a health care facility / Participant withdrew from study / Death / Other: Xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx	

Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.2.1
Protocol Deviations
Safety Population

Deviation type: Minor

Centre Participant ID	Date of Deviation	Deviation Category	Description of Deviation	Description of Deviation (Verbatim)	Action Taken to Resolve) Deviation (Verbatim)
Centre XX					
XXXXXXXX	ddMMMyyyy	Inappropriate enrollment: INCL / Inappropriate enrollment: EXCL / Missed visit / Visit completed outside permissible period: Trial month XX.X / Other (code) / Other: Xxxxxxxx			

Programmers Notes:
- Please populate Description of Deviation with the appropriate (IPM 027/DPR-naïve) INCL/EXCL criteria or Other (code) text
- Please repeat for Deviation type: Major / None

EXCL = Exclusion criteria; INCL = Inclusion criteria
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.3.1
Analysis Populations
Safety Population

Centre	Participant ID	Safety	m-ITT	Virology	PP
Centre XX	XXXXXXXX	Yes	Yes / No	Yes / No	Yes / No

m-ITT = Modified intent-to-treat population; PP = Per-protocol population
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.4.1
Demographics at Screening
Safety Population

Centre Participant ID	Visit Date	Date of Birth	Race	Age (Years)	Height (cm)	Weight (kg)	BMI (kg/m^2)	Education			Marital Status
								Primary School	Secondary School	Tertiary Level: No. of Years	
Centre XX XXXXXXXX	ddMMMyyyy	ddMMMyyyy	Coloured / Asian / Black / White / Indian / Other: Xxxxxx	XX	XXXX	XXX	XX.X	Yes / No	Yes / No	Yes: XX / No	Married / Separated / Divorced / Widowed / Single

Programmers Note: Please capture multiple STIs, separated with a ';'

Age = INT((Enrollment Date – Date of Birth)/365.25); Body Mass Index (BMI) = (Weight in kg)/(Height in $m)^2$
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.4.1
Demographics at Screening
Safety Population

Centre Participant ID	Main Sex Partner	Length of Partnership (Years)	Current Co-Residential Status with Main Partner	Co-Residential Status with Main Partner (Past Year)	Vaginal Sex Once a Week or More in Past Month	Usual No. of Vaginal Sex Acts	No. of Male Sex Partners at Baseline	Has Children
Centre XX								
XXXXXXXX	Yes No	XX / < 1	Yes / No	Lived together all the time / Lived together some of the time / Lived together none of the time	Yes / No	XX	XX	Yes / No

Programmers Note: Please capture multiple STIs, separated with a ';'

Age = INT((Enrollment Date – Date of Birth)/365.25); Body Mass Index (BMI) = (Weight in kg)/ (Height in m)^2
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.4.1
Demographics at Screening
Safety Population

Centre Participant ID	Genital Symptom STIs at Screening	Partner Knowledge of Ring Use / Study Participation	Directly From IPM 027?	IPM 027 Treatment	Comments
Centre XX					
XXXXXXXX	Trichomonas / Gonorrhoea / Chlamydia / Syphilis	Knows about the study and ring / Only knows that I am in a study / Only knows that I am wearing a ring / Doesn't know about the study or the ring / Don't know	Yes / No	Dapivirine / Placebo	

Programmers Note: Please capture multiple STIs, separated with a ';'

Age = INT((Enrollment Date – Date of Birth)/365.25); Body Mass Index (BMI) = (Weight in kg)/ (Height in m)^2
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.4.2
Demographics at Screening
Virology Population

Seroconverted	Centre - Participant ID	Age (Years)	Date of Seroconversion	Height (cm)	Weight (kg)	BMI (kg/m^2)	Country	Race	Marital Status
Yes (On IP)/ Yes (Prior to IP) / Yes (After IP) / No	XX- XXXXXXXX	XX	ddMMMyyyy	XXXX	XXX	XX.X	South Africa / Zimbabwe / Uganda	Coloured / Asian / Black / White / Indian / Other: Xxxxxx	Married / Separated / Divorced / Widowed / Single

Programmers Notes:
- Please capture multiple STIs, separated with a ';'
- Please sort listing by seroconversion status and PID

Age = INT((Enrollment Date – Date of Birth)/365.25); Body Mass Index (BMI) = (Weight in kg)/ (Height in m)^2
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.4.2
Demographics at Screening
Virology Population

Seroconverted[a]	Centre - Participant ID	Has Children	Genital Symptom STIs at Baseline	No. of Male Sex Partners at Screening	HIV-1 Subtype	Directly From IPM 027?	IPM 027 Treatment
No / Yes (on) / Yes (prior) / Yes (after)	XX- XXXXXXXX	Yes / No	Trichomonas / Gonorrhoea / Chlamydia / Syphilis	XX	C / A1	Yes / No	Dapivirine / Placebo

Programmers Notes:
- Please capture multiple STIs, separated with a ';'
- Please sort listing by seroconversion status and PID

Age = INT((Enrollment Date – Date of Birth)/365.25); Body Mass Index (BMI) = (Weight in kg)/ (Height in m)^2
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.4.3
Medical History at Screening
Safety Population

Centre Participant ID	Condition / Diagnosis	Severity Grade	Onset Date	Ongoing at Enrollment	Comments
Centre XX					
XXXXXXXX		X / Not gradable	ddMMMyyyy	Yes / No	

Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.4.4
Contraceptive/ Menstrual/ Obstetric History at Screening
Safety Population

Centre Participant ID	Visit Date	Contraceptive Method		Menstruation History		
		Current Method	CM Name	Menstrual Bleeding (Past 6 Months)	Duration of Menstrual Cycle (Days)	Duration of Menstrual Bleeding (Days)
Centre XX						
XXXXXXXX	ddMMMyyyy	Oral contraceptive regimen / Transdermal contraceptive patch / Long acting injectable progestins / Condoms / Subcutaneous implant / IUD / Surgical sterilization / Other: Xxxxxxxxxx		Regular cycle / Irregular cycle (associated with contraceptive use) / Amenorrhoeic	XX	XX

Programmers Note: Please list all Contraceptive Methods and applicable CM Names separated with a ';'

CM = Concomitant medication; IUD = Intrauterine device
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.4.4
Contraceptive/ Menstrual/ Obstetric History at Screening
Safety Population

		Menstruation History		Obstetric History				
Centre Participant ID	Visit Date	Menstrual Flow	Dysmenorrhea History	Gravidity	Parity	No. of Vaginal Deliveries	No. of C-Sections	Comments
Centre XX XXXXXXXX	ddMMMyyyy	Light / Moderate / Heavy	Yes / No	XX	XX	XX	XX	

Programmers Note: Please list all Contraceptive Methods and applicable CM Names separated with a ';'

CM = Concomitant medication; IUD = Intrauterine device
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.4.5
Gynaecological History at Screening
Safety Population

Centre Participant ID	Subcategory of Medical History	System Organ Class / Condition or Diagnosis	Severity Grade	Onset	Ongoing at enrollment
Centre XX XXXXXXX				ddMMMyyyy	Y / N

Gynaecological conditions were coded using Version 19.0 of the Medical Dictionary for Regulatory Activities (MedDRA)
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.4.6
Prior Medication
Safety Population

Centre Participant ID	Medication Name	Indication	Dose (Units)	Route	Frequency	Start Date	End Date
Centre XX XXXXXXXX		Contraceptive / Xxxxxxxxxxx	XXX (unit)	PO / IU / VAG / IM / TOP / REC / IV / UHL / SC / Other: Xxxxxxx	pm / bid / phs / once / tid / qd / qid / Other: Xxxxxx	ddMMMyyyy	ddMMMyyyy / Ongoing

Programmers note: Please add abbreciations of Frequency to the footnote (where applicable)

Prior medication is defined as any medication that started and ended before the first insertion of the investigational product (IP)
Medications were coded using the World Health Organization Drug Dictionary Enhanced (WHO DDE; version June 2017)
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.4.7
Concomitant Medication
Safety Population

Centre Participant ID	Medication Name	Taken for AE: Description	Indication	Dose (Units)	Route	Frequency	Start Date	End Date
Centre XX XXXXXXXX		Yes: Xxxxxxxxxxx / No	Contraceptive / Xxxxxxxxxxx	XXX (unit)	PO / IU / VAG / IM / TOP / REC / IV / UHL / SC / Other: Xxxxxxx	pm / bid / phs / once / tid / qd / qid / Other: Xxxxxx	ddMMMyyyy	ddMMMyyyy / Ongoing

Programmers note: Please add abbreciations of Frequency to the footnote (where applicable)

AE = Adverse event
Concomitant medication is defined as any medication taken in conjunction with the investigational product (IP). This includes any medication that started after the first insertion of the IP, or started before the first insertion of the IP but ended on/after the first insertion of the IP
Medications were coded using the World Health Organization Drug Dictionary Enhanced (WHO DDE; version June 2017)
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.1
Adherence to Investigational Product
Safety Population

Centre Participant ID	Used in Month No.	Enrollment Date	Parameter	Residual Dapivirine (mg)	Batch No.	IPM 027 Treatment	Comments
Centre XX							
XXXXXXXX	XX	ddMMMyyyy				Dapivirine / Placebo	

Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.2
Self-Reported Acceptability and Adherence to Investigational Product
Safety Population

Centre Participant ID	Visit Date	IPM 027 Treatment	Date Inserted	Date Removed	Duration of Treatment	Scheduled Duration	Adherence Rate	Adherence Rate Category
Centre XX								
XXXXXXXX	ddMMMyyyy	Dapivirine / Placebo	ddMMMyyyy	ddMMMyyyy	XX	XX	XXX	< 80% ≥ 80 to < 90% / ≥ 90%

Adherence rate = 100 x (Duration of Treatment / Scheduled Duration)
Missing or partial dates for when the ring was inserted or removed are treated as missing data during the calculation of the adherence rate
If a participant did not remember/know the date when a ring was expelled or removed, the number of days that the ring was out is counted as one day and applies to the ring that was dispensed during that time
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.2
Self-Reported Acceptability and Adherence to Investigational Product
Safety Population

Centre Participant ID	Visit Date	Do You Think It Is Possible To Use Ring As Requested (i.e. Without Removing It)?	Do You Think Women In Your Community Would Like To Use This Ring If It Were Available?
Centre XX			
XXXXXXXX	ddMMMyyyy	Yes / No: Xxxxxxxxxxxxxx / Don't know / Chose not to answer	Yes / No: Xxxxxxxxxxxxxxxxxxx / Chose not to answer

Adherence rate = 100 x (Duration of Treatment / Scheduled Duration)
Missing or partial dates for when the ring was inserted or removed are treated as missing data during the calculation of the adherence rate
If a participant did not remember/know the date when a ring was expelled or removed, the number of days that the ring was out is counted as one day and applies to the ring that was dispensed during that time
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.3
Returned Ring Log
Safety Population

Centre	Participant ID	Month of Ring Use	Replacement Ring	Shipped for Analysis	Shipped Date	Shared Results with Participant	Results Shared Date
XX	XXXXXXXXX	XX	Yes / No	Yes / No	ddMMMyyyy	Yes / No	ddMMMyyyy

Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.4
Ring Insertion/ Removal
Safety Population

	Dispensed					Insertion		
Centre Participant ID	Month To Be Used In	Batch No.	Replacement Ring	Visit Dispensed	Dispensed Date	Inserted Ring	Insertion Date	Re-Educated?
Centre XX								
XXXXXXXX	XX	XXXXXX	Yes / No	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	ddMMMyyyy	Yes / No: Xxxxxxxxxxx	ddMMMyyyy	Yes / No

Duration of Ring Use = (Removal Date – Inserted Date)+1
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.4
Ring Insertion/ Removal
Safety Population

	Removal					
Centre Participant ID	Removal Date	Duration of Ring Use (Days)	Required Assistance with Removal	Re-Educated?	Ring Returned to Research Centre	Reason Not Returned to Research Centre
Centre XX XXXXXXXX	ddMMMyyyy	XX	Yes / No	Yes / No	Yes / No	Lost ring / Flushed down toilet / Forgot ring / Discarded ring / Other: Xxxxxxxxx

Duration of Ring Use = (Removal Date – Inserted Date)+1
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.4
Ring Insertion/ Removal
Safety Population

Centre Participant ID	Return						Comments
	Visit Returned	Return Date	Package Opened	Appearance of Returned Ring	Color of Returned Ring	Other Comments on Appearance of Ring	
Centre XX							
XXXXXXXX	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	ddMMMyyyy	Yes / No	Appears used: Xxxxxxxx / Appears not used: Xxxxx / Not sure: Xxxxxxxxx	White to off-white cream-colored / Slight yellow to yellow / Tan / Brown / Other color: Xxxxxxxx		

Duration = (Removal Date – Inserted Date)+1
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.5
Accidental Expulsion/ Removal Log
Safety Population

Centre Participant ID	Date of Accidental Expulsion / Removal	Time of Expulsion / Removal	Expulsion / Removal	Date of Re-Insertion	Time of Re-Insertion	Why Was Ring Removed / Why Did Ring Come Out?	Category for Removal
Centre XX XXXXXXXX	ddMMMyyyy	hh:mm	Expulsion / Removal	ddMMMyyyy / Not re-inserted	hh:mm		Removed by participant / Colposcopy / Etc.

Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.6
Participant Questionnaire – Part A (Month 1, 2 and 3)
Safety Population

Question No.	Question
1	As per investigator decision, are you coming to the research centre next month, or in three months for your next visit?
2	Will you take your extra rings with you today or will you come back to the research centre each month to pick up your new ring?
3	What are your reasons for leaving the rings at the research centre today?
4	Does your main partner know you are in the study and wearing a vaginal ring?
5	The research centre staff showed you how to insert and remove your ring. You were also given an instruction sheet that explains this. Was the sheet helpful, or does it need to be changed?

Listing 16.2.5.6
Participant Questionnaire – Part A (Month 1, 2 and 3)
Safety Population

Centre Participant ID	Visit Date	Visit	Q1	Q2	Q3
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Next month / In 3 months	Take them all / Collect monthly from centre / Chose not to answer	Do not want anyone to see the rings / Do not have a private place to keep unused rings at home / Do not have a private place to keep used rings at home / Do not have an appropriate storage place to keep the rings (used or unused) at home / Do not have a private place to insert the rings at home / Worried I might lose the ring(s) / Feel I might forget to insert the new ring if I don't come each month / Like coming to the research centre for HIV tests each month / Like coming to the research centre monthly for social reasons / Other: Xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx / Chose not to answer

Programmers Note: Please capture multiple responses, separated with a ';'

Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.6
Participant Questionnaire – Part A (Month 1, 2 and 3)
Safety Population

Centre Participant ID	Visit Date	Visit	Q4	Q5
Centre XX				
XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Knows about the study and the ring / Only knows that I am in a study / Only knows that I am wearing a ring / Doesn't know about the study or the ring / Don't know / Chose not to answer	Good as is / Hard to understand / Needs more information: Xxxxxxxxxxxxxxxxxxx / Needs to be changed: Xxxxxxxxxxxxxxxxxxx / Did not read the instruction sheet / Can't remember the sheet / Chose not to answer

Programmers Note: Please capture multiple responses, separated with a ';'

Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.7
Participant Questionnaire – Part B (Month 2 and 3 Only)
Safety Population

Question No.	Question
1	Has your ring been removed/expelled since your last scheduled visit?
2	What was the reason the ring was removed/expelled since the last scheduled visit?
3	When the ring was removed/expelled did you clean the ring before reinsertion?
4	What did you use to clean the ring when it was removed or expelled?
5	For those participants who removed their ring: Thinking back since your last scheduled visit, was it easy or difficult to remove your ring?
6	Thinking back since your last scheduled visit, when you inserted a new ring, was it easy or difficult?
7	At each regularly scheduled visit, you gave a sample of blood and vaginal fluids. Please tell me what your preferences are.
8	Below is a list of things that some women may like about participating in this study (DREAM). Please order these, where 1 means you liked it the most and 5 means you liked it the least.
9	I'm going to read a list of things that some women have experienced during other study/studies. Please tell me if you have experienced any of these things in this study (DREAM).
9.a	Length of time spent at the research centre for the study visits was too long. If Yes, specify how long.
9.b	Transport to the research centre for scheduled visits was a problem. If Yes, specify.
9.c	I was treated well when coming to the research centre for regular visits.
9.d	If partner knows about participation: My partner id happy about my participation in the study.
9.e	My neighbors, family, or friends know about my participation in this study. If yes, specify if neighbor/friends/family.
9.f	If neighbor, friends, or family knows about participation (see above): My neighbors, family, or friends (as above) are happy about my participation in this study.
9.g	Other
10	If you were not in a study, would you prefer to come to the health care clinic/provider for new rings each month, or every three months?
11	If you were not in a study, would you prefer to come to the health care clinic/provider for an HIV test each month, or every three months?

Listing 16.2.5.7
Participant Questionnaire – Part B (Month 2 and 3 Only)
Safety Population

Centre Participant ID	Visit Date	Visit	Q1	Q2	Q3	Q4
Centre XX						
XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Yes / No / Chose not to answer	Removed: Uncomfortable/painful / Removed: Cleaning / Removed: Menses / Removed: Real/perceived side effects: Xxxxxxxxxxx / Removed: Partner request / Removed: Sex / Removed: Keep from partner / Accident: Xxxxxxxxxxxxxx / Other: Xxxxxxxxxxxxx / Chose not to answer	Yes / No / Chose not to answer	Water only / Body wash soap only / Water and body wash soap / Disinfectant: Xxxxxxxxxx / Herbal product: Xxxxxxxxxx / Traditional medicine: Xxxxxxx / Bubble bath: Xxxxxxxxxx / Bath salts: Xxxxxxxxx / Dishwashing liquid: Xxxxxxxxx / Other: Xxxxxxxxxxxxx / Chose not to answer

Programmers Note: Please capture multiple responses, separated with a ';'

Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.7
Participant Questionnaire – Part B (Month 2 and 3 Only)
Safety Population

Centre Participant ID	Visit Date	Visit	Q5	Q6	Q7a: Blood Samples	Q7b: Vaginal Fluid Samples
Centre XX						
XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Easy / Difficult / Bit of both / Neither / N/A / Chose not to answer	Easy / Difficult / Bit of both / Neither / N/A / Chose not to answer	Taken at every visit / Taken less often / N/A / Chose not to answer	Taken at every visit / Taken less often / N/A / Chose not to answer

Programmers Note: Please capture multiple responses, separated with a ';'

Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.7
Participant Questionnaire – Part B (Month 2 and 3 Only)
Safety Population

Centre Participant ID	Visit Date	Visit	Q8: Rank	Q9	Q9a	Q9b	Q9c	Q9d
Centre XX								
XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Regular HIV testing: X / Other health benefits: X / Reimbursement money: X / Meeting other study participants: X / Helping others in future: X / Chose not to answer	Answered / Chose not to answer	Yes: Xxxx / No	Yes: Xxxx / No	Yes / No	Yes / No / N/A

Programmers Note: Please capture multiple responses, separated with a ';'

Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.7
Participant Questionnaire – Part B (Month 2 and 3 Only)
Safety Population

Centre Participant ID	Visit Date	Visit	Q9e	Q9f	Q9g Experience	Q9g	Q10	Q11
Centre XX								
XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Yes: Friends / Yes: Family / Yes: Neighbor / No /	Yes / No / N/A		Yes / No / N/A	Each month / Every 3 months / Don't mind / Depends: Xxxxxxxxxx / Chose not to answer	Each month / Every 3 months / Don't mind / Depends: Xxxxxxxxxx / Chose not to answer

Programmers Note: Please capture multiple responses, separated with a ';'

Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.8
Participant Questionnaire – Part C (Month 1, 2, and 3)
Safety Population

Question No.	Question
1	Do you currently have a main sex partner?
1a	How long has he been your partner?
2	Do you and your main partner currently live together?
3	Have you had any other partners in the past 3 months?
3a	If yes, indicate number.
4	We need to know how often you usually have sex. Think about the past four weeks, which is about one month. Over the past four weeks, how many rounds of vaginal sex did you have?
5	In the past month, how frequently did you use a male condom during vaginal sex?
6	In the past month, how frequently did you use a female condom during vaginal sex?
7	During the last round of vaginal sex you had, did you use a condom?
8	In the past year, have you had anal sex?
8a	If yes, did you use a condom?
9	How worried are you that you might get infected with HIV in the next year?
10	In the past 3 months, have you had any menstrual bleeding or any menstrual spotting?
11	In the past 3 months, what have you used to control or manage the menstrual blood or spotting? Mark all that apply, using numbers for only those that apply - with 1 for the item used most, 2 for next most frequent, and so on until least frequent.
12	Since your last scheduled visit, have you inserted your fingers into your vagina for any reason?
13	What was the reason for inserting your fingers into your vagina?

Listing 16.2.5.8
Participant Questionnaire – Part C (Month 1, 2, and 3)
Safety Population

Centre Participant ID	Visit Date	Visit	Q1	Q1a	Q2	Q3	Q3a	Q4
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Yes / No / Chose not to answer	XXX months / XXX years / Chose not to answer	Yes / No / Chose not to answer	Yes / No / Chose not to answer	XXX / Chose not to answer	XXX / Chose not to answer

Programmers Note: Please capture multiple responses, separated with a ';'

Rank: 1 = Used most frequent; 2 = Used second most frequent; 3 = Frequently used; 4 = Used a little; 5 = Least used
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.8
Participant Questionnaire – Part C (Month 1, 2, and 3)
Safety Population

Centre Participant ID	Visit Date	Visit	Q5	Q6	Q7	Q8	Q8a	Q9
Centre XX								
XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Always / Sometimes / Often / Never / Chose not to answer	Always / Sometimes / Often / Never / Chose not to answer	Yes male condom / Yes female condom No / Chose not to answer	Yes / No / Chose not to answer	Yes / No / Sometimes / Chose not to answer	Very / A little / Not at all / Chose not to answer

Programmers Note: Please capture multiple responses, separated with a ';'

Rank: 1 = Used most frequent; 2 = Used second most frequent; 3 = Frequently used; 4 = Used a little; 5 = Least used
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.8
Participant Questionnaire – Part C (Month 1, 2, and 3)
Safety Population

Centre Participant ID	Visit Date	Visit	Q10	Q11	Q11. No	Q12	Q13
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Yes / No / Chose not to answer	Put inside the vagina: Xxxxxxx / Put inside the underwear/clothing: Xxxxxxx / Tampon / Sanitary pad / Menstrual cup / Water, no soap, inside the vagina / Water, with soap, inside the vagina / Anything else: Xxxxxxxxxxx / Nothing was used / Chose not to answer		Yes / No / Chose not to answer	Check position of ring / Insert/remove ring / Insert menses product / Cleaning / Sexual pleasure / Other: Xxxxxxxxxx / Chose not to answer

Programmers Note: Please capture multiple responses, separated with a ';'

Rank: 1 = Used most frequent; 2 = Used second most frequent; 3 = Frequently used; 4 = Used a little; 5 = Least used
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.9
Participant Questionnaire – 3 Month Follow-Up
Safety Population

Question No.	Question
1	Will you take your extra rings with you today or will you come back to the research centre each month to pick up your new ring?
2	What are your reasons for leaving the rings at the research centre today?
3	Did you have an additional HIV test at the research centre when you returned to collect your ring (in-between the study visits)?
4	Does your main partner know you are in the study and wearing a vaginal ring?
5	The research centre staff showed you how to insert and remove your ring. You were also given an instruction sheet that explains this. Was the sheet helpful, or does it need to be changed?
6	Thinking back since your last visit, was it easy or difficult to remove your ring?
7	Thinking back since your last visit, when you inserted a new ring, was it easy or difficult?
8	You were given a bag(s) to put the used ring in when returning it to the research centre. Please describe your experiences with the bag(s)?
9	For those who took extra rings: Where did you store the unused ring(s) before insertion?
10	For those who took extra rings: You personally stored the unused rings before using them. What was it like storing the unused ring(s)?
11	For those who did not return the used ring to the research centre straight away: Where did you store the used ring(s) after removing it/them?
12	For those who did not return the used ring to the research centre straight away: You stored the used ring before bringing it back to the research centre for your next scheduled visit. What was it like storing the used ring(s)?
13	At each regularly scheduled visit, you gave a sample of blood and vaginal fluids. Please tell me what your preferences are.
14	Below is a list of things that some women may like about participating in this study (DREAM). Please order these, where 1 means you liked it the most, and 5 means you liked it the least.
15	I'm going to read a list of things that some women have experienced during other study/studies. Please tell me if you have experienced any of these things in this study (DREAM).
15a	Length of time spent at the research centre for the study visits was too long. If yes, specify how long.
15b	Length of time spent at the research centre to pick up rings was too long. If yes, specify how long.
15c	Transport to the research centre for scheduled visits was a problem. If yes, specify.
15d	I was treated well when coming to the research centre for regular visits.
15e	I was treated well when I came to the research centre to pick up rings.
15f	Transport to pick up rings was a problem (if applicable). If yes, specify.
15g	If partner knows about participation (see question 4): My partner is happy about my participation in the study.
15h	My neighbors, family, or friends know about my participation in this study. If yes, specify if neighbor/friends/family.
15i	If neighbor, friends, or family knows about participation (see above): My neighbors, family, or friends (as above) are happy about my participation in this study
15j	Other
16	If you were not in a study, would you prefer to come to the health care clinic/provider for new rings each month, or every three months?
17	If you were not in a study, would you prefer to come to the health care clinic/provider for an HIV test each month, or every three months?
18	Do you currently have a main sex partner?
18a	How long has he been your partner?
19	Do you and your main partner currently live together?
20	Have you had any other partners since your last scheduled visit?

Listing 16.2.5.9
Participant Questionnaire – 3 Month Follow-Up
Safety Population

20a	If yes, indicate number.
21	We need to know how often you usually have sex. Think about the past four weeks, which is about one month. Over the past four weeks, how many rounds of vaginal sex did you have?
22	In the past month, how frequently did you use a male condom during vaginal sex?
23	In the past month, how frequently did you use a female condom during vaginal sex?
24	During the last round of vaginal sex you had, did you use a condom?
25	Since your last scheduled visit, have you had anal sex?
26	How worried are you that you might get infected with HIV in the next year?
27	Since your last scheduled visit, have you had any menstrual bleeding or any menstrual spotting?
28	Since your last scheduled visit, what have you used to control or manage the menstrual blood or spotting? Mark all that apply, using numbers for only those that apply - with 1 for the item used most, 2 for next most frequent, and so on until least frequent.
29	Since your last scheduled visit, has your ring been removed/expelled between scheduled removal dates?
30	What was the reason the ring was removed/expelled at this time?
31	When the ring was removed/expelled did you clean the ring before reinsertion?
32	What did you use to clean the ring when it was removed or expelled?
33	Since your last scheduled visit have you inserted your fingers into your vagina for any reason?
34	What was the reason for inserting your fingers into your vagina?

Listing 16.2.5.9
Participant Questionnaire – 3 Month Follow-Up
Safety Population

Centre Participant ID	Visit Date	Visit	Q1	Q2	Q3
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Take them all / Collect monthly from centre / Chose not to answer	Do not want anyone to see the rings / No private place to keep the unused rings / No private place to keep the used rings / No appropriate storage place to keep rings / No private place to insert the rings / Worried I might lose the ring(s) / I might forget to insert the new ring / Like coming to the centre for monthly HIV tests / Like coming to the centre monthly for social reasons / Other: Xxxxxxxxxxxxxxx / Chose not to answer	Yes / No / N/A / Chose not to answer

Programmers Note: Please capture multiple responses, separated with a ';'

Rank: 1 = Liked the most; 2 = Liked second most; 3 = Liked; 4 = Liked a little; 5 = Liked the least
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.9
Participant Questionnaire – 3 Month Follow-Up
Safety Population

Centre Participant ID	Visit Date	Visit	Q4	Q5	Q6
Centre XX					
XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	He knows about the study and the ring / He only knows that I am in a study / He only knows that I am wearing a ring / He doesn't know about the study or the ring / Don't know / Chose not to answer	Good as is / Hard to understand / Needs more information: Xxxxxxxxxxxxxxxx / Needs to be changed: Xxxxxxxxxxxxxxxxxx / Did not read the instruction sheet / Can't remember the sheet / Chose not to answer	Easy / Difficult / Bit of both / Got easier over time / Neither / N/A / Chose not to answer

Programmers Note: Please capture multiple responses, separated with a ';'

Rank: 1 = Liked the most; 2 = Liked second most; 3 = Liked; 4 = Liked a little; 5 = Liked the least
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.9
Participant Questionnaire – 3 Month Follow-Up
Safety Population

Centre Participant ID	Visit Date	Visit	Q7	Q8	Q9
Centre XX					
XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Easy / Difficult / Bit of both / Got easier over time / Neither /	Easy to open and close / Hard to open or close / Was sometimes lost / Used for something else: Xxxxxx / Bag was fine / Did not like keeping the empty bag(s) / Did not like the used ring(s) in the house / Did not like carrying the used ring(s) to the research centre / Someone found the ring bag(s): Xxxxxxx / Did not like the look of the bag: Xxxxxxxx / Difficult to bring the bags back to the clinic: Xxxxxxxxxx / Other: Xxxxxxxxxxx / N/A, did not use the bags / Chose not to answer	Bag/handbag / Shared cupboard/drawer / Personal cupboard/drawer / Locked place / At someone else's house: Xxxxxxx / Other: Xxxxxxxxxxxx / N/A / Chose not to answer

Programmers Note: Please capture multiple responses, separated with a ';'

Rank: 1 = Liked the most; 2 = Liked second most; 3 = Liked; 4 = Liked a little; 5 = Liked the least
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.9
Participant Questionnaire – 3 Month Follow-Up
Safety Population

Centre Participant ID	Visit Date	Visit	Q10	Q11	Q12
Centre XX					
XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	No problems / Worried someone might find it / Forgot where it was stored/lost it / Accidentally threw it away / Did not like it: Xxxxxxxxx / Someone found it and it was a problem: Xxxxxxxxxxx / Someone found it and it was not a problem: Xxxxxxxxxxx / Other: Xxxxxxxxx / N/A / Chose not to answer	Returned used rings / Bag/handbag / Shared cupboard/drawer / Personal cupboard/drawer / Locked place / At someone else's house: Xxxxxxx / Other: Xxxxxxxxxxx / N/A / Chose not to answer	No problems / Worried someone might find it / Forgot where it was stored/lost it / Accidentally threw it away / Did not like it: Xxxxxxxxx / Someone found it and it was a problem: Xxxxxxxxxxx / Someone found it and it was not a problem: Xxxxxxxxxxx / Other: Xxxxxxxxx / N/A / Chose not to answer

Programmers Note: Please capture multiple responses, separated with a ';'

Rank: 1 = Liked the most; 2 = Liked second most; 3 = Liked; 4 = Liked a little; 5 = Liked the least
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.9
Participant Questionnaire – 3 Month Follow-Up
Safety Population

Centre Participant ID	Visit Date	Visit	Q13: Blood Samples	Q13: Vaginal Fluid Samples	Q14: Rank	Q15
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Taken at every visit / Taken less often / N/A / Chose not to answer	Taken at every visit / Taken less often / N/A / Chose not to answer	Regular HIV testing: X / Other health benefits: X / Reimbursement money: X / Meeting other study participants: X / Helping others in future: X / Chose not to answer	Answered / Chose not to answer

Programmers Note: Please capture multiple responses, separated with a ';'

Rank: 1 = Liked the most; 2 = Liked second most; 3 = Liked; 4 = Liked a little; 5 = Liked the least
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.9
Participant Questionnaire – 3 Month Follow-Up
Safety Population

Centre Participant ID	Visit Date	Visit	Q15a	Q15b	Q15c	Q15d	Q15e	Q15f	Q15g	Q15h	Q15i
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Yes: Xxxx / No	Yes: Xxxx / No / N/A	Yes: Xxxx / No	Yes / No /	Yes / No / N/A	Yes: Xxxx / No / N/A	Yes / No / N/A	Yes: Friends / Yes: Family / Yes: Neighbor / No /	Yes / No / N/A

Programmers Note: Please capture multiple responses, separated with a ';'

Rank: 1 = Liked the most; 2 = Liked second most; 3 = Liked; 4 = Liked a little; 5 = Liked the least
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.9
Participant Questionnaire – 3 Month Follow-Up
Safety Population

Centre Participant ID	Visit Date	Visit	Q15j Experience	Q15j	Q16	Q17	Q18	Q18a
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit		Yes / No / N/A	Each month / Every 3 months / Don't mind / Depends: Xxxxxxxxxx / Chose not to answer	Each month / Every 3 months / Don't mind / Depends: Xxxxxxxxxx / Chose not to answer	Yes / No / Chose not to answer	XXX months / XXX years / Chose not to answer

Programmers Note: Please capture multiple responses, separated with a ';'

Rank: 1 = Liked the most; 2 = Liked second most; 3 = Liked; 4 = Liked a little; 5 = Liked the least
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.9
Participant Questionnaire – 3 Month Follow-Up
Safety Population

Centre Participant ID	Visit Date	Visit	Q19	Q20	Q20a	Q21	Q22	Q23	Q24
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Yes / No / Chose not to answer	Yes / No / Chose not to answer	XXX / Chose not to answer	XXX / Chose not to answer	Always / Sometimes / Often / Never / Chose not to answer	Always / Sometimes / Often / Never / Chose not to answer	Yes male condom / Yes female condom / No / Chose not to answer

Programmers Note: Please capture multiple responses, separated with a ';'

Rank: 1 = Liked the most; 2 = Liked second most; 3 = Liked; 4 = Liked a little; 5 = Liked the least
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.9
Participant Questionnaire – 3 Month Follow-Up
Safety Population

Centre Participant ID	Visit Date	Visit	Q25	Q25a	Q26	Q27	Q28	Q28 No.
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Yes / No / Chose not to answer	Yes / No / Sometimes	Very / A little / Not at all / Chose not answer	Yes / No / Chose not to answer	Put inside the vagina: Xxxxxxx / Put inside the underwear/clothing: Xxxxxxx / Tampon / Sanitary pad / Menstrual cup / Water, no soap, inside the vagina / Water, with soap, inside the vagina / Anything else: Xxxxxxxxxxx / Nothing was used / Chose not to answer	

Programmers Note: Please capture multiple responses, separated with a ';'

Rank: 1 = Liked the most; 2 = Liked second most; 3 = Liked; 4 = Liked a little; 5 = Liked the least
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.9
Participant Questionnaire – 3 Month Follow-Up
Safety Population

Centre Participant ID	Visit Date	Visit	Q29	Q30	Q31	Q32
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Yes / No / Chose not to answer	Removed: Uncomfortable/painful / Removed: Cleaning / Removed: Menses / Removed: Real/perceived side effects: Xxxxxxxxxxxxx / Removed: Partner request / Removed: Sex / Removed: Keep from partner / Accident: Xxxxxxxxxxxxxx / Other: Xxxxxxxxxxxxx / Chose not to answer	Yes / No / Chose not to answer	Water only / Body wash soap only / Water and body wash soap / Disinfectant: Xxxxxxxxxx / Herbal product: Xxxxxxxxxx / Traditional medicine: Xxxxxxx / Bubble bath: Xxxxxxxxxxx / Bath salts: Xxxxxxxxx / Dishwashing liquid: Xxxxxxxxx / Other: Xxxxxxxxxxxxx / Chose not to answer

Programmers Note: Please capture multiple responses, separated with a ';'

Rank: 1 = Liked the most; 2 = Liked second most; 3 = Liked; 4 = Liked a little; 5 = Liked the least
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.9
Participant Questionnaire – 3 Month Follow-Up
Safety Population

Centre Participant ID	Visit Date	Visit	Q33	Q34
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Yes / No / Chose not to answer	Check position of ring / Insert/remove ring / Insert menses product / Cleaning / Other: Xxxxxxxxxx / Sexual pleasure / Chose not to answer

Programmers Note: Please capture multiple responses, separated with a ';'

Rank: 1 = Liked the most; 2 = Liked second most; 3 = Liked; 4 = Liked a little; 5 = Liked the least
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.10
Participant Questionnaire – Last Product Use Visit
Safety Population

Question No.	Question
1	When you were doing your three monthly visits, did you take your extra rings with you or did you come back to the research centre each month to pick up your new ring?
1a	If sometimes took them, sometimes left them, did you: Initially leave it at the centre then later start taking it / Initially take it then start leaving it at the centre / It varied / Chose not to answer
2	What were your reasons for leaving the rings at the research centre?
3	Did your main partner know you were in the study and wearing a vaginal ring?
4	The research centre staff showed you how to insert and remove your ring. You were also given an instruction sheet that explains this. Was the sheet helpful, or does it need to be changed?
5	Thinking back over the study, when you removed your ring, was it easy or difficult?
6	Thinking back, when you inserted your ring, was it easy or difficult?
7	You were given a bag(s) to put the used ring in when returning it to the research centre. Please describe your experiences with the bag(s)?
8	For those who took extra rings: Over the duration of the study, Where did you store the unused ring(s) before insertion?
9	For those who took extra rings: You personally stored the unused rings before using them. What was it like storing the unused ring(s)?
10	For those who did not return the used ring to the research centre straight away: During the course of the study where did you store the used ring(s) after removing it/them?
11	For those who did not return the used ring to the research centre straight away: During the course of the study you stored the used ring before bringing it back to the research centre for your next scheduled visit. What was it like storing the used ring(s)?
12	At each regularly scheduled visit, you gave a sample of blood and vaginal fluids. Please tell me what your preferences are.
13	Below is a list of things that some women may like about participating in this study (DREAM). Please order these, where 1 means you liked it the most, and 5 means you liked it the least.
14	I'm going to read a list of things that some women have experienced during other study/studies. Please tell me if you have experienced any of these things at any time in this study (DREAM).
14a	In general, the length of time spent at the research centre for the study visits was too long. If yes, specify how long.
14b	In general, the length of time spent at the research centre to pick up rings was too long. If yes, specify how long.
14c	Transport to the research centre for scheduled visits was a problem. If yes, specify.
14d	I was treated well when coming to the research centre for regular visits.
14e	I was treated well when I came to the research centre to pick up rings.
14f	Transport to pick up rings was a problem (if applicable). If yes, specify.
14g	If partner knows about participation (see question 3): My partner is happy about my participation in the study.
14h	My neighbors, family, or friends know about my participation in this study. If yes, specify if neighbor/friends/family.

Listing 16.2.5.10
Participant Questionnaire – Last Product Use Visit
Safety Population

14i	If neighbor, friends, or family knows about participation (see above): My neighbors, family, or friends (as above) are happy about my participation in this study.
14j	Other, specify
15	Please tell us how much you like/do not like participating in this study.
16	If you were not in a study, would you prefer to come to the health care clinic/provider for new rings each month, or every three months?
17	If you were not in a study, would you prefer to come to the health care clinic/provider for an HIV test each month, or every three months?
18	Do you currently have a main sex partner?
18a	How long has he been your partner?
19	Do you and your main partner currently live together?
20	Have you had any other partners since your last scheduled visit?
20a	If yes, indicate number.
21	We need to know how often you usually have sex. Think about the past four weeks, which is about one month. Over the past four weeks, how many rounds of vaginal sex did you have?
22	In the past month, how frequently did you use a male condom during vaginal sex?
23	In the past month, how frequently did you use a female condom during vaginal sex?
24	During the last round of vaginal sex you had, did you use a condom?
25	Since your last scheduled visit, have you had anal sex?
25a	If yes, did you use a condom?
26	Since your last scheduled visit, have you had any menstrual bleeding or any menstrual spotting?
27	Since your last scheduled visit, what have you used to control or manage the menstrual blood or spotting? Mark all that apply, using numbers for only those that apply - with 1 for the item used most, 2 for next most frequent, and so on until least frequent.
28	Since your last scheduled visit, has your ring been removed/expelled between scheduled removal dates?
29	What was the reason the ring was removed/expelled at this time?
30	When the ring was removed/expelled did you clean the ring before reinsertion?
31	What did you use to clean the ring when it was removed or expelled?
32	How worried are you that you might get infected with HIV in the next year?
33	Since your last scheduled visit have you inserted your fingers into your vagina for any reason?
34	What was the reason for inserting your fingers into your vagina?
35	When you first joined the study you were told that we will do tests to see if a woman has been wearing her ring. If a woman was not able to wear her ring as she is meant to, she was not able to continue to participate in the study. The following tests could be used. Do you think these are good ways to check and make sure women are using the rings they are given?
35a	Test blood to see how much medicine is in the blood.
35b	Test used ring to see how much medicine is still in the ring.
35c	Ask the woman if she has been using the ring.
35d	Other, specify.
36	Sometimes women in microbicide studies can't/don't always keep their rings inserted. Do you think most women would be more likely to use their rings properly. if they knew the blood tests or used rings would show staff who was using the ring as intended and who was not?

Listing 16.2.5.10
Participant Questionnaire – Last Product Use Visit
Safety Population

37	It may be hard for women to use the ring all the time without taking it out. Do you think it is possible for women to use the ring as requested (i.e, without removing it)?
38	What do you think are the most likely reason(s) for a woman to take out her ring?
39	Please say whether you strongly agree, agree somewhat or disagree with the following statements below:
39a	All women can use the ring without taking it out.
39b	Women would need a break from using the ring every few months.
40	Do you think women in your community would want to use this ring if it were available?
41	If the ring is made available to the public, where do you think most women would want to get it from?
42	If the ring is made available to the public, how much would you be prepared to pay for it?
43	If the ring is made available to the public, where do you think it should be marketed/advertised?

Listing 16.2.5.10
Participant Questionnaire – Last Product Use Visit
Safety Population

Centre Participant ID	Visit Date	Visit	Q1	Q1a	Q2
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Always took it / Always left it at the centre to collect monthly / Sometimes took it sometimes left it at the centre / Chose not to answer	Initially leave it at the centre then later start taking it / Initially take it then start leaving it at the centre / It varied: Xxxxxxxxxxxxxxx / Chose not to answer	Did not want anyone to see the rings / Did not have a private place to keep the unused rings / Did not have a private place to keep the used rings / Did not have an appropriate storage place to keep the rings / Did not have a private place to insert the rings / Worried I might lose the ring(s) / Felt I might forget to insert the new ring if I didn't come each month / Liked coming to the centre for HIV tests each month / Liked coming to the research centre monthly for social reasons / Other: Xxxxxxxxxx / Chose not to answer

Programmers Note: Please capture multiple responses, separated with a ';'

LPUV = Last product use visit
Rank: 1 = Liked the most; 2 = Liked second most; 3 = Liked; 4 = Liked a little; 5 = Liked the least
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.10
Participant Questionnaire – Last Product Use Visit
Safety Population

Centre Participant ID	Visit Date	Visit	Q3	Q4	Q5
Centre XX					
XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	He knows about the study and the ring / He only knows that I am in a study / He only knows that I am wearing a ring / He doesn't know about the study or the ring / Don't know / Chose not to answer	Good as is / Hard to understand / Needs more information: Xxxxxxxxxxxxxx / Needs to be changed: Xxxxxxxxxxxxxxxxx / Did not read the instruction sheet / Can't remember the sheet / Chose not to answer	Easy / Difficult / Bit of both / Neither / Got easier over time / Neither / Chose not to answer

Programmers Note: Please capture multiple responses, separated with a ';'

LPUV = Last product use visit
Rank: 1 = Liked the most; 2 = Liked second most; 3 = Liked; 4 = Liked a little; 5 = Liked the least
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.10
Participant Questionnaire – Last Product Use Visit
Safety Population

Centre Participant ID	Visit Date	Visit	Q6	Q7	Q8
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Easy / Difficult / Bit of both / Neither / Got easier over time / Neither / Chose not to answer	Easy to open and close / Hard to open or close / Was sometimes lost / Used for something else: Xxxxxx / Bag was fine / Did not like keeping the empty bag(s) / Did not like the used ring(s) in the house / Did not like carrying the used ring(s) to the research centre / Someone found the ring bag(s): Xxxxxxx / Did not like the look of the bag: Xxxxxxxx / Difficult to bring the bags back to the clinic: Xxxxxxxxxx / Other: Xxxxxxxxxxx / N/A, did not use the bags / Chose not to answer	Bag/handbag / Shared cupboard/drawer / Personal cupboard/drawer / Locked place / At someone else's house: Xxxxxxx / Other: Xxxxxxxxxxxx / N/A, did not ever take rings / Chose not to answer

Programmers Note: Please capture multiple responses, separated with a ';'

LPUV = Last product use visit
Rank: 1 = Liked the most; 2 = Liked second most; 3 = Liked; 4 = Liked a little; 5 = Liked the least
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.10
Participant Questionnaire – Last Product Use Visit
Safety Population

Centre Participant ID	Visit Date	Visit	Q9	Q10	Q11
Centre XX					
XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	No problems / Worried someone might find it / Forgot where it was sorted/lost it / Accidentally threw it away / Did not like it: Xxxxxxxxx / Someone found it and it was a problem: Xxxxxxxxxxx / Someone found it and it was not a problem: Xxxxxxxxxxx / Other: Xxxxxxxxx / N/A, did not ever take extra rings / Chose not to answer	Returned used rings / Bag/handbag / Shared cupboard/drawer / Personal cupboard/drawer / Locked place / At someone else's house: Xxxxxxx / Other: Xxxxxxxxxxx / N/A, did not store extra rings / Chose not to answer	No problems / Worried someone might find it / Forgot where it was sorted/lost it / Accidentally threw it away / Did not like it: Xxxxxxxxx / Someone found it and it was a problem: Xxxxxxxxxxx / Someone found it and it was not a problem: Xxxxxxxxxxx / Other: Xxxxxxxxx / N/A, did not have/store extra rings / Chose not to answer

Programmers Note: Please capture multiple responses, separated with a ';'

LPUV = Last product use visit
Rank: 1 = Liked the most; 2 = Liked second most; 3 = Liked; 4 = Liked a little; 5 = Liked the least
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.10
Participant Questionnaire – Last Product Use Visit
Safety Population

Centre Participant ID	Visit Date	Visit	Q12: Blood Samples	Q12: Vaginal Fluid Sample	Q13: Rank	Q14	Q14a
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Taken at every visit / Taken less often / N/A / Chose not to answer	Taken at every visit / Taken less often / N/A / Chose not to answer	Regular HIV testing: X / Other health benefits: X / Reimbursement money: X / Meeting other participants: X / Chose not to answer	Answered / Chose not to answer	Yes: Xxxx / No

Programmers Note: Please capture multiple responses, separated with a ';'

LPUV = Last product use visit
Rank: 1 = Liked the most; 2 = Liked second most; 3 = Liked; 4 = Liked a little; 5 = Liked the least
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.10
Participant Questionnaire – Last Product Use Visit
Safety Population

Centre Participant ID	Visit Date	Visit	Q14b	Q14c	Q14d	Q14e	Q14f	Q14g	Q14h	Q14i
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Yes: Xxxx / No / N/A	Yes: Xxxx / No	Yes / No /	Yes / No / N/A	Yes: Xxxx / No / N/A	Yes / No / N/A	Yes: Family / Yes: Friends / Yes: Neighbor / No	Yes/ No / N/A

Programmers Note: Please capture multiple responses, separated with a ';'

LPUV = Last product use visit
Rank: 1 = Liked the most; 2 = Liked second most; 3 = Liked; 4 = Liked a little; 5 = Liked the least
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.10
Participant Questionnaire – Last Product Use Visit
Safety Population

Centre Participant ID	Visit Date	Visit	Q14j Experience	Q14j	Q15	Q16	Q17
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Xxxxxxxxxxx	Yes / No / N/A	Don't like it: Xxxxxxxxxxx / It's alright/okay / Really liked it: Xxxxxxxxxxxx / Other: Xxxxxxxxxxxxxxxxx / Chose not to answer	Each month / Every 3 months / Don't mind / Depends: Xxxxxxxxx / Chose not to answer	Each month / Every 3 months / Don't mind / Depends: Xxxxxxxxx / Chose not to answer

LPUV = Last product use visit
Rank: 1 = Liked the most; 2 = Liked second most; 3 = Liked; 4 = Liked a little; 5 = Liked the least
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.10
Participant Questionnaire – Last Product Use Visit
Safety Population

Centre Participant ID	Visit Date	Visit	Q18	Q18a	Q19	Q20	Q20a	Q21	Q22
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Yes / No / Chose not to answer	XXX months / XXX years / Chose not to answer	Yes / No / Chose not to answer	Yes / No / Chose not to answer	XXX / Chose not to answer	XXX / Chose not to answer	Always / Sometimes / Often / Never / Chose not to answer

Programmers Note: Please capture multiple responses, separated with a ';'

LPUV = Last product use visit
Rank: 1 = Liked the most; 2 = Liked second most; 3 = Liked; 4 = Liked a little; 5 = Liked the least
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.10
Participant Questionnaire – Last Product Use Visit
Safety Population

Centre Participant ID	Visit Date	Visit	Q23	Q24	Q25	Q26	Q27
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Always / Sometimes / Often / Never / Chose not to answer	Yes male condom / Yes female condom / No / Chose not to answer	Yes / No / Chose not to answer	Yes / No / Chose not to answer	Put inside the vagina: Xxxxxxx / Put inside the underwear/clothing: Xxxxxxx / Tampon / Sanitary pad / Menstrual cup / Water, no soap, inside the vagina / Water, with soap, inside the vagina / Anything else: Xxxxxxxxxxx / Nothing was used / Chose not to answer

Programmers Note: Please capture multiple responses, separated with a ';'

LPUV = Last product use visit
Rank: 1 = Liked the most; 2 = Liked second most; 3 = Liked; 4 = Liked a little; 5 = Liked the least
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.10
Participant Questionnaire – Last Product Use Visit
Safety Population

Centre Participant ID	Visit Date	Visit	Q27 No.	Q28	Q29	Q30	Q31
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit		Yes / No / Chose not to answer	Removed: Uncomfortable/painful / Removed: Cleaning / Removed: Menses / Removed: Real/perceived side effects: Xxxxxxxxxxxxx / Removed: Partner request / Removed: Sex / Removed: Keep from partner / Accident: Xxxxxxxxxxxxxx / Other: Xxxxxxxxxxxxx / Chose not to answer	Yes / No / Chose not to answer	Water only / Body wash soap only / Water and body wash soap / Disinfectant: Xxxxxxxxxx / Herbal product: Xxxxxxxxxx / Traditional medicine: Xxxxxxx / Bubble bath: Xxxxxxxxxx / Bath salts: Xxxxxxxxx / Dishwashing liquid: Xxxxxxxxx / Other: Xxxxxxxxxxxxx / Chose not to answer

Programmers Note: Please capture multiple responses, separated with a ';'

LPUV = Last product use visit
Rank: 1 = Liked the most; 2 = Liked second most; 3 = Liked; 4 = Liked a little; 5 = Liked the least
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.10
Participant Questionnaire – Last Product Use Visit
Safety Population

Centre Participant ID	Visit Date	Visit	Q32	Q33	Q34	Q35	Q35a	Q35b	Q35c	Q35d Specify
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Very / A little / Not at all	Yes / No / Chose not to answer	Check position of ring / Insert/remove ring / Insert menses product / Cleaning / Sexual pleasure / Other: Xxxxxxxxxx / Chose not to answer	Answered / Not answered	Yes / No	Yes / No	Yes / No	

Programmers Note: Please capture multiple responses, separated with a ';'

LPUV = Last product use visit
Rank: 1 = Liked the most; 2 = Liked second most; 3 = Liked; 4 = Liked a little; 5 = Liked the least
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.10
Participant Questionnaire – Last Product Use Visit
Safety Population

Centre Participant ID	Visit Date	Visit	Q35d	Q36	Q37	Q38
Centre XX						
XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Yes / No	Yes / No: Xxxxxxxxxx / Don't know: Xxxxxxxxx / Chose not to answer	Yes / No: Xxxxxxxxxx / Don't know: Xxxxxxxxx / Chose not to answer	Partner request / Fear of partner feeling it / Influence of others: Xxxxxxxxx / Break from having the ring inside / Mense / Side effects / Discomfort/pain / Belief that ring doesn't work / Chose not to answer

Programmers Note: Please capture multiple responses, separated with a ';'

LPUV = Last product use visit
Rank: 1 = Liked the most; 2 = Liked second most; 3 = Liked; 4 = Liked a little; 5 = Liked the least
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.10
Participant Questionnaire – Last Product Use Visit
Safety Population

Centre Participant ID	Visit Date	Visit	Q39a	Q39b	Q40	Q41
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Strongly agree / Somewhat agree / Strongly disagree / Chose not to answer /	Strongly agree / Somewhat agree / Strongly disagree / Chose not to answer	Yes / No: Xxxxxxxxxx / Chose not to answer	Clinic / Pharmacy / Private doctor / Other: Xxxxxx / Wouldn't want to wear it / Chose not to answer

Programmers Note: Please capture multiple responses, separated with a ';'

LPUV = Last product use visit
Rank: 1 = Liked the most; 2 = Liked second most; 3 = Liked; 4 = Liked a little; 5 = Liked the least
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.10
Participant Questionnaire – Last Product Use Visit
Safety Population

Centre Participant ID	Visit Date	Visit	Q42	Q43
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Free / Would pay: ZARXXXX / Would pay: UShXXXX / Chose not to answer	Qualified healthcare providers / Local clinic/hospital notice boards / Pamphlets in clinics only / Pamphlets in pharmacies/private doctor / Pamphlets in public areas: Xxxxxxxxxxxxx / Television and/or radio / Billboards / Other: Xxxxxxxxx / Chose not to answer

Programmers Note: Please capture multiple responses, separated with a ';'

LPUV = Last product use visit
Rank: 1 = Liked the most; 2 = Liked second most; 3 = Liked; 4 = Liked a little; 5 = Liked the least
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.11
Feasibility of a 3-Monthly Clinical Follow-Up Schedule
Safety Population

Participant Questionnaire	Question No.	Question
Part A	1	As per investigator decision, are you coming to the research centre next month or in three months for your next visit?
	2	Will you take your extra ring with you today or will you come back to the research centre each month to pick up your new ring?
	3	What are your reasons for leaving the rings at the research centre today?
Part B	10	If you were not in a study, would you prefer to come to the health care clinic / provider for new rings each month, or every three months?
	11	If you were not in a study, would you prefer to come to the health care clinic / provider for an HIV test each month, or every three months?
3 Month Follow-up	1	Will you take your extra rings with you today or will you come back to the research centre each month to pick up your new ring?
	2	What are your reasons for leaving the rings at the research centre today?
	16	If you were not in a study, would you prefer to come to the health care clinic / provider for new rings each month, or every three months?
	17	If you were not in a study, would you prefer to come to the health care clinic / provider for an HIV test each month, or every three months?
LPUV	1	When you were doing your three monthly visits, did you take your extra rings with you or did you come back to the research centre each month to pick up your new ring?
	1a	If sometimes took them, sometimes left them, did you: Initially leave them at the research centre then later start taking them / Initially take them, then start leaving them at the research centre / It varied / Chose not to answer
	2	What were your reasons for leaving the rings at the research centre?
	16	If you were not in a study, would you prefer to come to the health care clinic / provider for new rings each month, or every three months?
	17	If you were not in a study, would you prefer to come to the health care clinic / provider for an HIV test each month, or every three months?

Listing 16.2.5.11
Feasibility of a 3-Monthly Clinical Follow-Up Schedule
Safety Population

			Part A (Month 1, 2 and 3)		
Centre Participant ID	Visit Date	Visit	Q1	Q2	Q3
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Next month / In three months	Will take them all / Will leave them at the research centre to collect monthly / Chose not to answer	Do not want anyone to see rings / Do not have a private place to keep unused rings at home / Do not have a private place to keep the used rings at home / Do not have an appropriate storage place to keep the rings (used and unused) at home / Do not have a private place to insert the rings at home / Worried I might lose the ring(s) / Feel I might forget to insert the new ring if I don't come each month / Like coming to the research centre for HIV tests each month / Like coming to the research centre monthly for social reasons / Other: Xxxxxxxxxxxxxxx / Chose not to answer

Programmers Note: Please capture multiple responses, separated with a ';'

LPUV = Last product use visit
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.11
Feasibility of a 3-Monthly Clinical Follow-Up Schedule
Safety Population

			Part B (Month 2 and 3 Only)		3 Month Follow-up
Centre Participant ID	Visit Date	Visit	Q10	Q11	Q1
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Each month / Every three months / Don't mind / Depends (e.g. if working): Xxxxxxxxxxxxxxxxxx / Chose not to answer	Each month / Every three months / Don't mind / Depends (e.g. if working): Xxxxxxxxxxxxxxxxxx / Chose not to answer	Will take them all / Will leave them at the research centre to collect monthly / Chose not to answer

Programmers Note: Please capture multiple responses, separated with a ';'

LPUV = Last product use visit
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.11
Feasibility of a 3-Monthly Clinical Follow-Up Schedule
Safety Population

Centre Participant ID	Visit Date	Visit	3 Month Follow-up Q2	Q16	Q17
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Do not want anyone to see rings / Do not have a private place to keep unused rings at home / Do not have a private place to keep the used rings at home / Do not have an appropriate storage place to keep the rings (used and unused) at home / Do not have a private place to insert the rings at home / Worried I might lose the ring(s) / Feel I might forget to insert the new ring if I don't come each month / Like coming to the research centre for HIV tests each month / Like coming to the research centre monthly for social reasons / Other: Xxxxxxxxxxxxxxx / Chose not to answer	Each month / Every three months / Don't mind / Depends (e.g. if working): Xxxxxxxxxxxxxxxxxx / Chose not to answer	Each month / Every three months / Don't mind / Depends (e.g. if working): Xxxxxxxxxxxxxxxxxx / Chose not to answer

Programmers Note: Please capture multiple responses, separated with a ';'

LPUV = Last product use visit
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.11
Feasibility of a 3-Monthly Clinical Follow-Up Schedule
Safety Population

			LPUV	
Centre Participant ID	Visit Date	Visit	Q1	Q1a
Centre XX				
XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Always took them / Always left the research centre to collect monthly / Sometimes took them, sometimes left them at the research centre/ Chose not to answer	Initially leave them at the research centre then later start taking them / Initially take them, then start leaving them at the research centre / It varied: Xxxxxxxxxxxxxxxxxxxxxxxxxxxx / Chose not to answer

Programmers Note: Please capture multiple responses, separated with a ';'

LPUV = Last product use visit
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.11
Feasibility of a 3-Monthly Clinical Follow-Up Schedule
Safety Population

Centre Participant ID	Visit Date	Visit	LPUV Q2	Q16	Q17
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Did not want anyone to see the rings / Did not have a private place to keep the unused rings / Did not have a private place to keep the used rings / Did not have an appropriate storage place to keep the rings (used or unused) at home / Did not have a private place to insert the rings at home / Worried I might lose the ring(s) / Felt I might forget to insert the new ring if I didn't come each month / Liked coming to the research centre monthly for social reasons / Other: Xxxxxxxxxxxxxxxxxxxxxxxxx / Chose not to answer	Each month / Every three months / Don't mind / Depends (e.g. if working): Xxxxxxxxxxxxxxxxxx / Chose not to answer	Each month / Every three months / Don't mind / Depends (e.g. if working): Xxxxxxxxxxxxxxxxxx / Chose not to answer

Programmers Note: Please capture multiple responses, separated with a ';'

LPUV = Last product use visit
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.12
Participant Questionnaire – Vaginal Practices
Safety Population

			External Cleaning/ External Genital Washing				
Centre Participant ID	Visit Date	Visit	Done	Product(s) Used	Product(s) Applied Using	Removed Ring	Reason for Product Use
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Yes / No / Chose not to answer	Water only / Soap only: Xxxxxxx / Soap and water / Disinfectant/detergent: Xxxxxxx / Traditional: Xxxxxxxx / Other: Xxxxxxxx	Cloth / Hands / Other: Xxxxx /	Yes / No	General cleaning/hygiene / Cleaning/hygiene during menses / To clean for sex / To clean after sex / Prepare vagina for sexual pleasure / Improve/enhance sex / Dry/tighten vagina / Heal/treat vagina / Other: Xxxxxxxxxxx / Chose not to answer

Programmers Note: Please capture multiple responses, separated with a ';'

Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.12
Participant Questionnaire – Vaginal Practices
Safety Population

Centre Participant ID	Visit Date	Visit	Internal Cleaning/ Internal Vaginal Cleansing				
			Done	Product(s) Used	Product(s) Applied Using	Removed Ring	Reason for Product Use
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Yes / No / Chose not to answer	Water only / Soap only: Xxxxxxx / Soap and water / Disinfectant/detergent: Xxxxxxx / Traditional: Xxxxxxxx / Gels: Xxxxxxxxxx / Other: Xxxxxxxx	Cloth / Hands / Other: Xxxxx /	Yes / No	General cleaning/hygiene / Cleaning/hygiene during menses / To clean for sex / To clean after sex / Prepare vagina for sexual pleasure / Improve/enhance sex / Dry/tighten vagina / Heal/treat vagina / Other: Xxxxxxxxxxx / Chose not to answer

Programmers Note: Please capture multiple responses, separated with a ';'

Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.12
Participant Questionnaire – Vaginal Practices
Safety Population

Centre Participant ID	Visit Date	Visit	Vaginal Steaming/ Smoking				
			Done	Product(s) Used	Product(s) Applied Using	Removed Ring	Reason for Product Use
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Yes / No / Chose not to answer	Traditional: Xxxxxxxx / Commercial: Xxxxxxxxxx / Other: Xxxxxxxx	Cloth / Hands / Other: Xxxxx /	Yes / No	General cleaning/hygiene / Cleaning/hygiene during menses / To clean for sex / To clean after sex / Prepare vagina for sexual pleasure / Improve/enhance sex / Dry/tighten vagina / Heal/treat vagina / Other: Xxxxxxxxxxx / Chose not to answer

Programmers Note: Please capture multiple responses, separated with a ';'

Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.12
Participant Questionnaire – Vaginal Practices
Safety Population

Centre Participant ID	Visit Date	Visit	Inserted Products Into Vagina Done	Product(s) Used	Product(s) Applied Using	Removed Ring	Reason for Product Use
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Yes / No / Chose not to answer	Tampon / Cloth / Type of paper: Xxxxxxxx / Cotton wool / Snuff, Kuber: Xxxxxxxxxx / Zambuk / Talc / Other commercial: Xxxxxxxxx / Traditional: Xxxxxx / Other: Xxxxxxxxxxxxx	Cloth / Hands / Other: Xxxxx /	Yes / No	General cleaning/hygiene / Cleaning/hygiene during menses / To clean for sex / To clean after sex / Prepare vagina for sexual pleasure / Improve/enhance sex / Dry/tighten vagina / Heal/treat vagina / Other: Xxxxxxxxxxx / Chose not to answer

Programmers Note: Please capture multiple responses, separated with a ';'

Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.12
Participant Questionnaire – Vaginal Practices
Safety Population

Centre Participant ID	Visit Date	Visit	External Application Done	Product(s) Used	Product(s) Applied Using	Removed Ring	Reason for Product Use
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Yes / No / Chose not to answer	Commercial cream: Xxxxxxxx / Talc / Intimate sprays / Traditional: Xxxxxxxx / Other: Xxxxxxxx	Cloth / Hands / Other: Xxxxx /	Yes / No	General cleaning/hygiene / Cleaning/hygiene during menses / To clean for sex / To clean after sex / Prepare vagina for sexual pleasure / Improve/enhance sex / Dry/tighten vagina / Heal/treat vagina / Other: Xxxxxxxxxxx / Chose not to answer

Programmers Note: Please capture multiple responses, separated with a ';'

Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.13
Dapivirine Concentration Sample Collection
Safety Population

Centre Participant ID	Visit Date	Visit	Plasma Sample for Dapivirine Concentration Collected	Vaginal Fluid Sample for Dapivirine Concentration Collected	Wet Tear Test Strip Mass (g)	Dry Tear Test Strip Mass (g)
Centre XX						
XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Yes / No: Xxxxxxxxxxx	Yes / No: Xxxxxxxxxxx	XX.XXXX	XX.XXXX

Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.13
Dapivirine Concentration Sample Collection
Safety Population

Centre Participant ID	Visit Date	Visit	Sample Mass (g)	Comments
Centre XX				
XXXXXXXX	ddMMMyyyy	Screening / Enrollment / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	XX.XXXX	

Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.5.14
Dapivirine Ring Residual Levels (mg) in the Last Three Returned Rings Prior to HIV-1 Seroconversion
m-ITT Population

Participant ID	Day of HIV-1 Seroconversion	Visit	Residual Dapivirine in Ring (mg)	Appearance of Ring	Color of Ring	Average Residual Levels of HIV-Neg. Participants Over the Duration of the Trial	IPM 027 Treatment
XXXXXXXX	XX	Trial Month XX	XX	Appears used: Xxxxxxxx / Appears not used: Xxxxx / Not sure: Xxxxxxxxx	White to off-white cream-colored / Slight yellow to yellow / Tan / Brown / Other color: Xxxxxxxx	XX.X	Dapivirine / Placebo

HIV-1 = Human immunodeficiency virus type 1; RNA = Ribonucleic acid

Listing 16.2.5.15
Dapivirine Concentration in the Last Two Returned Rings Prior to First Positive HIV RNA PCR Test
m-ITT Population

Participant ID	Date of HIV-1 RNA Detection	Day of HIV-1 RNA Detection	Ring No.	Residual Dapivirine in Ring (mg)	Appearance of Ring	Color of Ring	Average Residual Levels of HIV-Neg. Participants Over the Duration of the Trial	IPM 027 Treatment
XXXXXXXX	ddMMMyyyy	XX	XX	XX	Appears used: Xxxxxxxx / Appears not used: Xxxxx / Not sure: Xxxxxxxxx	White to off-white cream-colored / Slight yellow to yellow / Tan / Brown / Other color: Xxxxxxxx	XX	Dapivirine / Placebo

HIV-1 = Human immunodeficiency virus type 1; RNA = Ribonucleic acid

Listing 16.2.7.1
Treatment Emergent Adverse Events
Safety Population

Centre Participant ID	System Organ Class / Preferred Term / AE Term (Verbatim)	Start Date	End Date	Study Day of Start of AE	Duration of AE (Days)	Related to IP	Worsening of Pre-Existing Condition?	Severity Grade	SAE?
Centre XX XXXXXXXX		ddMMMyyyy	ddMMMyyyy / Ongoing	XXX	XX / > XX	Yes / No	Yes / No	1 / 2 / 3 / 4 / 5	Yes / No

Programmers Notes:
- List all CMs captured, separated with a ;
- If AESTDTC and AEENDTC are both known then DURATION = AEENDTC – AESTDTC +1; else if AESTDTC is known and AE is ongoing at trial end then DURATION = "> (Trial Termination Date – AESTDTC+1)"
- Duration of ring removal = Date re-introduced – Date withdrawn+1
- Concatenate SOC, PT and AE Term separated by '/'

AE = Adverse event; CM = Concomitant medication; IP = Investigational product; SAE = Serious adverse event; SPL = Surgical intervention/procedure log
Severity grade: 1 = Mild; 2 = Moderate; 3 = Severe; 4 = Potentially life-threatening; 5 = Death
System organ class and preferred term were coded using MedDRA (Version 19.0)
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.7.1
Treatment Emergent Adverse Events
Safety Population

Centre Participant ID	System Organ Class / Preferred Term / AE Term (Verbatim)	IPM 027 Treatment	Action Taken with IP	Date IP Withdrawn	Duration of Ring Removal (Days)	Other Action Taken: CM Name	Procedures Performed / SPL Page No.
Centre XX XXXXXXXX		Dapivirine / Placebo	Dose not changed / Drug interrupted / Drug withdrawn / Not applicable	ddMMMyyyy	XX	None / Treatment medication: Xxxxxx / Non-drug therapy / Other: Xxxxxxxxx	Yes: XX / No

Programmers Notes:
- List all CMs captured, separated with a ;
- If AESTDTC and AEENDTC are both known then DURATION = AEENDTC – AESTDTC +1; else if AESTDTC is known and AE is ongoing at trial end then DURATION = "> (Trial Termination Date – AESTDTC+1)"
- Duration of ring removal = Date re-introduced – Date withdrawn+1
- Concatenate SOC, PT and AE Term separated by '/'

AE = Adverse event; CM = Concomitant medication; IP = Investigational product; SAE = Serious adverse event; SPL = Surgical intervention/procedure log
Severity grade: 1 = Mild; 2 = Moderate; 3 = Severe; 4 = Potentially life-threatening; 5 = Death
System organ class and preferred term were coded using MedDRA (Version 19.0)
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.7.1
Treatment Emergent Adverse Events
Safety Population

Centre Participant ID	System Organ Class / Preferred Term / AE Term (Verbatim)	Outcome	Comments
Centre XX			
XXXXXXXX		Fatal / Unknown / Not recovered/not resolved / Recovering/resolving / Recovered/resolved / Recovered/resolved with sequelae: Xxxxxxxxxxxxxxxxx	

Programmers Notes:
- List all CMs captured, separated with a ;
- If AESTDTC and AEENDTC are both known then DURATION = AEENDTC – AESTDTC +1; else if AESTDTC is known and AE is ongoing at trial end then DURATION = "> (Trial Termination Date – AESTDTC+1)"
- Duration of ring removal = Date re-introduced – Date withdrawn+1
- Concatenate SOC, PT and AE Term separated by '/'

AE = Adverse event; CM = Concomitant medication; IP = Investigational product; SAE = Serious adverse event SPL = Surgical intervention/procedure log
Severity grade: 1 = Mild; 2 = Moderate; 3 = Severe; 4 = Potentially life-threatening; 5 = Death
System organ class and preferred term were coded using MedDRA (Version 19.0)
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.7.2
Product-Related Treatment Emergent Adverse Events
Safety Population

Centre Participant ID	System Organ Class / Preferred Term / AE Term (Verbatim)	Start Date	End Date	Study Day of Start of AE	Duration of AE (Days)	Severity Grade	SAE?	IPM 027 Treatment
Centre XX								
XXXXXXXX		ddMMMyyyy	ddMMMyyyy / Ongoing	XXX	XX / > XX	1 / 2 / 3 / 4 / 5	Yes / No	Dapivirine / Placebo

Programmers Notes:
- If AESTDTC and AEENDTC are both known then DURATION = AEENDTC – AESTDTC +1; else if AESTDTC is known and AE is ongoing at trial end then DURATION = "> (Trial Termination Date – AESTDTC+1)"
- Duration of ring removal = Date re-introduced – Date withdrawn+1
- Concatenate SOC, PT and AE Term separated by '/'

AE = Adverse event; IP = Investigational product; SAE = Serious adverse event
Severity grade: 1 = Mild; 2 = Moderate; 3 = Severe; 4 = Potentially life-threatening; 5 = Death
System organ class and preferred term were coded using MedDRA (Version 19.0)
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.7.2
Product-Related Treatment Emergent Adverse Events
Safety Population

Centre Participant ID	System Organ Class / Preferred Term / AE Term (Verbatim)	Action Taken with IP	Date IP Withdrawn	Duration of Ring Removal (Days)	Other Action Taken	Outcome	Comments
Centre XX XXXXXXXX		Dose not changed / Drug interrupted / Drug withdrawn / Not applicable	ddMMMyyyy	XX	None / Treatment medication: Xxxxxxxxx / Non-drug therapy / Other: Xxxxxxxxx	Fatal / Not recovered/ not resolved / Unknown / Recovering/ resolving / Recovered/ resolved / Recovered/ resolved with sequelae: Xxxxxxxxxxxxx	

Programmers Notes:
- If AESTDTC and AEENDTC are both known then DURATION = AEENDTC – AESTDTC +1; else if AESTDTC is known and AE is ongoing at trial end then DURATION = "> (Trial Termination Date – AESTDTC+1)"
- Duration of ring removal = Date re-introduced – Date withdrawn+1
- Concatenate SOC, PT and AE Term separated by '/'

AE = Adverse event; IP = Investigational product; SAE = Serious adverse event
Severity grade: 1 = Mild; 2 = Moderate; 3 = Severe; 4 = Potentially life-threatening; 5 = Death
System organ class and preferred term were coded using MedDRA (Version 19.0)
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.7.3
Treatment Emergent Adverse Events Leading to Temporary Product Discontinuation
Safety Population

Centre Participant ID	System Organ Class / Preferred Term / AE Term (Verbatim)	Start Date	End Date	Study Day of Start of AE	Duration of AE (Days)	Related to IP	Severity Grade	SAE?
Centre XX XXXXXXXX		ddMMMyyyy	ddMMMyyyy / Ongoing	XXX	XX / > XX	Yes / No	1 / 2 / 3 / 4 / 5	Yes / No

Programmers Notes:
- Source: A participant reported as having an AE with an action taken of "drug interrupted" per the AE CRF
- If AESTDTC and AEENDTC are both known then DURATION = AEENDTC – AESTDTC +1; else if AESTDTC is known and AE is ongoing at trial end then DURATION = "> (Trial Termination Date – AESTDTC+1)"
- Concatenate SOC, PT and AE Term separated by '/'

AE = Adverse event; IP = Investigational product; SAE = Serious adverse event
Severity grade: 1 = Mild; 2 = Moderate; 3 = Severe; 4 = Potentially life-threatening; 5 = Death
System organ class and preferred term were coded using MedDRA (Version 19.0)
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.7.3
Treatment Emergent Adverse Events Leading to Temporary Product Discontinuation
Safety Population

Centre Participant ID	System Organ Class / Preferred Term / AE Term (Verbatim)	IPM 027 Treatment	Action Taken with IP	Duration of Ring Removal (Days)	Other Action Taken	Outcome
Centre XX						
XXXXXXXX		Dapivirine / Placebo	Drug interrupted	XX	None / Treatment medication: Xxxxxxx / Non-drug therapy / Other: Xxxxxxxxx	Fatal / Unknown / Not recovered/not resolved / Recovering/resolving / Recovered/resolved / Recovered/resolved with sequelae: Xxxxxxxxxxxxxxxxx

Programmers Notes:
- Source: A participant reported as having an AE with an action taken of "drug interrupted" per the AE CRF
- If AESTDTC and AEENDTC are both known then DURATION = AEENDTC – AESTDTC +1; else if AESTDTC is known and AE is ongoing at trial end then DURATION = "> (Trial Termination Date – AESTDTC+1)"
- Concatenate SOC, PT and AE Term separated by '/'

AE = Adverse event; IP = Investigational product; SAE = Serious adverse event
Severity grade: 1 = Mild; 2 = Moderate; 3 = Severe; 4 = Potentially life-threatening; 5 = Death
System organ class and preferred term were coded using MedDRA (Version 19.0)
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.7.4
Treatment Emergent Adverse Events Leading to Permanent Product Discontinuation
Safety Population

Centre Participant ID	System Organ Class / Preferred Term / AE Term (Verbatim)	Start Date	End Date	Study Day of Start of AE	Duration of AE (Days)	Related to IP	Severity Grade	SAE?
Centre XX								
XXXXXXXX		ddMMMyyyy	ddMMMyyyy / Ongoing	XXX	XX / > XX	Yes / No	1 / 2 / 3 / 4 / 5	Yes / No

Programmers Notes:
- Source: A participant reported as having an AE with an action taken of "drug withdrawn" per the AE CRF
- If AESTDTC and AEENDTC are both known then DURATION = AEENDTC – AESTDTC +1; else if AESTDTC is known and AE is ongoing at trial end then DURATION = "> (Trial Termination Date – AESTDTC+1)"
- Concatenate SOC, PT and AE Term separated by '/'

AE = Adverse event; IP = Investigational product; SAE = Serious adverse event
Severity grade: 1 = Mild; 2 = Moderate; 3 = Severe; 4 = Potentially life-threatening; 5 = Death
System organ class and preferred term were coded using MedDRA (Version 19.0)
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.7.4
Treatment Emergent Adverse Events Leading to Permanent Product Discontinuation
Safety Population

Centre Participant ID	System Organ Class / Preferred Term / AE Term (Verbatim)	IPM 027 Treatment	Action Taken with IP	Date IP Withdrawn	Other Action Taken	Outcome
Centre XX XXXXXXXX		Dapivirine / Placebo	Drug withdrawn	ddMMMyyyy	None / Treatment medication: Xxxxxxxx / Non-drug therapy / Other: Xxxxxxxxx	Fatal / Unknown / Not recovered/not resolved / Recovering/resolving / Recovered/resolved / Recovered/resolved with sequelae: Xxxxxxxxxxxxxxxxx

Programmers Notes:
- Source: A participant reported as having an AE with an action taken of "drug withdrawn" per the AE CRF
- If AESTDTC and AEENDTC are both known then DURATION = AEENDTC – AESTDTC +1; else if AESTDTC is known and AE is ongoing at trial end then DURATION = "> (Trial Termination Date – AESTDTC+1)"
- Concatenate SOC, PT and AE Term separated by '/'

AE = Adverse event; IP = Investigational product; SAE = Serious adverse event
Severity grade: 1 = Mild; 2 = Moderate; 3 = Severe; 4 = Potentially life-threatening; 5 = Death
System organ class and preferred term were coded using MedDRA (Version 19.0)
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.7.5
Treatment Emergent Adverse Events Leading to Premature Trial Discontinuation
Safety Population

Centre Participant ID	System Organ Class / Preferred Term / AE Term (Verbatim)	Start Date	End Date	Study Day of Start of AE	Duration of AE (Days)	Related to IP	Severity Grade	SAE?
Centre XX								
XXXXXXXX		ddMMMyyyy	ddMMMyyyy / Ongoing	XXX	XX / > XX	Yes / No	1 / 2 / 3 / 4 / 5	Yes / No

Programmers Notes:
- Source: A participant reported as having a Trial Completion status of "Participant discontinued from the trial early" and a reason of "Adverse event/intercurrent illness" per the TC CRF
- If AESTDTC and AEENDTC are both known then DURATION = AEENDTC – AESTDTC +1; else if AESTDTC is known and AE is ongoing at trial end then DURATION = "> (Trial Termination Date – AESTDTC+1)"
- Concatenate SOC, PT and AE Term separated by '/'

AE = Adverse event; IP = Investigational product; SAE = Serious adverse event
Severity grade: 1 = Mild; 2 = Moderate; 3 = Severe; 4 = Potentially life-threatening; 5 = Death
System organ class and preferred term were coded using MedDRA (Version 19.0).
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.7.5
Treatment Emergent Adverse Events Leading to Premature Trial Discontinuation
Safety Population

Centre Participant ID	System Organ Class / Preferred Term / AE Term (Verbatim)	IPM 027 Treatment	Action Taken with IP	Date IP Withdrawn	Other Action Taken	Outcome
Centre XX XXXXXXXX		Dapivirine / Placebo	Dose not changed / Drug interrupted / Drug withdrawn / Not applicable	ddMMMyyyy	None / Treatment medication: Xxxxxxx / Non-drug therapy / Other: Xxxxxxxxx	Fatal / Unknown / Not recovered/not resolved / Recovering/resolving / Recovered/resolved / Recovered/resolved with sequelae: Xxxxxxxxxxxxxxxxx

Programmers Notes:
- Source: A participant reported as having a Trial Completion status of "Participant discontinued from the trial early" and a reason of "Adverse event/intercurrent illness" per the TC CRF
- If AESTDTC and AEENDTC are both known then DURATION = AEENDTC – AESTDTC +1; else if AESTDTC is known and AE is ongoing at trial end then DURATION = "> (Trial Termination Date – AESTDTC+1)"
- Concatenate SOC, PT and AE Term separated by '/'

AE= Adverse event; IP = Investigational product; SAE = Serious adverse event
Severity grade: 1 = Mild; 2 = Moderate; 3 = Severe; 4 = Potentially life-threatening; 5 = Death
System organ class and preferred term were coded using MedDRA (Version 19.0).
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.7.6
Serious Treatment Emergent Adverse Events
Safety Population

Centre Participant ID	System Organ Class / Preferred Term / AE Term (Verbatim)	Start Date	End Date	Study Day of Start of AE	Duration of AE (Days)	Related to IP	Severity Grade	Criteria for Seriousness	IPM 027 Treatment
Centre XX XXXXXXXX		ddMMMyyyy	ddMMMyyyy / Ongoing	XXX	XX / > XX	Yes / No	1 / 2 / 3 / 4 / 5	Death / Life-threatening / Hospitalization/prolonged hospitalization / Significant disability/incapacity / Congenital anomaly/birth defect / Medically significant: Xxxxxxxxxxxxxxx	Dapivirine / Placebo

Programmers Notes:
- List all Criteria for Seriousness, separated with a ;
- If AESTDTC and AEENDTC are both known then DURATION = AEENDTC – AESTDTC +1; else if AESTDTC is known and AE is ongoing at trial end then DURATION = "> (Trial Termination Date – AESTDTC+1)"
- Duration of ring removal = Date re-introduced – Date withdrawn+1
- Concatenate SOC, PT and AE Term separated by '/'

AE = Adverse event; IP = Investigational product; SAE = Serious adverse event
Severity grade: 1 = Mild; 2 = Moderate; 3 = Severe; 4 = Potentially life-threatening; 5 = Death
System organ class and preferred term were coded using MedDRA (Version 19.0).
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.7.6
Serious Treatment Emergent Adverse Events
Safety Population

Centre Participant ID	System Organ Class / Preferred Term / AE Term (Verbatim)	Action Taken with IP	Date IP Withdrawn	Duration of Ring Removal (Days)	Other Action Taken	Outcome
Centre XX XXXXXXXX		Dose not changed / Drug interrupted / Drug withdrawn / Not applicable	ddMMMyyyy	XX	None / Treatment medication: Xxxxxxx / Non-drug therapy / Other: Xxxxxxxxx	Fatal / Not recovered/ not resolved / Unknown / Recovering/ resolving / Recovered/ resolved / Recovered/ resolved with sequelae: Xxxxxxxxxxxxx

Programmers Notes:
- List all Criteria for Seriousness, separated with a ;
- If AESTDTC and AEENDTC are both known then DURATION = AEENDTC – AESTDTC +1; else if AESTDTC is known and AE is ongoing at trial end then DURATION = "> (Trial Termination Date – AESTDTC+1)"
- Duration of ring removal = Date re-introduced – Date withdrawn+1
- Concatenate SOC, PT and AE Term separated by '/'

AE = Adverse event; IP = Investigational product; SAE = Serious adverse event
Severity grade: 1 = Mild; 2 = Moderate; 3 = Severe; 4 = Potentially life-threatening; 5 = Death
System organ class and preferred term were coded using MedDRA (Version 19.0).
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.7.7
Grade 3 or 4 Treatment Emergent Adverse Events
Safety Population

Centre Participant ID	System Organ Class / Preferred Term / AE Term (Verbatim)	Start Date	End Date	Study Day of Start of AE	Duration of AE (Days)	Related to IP	Severity Grade	SAE?	IPM 027 Treatment
Centre XX XXXXXXXX		ddMMMyyyy	ddMMMyyyy / Ongoing	XXX	XX / > XX	Yes / No	3 / 4 /	Yes / No	Dapivirine / Placebo

Programmers Notes:
- If AESTDTC and AEENDTC are both known then DURATION = AEENDTC – AESTDTC +1; else if AESTDTC is known and AE is ongoing at trial end then DURATION = "> (Trial Termination Date – AESTDTC+1)"
- Duration of ring removal = Date re-introduced – Date withdrawn+1
- Concatenate SOC, PT and AE Term separated by '/'

AE = Adverse event; IP = Investigational product; SAE = Serious adverse event
Severity grade: 3 = Severe; 4 = Potentially life-threatening
System organ class and preferred term were coded using MedDRA (Version 19.0)
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.7.7
Grade 3 or 4 Treatment Emergent Adverse Events
Safety Population

Centre Participant ID	System Organ Class / Preferred Term / AE Term (Verbatim)	Action Taken with IP	Date IP Withdrawn	Duration of Ring Removal (Days)	Other Action Taken	Outcome
Centre XX XXXXXXXX		Dose not changed / Drug interrupted / Drug withdrawn / Not applicable	ddMMMyyyy	XX	None / Treatment medication: Xxxxxxx / Non-drug therapy / Other: Xxxxxxxxx	Fatal / Not recovered/ not resolved / Unknown / Recovering/ resolving / Recovered/ resolved / Recovered/ resolved with sequelae: Xxxxxxxxxxxxx

Programmers Notes:
- If AESTDTC and AEENDTC are both known then DURATION = AEENDTC – AESTDTC +1; else if AESTDTC is known and AE is ongoing at trial end then DURATION = "> (Trial Termination Date – AESTDTC+1)"
- Duration of ring removal = Date re-introduced – Date withdrawn+1
- Concatenate SOC, PT and AE Term separated by '/'

AE = Adverse event; IP = Investigational product; SAE = Serious adverse event
Severity grade: 3 = Severe; 4 = Potentially life-threatening
System organ class and preferred term were coded using MedDRA (Version 19.0)
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.7.8
Treatment Emergent Adverse Events Leading to Death
Safety Population

Centre Participant ID	System Organ Class / Preferred Term / AE Term (Verbatim)	Start Date	End Date	Study Day of Start of AE	Duration of AE (Days)	Worsening of Pre-existing Condition	Related to IP	SAE?
Centre XX								
XXXXXXXX		ddMMMyyyy	ddMMMyyyy / Ongoing	XXX	XX / > XX	Yes / No	Yes / No	Yes / No

Programmers Notes:
- If AESTDTC and AEENDTC are both known then DURATION = AEENDTC – AESTDTC +1; else if AESTDTC is known and AE is ongoing at trial end
then DURATION = "> (Trial Termination Date – AESTDTC+1)"
- Duration of ring removal = Date re-introduced – Date withdrawn+1
- Concatenate SOC, PT and AE Term separated by '/'

AE = Adverse event; IP = Investigational product; SAE = Serious adverse event
System organ class and preferred term were coded using MedDRA (Version 19.0)
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.7.8
Treatment Emergent Adverse Events Leading to Death
Safety Population

Centre Participant ID	System Organ Class / Preferred Term / AE Term (Verbatim)	IPM 027 Treatment	Action Taken with IP	Date IP Withdrawn	Other Action Taken
Centre XX					
XXXXXXXX		Dapivirine / Placebo	Dose not changed / Drug interrupted / Drug withdrawn / Not applicable	ddMMMyyyy	None / Treatment medication: Xxxxxxx / Non-drug therapy / Other: Xxxxxxxxx

Programmers Notes:
- If AESTDTC and AEENDTC are both known then DURATION = AEENDTC – AESTDTC +1; else if AESTDTC is known and AE is ongoing at trial end then DURATION = "> (Trial Termination Date – AESTDTC+1)"
- Concatenate SOC, PT and AE Term separated by '/'

AE = Adverse event; IP = Investigational product; SAE = Serious adverse event
System organ class and preferred term were coded using MedDRA (Version 19.0)
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.7.9
Urogenital Treatment Emergent Adverse Events
Safety Population

Centre Participant ID	System Organ Class / Preferred Term / AE Term (Verbatim)	Start Date	End Date	Study Day of Start of AE	Duration of AE (Days)	Related to IP	Severity Grade	SAE?	IPM 027 Treatment
Centre XX XXXXXXXX		ddMMMyyyy	ddMMMyyyy / Ongoing	XXX	XX / > XX	Yes / No	3 / 4 /	Yes / No	Dapivirine / Placebo

Programmers Notes:
- If AESTDTC and AEENDTC are both known then DURATION = AEENDTC – AESTDTC +1; else if AESTDTC is known and AE is ongoing at trial end then DURATION = "> (Trial Termination Date – AESTDTC+1)"
- Duration of ring removal = Date re-introduced – Date withdrawn+1
- Concatenate SOC, PT and AE Term separated by '/'

AE = Adverse event; IP = Investigational product; SAE = Serious adverse event
Severity grade: 3 = Severe; 4 = Potentially life-threatening
System organ class and preferred term were coded using MedDRA (Version 19.0)
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.7.9
Urogenital Treatment Emergent Adverse Events
Safety Population

Centre Participant ID	System Organ Class / Preferred Term / AE Term (Verbatim)	Action Taken with IP	Date IP Withdrawn	Duration of Ring Removal (Days)	Other Action Taken	Outcome
Centre XX XXXXXXXX		Dose not changed / Drug interrupted / Drug withdrawn / Not applicable	ddMMMyyyy	XX	None / Treatment medication: Xxxxxxx / Non-drug therapy / Other: Xxxxxxxxx	Fatal / Not recovered/ not resolved / Unknown / Recovering/ resolving / Recovered/ resolved / Recovered/ resolved with sequelae: Xxxxxxxxxxxxx

Programmers Notes:
- If AESTDTC and AEENDTC are both known then DURATION = AEENDTC – AESTDTC +1; else if AESTDTC is known and AE is ongoing at trial end then DURATION = "> (Trial Termination Date – AESTDTC+1)"
- Duration of ring removal = Date re-introduced – Date withdrawn+1
- Concatenate SOC, PT and AE Term separated by '/'

AE = Adverse event; IP = Investigational product; SAE = Serious adverse event
Severity grade: 3 = Severe; 4 = Potentially life-threatening
System organ class and preferred term were coded using MedDRA (Version 19.0)
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.7.10
Social Harms Reported as Treatment Emergent Adverse Events
Safety Population

Centre Participant ID	System Organ Class / Preferred Term / AE Term (Verbatim)	Start Date	End Date	Study Day of Start of AE	Duration of AE (Days)	Related to IP	Severity Grade	SAE?	IPM 027 Treatment
Centre XX									
XXXXXXXX		ddMMMyyyy	ddMMMyyyy / Ongoing	XXX	XX / > XX	Yes / No	3 / 4 /	Yes / No	Dapivirine / Placebo

Programmers Notes:
- If AESTDTC and AEENDTC are both known then DURATION = AEENDTC – AESTDTC +1; else if AESTDTC is known and AE is ongoing at trial end then DURATION = "> (Trial Termination Date – AESTDTC+1)"
- Duration of ring removal = Date re-introduced – Date withdrawn+1
- Concatenate SOC, PT and AE Term separated by '/'

AE = Adverse event; IP = Investigational product; SAE = Serious adverse event
Severity grade: 3 = Severe; 4 = Potentially life-threatening
System organ class and preferred term were coded using MedDRA (Version 19.0)
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.7.10
Social Harms Reported as Treatment Emergent Adverse Events
Safety Population

Centre Participant ID	System Organ Class / Preferred Term / AE Term (Verbatim)	Action Taken with IP	Date IP Withdrawn	Duration of Ring Removal (Days)	Other Action Taken	Outcome	Related to Trial
Centre XX XXXXXXXX		Dose not changed / Drug interrupted / Drug withdrawn / Not applicable	ddMMMyyyy	XX	None / Treatment medication: Xxxxxxx / Non-drug therapy / Other: Xxxxxxxxx	Fatal / Not recovered/ not resolved / Unknown / Recovering/ resolving / Recovered/ resolved / Recovered/ resolved with sequelae: Xxxxxxxxxxxxx	Yes / No

Programmers Notes:
- If AESTDTC and AEENDTC are both known then DURATION = AEENDTC – AESTDTC +1; else if AESTDTC is known and AE is ongoing at trial end then DURATION = "> (Trial Termination Date – AESTDTC+1)"
- Duration of ring removal = Date re-introduced – Date withdrawn+1
- Concatenate SOC, PT and AE Term separated by '/'

AE = Adverse event; IP = Investigational product; SAE = Serious adverse event
Severity grade: 3 = Severe; 4 = Potentially life-threatening
System organ class and preferred term were coded using MedDRA (Version 19.0)
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.7.11
Congenital Anomalies or Birth Defects
Safety Population

Participant ID	System Organ Class / Preferred Term / AE Term (Verbatim)	Start Date	End Date	Duration of AE (Days)	Worsening of Pre-existing Condition	IPM 027 Treatment	Other Action Taken
Centre XX							
XXXXXXXX		ddMMMyyyy	ddMMMyyyy	XX	Yes / No	Dapivirine / Placebo	None / Treatment medication: Xxxxxxx / Non-drug therapy / Other: Xxxxxxxxx

Programmers Notes:
- If AESTDTC and AEENDTC are both known then DURATION = AEENDTC – AESTDTC +1
- Concatenate SOC, PT and AE Term separated by '/'

AE = Adverse event
System organ class and preferred term were coded using MedDRA (Version 19.0)
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.7.1
Non-Treatment Emergent Adverse Events
Safety Population

Participant ID	System Organ Class / Preferred Term / AE Term (Verbatim)	Start Date	End Date	Duration of AE (Days)	Worsening of Pre-existing Condition	IPM 027 Treatment	Other Action Taken
Centre XX							
XXXXXXXX		ddMMMyyyy	ddMMMyyyy	XX	Yes / No	Dapivirine / Placebo	None / Treatment medication: Xxxxxxx / Non-drug therapy / Other: Xxxxxxxxx

Programmers Notes:
- If AESTDTC and AEENDTC are both known then DURATION = AEENDTC – AESTDTC +1
- Concatenate SOC, PT and AE Term separated by '/'

AE = Adverse event
System organ class and preferred term were coded using MedDRA (Version 19.0)
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.8.1
Haematology Results
Safety Population

Centre Participant ID	Visit	Collection Date	Parameter (Unit)	Result	Reference Range			DAIDS Grade	Clinically Significant	Clinical Assessment
					Lower Limit	Upper Limit	Indicator			
Centre XX XXXXXXXX	Screening / Trial Month XX / Trial Month XX (Unschedulead X) / Exit visit	ddMMMyyyy	Erythrocytes (x10^{12}/L) / Haemoglobin (g/dL) / Haematocrit (L/L) / Haematocrit (%) / Platelets (x10^{9} /L) / Leukocytes (x10^{9} /L) / Neutrophils (abs.) (x10^{9} /L) / Lymphocytes (abs.) (x10^{9} /L) / Monocytes (abs.) (x10^{9} /L) / Eosinophils (abs.) (x10^{9} /L) / Basophils (abs.) (x10^{9} /L) /	XX.XX / Not done	XX	XX	High / Low / Normal	1 / 2 / 3 / 4 / N/A	Yes / No	

AE = Adverse event
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.8.1
Haematology Results
Safety Population

Centre Participant ID	Visit	Collection Date	Parameter (Unit)	Any Findings AEs?	Description of AE	IPM 027 Treatment	Comments
Centre XX XXXXXXXX	Screening / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	ddMMMyyyy	Erythrocytes ($x10^{12}$/L) / Haemoglobin (g/dL) / Haematocrit (L/L) / Haematocrit (%) / Platelets ($x10^9$ /L) / Leukocytes ($x10^9$ /L) / Neutrophils (abs.) ($x10^9$ /L) / Lymphocytes (abs.) ($x10^9$ /L) / Monocytes (abs.) ($x10^9$ /L) / Eosinophils (abs.) ($x10^9$ /L) / Basophils (abs.) ($x10^9$ /L)	Yes / No / N/A		Dapivirine / Placebo	

AE = Adverse event
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.8.2
Biochemistry Results
Safety Population

Centre Participant ID	Visit	Collection Date	Parameter (Unit)	Result	Reference Range			DAIDS Grade	Clinically Significant	Clinical Assessment
					Lower Limit	Upper Limit	Indicator			
Centre XX										
XXXXXXXX	Screening / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	ddMMMyyyy	Creatinine (µmol/L) / ALT (IU/L) / AST (IU/L) / Sodium (mmol/L) / Potassium (mmol/L) / Chloride (mmol/L) / Urea (mmol/L) / Bilirubin (total) (µmol/L) / Alkaline phosphatase (IUL/L) / Calcium (mmol/L) / Phosphate (mmol/L)	XX.XX / Not done	XX	XX	High / Low / Normal	1 / 2 / 3 / 4 / N/A	Yes / No	

AE = Adverse event; ALT = Alanine aminotransferase; AST = Aspartate aminotransferase
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.8.2
Biochemistry Results
Safety Population

Centre Participant ID	Visit	Collection Date	Parameter (Unit)	Any Findings AEs?	Description of AE	IPM 027 Treatment	Comments
Centre XX							
XXXXXXXX	Screening / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	ddMMMyyyy	Creatinine (µmol/L) / ALT (IU/L) / AST (IU/L) / Sodium (mmol/L) / Potassium (mmol/L) / Chloride (mmol/L) / Urea (mmol/L) / Bilirubin (total) (µmol/L) / Alkaline phosphatase (IUL/L) / Calcium (mmol/L) / Phosphate (mmol/L)	Yes / No / N/A		Dapivirine / Placebo	

AE = Adverse event; ALT = Alanine aminotransferase; AST = Aspartate aminotransferase
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.8.3
Urinalysis and Microscopy Results
Safety Population

Centre Participant ID	Collection Date	Visit	Test Done / Clinically Indicated	Category	Parameter	Result	DAIDS Grade	Clinically Significant	Other Clinically Significant Findings
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Yes / No	Urinalysis / Microscopy			1 / 2 / 3 / 4	Yes / No	No / Yes: Xxxxxxxxxxxxxx

AE = Adverse event
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.8.3
Urinalysis and Microscopy Results
Safety Population

Centre Participant ID	Collection Date	Visit	Test Done / Clinically Indicated	Category	Parameter	Clinical Assessment	Any Findings AEs?	Description of AE	IPM 027 Treatment
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Yes / No	Urinalysis / Microscopy			Yes / No / N/A		Dapivirine / Placebo

AE = Adverse event
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.8.4
Abnormal Clinical Laboratory Data
Safety Population

Centre Participant ID	Date of Exam	Visit	Parameter	Sample Type	Result	Abnormal Result Specifics	Clinically Significant	Any Findings AEs?	IPM 027 Treatment
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit			Not examined / Normal / Abnormal / Not Applicable		Yes / No	Yes / No / N/A	Dapivirine / Placebo

Programmers Note: If a subject presents with an abnormal result, include all other relevant test for the subject (i.e. show all results for all visits)

AE = Adverse event
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.8.5
Vital Signs
Safety Population

Centre Participant ID	Date of Exam	Visit	Weight (kg)	Temperature (°C)	Pulse (beats/min)	Respiration Rate (breaths/min)	Blood Pressure (mmHg)
Centre XX							
XXXXXXXX	ddMMMyyyy	Screening / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	XXX / Not done	XX.X / Not done	XXX / Not done	XX / Not done	XXX/XXX / Not done

Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.8.6
Physical Examination
Safety Population

Centre Participant ID	Date of Exam	Visit	Body System or Part	Result	Abnormal Result Specifics	Clinically Significant	Any Findings AEs?
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	General appearance / Gastrointestinal/ Abdomen / Neck / Lymph node / Cardiovascular/ Heart / Respiratory/Lungs / Neurological / Skin / Eyes / Ears, nose, throat / Other: Xxxxxxxxx	Not examined / Normal / Abnormal / Not Applicable		Yes / No	Yes / No / N/A

AE = Adverse event; CRF = Case report form
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.8.6
Physical Examination
Safety Population

Centre Participant ID	Date of Exam	Visit	Body System or Part	Description of AE	IPM 027 Treatment	Comments
Centre XXX						
XXXXXXXX	ddMMMyyyy	Screening / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	General appearance / Gastrointestinal/ Abdomen / Neck Lymph node / Cardiovascular/ Heart / Respiratory/Lungs / Neurological / Skin / Eyes / Ears, nose, throat / Other: Xxxxxxxxx		Dapivirine / Placebo	

AE = Adverse event; CRF = Case report form
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.8.7
Menses Information and Pregnancy Test Results
Safety Population

			Menses Information			Pregnancy Test		
Centre Participant ID	Collection Date	Visit	N/A at Scheduled Visits	First Day of Last Menstrual Period	Changes to Menses from Previous Visit	Urine Test Result	Serum Collection Date	Serum Test Result
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Yes	ddMMMyyyy / N/A	No / N/A / Yes: Xxxxxxxxxxx	Negative / Positive / Not done	ddMMMyyyy / N/A	Negative / Equivocal / positive

Programmers Note: Capture all methods used to estimate date of deliver, separated by ';'

Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.8.7
Menses Information and Pregnancy Test Results
Safety Population

				Pregnancy Report	
Centre Participant ID	Collection Date	Visit	On Contraceptive at Positive Pregnancy Test: Name	Estimated Day of Delivery	Information Used to Estimate Date of Delivery
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Yes: Xxxxxxxxxxx / No	ddMMMyyyy / N/A	Last menstrual period / Initial ultrasound <20 w / Initial ultrasound ≥ 20 w / Physical exam / Other: Xxxxxxxxxxxxxxxx

Programmers Note: Capture all methods used to estimate date of deliver, separated by ';'

Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.8.7
Menses Information and Pregnancy Test Results
Safety Population

Centre Participant ID	Collection Date	Visit	Pregnancy Report	Pregnancy Outcome		
			History of Pregnancy Complications or Fetal/Infant Congenital Anomalies	No. of Pregnancy Outcomes Resulted From Report	Outcome Date	Delivery / Outcome Place
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	No / Yes: Xxxxxxxxxxxxxxxxxx	X	ddMMMyyyy	Home / Hospital / Clinic / Unkown / Other: Xxxxxxxxx

Programmers Note: Capture all methods used to estimate date of deliver, separated by ';'

Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.8.7
Menses Information and Pregnancy Test Results
Safety Population

Centre Participant ID	Collection Date	Visit	Pregnancy Outcome Outcome	Pregnancy Outcome Delivery-Related Complications
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Full term live birth (≥37 weeks): C-section / Full term live birth (≥37 weeks): Standard vaginal / Full term live birth (≥37 weeks): Operative vaginal / Premature term live birth (< 37 weeks): C-section / Premature term live birth (< 37 weeks): Standard vaginal / Premature term live birth (< 37 weeks): Operative vaginal / Stillbirth/intrauterine fetal demise (≥20 weeks) / Spontaneous abortion (< 20 weeks) / Ectopic pregnancy / Therapeutic abortion / Non-therapeutic abortion / Ongoing at trial end / Other: Xxxxxxxxxxxxxxxxxxxx /	None / Intrapartum hemorrhage / Postpartum hemorrhage / Non-reassuring fetal status / Chorioamnionitis / Other: Xxxxxxxxxxxx

Programmers Note: Capture all methods used to estimate date of deliver, separated by ';'

Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.8.7
Menses Information and Pregnancy Test Results
Safety Population

Centre Participant ID	Collection Date	Visit	Pregnancy Outcome Non-Delivery-related Complications	Pregnancy Outcome Congenital Anomalies Indicator
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	None / Hypertensive disorders of pregnancy / Gestational diabetes / Other: Xxxxxxxxxxxxxx	

Programmers Note: Capture all methods used to estimate date of deliver, separated by ';'

Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.8.8
Sexually Transmitted Infections
Safety Population

Centre Participant ID	Collection Date	Visit	Parameter	Result	Blood Present at Collection of Cervico-vaginal Samples	Any Findings AEs?	AE Description
Centre XX							
XXXXXXXX	ddMMMyyyy	Screening / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Trichomonas rapid test / Gonorrhea / Chlamydia / Syphilis RPR screening test / Syphilis RPR titre / Syphilis confirmatory test TPHA/TPPA		Yes / No	Yes / No / N/A	

AE = Adverse event; RPR = Rapid plasma reagin; TPHA = Treponema pallidum haemagglutination test; TPPA = Treponema pallidum particle agglutination assay
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.8.8
Sexually Transmitted Infections
Safety Population

Centre Participant ID	Collection Date	Visit	Parameter	Comments
Centre XX				
XXXXXXXX	ddMMMyyyy	Screening / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Trichomonas rapid test / Gonorrhea / Chlamydia / Syphilis RPR screening test / Syphilis RPR titre / Syphilis confirmatory test TPHA/TPPA	

AE = Adverse event; RPR = Rapid plasma reagin; TPHA = Treponema pallidum haemagglutination test; TPPA = Treponema pallidum particle agglutination assay
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.8.9
HIV-1 Seroconversion
m-ITT Population

Centre IPM 027 Treatment Participant ID	Collection Date	Visit	Seroconversion Timepoint	Category	Parameter	Result
Centre XX Dapivirine/ Placebo XXXXXXXX	ddMMMyyyy	Screening / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	On IP / Prior to IP / After IP	HIV Rapid test / Seroconversion / Seroconversion additional testing / HIV RNA PCR / HIV seroconversion evaluation /	Test 1: Determine / Test 1: Xxxxxxxxxx / Test 2: OraQuick / Test 2: Xxxxxxx / Test 3: UniGold / Test 3: Xxxxxxx / HIV-1 Western Blot / Repeat HIV-1 Western Blot / HIV-2 Western Blot / Reapeat HIV-2 Western Blot / RNA PCR Testing: Confirmed seroconversion / Etc.	Reactive / Non-reactive / Negative / Positive / Indeterminate / < 40 cop/mL / >= 40 cop/mL: XXXX / Xxxxxxxx / Yes / No / N/A / Not done

AE = Adverse event; HIV-1 = Human immunodeficiency virus type 1; IP = Investigational product; IRE = Immediately reportable event; PCR = Polymerase chain reaction; RNA = Ribonucleic acid
[a] Based on Retrospective HIV RNA PCR results
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM); Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.8.9
HIV-1 Seroconversion
m-ITT Population

Centre IPM 027 Treatment Participant ID	Collection Date	Visit	HIV Subtype	Genotype Sample Taken / Analysed / Successful Assessment	Reported as IRE[b]	Contraceptive When Seroconverted: Method and Name	Estimated Point of Infection On IP?[a]
Centre XX Dapivirine/ Placebo XXXXXXXX	ddMMMyyyy	Screening / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit		Yes/Yes/Yes / Yes/Yes/No / Yes/No/No No	Yes / No	Oral: Xxxxxxxxx / Transdermal patch / Long acting injectable Condoms /progestins / Subcutaneous implant / IUD / Surgical sterilization / Other: Xxxxxxxxxx	

AE = Adverse event; HIV-1 = Human immunodeficiency virus type 1; IP = Investigational product; IRE = Immediately reportable event; PCR = Polymerase chain reaction; RNA = Ribonucleic acid
[a] Based on Retrospective HIV RNA PCR results
[b] A positive/reactive HIV rapid test result is reported as an IRE
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.8.9
HIV-1 Seroconversion
m-ITT Population

Centre IPM 027 Treatment Participant ID	Collection Date	Visit	Specifics of Point of Infection	ARV Treatment Initiated	Comments
Centre XX Dapivirine/ Placebo XXXXXXXX	ddMMMyyyy	Screening / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	HIV RNA copies present at enrollment / IP discontinued due to pregnancy / IP removed for an extended period due to AE: Xxxxxxxxx / Ring non-user / Other: Xxxxxxxx	Yes: Xxxxxx / No	

AE = Adverse event; HIV-1 = Human immunodeficiency virus type 1; IP = Investigational product; IRE = Immediately reportable event; PCR = Polymerase chain reaction; RNA = Ribonucleic acid
[a]Based on Retrospective HIV RNA PCR results
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM); Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.8.11
HIV-1 Seroconversion on Investigational Product
Safety Population

IPM 027 Treatment Participant ID	Date of HIV-1 Seroconversion	Date of Last Neg. HIV-1 RNA Result	Date of First HIV-1 Detection	Days between Last Neg. and First HIV-1 RNA Detection	Time to First HIV-1 RNA Detection	Residual Dapivirine in Ring (mg) at First HIV-1 RNA Detection	Appearance of Ring At First HIV-1 RNA Detection	Colour of Ring At First HIV-1 RNA Detection
Dapivirine/ Placebo XXXXXXXX	ddMMMyyyy	ddMMMyyyy	ddMMMyyyy	XXX	XXX	XX.X	Appears used/ Appears not used	Tan / White to off-white/ Etc.

Programmers Note: Please list Mutations as a string ordered by position

HIV-1 = Human immunodeficiency virus type 1; RNA = Ribonucleic acid

Listing 16.2.8.12
Participants with Drug Resistance Mutations
Safety Population

IPM 027 Treatment Participant ID	Date of HIV-1 Seroconversion	Seroconversion Timepoint	Trial Visit	Collection Date	HIV-1 RNA Results (cop/mL)	Associated Drug Resistance Mutations	Days Since HIV-1 Sero-conversion	Days Since HIV-1 RNA Detection
Dapivirine/ Placebo								
XXXXXXXX	ddMMMyyyy	On IP / After IP / Prior to IP	Trial Month XX		XX / Not detected	NNRTI: Xxxxxxx / NTRI: Xxxxxxx / PI Major: Xxxxxx / No mutations	XXX	XXX

Programmers Note: Please list Mutations as a string ordered by position

HIV-1 = Human immunodeficiency virus type 1; NNRTI = Non-nucleoside reverse transcriptase inhibitor; NTRI = Nucleoside reverse transcriptase inhibitor; RNA = Ribonucleic acid
The Stanford University HIV-1 Drug Resistance Database version 8.4 (dated 2017-06-16) was used

Listing 16.2.8.13
HIV-1 NNRTI Drug Susceptibility: Stanford Interpretation of Genotype
Safety Population

IPM 027 Treatment Participant ID	Seroconversion Timepoint	Sample Date	Visit	Date of HIV-1 Seroconversion	Days Since HIV-1 Seroconversion	Date of HIV-1 RNA Detection	Days Since HIV-1 RNA Detection	HIV Subtype	NNRTI mutations	NNRTI Stanford Mutation Score / Classification			
										Efavirenz	Etravirine	Nevirapine	Rilpivirine
Dapivirine/ Placebo													
XXXXXXXX	On IP /	ddMMM Myyyy	Trial Month XX / LPUV / Exit Visit	ddMMMyyyy	XXX	ddMMMyyyy	XXX		XXXX	XX: 1 /	XX: 1 /	XX: 1 /	XX: 1 /
	After IP /									XX: 2 /	XX: 2 /	XX: 2 /	XX: 2 /
	Prior to IP									XX: 3 /	XX: 3 /	XX: 3 /	XX: 3 /
										XX: 4 /	XX: 4 /	XX: 4 /	XX: 4 /
										XX: 5	XX: 5	XX: 5	XX: 5

Programmers Note: Please list Mutations as a string ordered by position

HIV-1 = Human immunodeficiency virus type 1; LPUV = Last product use visit; NNRTI = Non-nucleoside reverse transcriptase inhibitor; RNA = Ribonucleic acid
NNRTI resistance mutation score: 1 = Susceptible (< 10); 2 = Potential low-lebel resistance (10 -< 15); 3 = Low-level resistance (15 - < 30); 4 = Intermediate resistance (30 -< 60); 5 = High-level resistance (> 60)
The Stanford University HIV-1 Drug Resistance Database version 8.4 (dated 2017-06-16) was used to identify mutations associated with any resistance score to NRTI, NRTI or PI

Listing 16.2.8.14
Population-Based Sequencing: Mutations per Region
Safety Population

HIV-1 Serovonversions

IPM 027 Treatment Participant ID	Date of HIV-1 Sero-conversion	Seroconversion Timepoint	Day of HIV-1 Sero-conversion	Days Since HIV-1 Sero-conversion	Date of First HIV-1 RNA Detection	Days Since HIV-1 RNA Detection	Sample Date	Visit Sample Taken	Visit Day	Region	Mutations
Dapivirine/ Placebo											
XXXXXXXX	ddMMMyyyy	On IP /	XXX	XX		XXX	ddMMMyyyy	Trial Month XX /	XXX	RT	XXXX
		After IP / Prior to IP						LPUV / Exit Visit		PR	

Programmers Notes:
- *Populate Mutations with RT changes from reference sequence as a string ordered by position*
- *Please repeat the listing for the following subgroups: HIV-1 Seroconconverted On Treatment; HIV-1 Seroconverted After Treatment*

HIV-1 = Human immunodeficiency virus type 1; LPUV = Last product use visit; RNA = Ribonucleic acid
The consensus subtype B sequence from the Stanford University HIV-1 database was used as reference

Listing 16.2.8.15
Population-Based Genotyping Amongst Participants who HIV-1 Seroconverted
Saftey Population

IPM 027 Treatment Participant ID	HIV-1 Sero-Conversion Timepoint	Date of of HIV-1 Sero-conversion	Day of HIV-1 Serocon-version	Date of Last Ring Exposure	RNA PCR Sample Date	Visit Sample Taken	Genotyping Performed?	Days Since HIV-1 Seroconversion
Dapivirine/ Placebo XXXXXXXX	Prior to IP/ On IP / After IP	ddMMMyyyy	XXX	ddMMMyyyy	ddMMMyyyy	Trial Month X / LPUV / Exit Visit	Yes / No	

HIV-1 = Human immunodeficiency virus type 1; LPUV = Last product use visit; RNA = Ribonucleic acid

Listing 16.2.8.15
Population-Based Genotyping Amongst Participants who HIV-1 Seroconverted
Saftey Population

IPM 027 Treatment Participant ID	HIV-1 Sero-Conversion Timepoint	Date of of HIV-1 Sero-conversion	Days Since Study Start	Date of First HIV-1 RNA Detection	Days Since HIV-1 RNA Detection	Days Since Last Ring Exposure	HIV RNA PCR Results (cop/mL) At Seroconversion
Dapivirine/ Placebo							
XXXXXXXX	Prior to IP/ On IP / After IP	ddMMMyyyy	XXX	ddMMMyyyy	XXX	XXX	XXXX

HIV-1 = Human immunodeficiency virus type 1; LPUV = Last product use visit; RNA = Ribonucleic acid

Listing 16.2.8.16
Pelvic/ Speculum Examinations
Safety Population

Centre Participant ID	Date of Examination	Visit	Examined	Abnormal Findings	Vulvar			
					Indicator	Parameter	Clinically Significant	Grade
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Yes / No	Yes / No	Vulvar erythema / Vulvar edema / Vulvar rash / Vulvar tenderness / Bartholin's or Skene's gland abnormality / Not done	Ulcer / Blister / Pustule / Peeling / Ecchymosis / Other: Xxxxxxxxxxxxxx	Yes / No	X

Programmers Note: Please capture multiple responses, separated with a ';'

AE = Adverse event
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.8.16
Pelvic/ Speculum Examinations
Safety Population

				Vaginal			
Centre Participant ID	Examination Date	Visit	Examined	Indicator	Parameter	Clinically Significant	Grade
Centre XX							
XXXXXXXX	ddMMMyyyy	Screening / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Yes / No	Vaginal erythema / Vaginal edema / Vaginal masses / Vaginal abrasions or lacerations / Vaginal tenderness / Vaginal discharge: Slight / Vaginal discharge: Mild / Vaginal discharge: Pooling	Ulcer / Blister / Pustule / Peeling / Ecchymosis / Other: Xxxxxxxxxxxxxx	Yes / No	X

Programmers Note: Please capture multiple responses, separated with a ';'

AE = Adverse event
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.8.16
Pelvic/ Speculum Examinations
Safety Population

Centre Participant ID	Examination Date	Visit	Examined	Cervical			
				Indicator	Parameter	Clinically Significant	Grade
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Yes / No	Cervical erythema / Cervical edema and/or friability/ Cervical masses / Cervical motion tenderness / Cervical discharge	Ulcer / Blister / Pustule / Peeling / Ecchymosis / Other: Xxxxxxxxxxxxxx	Yes / No	X

Programmers Note: Please capture multiple responses, separated with a ';'

AE = Adverse event
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.8.16
Pelvic/ Speculum Examinations
Safety Population

Centre Participant ID	Examination Date	Visit	Examined	General / Other			
				Indicator	Parameter	Clinically Significant	Grade
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Yes / No			Yes / No	X

Programmers Note: Please capture multiple responses, separated with a ';'

AE = Adverse event
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.8.16
Pelvic/ Speculum Examinations
Safety Population

Centre Participant ID	Examination Date	Visit	Examined	Description of AE	Cervical Ectopy	IPM 027 Treatment	Comments
Centre XX							
XXXXXXXX	ddMMMyyyy	Screening / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Yes / No	Xxxxxxxxxx	0% / 1 – 25% / 26 – 50% / 51 – 75% / 76 – 100%	Dapivirine / Placebo	

Programmers Note: Please capture multiple responses, separated with a ';'

AE = Adverse event
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.8.17
Cervical Cytology Results
Safety Population

Centre Participant ID	Sample Date	Visit	Pap Test Results: End of Form Date	Reported as AE: Description	Comments
Centre XX					
XXXXXXXX	ddMMMyyyy	Screening / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit	Not done / Documentation of normal cervical cytology / results within 1 year of Screening: ddMMMyyyy / Negative for intraepithelial lesion or cancer (malignancy) / ASCUS / ASC-H / SIL-low grade (LSIL) / SIL-high grade (HSIL) / AGC / AGC-favor neoplastic / Cancer / Other: Xxxxxxxxxxxxxxxxxxxxxxx	Yes: Xxxxxxx / No / N/A	

AE = Adverse event
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.8.18.1
Social Harms Report
Safety Population

Centre Participant ID	Report Date	Visit	Reported Social Harm (Verbatim)	Person Responsible	Similar Event Happened Before	Event Due To Your Involvement in Trial
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit		Sex partner / Family member / Friends/neigbours / Health worker / Co-workers / Church member / Known community members / Strangers / Other: Xxxxxxxxxxxxxxxxxxxx	No / Yes: Xxxxxxxxxxx	No / Yes: Xxxxxxxxxxxxx / Not sure: Xxxxxxxxxx

Programmers Note: Please capture multiple responses, separated with a ';'

AE = Adverse event; RC = Research centre
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.8.18.1
Social Harms Report
Safety Population

Centre Participant ID	Report Date	Visit	Reported Social Harm (Verbatim)	Resolution Status (Participant Opinion)	Referral for Support	Impact on Quality of Life
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit		Yes / No / Not sure	Yes / No	Minor disturbance / Major disturbance / Moderate disturbance

Programmers Note: Please capture multiple responses, separated with a ';'

AE = Adverse event; RC = Research centre
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.8.18.1
Social Harms Report
Safety Population

Centre Participant ID	Report Date	Visit	Reported Social Harm (Verbatim)	Type of Social Harm		
				Physical	Description of Reported AE	Emotional
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit		None / Beating/hitting/slapping / Shoving/tripping / Cutting/burning/shooting Witholding basic needs / Other: Xxxxxxxxxx	Xxxxxxxx / No AE	None / Yelling/shouting / Shunning/ignoring / Gossiping / Emotional harm to others / Physical harm to others / Financial harm to others / Other: Xxxxxxxxxxxxxxxx

Programmers Note: Please capture multiple responses, separated with a ';'

AE = Adverse event; RC = Research centre
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.8.18.1
Social Harms Report
Safety Population

Centre Participant ID	Report Date	Visit	Reported Social Harm (Verbatim)	Type of Social Harm Financial	Action(s) Taken By Participant
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit		None / Lost source of income / Lost home / Victim of theft / Cost of care for physical/emotional harm / Loss of resources / Other: Xxxxxxxxxxxxxxxxxxx	None / Sought support services / Sought counselling / Sought medical care / Other: Xxxxxxxxxxxxxxxx

Programmers Note: Please capture all responses, separated by ';'

AE = Adverse event; RC = Research centre
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.8.18.1
Social Harms Report
Safety Population

Centre Participant ID	Report Date	Visit	Reported Social Harm (Verbatim)	Action(s) Taken		Resolution Status (RC Opinion)
				By RC	Other	
Centre XX						
XXXXXXXX	ddMMMyyyy	Screening / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit		None / Referred to support services / Referred for counselling / Medical Care / Other: Xxxxxxxxxxxxxxxx	None / Xxxxxxxxx	Resolved / Unresolved at this visit /

Programmers Note: Please capture all responses, separated by ';'

AE = Adverse event; RC = Research centre
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.8.18.1
Social Harms Report
Safety Population

Centre Participant ID	Date of Report	Follow-up Report Visit	Reported Social Harm (Verbatim)	Resolution Date	Comments
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit		ddMMMyyyy	

Programmers Note: Please capture all responses, separated by ';'

AE = Adverse event; RC = Research centre
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.8.18.2
Social Harms Follow-up Report
Safety Population

Centre Participant ID	Date of Report	Follow-up Report Visit	Reported Social Harm (Verbatim)	Additional Info Report Date	Additional Information (Verbatim)	Resolution Status (RC Opinion)
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit		ddMMMyyyy		Resolved / Unresolved at the visit / Ongoing at participant's last visit: xxxxxxxxxxxxxxxxxx

Programmers Note: Please capture all responses, separated by ';'

AE = Adverse event; RC = Research centre
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.8.18.2
Social Harms Follow-up Report
Safety Population

Centre Participant ID	Date of Report	Follow-up Report Visit	Reported Social Harm (Verbatim)	Resolution Date	Comments
Centre XX XXXXXXXX	ddMMMyyyy	Screening / Trial Month XX / Trial Month XX (Unscheduled X) / Exit visit		ddMMMyyyy	

Programmers Note: Please capture all responses, separated by ';'

AE = Adverse event; RC = Research centre
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.8.19
Timing Profile
Safety Population

Centre Participant ID	IPM 027 Treatment	Trial	Date Category	Start Date	End Date	Duration (Days)	Directly Enrolled In IPM 032?
Centre XX							
XXXXXXXX	Dapivirine / Placebo	IPM 032 / IPM 027	Time on IP / Time on open-label IP / Time off IP / Total time on IP / Time off between IPM 027 and IPM 032 / Time on randomized IP / IPM 027 exit date / IPM 032 exit date Time to seroconversion / Time to first positive HIV RNA / Etc.	ddMMMyyyy	ddMMMyyyy	XXX	Yes / No

IP = Investigational product
Centre 01: Madibeng Centre for Research (MCR); Centre 02: MatCH Research Unit (MRU); Centre 04: Qhakaza Mbokodo (QM);
Centre 06: MRC/UVRI & LSHTM Uganda Research Unit (MRC/UVRI); Centre 07: Desmond Tutu HIV Foundation (DTHF), Masiphumelele; Centre 08: Ndlovu Care Group (NCG)

Listing 16.2.8.19
Timing Profile
Safety Population

Centre Participant ID	IPM 027 Treatment	Trial	Date Category	IPM 027 Participant ID	End of Treatment Status
Centre XX XXXXXXXX	Dapivirine / Placebo	IPM 032 / IPM 027	Time on IP / Time on open-label IP / Time off IP / Total time on IP / Time off between IPM 027 and IPM 032 / Time on randomized IP / IPM 027 exit date / IPM 032 exit date Time to seroconversion / Time to first positive HIV RNA / Etc.	XXXXXX	Completed / Discomtinued: Xxxxxxxx / Etc.

Appendix 4 – Stanford HIV-1 Drug Resistance (database version 8.4 - dated 2017-06-16)

Stanford Mutation List NNRTI Version 8.4

NNRTI

A98G, L100I, L100V, K101E, K101H, K101P, K103E, K103Q, K103H, K103N, K103S, K103T, V106A, V106M, V108I, E138A, E138K, E138Q, E138G, E138R, V179D, V179E, V179F, V179L, V179T, Y181C, Y181F, Y181S, Y181G, Y181I, Y181V, Y188C, Y188F, Y188H, Y188L, G190A, G190C, G190T, G190V, G190E, G190Q, G190S, H221Y, P225H, F227C, F227L, M230I, M230L, P236L, K238T, K238N, Y318F, N348I.

Stanford Mutation List NRTI Version 8.4

NRTI

E40F, M41L, E44A, E44D, A62V, K65E, K65N, K65R, D67Deletion, D67G, D67E, D67S, D67T, D67H, D67N, S68Deletion, T69Deletion, T69D, T69G, T69Insertion, K70Deletion, K70E, K70G, K70Q, K70N, K70S, K70T, K70R, L74V, L74I, V75I, V75M, V75S, V75A, V75T, F77L, Y115F, F116Y, Q151L, Q151M, M184V, M184I, L210W, T215F, T215S, T215C, T215D, T215E, T215I, T215V, T215A, T215L, T215N, T215Y, K219N, K219R, K219Q, K219E, K219W.

Stanford Mutation List PI Version 8.4

Major

D30N, V32I, L33F, M46I, M46L, I47A, I47V, G48M, G48V, I50L, I50V, I54A, I54T, I54L, I54M, I54V, L76V, V82A, V82F, V82L, V82T, V82S, I84V, N88S, N88D, L90M

System Organ Class (SOC)	Preferred Term (PT) of Interest	Lower Level Term (if applicable)	Descriptive Term
Infections and infestations	Bacterial vaginosis	N/A	N/A
	Bartholin's abscess	N/A	N/A
	Vulval abscess	N/A	N/A
	Cervicitis	N/A	N/A
	Cystitis	N/A	N/A
	Genital infection female	N/A	N/A
	Genitourinary tract gonococcal infection	N/A	Gonococcal urogenital events
	Vulvovaginitis gonococcal		
	Gynaecological chlamydia infection	N/A	Chlamydia urogenital events
	Vulvovaginitis chlamydial		
	Oophoritis	N/A	N/A
	Pelvic inflammatory disease	N/A	N/A
	Pyelonephritis	N/A	N/A
	Syphilis	N/A	N/A
	Trichomoniasis	N/A	Trichomonal urogenital events
	Vulvovaginitis trichomonal		
	Urinary tract infection	N/A	N/A
	Vaginal infection	N/A	N/A

System Organ Class (SOC)	Preferred Term (PT) of Interest	Lower Level Term (if applicable)	Descriptive Term
Infections and infestations (cont.)	Vulval cellulitis	N/A	N/A
	Vulvovaginal candidiasis	N/A	N/A
	Vulvovaginitis	N/A	N/A
Reproductive system and breast disorders	Adnexa uteri cyst	N/A	Adnexa uteri symptoms
	Adnexa uteri mass		
	Adnexa uteri pain		
	Adnexa uteri pain		
	Amenorrhoea	N/A	Bleeding disorders
	Menorrhagia		
	Metrorrhagia		
	Menstruation irregular		
	Cervix disorder	Cervix lesion*	N/A
	Cervix inflammation	Cervix inflammation**	N/A
	Dysmenorrhoea	N/A	N/A
	Dyspareunia	N/A	N/A
	Ovarian mass	N/A	N/A
	Pelvic discomfort	N/A	N/A
	Pelvic pain	N/A	N/A

System Organ Class (SOC)	Preferred Term (PT) of Interest	Lower Level Term (if applicable)	Descriptive Term
Reproductive system and breast disorders (cont.)	Pruritus genital	N/A	N/A
	Uterine cervix ulcer	N/A	N/A
	Uterine pain	N/A	N/A
	Uterine tenderness	N/A	N/A
	Vaginal discharge	N/A	N/A
	Vaginal odour	N/A	N/A
	Vaginal ulceration	Vulval lesion*	N/A
	Vulval disorder	N/A	N/A
	Vulval ulceration	N/A	N/A
	Vulvovaginal discomfort	N/A	N/A
	Vulvovaginal dryness	N/A	N/A
	Vulvovaginal pain	N/A	N/A
	Vulvovaginal pruritus	N/A	N/A
	Vulvovaginal rash	N/A	N/A
	Vulvovaginal swelling	N/A	N/A
Renal and urinary disorders	Bladder pain	N/A	N/A
	Dysuria	N/A	N/A
	Urine odour abnormal	N/A	N/A

System Organ Class (SOC)	Preferred Term (PT) of Interest	Lower Level Term (if applicable)	Descriptive Term
General disorders and administration site conditions	Application site pain	N/A	N/A
	Suprapubic pain	N/A	N/A
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Anogenital warts	N/A	N/A
	Uterine leiomyoma	N/A	N/A
	Vulvovaginal warts	N/A	N/A
Pregnancy, puerperium and perinatal conditions	Abortion spontaneous	N/A	N/A
	Abortion spontaneous incomplete	N/A	N/A
	Retained products of conception	N/A	N/A

*IPM convention for vesicular ulcerative lesion

**The reported term for the AE was “Granuloma in cervical os due to gynaecological infection”

Sections in Protocol Version 2.0 Amendment 2.0 dated 16 Jan 2017 to be implemented

NOTE: Text highlighted in this document is the text in the specific sections that will be implemented with regards to Amendment 2.0. These sections will be implemented in addition to the Protocol Version 2.0 Amendment 1.0 dated 22 Oct 2015 that is currently implemented at the research centres in its entirety.

Sections:

Protocol Synopsis

The Exploratory Trial Objectives are:

1. To assess the feasibility of 3-monthly follow-up visits, as a possible schedule for post-licensure vaginal ring clinical follow-up
2. To explore the correlation between drug concentrations and results from the visual inspection of the returned vaginal rings by research staff between the monthly and 3-monthly research centre follow-up schedules
3. To determine the proportion of participants electing to undergo HIV rapid tests at the research centres between scheduled 3-monthly visits
4. To characterize the IPM 027 participants who decline enrollment into IPM 032 (Decliner Population)
5. To explore self-reported acceptability of and adherence to the 25 mg Dapivirine Vaginal Ring-004.

The exploratory endpoints are:

- Feasibility of 3-monthly clinical follow-up schedule
- Dapivirine residual amounts in returned used vaginal rings and/or dapivirine concentrations in blood and/or vaginal fluid in correlation with results from the visual inspection of the returned used vaginal rings by research staff
- Proportion of participants opting for HIV rapid tests at the research centre between scheduled 3-monthly research centre follow-up visits
- Characteristics of IPM 027 participants who decline enrollment into IPM 032 (Decliner Population) and reasons for declining
- The proportion of women who report the use of the vaginal ring as acceptable
- Participant self-reported patterns of ring use

The exploratory endpoints will be assessed through:
• Participant report of feasibility regarding a 3-monthly clinical follow-up schedule (Participant Questionnaire) • Number of women opting not to receive two additional rings at the 3-monthly visits • Proportion of returned rings (used and unused) during the 3-monthly clinical follow-up schedule • Dapivirine residual amounts in returned used vaginal rings and/or dapivirine concentrations in blood and/or vaginal fluid • Visual inspection of the returned used vaginal rings by research centre staff • Number of participants undergoing HIV rapid tests at the research centre between scheduled 3-monthly research centre follow-up visits • Questionnaires and qualitative data regarding reasons for declining participation, ring acceptability and self-reported patterns of ring use.
METHODS: Qualitative and Quantitative Behavioural Assessments: Each research centre will conduct two to three in-depth individual interviews (IDIs) with approximately six participants in each of the following categories: • Decliner Population • Ring Users • Ring Non-users In cases of interest IDIs will be conducted; approximately three participants will be interviewed per site. These cases of interest may include, but will not be limited to participants who may have experienced social harms, may have had problems using the ring, or who HIV seroconverted. Focus group discussions may be conducted with the above mentioned groups. Efforts will be made to ensure the sample size is representative of both previous IPM 027 participants as well as the two ring-naïve cohorts of women. Additionally, IDIs and/or FGDs with approximately six males from the community and/or male partners will be conducted at each research centre. DVR-naïve participants will complete a behavioural questionnaire at enrolment, in addition to the participant questionnaire collected at other trial visits.

These assessments will provide data on acceptability and influencers of ring use. The recruitment and sampling strategy will be specified in the study operations manual.

2.2. Trial Endpoints and Assessments

The Exploratory Trial Objectives are:

1. To assess the feasibility of 3-monthly follow-up visits, as a possible schedule for post-licensure vaginal ring clinical follow-up
2. To explore the correlation between drug concentrations and results from the visual inspection of the returned vaginal rings by research staff between the monthly and 3-monthly research centre follow-up schedules
3. To determine the proportion of participants electing to undergo HIV rapid tests at the research centres between scheduled 3-monthly visits
4. To characterize the IPM 027 participants who decline enrollment into IPM 032 (Decliner Population)
5. To explore self-reported acceptability of and adherence to the 25 mg Dapivirine Vaginal Ring-004.

The exploratory endpoints are:

- Feasibility of 3-monthly clinical follow-up schedule
- Dapivirine residual amounts in returned used vaginal rings and/or dapivirine concentrations in blood and/or vaginal fluid in correlation with results from the visual inspection of the returned used vaginal rings by research staff
- Proportion of participants opting for HIV rapid tests at the research centre between scheduled 3-monthly research centre follow-up visits
- Characteristics of IPM 027 participants who decline enrollment into IPM 032 (Decliner Population) and reasons for declining
- The proportion of women who report the use of the vaginal ring as acceptable
- Participant self-reported patterns of ring use

The exploratory endpoints will be assessed through:

- Participant report of feasibility regarding a 3-monthly clinical follow-up schedule (Participant Questionnaire)
- Number of women opting not to receive two additional rings at the 3-monthly visits
- Proportion of returned rings (used and unused) during the 3-monthly clinical follow-up schedule
- Dapivirine residual amounts in returned used vaginal rings and/or dapivirine concentrations in blood and/or vaginal fluid

- Visual inspection of the returned used vaginal rings by research centre staff
- Number of participants undergoing HIV rapid tests at the research centre between scheduled 3-monthly research centre follow-up visits
- Questionnaires and qualitative data regarding reasons for declining participation, ring acceptability and self-reported patterns of ring use.

5.16 Qualitative Behavioural Assessments

Each research centre will conduct two to three in-depth individual interview (IDIs) with approximately six participants in each of the following categories:

- Decliner Population
- Ring Users
- Ring Non-users

In cases of interest IDIs will be conducted; approximately three participants will be interviewed per site. These cases of interest may include, but will not be limited to participants who may have experienced social harms, may have had problems using the ring, or who HIV seroconverted

Focus group discussions may also be conducted with the above mentioned groups. Efforts will be made to ensure the sample size is representative of both previous IPM 027 participants as well as the two ring-naïve cohorts of women. Additionally, IDIs and/or FGDs with approximately six males from the community and/or male partners will be conducted at each research centre.

DVR-naïve participants will complete a behavioural questionnaire at enrolment, in addition to the participant questionnaire collected at other trial visits.

These assessments will provide data on acceptability and influencers of ring use. The recruitment and sampling strategy will be specified in the study operations manual.

8.4.5 Other results from Qualitative/Quantitative Behavioural assessments

Each research centre will conduct two to three in-depth individual interviews (IDIs) with approximately six participants in each of the following categories:
Decliner Population
Ring Users
Ring Non-users

In cases of interest IDIs will be conducted; approximately three participants will be interviewed per site. These cases of interest may include, but will not be limited to participants who may have experienced social harms, may have had problems using the ring, or who HIV seroconverted. Focus group discussions may be conducted with the above mentioned groups. Efforts will be made to ensure the sample size is representative of both previous IPM 027 participants as well as the two ring-naïve cohorts of women. Additionally, IDIs and/or FGDs with approximately six males from the community and / or male partners will be conducted at each research centre.

DVR-naïve participants will complete a behavioural questionnaire at enrolment, in addition to the participant questionnaire collected at other trial visits.

8.5 Data and Safety Monitoring Board

Safety data from the trial will be evaluated by an independent Data and Safety Monitoring Board (DSMB). The first scheduled meeting will take place approximately six months after all research centres have been activated and thereafter at approximately annual intervals for the duration of IPM 032. Based on the review of the data, the DSMB is required to provide recommendations about continuation, pausing, termination or other modifications to the trial, including changes to the information provided to participants for obtaining their informed consent. An IPM 032 DSMB charter will describe the roles and responsibilities of the DSMB, its composition, data to be provided to the DSMB, the process for disseminating trial data to the DSMB, and the communication plan between the DSMB and IPM.

	Deviation Category	Description	Classification	Comment
1	Inappropriate enrolment	More than one Inclusion or Exclusion criterion not met.	Major	
		<u>Inclusion Criteria:</u> Inclusion criterion 1: Previously enrolled in the IPM 027 trial	Major	
		Inclusion criterion 2: Available for all visits and consent to follow all procedures scheduled for the trial	To review	
		Inclusion criterion 3: Using an effective method of contraception at the Enrolment Visit, and intending to use an effective contraceptive method for the duration of trial participation, unless post-menopausal with no history of menses for one year prior to screening.	Major	
		Inclusion criterion 4: HIV-negative as determined by the HIV algorithm applied at Screening/Pre-Enrolment	Major	
		Inclusion criterion 5: Willing to refrain from participation in another research trial using drugs, vaccines, medical devices and microbicides for the duration of the IPM 032 trial	Major	
		Inclusion criterion 6: Willing to provide adequate locator information for trial retention purposes and be reachable per local standard procedures (*e.g.*, by home visit or telephone; or *via* family or close neighbour contacts); confidentiality to be maintained	Minor	

	Deviation Category	Description	Classification	Comment
		<u>Exclusion Criteria:</u> Exclusion criterion 1: Investigational product use permanently discontinued in response to an AE (where the AE was considered related to investigational product) or safety-related concern while taking part in the IPM 027 trial	Major	
		Exclusion criterion 2: Participant self-report of taking post-exposure prophylaxis (PEP)within ≤ 2 months at Screening Visit ***Note:*** *Participants may be enrolled after completing the PEP regimen and a negative HIV test was documented at least 2 months prior to screening for IPM 032*	To review	
		Exclusion criterion 3: Currently pregnant, or currently breast-feeding	Major	
		Intends to become pregnant	To review	
		Exclusion criterion 4: Known drug abuse or alcohol dependence in the 12 months prior to screening	To review	
		Exclusion criterion 5: Participated in another research trial (other than IPM 027) using drugs, medical devices, microbicides or oral pre-exposure prophylaxis agents within 30 days prior to screening	To review	
		Exclusion criterion 6: Any new illness or condition(s), chronic condition(s) or abnormal laboratory finding(s) that, in the opinion of the investigator, might put the participant at risk, or interfere with the trial objectives or the	To review	

	Deviation Category	Description	Classification	Comment
		participant's adherence to trial requirements		
2	**Missed visit**		To Review	
3	**Visit completed outside of permissible windows**		To review	
4	**Informed consent process deviations**		To review	Deviations will be discussed on a case-by-case basis, and the severity will be determined by the nature of the deviation. Absence of documented informed consent prior to trial related procedures will be considered major.
5	**IP deviations** *(dispensing, timing and dosing*	IP incorrectly dispensed and used by participant	Major	
		Expired IP dispensed and used by participant	Major	
		Quarantined/not fit for use IP dispensed and used by participant	Major	Occurrence and extent of temperature excursions, for example, to be evaluated on a case-by-case basis.
6	**Safety Reporting** *(IREs not reported within timeframe, unreported AEs)*	SAE not reported within 24 hours	Minor	For definition of PP population this would be considered minor (i.e. participant would not be excluded from PP population) as the deviation does not have effect on data).
		Multiple unreported AEs for the same participant	To be reviewed	
		Any non-serious AE leading to permanent discontinuation of the IP not reported within 48 hours	Minor	
		Seroconversion not reported within 48 hours	Minor	
		Pregnancy not reported within 48 hours	Minor	

	Deviation Category	Description	Classification	Comment
7	**Failure to discontinue (temporarily or permanently) IP use for whom it is indicated**	HIV Seroconversion	Minor	For definition of PP population this would be considered minor (i.e. participant would not be excluded from PP population) as the deviation occurred after the seroconversion (endpoint).
		Pregnancy	Major	
		SAE or non-serious AE (including laboratory abnormality) indicating need for IP discontinuation	Major	
8	**Inappropriate treatment/ management of medical conditions and follow-up of AEs**		To review	Deviation will be discussed on a case-by-case basis, and the severity will be determined by the nature of the deviation
9	**Mishandled laboratory samples** *(including samples that have been collected, processed, stored or transported incorrectly)*	Incorrectly labelled samples, resulting in redraw	Minor	
		Incorrect storage (e.g. loss of cold chain with loss of samples)	Minor	
		Incorrect sampling (preservative contamination)	Minor	
		Data not recorded, resulting in loss of data (tear strip weight not recorded; rapid test result not recorded on log)	Minor	
		Lost samples (storage/shipping)	Minor	
10	**Missing or incorrectly timed trial procedures**	Pregnancy tests not performed as per protocol schedule	To review	
		Other trial procedures not performed as per protocol schedule.	To review	

	Deviation Category	Description	Classification	Comment
11	**Conduct of additional non-study related procedures**		To review	Deviation will be discussed on a case-by-case basis, and the severity will be determined by the nature of the deviation
12	**Participant non-adherence to trial requirements**	Participant fails to follow protocol requirements which are deemed to be serious enough by the Investigator to warrant discontinuation, e.g. in the absence of an AE or discomfort, participant refuses to keep vaginal ring inserted for the duration of the relevant treatment period	To review	
13	**Failure to discontinue participants who meet trial discontinuation criteria**	Participant withdraws her consent	Major	
		Participant tests HIV-positive according to the HIV-testing algorithm	Minor	
		Participant is lost to follow-up, i.e. the research centre is unsuccessful (following reasonable attempts as defined in the local SOP) in contacting participant or bringing the participant back to the research centre l	Minor	
		If for safety reasons, the Investigator considers it in the best interest of the participant to discontinue her from the trial	To review	For laboratory values: Major in cases where investigator has indicated the findings to be related to IP.
		At the discretion of the Investigator, IPM, the relevant Institutional Review Board/Independent Ethics Committee (IRB/IEC), or the government health authority	Minor	
14	**Other, specify**		To review	

Version 1.0 compiled by:

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Approved by:

Annalene Nel

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14 Nov 2016
Date

INTERNATIONAL PARTNERSHIP FOR MICROBICIDES

Statistical Analysis Plan

Virology Addendum Analysis of Dapivirine Vaginal Ring-004 Clinical Trial IPM 032

(Phase IIIb Clinical Trial)

Version 1.0

International Partnership for Microbicides
8405 Colesville Road, Suite 600
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APPROVAL SIGNATURE PAGE

IPM 032 Virology Addendum – Statistical Analysis Plan

I have read the above referenced Statistical Analysis Plan and approve its contents.

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IPM 032 Virology Addendum – Statistical Analysis Plan

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ABBREVIATIONS

CSR	Clinical Study Report
DNA	Deoxyribonucleic acid
DVR-004	Dapivirine Vaginal Ring-004
EFV	Efavirenz
ETR	Etravirine
FC	Fold-change
HIV-1	Human immunodeficiency virus type 1
HIVdb	HIV Drug Resistance Database
IC_{50}	50% inhibitory concentration
IP	Investigational product (ie, the DVR-004 and placebo ring)
IPM	International Partnership for Microbicides
ITT	Intent-to-treat
MTN	Microbicide Trials Network
NGS	Next generation sequencing
NNRTI	Non-nucleoside reverse transcriptase inhibitor
NVP	Nevirapine
PCR	Polymerase chain reaction
RAM	Resistance-associated mutation
RNA	Ribonucleic acid
RPV	Rilpivirine
RT	Reverse transcriptase
SAP	Statistical Analysis Plan
STI	Sexually transmitted infection
T&L	Tables and Listings
UMI	Unique molecular identifier
USA	United States of America

TABLE OF CONTENTS

1. INTRODUCTION

This document serves as the Statistical Analysis Plan (SAP) for the supplementary virology analysis of the Dapivirine Vaginal Ring-004 (DVR-004) Phase IIIb open-label extension trial, IPM 032. Specifically, this document describes the process for identification of samples and statistical methods that will be used to analyze the data resulting from retrospective resistance testing using a unique molecular identifier (UMI) next generation sequencing (NGS) methodology[1-3], as well as phenotypic susceptibility analysis recombinant retroviral system[4].

There are several advantages of the NGS method employed in this analysis over standard NGS methodologies. The current methodology uses UMI 'barcodes' built into polymerase chain reaction (PCR) primers, which allows sequences originating from the same human immunodeficiency virus type 1 (HIV-1) ribonucleic acid (RNA) template to be grouped and aligned. Building consensus sequences from these alignments provides improved control of PCR and sequencing error, PCR bias, and PCR recombination. The number of UMI with consensus sequences allows the depth of sequencing to be calculated based on the number of HIV-1 RNA templates sampled, which can in turn be used to estimate the sensitivity of the individual sample analysis using an adaptation of the Clarke and Carbon equation

$[P=1-(1-f)^N$

where P = probability, N = number of sequences, f = fraction of sequences with variant][5,6] to obtain the proportion of a minority species that can be detected with 95% confidence. The assay has been validated to detect resistance-associated mutations (RAMs) down to 1% prevalence, subject to the number of consensus sequences (UMIs) observed. Despite the robust nature of the assay and the analysis of its results, the NGS analysis should still be considered as exploratory. Of note, clinical interpretation of these data remains challenging. In addition to technical challenges, there is an absence of cross-laboratory standardization of outputs and of accredited means for external quality assessment[7,8]. In the absence of resolution of these issues, the clinical relevance of the increased sensitivity for detection of resistance-associated mutations using NGS remains unknown.

Templates for all tables and listings that will be used to present the virology results are also provided. These analyses will be described in an addendum to the IPM 032 Clinical Study Report (CSR).

Table shells and listing shells that will accompany the analyses are provided in a separate document of mock tables and listings (T&L) (Appendix 1). This document is viewed as supporting material for the analyses and will not require signature approval if formatting changes are made.

2. OBJECTIVE

The primary purpose of this analysis is to further address, with supplementary information, the secondary objective for trial IPM 032:

- To assess the frequency of HIV-1 drug resistance in women who acquire HIV-1 infection while using the DVR-004.

Specifically, the analyses will facilitate the description of:

- the prevalence of all variants detectable to a minimum prevalence of 1%, 5%, or 10% in reverse transcriptase (RT) at seroconversion using NGS.
- the fold-change (FC) in phenotypic susceptibility of virus at seroconversion to dapivirine, efavirenz, etravirine, nevirapine, and rilpivirine relative to a wild-type control.
- the findings in relation to the population-based genotyping results described in the IPM 032 CSR and the Phase III Clinical Virology Report Version 4.0.

2.1. Endpoints

Primary Endpoints:

- The presence of non-nucleoside reverse transcriptase inhibitor (NNRTI) resistance-associated mutations (RAMs), including minority species RAMS at seroconversion, using NGS.
- Phenotypic susceptibility of virus to dapivirine and the approved NNRTIs: efavirenz, etravirine, nevirapine and rilpivirine, measured at seroconversion.

Secondary Endpoint:

- Comparison of specific NNRTI RAM detection using population-based genotyping and NGS.

Exploratory Endpoints:

- Correlation between phenotypic susceptibility findings and population-based genotype.
- Longitudinal NGS-based genotyping of virus from one selected participant with emergence of K103N determined using population-based genotyping (Participant Identifier 3201198).

2.2. Assessments of Endpoints

Primary Endpoints Assessed by:

- Determination of the prevalence of all variants reported from NGS tests with sensitivity to detect viruses present at ≥ 10.0%, ≥ 5.0%, and ≥ 1.0% prevalence in HIV-1 RT at seroconversion.
- Determination of the 50% inhibitory concentration (IC_{50}) and FC in phenotypic susceptibility of virus at seroconversion to dapivirine, efavirenz, etravirine, nevirapine, and rilpivirine relative to a wild-type control virus.

Secondary Endpoint Assessed by:

- Summarizing numbers and prevalence of additional NNRTI RAMs observed using NGS compared with population-based genotyping, within the limits of the NGS sequence region (reverse transcriptase codons 81 to 149 and 152 to 212).

Exploratory Endpoints Assessed by:

- Summarizing viral fold-change in susceptibility to dapivirine by mutation patterns determined using population-based genotyping assessment.
- Comparison of IC_{50} values between viruses with known NNRTI RAMs and those with wild-type genotypes.
- Comparison of pre-seroconversion and seroconversion NGS analyses in samples from participant with emergent K103N at seroconversion (Participant Identifier 3201198).

3. ANALYSIS POPULATIONS

3.1. Safety Population

The safety population includes all trial participants who were enrolled from the parent trial, IPM 027, and received and inserted at least one DVR-004.

3.2. Virology Population

The virology population includes all participants in the safety population who experienced seroconversion (either using HIV-1 Rapid test result algorithms or determined to have been HIV-1 infected while using the DVR-004 based on reverse sequential HIV-1 RNA PCR testing) during investigational product (IP) use except:

- Participants who were deemed to be HIV-1 RNA positive at the time of enrolment.
- Participants who seroconverted after last product use (ie, at the Exit Visit) and were not HIV-1 RNA positive at the last product use visit, ie, were infected after they discontinued product use.

The virology population will be the main focus of this analysis. Available data for any participants infected with HIV-1 prior to enrolment or after last product use will be listed and described separately. Phenotypic analyses will be performed only on samples obtained at seroconversion during DVR-004 use.

4. GENERAL STATISTICAL CONSIDERATIONS

4.1. Analysis Software

Statistical analyses will be conducted by an external service provider of the International Partnership for Microbicides (IPM) and will be reviewed by IPM and the University of Pittsburgh Virology Laboratory. The analyses will be performed using SAS® for Windows or Linux/Unix (Version 9.2 or higher, SAS Institute Inc., Cary, North Carolina, United States of America [USA]).

4.2. Planned Subgroups

As numbers are small, there are no plans to perform analyses in subgroups. Should individual outlier results be observed, additional relevant characteristics may be described from the IPM 032 CSR listings or listings from this addendum.

4.3. Data Used for Analysis

Next generation sequencing will be attempted for all available seroconversion samples from all participants in the virology population, although results showing sensitivity to detect viruses present only at >10.0% prevalence (ie, with detection of < 28 UMI) will be summarized, although, due to inadequate sensitivity, these results will not be used to infer the absence of NNRTI RAMs. Analyses will be performed with cut-offs set to include the detection of minority species present in at least 10.0%, 5.0%, or 1.0% of UMI.

Results showing sensitivity to detect only minority species present with > 10.0% prevalence (ie, UMI < 28) will be described individually.

Phenotypic susceptibility and NGS will be performed on plasma samples taken at the time of HIV-1 seroconversion ± 14 days. Any results from other time points will be listed and may be discussed separately, but not included in summary analyses.

4.4. Methods for Handling Missing Data

While every effort will be made to minimize the amount of missing data, as this is a retrospective analysis, some degree of missing data associated with sample availability and participant consent, is expected. Numbers of missing analyses will be provided along with numbers of participants included in the analysis, and tests conducted with and without successful outcomes.

If the date of the last IP exposure (ie, last ring removal) is incomplete or missing, the following imputation will be made:

- when only the day is missing, impute with min (last ring insertion date + 28 days, last day of the month), else
- impute with last ring insertion date + 28 days.

This should be added in a footnote in the applicable tables/listings. If the date itself should be printed, the original (not the imputed) date should be printed.

5. ANALYSIS OF DEMOGRAPHIC AND BASELINE CHARACTERISTICS

As numbers are small, the demographic and baseline characteristics of participants in the virology population will not be described. The overall population characteristics are available in the IPM 032 CSR Version 1.0.

6. ANALYSIS OF GENOTYPING DATA

Antiretroviral drug NNRTI RAMs in virus from women who acquire HIV-1 while using the DVR-004 will be determined by means of NGS. (Population-based genotypes are reported in the IPM 032 CSR Version 1.0, dated 09 April 2020 and the Clinical Virology Report, Version 4.0.) Next generation sequencing provides the supplementary, exploratory results primarily addressed in the current SAP.

6.1. Definition of Resistance-associated Mutations

Summary analyses of NNRTI RAMs will be based on mutations identified in the Stanford HIV Drug Resistance Database (HIVdb) Version 8.4 (dated 16 June 2017, https://hivdb.stanford.edu/)[9]. The NNRTI RAMs with scores in the Stanford HIVdb algorithm Version 8.4 within the range of the NGS test include:

A98G, L100I, L100V, K101E, K101H, K101P, K103H, K103N, K103S, K103T, V106A, V106M, V108I, E138A, E138G, E138K, E138Q, E138R, V179D, V179E, V179F, V179L, V179T[a], Y181C, Y181F, Y181G, Y181I, Y181S, Y181V, M184I[a], Y188C, Y188F, Y188H, Y188L, G190A, G190C, G190E, G190Q, G190S, G190T, G190V (Appendix 2).

In addition, a summary of all amino acid variants from the reference sequence will be provided for both sequencing methodologies.

6.2. Population-based Sequencing

Population-based sequencing results at seroconversion have been described in the IPM 032 CSR (IPM 032 CSR Version 1.0, dated 09 April 2020) and in the Clinical Virology Report, Version 4.0; individual participant results are provided in the listings associated with the IPM 032 CSR.

The population-based genotyping sequences and resistance predictions will also be used to examine consistency with the NGS findings and the phenotypic susceptibility results. The reference sequence for the population-based sequencing analysis was the Stanford HIVdb consensus subtype B sequence.

6.3. Next Generation Sequencing

For NGS, the wild-type subtype B sequence, HXB2 (accession number K03455-1), will be used as reference. In the region sequenced, the only difference from the Stanford HIVdb consensus subtype B sequence is at codon 122 (HXB2: K122; Stanford: E122, respectively); K122 (or E122K) and E122 (or K122E) will be considered to be polymorphisms not related to NNRTI resistance in the analysis. The sensitivity for each NGS determination indicates the required prevalence for changes from the reference sequence to be detectable in the sample. The prevalences required are determined based on the statistical consideration of requiring at least 298 UMI for sensitivity to detect a 1.0% minority, 58 UMI for a 5.0% minority and 28 UMI for a 10.0% minority and will be summarized in tabulations. Samples with results showing less than 298, 58 or 28 UMI will be censored from each analysis performed to sensitivities to detect 1.0%, 5.0%, and 10.0% minority species, respectively.

[a] These mutations do not have a resistance score when present alone; V179T with Y181C and M184I with K101E contribute to the score as a combination.

Frequency tabulations per minimum detectable prevalence (1.0%, 5.0%, 10.0%), as well as any additional NNRTI RAMs observed when results indicate UMI < 28, will be presented showing the percentage of participants with an amino acid change from reference at each position of the sequenced RT region.

All NGS results will be listed relative to the reference virus' amino acid sequence together with percent prevalence in the sample.

Frequency tabulations will be created per sensitivity cut-off (1.0%, 5.0%, 10.0%) for:

- The number (and percentage) of participants who had a resistance test performed.
- The number (and percentage) of participants with each individual NNRTI RAM.
- The number (and percentage) of participants with 0, 1, 2 or ≥ 3 mutations by class (NNRTI).
- The number (and percentage) of participants with combinations of specified NNRTI RAMs.

6.4. Phenotypic Susceptibility

Phenotyping data will be obtained for virus from women with HIV-1 seroconversion and who had a seroconversion sample with sufficient HIV-1 RNA for analysis.

Recombinant HIV-1 will be generated containing cloned RT from the participant's HIV-1 RNA from plasma that was sampled at the time of HIV seroconversion. Recombinant viruses will be tested in the TZM-bl cell line for susceptibility to dapivirine as well as to the NNRTIs: efavirenz, etravirine, nevirapine, and rilpivirine.

For each NNRTI, susceptibility will be reported as the half maximal inhibitory concentration (IC_{50}). Fold-change resistance will be calculated for each individual NNRTI as:

$$FC = IC_{50}/IC_{50control}$$

- with $IC_{50control}$ = reference wild-type virus value or the geometric mean of results from the nearest match wild-type viruses in the analysis. The reference wild-type virus will be a recombinant virus with an anonymized HIV-1 RT amplicon from South Africa with no RT resistance-associated mutations cloned into an xxLAI vector (4).
- when more than one IC_{50} value is available for a sample (replicate test results), the geometric mean IC_{50} value of all replicates will be taken prior to the FC calculation.

Descriptive statistics of IC_{50} and FC values will be presented for each NNRTI and will include geometric mean and standard deviation, median, quartiles, range, and number of observations.

Additionally, descriptive statistics (geometric mean and standard deviation) of NNRTI FCs will be presented by NNRTI RAM pattern.

All individual participant data (IC_{50}, FC) will be listed. Individual IC_{50} determinations and FCs will be averaged using geometric means for each virus when multiple determinations are available.

7. REFERENCES

1. Zhou S, Jones C, Mieczkowski P, Swanstrom R. Primer ID Validates Template Sampling Depth and Greatly Reduces the Error Rate of Next-Generation Sequencing of HIV-1 Genomic RNA Populations. Journal of virology. 2015;89(16):8540-55.
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3. Boltz VF, Rausch J, Shao W, Hattori J, Luke B, Maldarelli F, et al. Ultrasensitive single-genome sequencing: accurate, targeted, next generation sequencing of HIV-1 RNA. Retrovirology. 2016;13(1):87.
4. Shi C, Mellors JW. A recombinant retroviral system for rapid in vivo analysis of human immunodeficiency virus type 1 susceptibility to reverse transcriptase inhibitors. Antimicrob Agents Chemother. 1997;41(12):2781-5.
5. Clarke L, Carbon J. A colony bank containing synthetic Col El hybrid plasmids representative of the entire E. coli genome. Cell. 1976;9(1):91-9.
6. Hogg S. Essential Microbiology. Second edition. ed: Wiley-Blackwell, Chichester, West Sussex, United Kingdom, 2013.
7. Avila-Rios S, Parkin N, Swanstrom R, Paredes R, Shafer R, Ji H, et al. Next-Generation Sequencing for HIV Drug Resistance Testing: Laboratory, Clinical, and Implementation Considerations. Viruses. 2020;12(6).
8. Ji H, Sandstrom P, Paredes R, Harrigan PR, Brumme CJ, Avila Rios S, et al. Are We Ready for NGS HIV Drug Resistance Testing? The Second "Winnipeg Consensus" Symposium. Viruses. 2020;12(6).
9. Stanford NNRTI Resistance Mutation Scores, Database Version 8.4, dated 16 June 2017. Available at: https://hivdb.stanford.edu/ (last accessed 21 May 2021.
10. Wensing AM, Calvez V, Ceccherini-Silberstein F, Charpentier C, Günthard HF, Paredes R, et al. 2019 update of the drug resistance mutations in HIV-1. Topic Antivir Med 2019, 27(3):111-121.

8. APPENDICES

8.1. Appendix 1 – Tables and Listings Titles

Tables

Table number	Title
14.3.9	**Next Generation Sequencing (NGS) and Phenotypic Susceptibility Analysis**
14.3.9.1	**Accountability**
14.3.9.1.1	Sample Availability
14.3.9.2	**Summary of NGS and Paired Population-based Genotype Analysis**
14.3.9.2.1	Summary of Number of Participants with an Amino Acid Change from Reference per Residue in the RT Region Among HIV-1 Seroconversions using Next Generation Sequencing with Paired Population-Based Genotypes
14.3.9.2.2	Summary of Numbers and Combinations of HIV-1 NNRTI Resistance-associated Mutations Among HIV-1 Seroconversions using Next Generation Sequencing with Paired Population-Based Genotypes
14.3.9.3	**Phenotypic Susceptibility Analysis**
14.3.9.3.1	Summary of Phenotypic Susceptibility to Dapivirine and Other NNRTIs by Population-based Genotype
14.3.9.4	**Summary of Population-Based Genotype Analysis (All Seroconversion Data)**
14.3.9.4.1	Summary of Number of Participants with an Amino Acid Change from Reference per Residue in the RT Region Among HIV-1 Seroconversions using Population-Based Genotyping

Listings

Listing number	Title
16.2.8.20	**Next Generation Sequencing and Phenotypic Data**
16.2.8.20.1	Next Generation Sequencing: Listing of All Available Data
16.2.8.20.2	Next Generation Sequencing: Listing of Detected NNRTI Resistance-associated Mutations
16.2.8.20.3	Phenotypic Data: Listing of All Available Data
16.2.8.20.4	Genotypic Interpretations with Phenotypic Data: Full Listing for HIV-1 Seroconverters

Note: Table and listing shells are provided in a separate document.

8.2. Appendix 2 – Stanford Human Immunodeficiency Virus Type 1 Drug Resistance (Database Version 8.4 Provided by Stanford HIVdb)

Stanford Mutation List NNRTI Version 8.4 (9)

NNRTI

A98G, L100I, L100V, K101E, K101H, K101P, K103E, K103H, K103N, K103Q, K103R[b], K103S, K103T, V106A, V106M, V108I, E138A, E138K, E138Q, E138G, E138R, V179D, V179E, V179F, V179L, V179T, Y181C, Y181F, Y181G, Y181I, Y181S, Y181V, M184I, Y188C, Y188F, Y188H, Y188L, G190A, G190C, G190E, G190Q, G190S, G190T, G190V (H221Y, P225H, F227C, F227L, M230I, M230L, P236L, K238T, K238N, Y318F, N348I).

Other

V90I, A98S, K101N, K101Q, K101R, K103E, K103M, K103Q, K103R, V106I, V108A, I132M, I132L, V179A, V179I, V179M, Y181N, (F227I[c], F227R[c], F227V[c], Y232H, L234I[c], P236L[c]).

These 'other' mutations do not contribute to the Stanford Mutation Score for EFV, ETV, NVP or RPV, so they are not included in the NNRTI RAM summary tables. However, they are listed among the NNRTI Resistance Notes on the Stanford web page (https://hivdb.stanford.edu/dr-summary/resistance-notes/NNRTI/ accessed 24 March 2021), the IAS USA 2019 update of drug resistance mutations in HIV-1 (10) or during in vitro passage experimentation (Module 2.7.2.4) and will be included in summaries of sequence data by codon.

[b] K103R, which by itself is polymorphic and non-scoring in the Stanford HIVdb algorithm Version 8.4, augments the V179D resistance scores for efavirenz and nevirapine from potential low-level- to intermediate resistance.

[c] These mutations are associated with resistance to doravirine.

8.3. Appendix 3 – Stanford Non-nucleoside Reverse Transcriptase Inhibitor Resistance Mutation Scores (Database Version 8.4, dated 18 July 2018)

Rule	EFV	ETR	NVP	RPV
A98G	15	10	30	15
L100I	60	30	60	60
L100V	30	10	30	15
K101E	15	15	30	45
K101H	10	10	15	10
K101P	60	60	60	60
K103H	60	0	60	0
K103N	60	0	60	0
K103S	45	0	60	0
K103T	15	0	60	0
V106A	45	0	60	0
[V106I][a]	[0]	[10]	[10]	[10]
V106M	60	0	60	0
V108I	10	0	15	0
E138A	0	10	0	15
E138G	10	10	10	15
E138K	10	10	10	45
E138Q	10	10	10	15
E138R	10	10	10	15
V179D	10	10	10	10
V179E	10	10	10	10
V179F	10	15	15	15
V179L	10	10	10	15
Y181C	30	30	60	45
Y181F	15	15	60	30
Y181G	15	15	60	30
Y181I	30	60	60	60
Y181S	15	15	60	30
Y181V	30	60	60	60
Y188C	60	0	60	0
Y188F	60	0	60	30
Y188H	30	0	60	0
Y188L	60	10	60	60

Rule	EFV	ETR	NVP	RPV
G190A	45	10	60	15
G190C	60	10	60	10
G190E	60	45	60	60
G190Q	60	45	60	45
G190S	60	10	60	15
G190T	60	10	60	10
G190V	60	10	60	10
H221Y	10	10	15	15
P225H	45	0	45	0
F227C	45	30	45	45
F227L	15	0	30	0
M230I	15	15	30	30
M230L	45	30	60	60
K238N	10	0	10	0
K238T	30	0	30	0
Y318F	10	0	30	0
N348I	0	0	15	0
K101E + Y181C	5	5	5	0
K101E + M184I	0	0	0	15
K101E + Y188L	0	5	0	0
K101E + G190A	0	5	0	0
K101E + G190S	0	5	0	0
K103R + V179D	20	0	20	15
V106A + F227L	15	0	0	0
E138K + M184I	0	0	0	15
V179F + Y181C	0	15	0	15
V179T + Y181C	0	10	0	10
Y181C + G190ACSTV	0	10	0	10
A98G + Y181C	5	5	5	

EFV = efavirenz; ETR = etravirine; NVP = nevirapine; RPV = rilpivirine
[a] Scoring is included in the current version of the Stanford HIVdb algorithm (Version 8.9-1; dated 25 October 2019).
Note: When a participant has multiple mutations, the scores for the individual mutations and for the combination of mutations have to be added in order to obtain the total score.
Example**:** A participant with mutations K101E and Y181C will have a EFV mutation score of 15 + 30 + 5 = 50.

IPM 032 VIROLOGY ADDENDUM SAP

APPENDIX 1

TABLE AND LISTING SHELLS – VERSION 1.0, 24 MAY 2021

TABLE SHELLS

Table 14.3.9.1.1
Sample Availability
Virology Population

	Statistic
HIV-1 Seroconversion Participants, N1	XX
Seroconversion Samples Available, N2 (%) (a)	xx (x.x%)
No sample n (%) (a)	xx (x.x%)
Sample not suitable n (%) (a)	xx (x.x%)
No consent n (%) (a)	xx (x.x%)
Seroconversion Samples with NGS Analysis Attempted, n (%) (b)	xx (x.x%)
HIV-1 seroconversion participants with a successful NGS genotype, N3 (%) (b)	xx (x.x%)
Sensitivity to detect RAMs present with at least:	
≤ 1% variant, n (%) (c)	xx (x.x%)
> 1% to 5% variant, n (%) (c)	xx (x.x%)
> 5% to 10% variant, n (%) (c)	xx (x.x%)
Invalid Result, n (%) (b, d)	xx (x.x%)
Test performed, no output (c)	xx (x.x%)
Sensitivity to detect RAMs present at:	
>10% to 20% variant, n (%) (c,d)	xx (x.x%)
> 20% variant, n (%) (c,d)	xx (x.x%)
Seroconversion Samples with Phenotypic Susceptibility Analysis Attempted, n (%) (b)	xx (x.x%)
HIV-1 seroconversion participants with any successful Phenotypic analysis (%) (b, e)	xx (x.x%)
Invalid or No Test Result, n (%) (b)	xx (x.x%)
Failed Testing (All phenotypes), n (%) (b)	xx (x.x%)
No test (Insufficient sample volume), n (%) (b,f)	xx (x.x%)

The percentage calculation is based on the total number of participants in the denoted section.
(a) Denominator = N1. (b) Denominator = N2. (c) Denominator = N3.
(d) Due to low UMI (< 28), these are considered to provide invalid results. Mutations detected in these samples will be reported separately.
(e) In the unlikely event of one to four of the five phenotypic test results for successful analysis being missing, this should be footnoted with the affected participant identifier.
(f) Some samples may have had inadequate volume to perform both the NGS and the phenotypic tests and so analysis was performed with NGS as priority, followed by phenotype determination.

Table 14.3.9.2.1
Summary of Numbers of Participants with an Amino Acid Change from Reference per Residue in the NGS Sequenced RT Region Among HIV-1 Seroconverters using Next Generation Sequencing with Paired Population-Based Genotyping
Virology Population

Next Generation Sequencing: Number of Participants with an Amino Acid Change from Reference per Residue in the RT Region Among HIV-1 Seroconverters

	Statistic	
Sensitivity Level 1%		
Participants with a Next Generation Sequencing Assessment (1% sensitivity: UMI >/= 298) at seroconversion time point (N)	XX	
Amino Acid Change in RT (a)	**NGS n (%)**	**Paired Population-based Genotype n (%)**
Y82X	X (XX.X%)	X (XX.X%)
Y87X	X (XX.X%)	X (XX.X%)
Y88X	X (XX.X%)	X (XX.X%)
Y88X + Y88Z or Y88X/Z	X (XX.X%)	X (XX.X%)
Y90X	X (XX.X%)	X (XX.X%)
etc.		
Sensitivity Level 5%		
Participants with a Next Generation Sequencing Assessment (5% sensitivity: UMI >/= 58) at seroconversion time point (N)	XX	
Amino Acid Change in RT (a)	**NGS n (%)**	**Paired Population-based Genotype n (%)**
Y82X	X (XX.X%)	X (XX.X%)
Y87X	X (XX.X%)	X (XX.X%)
Y88X	X (XX.X%)	X (XX.X%)

Y88X + Y88Z or Y88X/Z	X (XX.X%)	X (XX.X%)
Y90X	X (XX.X%)	X (XX.X%)
etc.		

Sensitivity Level 10%

Participants with a Next Generation Sequencing Assessment (10% sensitivity: UMI >/= 28) at seroconversion time point (N) XX

Amino Acid Change in RT (a)	**NGS n (%)**	**Paired Population-based Genotype n (%)**
Y82X	X (XX.X%)	X (XX.X%)
Y87X	X (XX.X%)	X (XX.X%)
Y88X	X (XX.X%)	X (XX.X%)
Y88X + Y88Z or Y88X/Z	X (XX.X%)	X (XX.X%)
Y90X	X (XX.X%)	X (XX.X%)
etc.		

Sensitivity Level > 10%

Participants with a Next Generation Sequencing Assessment (> 10% sensitivity: UMI < 28) at seroconversion time point (N). XX

Amino Acid Change in RT (a)	**NGS n (%) (a)**	**Paired Population-based Genotype n (%)**
Y82X	X (XX.X%)	X (XX.X%)
Y87X	X (XX.X%)	X (XX.X%)
Y88X	X (XX.X%)	X (XX.X%)
Y88Z	X (XX.X%)	X (XX.X%)
Y88X + Y88Z or Y88X/Z	X (XX.X%)	X (XX.X%)
Y90X	X (XX.X%)	X (XX.X%)

etc.

N = Number of participants with data; n = number of participants with that observation.
NGS analyses should be considered exploratory.
The percentage calculation is based on the total number of participants with a next-generation sequencing assessment.
The sequenced region contains RT amino acids 80 – 150 and 152 - 212.
Participants may be counted more than once.
The reference sequence was the HXB2 sequence (NCBI accession number K03455.1, https://www.ncbi.nlm.nih.gov/nuccore/1906382 accessed 13th January 2021). Within the NGS sequencing range, this differs from the Stanford consensus B sequence only at residue 122 (consensus amino acid: lysine, 'K'; HXB2: glutamic acid, 'E').
(a) Mixtures of variants with wild-type and mutant viral species (e.g. K103N at ≤ 99% prevalence) for NGS data will be counted as the mutation being present (i.e. as 'K103N'). Similar mixtures detected using population-based genotyping (e.g. K103K/N) should be reported and counted as such. For NGS data, each mutant viral species will be counted (e.g. K103N and K103S from the same sample are counted in separate rows). Population-based genotypes having mixtures of mutations (e.g. K103N/S), will be reported as such and counted only once. Codons will be counted separately, therefore one participant with multiple mutations (e.g. K103N, E138A) will be counted more than once (i.e. twice in the example given).

[Note to programmer: Amino acids are listed in numeric order; population-based genotyping data is included as numbers are different from main analysis; residues with only null entries should be omitted; more than one variant at any residue should be reported separately; mixtures in the population-based genotypes should be counted if the mutation is present in the mixture (e.g. V108V/I would be counted with V108I in the NGS row). A separate line showing the mixture in the population-based genotype column only should then be included – mixtures will not be present by NGS. See above for Sensitivity > 10%]

Table 14.3.9.2.2
Summary of Numbers and Combinations of HIV-1 NNRTI Resistance-associated Mutations Among HIV-1 Seroconverters using Next Generation Sequencing with Paired Population-Based Genotyping
Virology Population

	Statistic	
Sensitivity Level 1%		
Participants with a Next Generation Sequencing Assessment (1% sensitivity: UMI >/= 298) at seroconversion time point (N)	XX	
	NGS n (%)	**Population-based Genotype n (%)**
Stanford Number of NNRTI RAMs per participant (a)		
None	XX (X.X%)	XX (X.X%)
Any	X (X.X%)	X (X.X%)
One	X (X.X%)	X (X.X%)
Two	X (X.X%)	X (X.X%)
Three or more	X (X.X%)	X (X.X%)
Average	0.XX	0.XX
Stanford NNRTI resistance mutation combinations (a)		
A98G	X (X.X%)	X (X.X%)
K101E	X (X.X%)	X (X.X%)
K101E + E138A	X (X.X%)	X (X.X%)
K101E + E138A + E138K (or K101E + E138A/K (b))	X (X.X%)	X (X.X%)
etc.		
Sensitivity Level 5%		
Participants with a Next Generation Sequencing Assessment (5% sensitivity: UMI >/= 58) at seroconversion time point (N)	XX	

	NGS n (%)	**Population-based Genotype n (%)**
Stanford Number of NNRTI RAMs per participant (a)		
None	XX (X.X%)	XX (X.X%)
Any	X (X.X%)	X (X.X%)
One	X (X.X%)	X (X.X%)
Two	X (X.X%)	X (X.X%)
Three or more	X (X.X%)	X (X.X%)
Average	0.XX	0.XX
Stanford NNRTI resistance mutation combinations (a)		
A98G	X (X.X%)	X (X.X%)
K101E	X (X.X%)	X (X.X%)
K101E + E138A	X (X.X%)	X (X.X%)
K101E + E138A + E138K (or K101E + E138A/K (b))	X (X.X%)	X (X.X%)
etc.		

Sensitivity Level 10%
Participants with a Next Generation Sequencing Assessment (10% sensitivity: UMI >/= 28) at seroconversion time point (N) XX

	NGS n (%)	**Population-based Genotype n (%)**
Stanford Number of NNRTI RAMs per participant (a)		
None	XX (X.X%)	XX (X.X%)
Any	X (X.X%)	X (X.X%)
One	X (X.X%)	X (X.X%)
Two	X (X.X%)	X (X.X%)
Three or more	X (X.X%)	X (X.X%)
Average	0.XX	0.XX
Stanford NNRTI resistance mutation combinations (a)		
A98G	X (X.X%)	X (X.X%)
K101E	X (X.X%)	X (X.X%)
K101E + E138A	X (X.X%)	X (X.X%)
K101E + E138A + E138K (or K101E + E138A/K (b))	X (X.X%)	X (X.X%)
etc. as above		

Sensitivity Level > 10%

Participants with a Next Generation Sequencing Assessment (> 10% sensitivity: UMI < 28) at seroconversion time point (N) XX

	NGS n (%)	**Population-based Genotype n (%)**
Stanford Number of NNRTI RAMs per participant (a)		
None	XX (X.X%)	XX (X.X%)
Any	X (X.X%)	X (X.X%)
One	X (X.X%)	X (X.X%)
Two	X (X.X%)	X (X.X%)
Three or more	X (X.X%)	X (X.X%)
Average	0.XX	0.XX
Stanford NNRTI RAM combinations (a)		
A98G	X (X.X%)	X (X.X%)
K101E	X (X.X%)	X (X.X%)
K101E + E138A	X (X.X%)	X (X.X%)
K101E + E138A + E138K (or K101E + E138A/K (b))	X (X.X%)	X (X.X%)
etc. as above		

N = Number of participants with data; n = number of participants with that observation; N/A = not applicable (mutations pattern was not detected); NNRTI = Non-nucleoside Reverse Transcriptase Inhibitor.
The percentage calculation is based on the total number of participants in the Virology Population and with a qualifying NGS assessment.
Participants are counted only once for each analysis (i.e. number of NNRTI RAMs per participant and number of each NNRTI RAM combination) within each sensitivity level.
The sequenced region contains RT amino acids 80 – 150 and 152 - 212. NGS analyses should be considered exploratory.
The Stanford HIV-1 Drug Resistance Database version 8.4 (dated 2017-06-16) was used.
(a) Mixtures of variants with wild-type and mutant viral minority species (e.g. K103N at ≤ 99% prevalence for NGS data or K103K/N for population-based genotyping) will be counted as the mutation being present (i.e. as 'K103N' in this example). Each sequence will be counted only once.
(b) Mixtures observed using population-based genotyping will be reported as 'E138A/K', whereas these will be reported separately as 'E138A' and 'E138K' using NGS.

[Note to programmer: Amino acids are listed in numeric order; population-based genotyping included as numbers might be different from main analysis. To simplify the analysis of population-based genotype mixtures, include the count if the mixture includes a variant from the NGS analysis. Also, if there is more than one variant detected by NGS, these should be included in the listed row. The example: K101E + E138A + E138K + Y181C might be represented in the population-based genotype as K101E + E138A/K + Y181C the E138A + E138K would count as one mutation, but subsequently broken down by sequence. The example shows all possible population-based genotypes, only ones that apply should be included.]

Table 14.3.9.3.1
Summary of Phenotypic Susceptibility to Dapivirine and Other NNRTIs by Population-based Genotype
Virology Population

All Viruses	**Dapivirine**	**Efavirenz**	**Etravirine**	**Nevirapine**	**Rilpivirine**
N	XX	XX	XX	XX	XX
IC_{50} (nM)					
Geometric mean (SD)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)
(25th/median/75th)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)
(Min,max)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)
Fold change (a)					
Geometric mean (SD)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)
(25th/median/75th)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)
(Min,max)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)
Wild-type viruses (b)					
N	XX	XX	XX	XX	XX
IC_{50} (nM)					
Geometric mean (SD)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)
(25th/median/75th)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)
(Min,max)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)
Fold change (a)					
Geometric mean (SD)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)
(25th/median/75th)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)
(Min,max)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)

Viruses with any NNRTI RAM					
N	XX	XX	XX	XX	XX
IC_{50} (nM)					
Geometric mean (SD)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)
(25th/median/75th)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)
(Min,max)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)
Fold change (a)					
Geometric mean (SD)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)
(25th/median/75th)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)
(Min,max)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)
Viruses with one NNRTI RAM					
N	XX	XX	XX	XX	XX
IC_{50} (nM)					
Geometric mean (SD)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)
(25th/median/75th)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)
(Min,max)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)
Fold change (a)					
Geometric mean (SD)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)
(25th/median/75th)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)
(Min,max)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)
Viruses with two NNRTI RAMs					
N	XX	XX	XX	XX	XX
IC_{50} (nM)					
Geometric mean (SD)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)
(25th/median/75th)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)

(Min,max)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)
Fold change (a)					
Geometric mean (SD)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)
(25th/median/75th)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)
(Min,max)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)
Viruses with three or more NNRTI RAMs					
N	XX	XX	XX	XX	XX
IC_{50} (nM)					
Geometric mean (SD)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)
(25th/median/75th)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)
(Min,max)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)
Fold change (a)					
Geometric mean (SD)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)
(25th/median/75th)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)
(Min,max)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)
Viruses with A98G					
etc.					
Viruses with K101E					
etc.					
Viruses with K101E + E138A					
etc.					

(a) Fold change = IC_{50}/IC_{50}wild-type reference control.
(b) Mutations are included from population-based genotyping results (minority species mutations are less likely to influence phenotypes).

Table 14.3.9.4.1
Summary of Number of Participants with an Amino Acid Change from Reference per Residue in the RT Region Among HIV-1 Seroconversions using Population-Based Genotyping (All Seroconversion ± 14-Days Data)
Virology Population

	Population-based Genotype n (%)
Participants with a population-based genotyping assessment at seroconversion time point (N)	XX
Stanford Number of NNRTI RAMs per participant (a)	
None	XX (X.X%)
Any	X (X.X%)
One	X (X.X%)
Two	X (X.X%)
Three or more	X (X.X%)
Average	0.XX
Stanford NNRTI resistance mutation combinations (b)	
A98G	X (X.X%)
K101E	X (X.X%)
K101E + E138A	X (X.X%)
K101E + E138A/K + Y181C	X (X.X%)
etc.	

N = Number of participants with data; n = number of participants with that observation; NNRTI = Non-nucleoside Reverse Transcriptase Inhibitor.
The percentage calculation is based on the total number of participants with a successful population-based genotyping assessment at seroconversion.
The Stanford HIV-1 Drug Resistance Database version 8.4 (dated 2017-06-16) was used.
(a) Instances of mixtures among the population-based genotypes that include one or more NNRTI RAM, are counted as if the mutation with the greatest drug resistance score was present.

LISTING SHELLS

Listing	Title
16.2.8.20	**Next Generation Sequencing and Phenotype Susceptibility Data**
16.2.8.20.1	Next Generation Sequencing: Listing of All Available Data
16.2.8.20.2	Next Generation Sequencing: Listing of Detected NNRTI Resistance-associated Mutations
16.2.8.20.4	Phenotypic Data: Listing of All Available Data
16.2.8.20.5	Genotypic Interpretations with Phenotypic Data: Full Listing for HIV-1 Seroconverters

Note: Population-based genotyping data are listed in the IPM 032 CSR Listings.

Listing 16.2.8.20.1
Next Generation Sequencing: Listing of All Available Data
Safety Population

PID (a)	Sample Date	Days (b)	Days (c)	Visit Day (d)	Log_{10} HIV-1 RNA (copies/mL)	Number UMI with Consensus	Sample Sensitivity (%)	Valid Result	Amino acid (% UMI) Change from Reference (e)
XXX-XXXXXX	DDMMMYYYY	XX	XX	XXX	X.XXX	XXXX	X	Yes/No	YxxX (xx), YxxX (xx), YxxxX (xx),….
etc.									

(a) PIDs infected on enrolment indicated with 'α'; PIDs with seroconversion off DVR-004 use indicated with 'β'.

(b) Days since seroconversion (negative values indicate evaluation prior to seroconversion).

(c) Days since first HIV-1 RNA detection.

(d) Visits indicated with a * are not within 14 days of the seroconversion time point.

(e) Reference sequence: HXB2 (accession number K03455-1).

The sequenced region contains RT amino acids 81 – 150, 152 - 212. NGS analyses are considered exploratory.

[Notes to programmer: Amino acids are listed in numeric order (Note e); choose appropriate markers for different populations (Note a).]

Listing 16.2.8.20.2
Next Generation Sequencing: Listing of Detected NNRTI Resistance-associated Mutations
Safety Population

PID (a)	Sample Date	Days (b)	Days (c)	Visit Day	Visit (d)	Number UMI with Consensus	Sample Sensitivity (%)	Number of Mutations	NNRTI RAMs (e)
XXX-XXXXXX	DDMMMYYYY	XX	XX	XXX	Month XX/ Week XX	XXXX	X	X	YxxZ (xx), YxxZ (xx),….
XXX-XXXXXX	DDMMMYYYY	XX	XX	XXX	Month XX/ Week XX	XXXX	X	X	None
XXX-XXXXXX	DDMMMYYYY	XX	XX	XXX	Month XX/ Week XX	XXXX	X	X	No Test

etc.

Table includes PIDS only if NNRTI RAMs were detected in NGS analysis.

(a) PIDs infected on enrolment indicated with 'α'; PIDs with seroconversion off DVR-004 use indicated with 'β'.

(b) Days since seroconversion (negative values indicate evaluation prior to seroconversion).

(c) Days since first HIV-1 RNA detection.

(d) Visits indicated with a * are not within 14 days of the seroconversion time point.

(e) Mutations reported according to Stanford HIVdb algorithm version 8.4 (see SAP).

The sequenced region contains RT amino acids 81 – 150, 152 - 212. NGS analyses should be considered exploratory.

[Notes to programmer: Amino acids are listed in numeric order (Note e); choose appropriate markers for different populations (Note a).]

Listing 16.2.8.20.4
Phenotypic Data: Listing of All Available Data
Safety Population

				DPV		EFV		ETR		NVP		RPV	
PID	Sample Date	NNRTI RAMs	Result ID	IC_{50} (nM)	FC (a)	IC_{50} (nM)	FC (a)	IC_{50} (nM)	FC (a)	IC_{50} (nM)	FC (a)	IC_{50} (nM)	FC (a)
XXX-XXXXXX	DDMMMYYYY	None	1	x.xx (x.xx)		x.xx (x.xx)		x.xx (x.xx)		x.xx (x.xx)		x.xx (x.xx)	
			2	x.xx (x.xx)									
			3	x.xx (x.xx)									
			Avg	x.xx (x.xx)	x.x	x.xx (x.xx)	x.x	x.xx (x.xx)	x.x	x.xx (x.xx)	x.x	x.xx (x.xx)	x.x

etc.

DPV = Dapivirine; EFV = Efavirenz; ETR = Etravirine; FC: Fold change; IC_{50}: 50% Inhibitory concentration; NNRTI: Non-nucleoside reverse transcriptase inhibitor; NVP = Nevirapine; PID: Participant identifier; RAM: Resistance-associated mutation; RPV = Rilpivirine
(a) FC = IC50/IC50CONTROL (Control IC50 [nM] range: DPV: n = X: X.XX - X.XX; EFV: n = X: X.XX - X.XX ; ETR: n = X: X.XX - X.XX; NVP: n = X: X.XX - X.XX; RPV: n = X: X.XX - X.XX). n: number of runs to complete the analysis.
(b) IC50 sample and (IC50 reference virus) are given.

[Note to programmer: Order by PID and then by NNRTI RAMs with 'None' first, then mutations in numeric order. Note the reference virus will be different from that in IPM 027 - a single lab-strain has been used per run.]

Listing 16.2.8.20.5
Genotypic Interpretations with Phenotypic Data: Full Listing for HIV-1 Seroconverters
Safety Population

		NNRTI RAMs			NNRTI Genotypic Susceptibility (Population-based sequencing)	Phenotype	
PID	Sample Date	Population	NGS	NNRTI	(a)	IC_{50} (nM)	FC (b)
XXX-XXXXXX	DDMMMYYYY	None	None	Dapivirine	N/A	X.XX	X.X
				Efavirenz	XX (YYY)	X.XX	X.X
				Etravirine	XX (YYY)	X.XX	X.X
				Nevirapine	XX (YYY)	X.XX	X.X
				Rilpivirine	XX (YYY)	X.XX	X.X
XXX-XXXXXX	DDMMMYYYY	YXXY	YXXY	Dapivirine	N/A	X.XX	X.X
				Efavirenz	XX (YYY)	X.XX	X.X
				Etravirine	XX (YYY)	X.XX	X.X
				Nevirapine	XX (YYY)	X.XX	X.X
				Rilpivirine	XX (YYY)	X.XX	X.X

etc.

HLR = High-level resistant; Interm = Intermediate resistant; LLR = Low-level resistant; N/A = Not applicable; NNRTI = Non-nucleoside Reverse Transcriptase Inhibitor; PLLR = Potential low-level resistant; RAM: Resistance-associated mutation; Sus = Susceptibility.

(a) Stanford HIVdb algorithm version 8.4 drug resistance score (interpretation: Sus, PLLR, LLR, Interm, HLR).

(b) FC = $IC_{50}/IC_{50Control}$ (Control IC50 [nM] range: DPV: n = X: X.XX - X.XX; EFV: n = X: X.XX - X.XX ; ETR: n = X: X.XX - X.XX; NVP: n = X: X.XX - X.XX; RPV: n = X: X.XX - X.XX)

[Note to programmer: Order by PID then by NNRTI RAMs with 'None' first, then mutations in numeric order (as per Phenotype Listing 16.2.8.20.4).]

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Charles Craig jcccrv@gmail.com Security Level: Email, Account Authentication (Required)	Charles Craig Signature Adoption: Pre-selected Style Signature ID: ACB6AE41-8A0B-4DCE-81DD-5FD6BC77A3B6 Using IP Address: 109.148.254.104 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	Sent: 5/24/2021 11:28:08 AM Viewed: 5/26/2021 4:48:46 AM Signed: 5/26/2021 6:58:55 AM
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John Steytler jsteytler@ipmglobal.org VP, Pharmacovigilance and Clinical Development International Partnership For Microbicides, Inc. Security Level: Email, Account Authentication (Required)	John Steytler Signature Adoption: Pre-selected Style Signature ID: 910A8946-697A-4AC0-B448-39A5F9A90235 Using IP Address: 45.222.24.44 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	Sent: 5/24/2021 11:28:08 AM Viewed: 5/24/2021 11:34:35 AM Signed: 5/24/2021 11:35:43 AM
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Neliette van Niekerk nvanniekerk@ipmglobal.org Senior Director Biometrics, Clinical Affairs Security Level: Email, Account Authentication (Required)	Neliette van Niekerk Signature Adoption: Pre-selected Style Signature ID: C949EDC4-4EBD-4938-A630-06F485AEDC71 Using IP Address: 105.209.232.100 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	Sent: 5/24/2021 11:28:08 AM Viewed: 5/24/2021 11:40:51 AM Signed: 5/24/2021 11:43:40 AM
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IPM 032 VIROLOGY ADDENDUM SAP

APPENDIX 1

TABLE AND LISTING SHELLS – VERSION 1.0, 24 MAY 2021

TABLE SHELLS

Table 14.3.9.1.1
Sample Availability
Virology Population

	Statistic
HIV-1 Seroconversion Participants, N1	XX
Seroconversion Samples Available, N2 (%) (a)	xx (x.x%)
No sample n (%) (a)	xx (x.x%)
Sample not suitable n (%) (a)	xx (x.x%)
No consent n (%) (a)	xx (x.x%)
Seroconversion Samples with NGS Analysis Attempted, n (%) (b)	xx (x.x%)
HIV-1 seroconversion participants with a successful NGS genotype, N3 (%) (b)	xx (x.x%)
Sensitivity to detect RAMs present with at least:	
≤ 1% variant, n (%) (c)	xx (x.x%)
> 1% to 5% variant, n (%) (c)	xx (x.x%)
> 5% to 10% variant, n (%) (c)	xx (x.x%)
Invalid Result, n (%) (b, d)	xx (x.x%)
Test performed, no output (c)	xx (x.x%)
Sensitivity to detect RAMs present at:	
>10% to 20% variant, n (%) (c,d)	xx (x.x%)
> 20% variant, n (%) (c,d)	xx (x.x%)
Seroconversion Samples with Phenotypic Susceptibility Analysis Attempted, n (%) (b)	xx (x.x%)
HIV-1 seroconversion participants with any successful Phenotypic analysis (%) (b, e)	xx (x.x%)
Invalid or No Test Result, n (%) (b)	xx (x.x%)
Failed Testing (All phenotypes), n (%) (b)	xx (x.x%)
No test (Insufficient sample volume), n (%) (b,f)	xx (x.x%)

The percentage calculation is based on the total number of participants in the denoted section.
(a) Denominator = N1. (b) Denominator = N2. (c) Denominator = N3.
(d) Due to low UMI (< 28), these are considered to provide invalid results. Mutations detected in these samples will be reported separately.
(e) In the unlikely event of one to four of the five phenotypic test results for successful analysis being missing, this should be footnoted with the affected participant identifier.
(f) Some samples may have had inadequate volume to perform both the NGS and the phenotypic tests and so analysis was performed with NGS as priority, followed by phenotype determination.

Table 14.3.9.2.1
Summary of Numbers of Participants with an Amino Acid Change from Reference per Residue in the NGS Sequenced RT Region Among HIV-1 Seroconverters using Next Generation Sequencing with Paired Population-Based Genotyping
Virology Population

Next Generation Sequencing: Number of Participants with an Amino Acid Change from Reference per Residue in the RT Region Among HIV-1 Seroconverters

	Statistic	
Sensitivity Level 1%		
Participants with a Next Generation Sequencing Assessment (1% sensitivity: UMI >/= 298) at seroconversion time point (N)	XX	
Amino Acid Change in RT (a)	**NGS n (%)**	**Paired Population-based Genotype n (%)**
Y82X	X (XX.X%)	X (XX.X%)
Y87X	X (XX.X%)	X (XX.X%)
Y88X	X (XX.X%)	X (XX.X%)
Y88X + Y88Z or Y88X/Z	X (XX.X%)	X (XX.X%)
Y90X	X (XX.X%)	X (XX.X%)
etc.		
Sensitivity Level 5%		
Participants with a Next Generation Sequencing Assessment (5% sensitivity: UMI >/= 58) at seroconversion time point (N)	XX	
Amino Acid Change in RT (a)	**NGS n (%)**	**Paired Population-based Genotype n (%)**
Y82X	X (XX.X%)	X (XX.X%)
Y87X	X (XX.X%)	X (XX.X%)
Y88X	X (XX.X%)	X (XX.X%)

Y88X + Y88Z or Y88X/Z	X (XX.X%)	X (XX.X%)
Y90X	X (XX.X%)	X (XX.X%)
etc.		

Sensitivity Level 10%

Participants with a Next Generation Sequencing Assessment (10% sensitivity: UMI >/= 28) at seroconversion time point (N) XX

Amino Acid Change in RT (a)	**NGS n (%)**	**Paired Population-based Genotype n (%)**
Y82X	X (XX.X%)	X (XX.X%)
Y87X	X (XX.X%)	X (XX.X%)
Y88X	X (XX.X%)	X (XX.X%)
Y88X + Y88Z or Y88X/Z	X (XX.X%)	X (XX.X%)
Y90X	X (XX.X%)	X (XX.X%)
etc.		

Sensitivity Level > 10%

Participants with a Next Generation Sequencing Assessment (> 10% sensitivity: UMI < 28) at seroconversion time point (N). XX

Amino Acid Change in RT (a)	**NGS n (%) (a)**	**Paired Population-based Genotype n (%)**
Y82X	X (XX.X%)	X (XX.X%)
Y87X	X (XX.X%)	X (XX.X%)
Y88X	X (XX.X%)	X (XX.X%)
Y88Z	X (XX.X%)	X (XX.X%)
Y88X + Y88Z or Y88X/Z	X (XX.X%)	X (XX.X%)
Y90X	X (XX.X%)	X (XX.X%)

etc.

N = Number of participants with data; n = number of participants with that observation.
NGS analyses should be considered exploratory.
The percentage calculation is based on the total number of participants with a next-generation sequencing assessment.
The sequenced region contains RT amino acids 80 – 150 and 152 - 212.
Participants may be counted more than once.
The reference sequence was the HXB2 sequence (NCBI accession number K03455.1, https://www.ncbi.nlm.nih.gov/nuccore/1906382 accessed 13th January 2021). Within the NGS sequencing range, this differs from the Stanford consensus B sequence only at residue 122 (consensus amino acid: lysine, 'K'; HXB2: glutamic acid, 'E').
(a) Mixtures of variants with wild-type and mutant viral species (e.g. K103N at ≤ 99% prevalence) for NGS data will be counted as the mutation being present (i.e. as 'K103N'). Similar mixtures detected using population-based genotyping (e.g. K103K/N) should be reported and counted as such. For NGS data, each mutant viral species will be counted (e.g. K103N and K103S from the same sample are counted in separate rows). Population-based genotypes having mixtures of mutations (e.g. K103N/S), will be reported as such and counted only once. Codons will be counted separately, therefore one participant with multiple mutations (e.g. K103N, E138A) will be counted more than once (i.e. twice in the example given).

[Note to programmer: Amino acids are listed in numeric order; population-based genotyping data is included as numbers are different from main analysis; residues with only null entries should be omitted; more than one variant at any residue should be reported separately; mixtures in the population-based genotypes should be counted if the mutation is present in the mixture (e.g. V108V/I would be counted with V108I in the NGS row). A separate line showing the mixture in the population-based genotype column only should then be included – mixtures will not be present by NGS. See above for Sensitivity > 10%]

Table 14.3.9.2.2
Summary of Numbers and Combinations of HIV-1 NNRTI Resistance-associated Mutations Among HIV-1 Seroconverters using Next Generation Sequencing with Paired Population-Based Genotyping
Virology Population

	Statistic	
Sensitivity Level 1%		
Participants with a Next Generation Sequencing Assessment (1% sensitivity: UMI >/= 298) at seroconversion time point (N)	XX	
	NGS n (%)	**Population-based Genotype n (%)**
Stanford Number of NNRTI RAMs per participant (a)		
None	XX (X.X%)	XX (X.X%)
Any	X (X.X%)	X (X.X%)
One	X (X.X%)	X (X.X%)
Two	X (X.X%)	X (X.X%)
Three or more	X (X.X%)	X (X.X%)
Average	0.XX	0.XX
Stanford NNRTI resistance mutation combinations (a)		
A98G	X (X.X%)	X (X.X%)
K101E	X (X.X%)	X (X.X%)
K101E + E138A	X (X.X%)	X (X.X%)
K101E + E138A + E138K (or K101E + E138A/K (b))	X (X.X%)	X (X.X%)
etc.		
Sensitivity Level 5%		
Participants with a Next Generation Sequencing Assessment (5% sensitivity: UMI >/= 58) at seroconversion time point (N)	XX	

	NGS n (%)	**Population-based Genotype n (%)**
Stanford Number of NNRTI RAMs per participant (a)		
None	XX (X.X%)	XX (X.X%)
Any	X (X.X%)	X (X.X%)
One	X (X.X%)	X (X.X%)
Two	X (X.X%)	X (X.X%)
Three or more	X (X.X%)	X (X.X%)
Average	0.XX	0.XX
Stanford NNRTI resistance mutation combinations (a)		
A98G	X (X.X%)	X (X.X%)
K101E	X (X.X%)	X (X.X%)
K101E + E138A	X (X.X%)	X (X.X%)
K101E + E138A + E138K (or K101E + E138A/K (b))	X (X.X%)	X (X.X%)
etc.		

Sensitivity Level 10%
Participants with a Next Generation Sequencing Assessment (10% sensitivity: UMI >/= 28) at seroconversion time point (N) XX

	NGS n (%)	**Population-based Genotype n (%)**
Stanford Number of NNRTI RAMs per participant (a)		
None	XX (X.X%)	XX (X.X%)
Any	X (X.X%)	X (X.X%)
One	X (X.X%)	X (X.X%)
Two	X (X.X%)	X (X.X%)
Three or more	X (X.X%)	X (X.X%)
Average	0.XX	0.XX
Stanford NNRTI resistance mutation combinations (a)		
A98G	X (X.X%)	X (X.X%)
K101E	X (X.X%)	X (X.X%)
K101E + E138A	X (X.X%)	X (X.X%)
K101E + E138A + E138K (or K101E + E138A/K (b))	X (X.X%)	X (X.X%)
etc. as above		

Sensitivity Level > 10%

Participants with a Next Generation Sequencing Assessment (> 10% sensitivity: UMI < 28) at seroconversion time point (N) XX

	NGS n (%)	**Population-based Genotype n (%)**
Stanford Number of NNRTI RAMs per participant (a)		
None	XX (X.X%)	XX (X.X%)
Any	X (X.X%)	X (X.X%)
One	X (X.X%)	X (X.X%)
Two	X (X.X%)	X (X.X%)
Three or more	X (X.X%)	X (X.X%)
Average	0.XX	0.XX
Stanford NNRTI RAM combinations (a)		
A98G	X (X.X%)	X (X.X%)
K101E	X (X.X%)	X (X.X%)
K101E + E138A	X (X.X%)	X (X.X%)
K101E + E138A + E138K (or K101E + E138A/K (b))	X (X.X%)	X (X.X%)
etc. as above		

N = Number of participants with data; n = number of participants with that observation; N/A = not applicable (mutations pattern was not detected); NNRTI = Non-nucleoside Reverse Transcriptase Inhibitor.
The percentage calculation is based on the total number of participants in the Virology Population and with a qualifying NGS assessment.
Participants are counted only once for each analysis (i.e. number of NNRTI RAMs per participant and number of each NNRTI RAM combination) within each sensitivity level.
The sequenced region contains RT amino acids 80 – 150 and 152 - 212. NGS analyses should be considered exploratory.
The Stanford HIV-1 Drug Resistance Database version 8.4 (dated 2017-06-16) was used.
(a) Mixtures of variants with wild-type and mutant viral minority species (e.g. K103N at ≤ 99% prevalence for NGS data or K103K/N for population-based genotyping) will be counted as the mutation being present (i.e. as 'K103N' in this example). Each sequence will be counted only once.
(b) Mixtures observed using population-based genotyping will be reported as 'E138A/K', whereas these will be reported separately as 'E138A' and 'E138K' using NGS.

[Note to programmer: Amino acids are listed in numeric order; population-based genotyping included as numbers might be different from main analysis. To simplify the analysis of population-based genotype mixtures, include the count if the mixture includes a variant from the NGS analysis. Also, if there is more than one variant detected by NGS, these should be included in the listed row. The example: K101E + E138A + E138K + Y181C might be represented in the population-based genotype as K101E + E138A/K + Y181C the E138A + E138K would count as one mutation, but subsequently broken down by sequence. The example shows all possible population-based genotypes, only ones that apply should be included.]

Table 14.3.9.3.1
Summary of Phenotypic Susceptibility to Dapivirine and Other NNRTIs by Population-based Genotype
Virology Population

All Viruses	**Dapivirine**	**Efavirenz**	**Etravirine**	**Nevirapine**	**Rilpivirine**
N	XX	XX	XX	XX	XX
IC_{50} (nM)					
Geometric mean (SD)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)
(25th/median/75th)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)
(Min,max)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)
Fold change (a)					
Geometric mean (SD)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)
(25th/median/75th)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)
(Min,max)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)
Wild-type viruses (b)					
N	XX	XX	XX	XX	XX
IC_{50} (nM)					
Geometric mean (SD)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)
(25th/median/75th)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)
(Min,max)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)
Fold change (a)					
Geometric mean (SD)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)
(25th/median/75th)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)
(Min,max)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)

Viruses with any NNRTI RAM					
N	XX	XX	XX	XX	XX
IC_{50} (nM)					
Geometric mean (SD)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)
(25th/median/75th)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)
(Min,max)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)
Fold change (a)					
Geometric mean (SD)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)
(25th/median/75th)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)
(Min,max)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)
Viruses with one NNRTI RAM					
N	XX	XX	XX	XX	XX
IC_{50} (nM)					
Geometric mean (SD)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)
(25th/median/75th)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)
(Min,max)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)
Fold change (a)					
Geometric mean (SD)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)
(25th/median/75th)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)
(Min,max)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)
Viruses with two NNRTI RAMs					
N	XX	XX	XX	XX	XX
IC_{50} (nM)					
Geometric mean (SD)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)
(25th/median/75th)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)

(Min,max)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)
Fold change (a)					
Geometric mean (SD)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)
(25th/median/75th)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)
(Min,max)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)
Viruses with three or more NNRTI RAMs					
N	XX	XX	XX	XX	XX
IC_{50} (nM)					
Geometric mean (SD)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)
(25th/median/75th)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)
(Min,max)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)
Fold change (a)					
Geometric mean (SD)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)	x.xx (x.xxx)
(25th/median/75th)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)	(x.xx/x.xx/x.xx)
(Min,max)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)	(x.xx/xx.xx)
Viruses with A98G					
etc.					
Viruses with K101E					
etc.					
Viruses with K101E + E138A					
etc.					

(a) Fold change = IC_{50}/IC_{50}wild-type reference control.
(b) Mutations are included from population-based genotyping results (minority species mutations are less likely to influence phenotypes).

Table 14.3.9.4.1
Summary of Number of Participants with an Amino Acid Change from Reference per Residue in the RT Region Among HIV-1 Seroconversions using Population-Based Genotyping (All Seroconversion ± 14-Days Data)
Virology Population

	Population-based Genotype n (%)
Participants with a population-based genotyping assessment at seroconversion time point (N)	XX
Stanford Number of NNRTI RAMs per participant (a)	
None	XX (X.X%)
Any	X (X.X%)
One	X (X.X%)
Two	X (X.X%)
Three or more	X (X.X%)
Average	0.XX
Stanford NNRTI resistance mutation combinations (b)	
A98G	X (X.X%)
K101E	X (X.X%)
K101E + E138A	X (X.X%)
K101E + E138A/K + Y181C	X (X.X%)
etc.	

N = Number of participants with data; n = number of participants with that observation; NNRTI = Non-nucleoside Reverse Transcriptase Inhibitor.
The percentage calculation is based on the total number of participants with a successful population-based genotyping assessment at seroconversion.
The Stanford HIV-1 Drug Resistance Database version 8.4 (dated 2017-06-16) was used.
(a) Instances of mixtures among the population-based genotypes that include one or more NNRTI RAM, are counted as if the mutation with the greatest drug resistance score was present.

LISTING SHELLS

Listing	Title
16.2.8.20	**Next Generation Sequencing and Phenotype Susceptibility Data**
16.2.8.20.1	Next Generation Sequencing: Listing of All Available Data
16.2.8.20.2	Next Generation Sequencing: Listing of Detected NNRTI Resistance-associated Mutations
16.2.8.20.4	Phenotypic Data: Listing of All Available Data
16.2.8.20.5	Genotypic Interpretations with Phenotypic Data: Full Listing for HIV-1 Seroconverters

Note: Population-based genotyping data are listed in the IPM 032 CSR Listings.

Listing 16.2.8.20.1
Next Generation Sequencing: Listing of All Available Data
Safety Population

PID (a)	Sample Date	Days (b)	Days (c)	Visit Day (d)	Log_{10} HIV-1 RNA (copies/mL)	Number UMI with Consensus	Sample Sensitivity (%)	Valid Result	Amino acid (% UMI) Change from Reference (e)
XXX-XXXXXX	DDMMMYYYY	XX	XX	XXX	X.XXX	XXXX	X	Yes/No	YxxX (xx), YxxX (xx), YxxxX (xx),….
etc.									

(a) PIDs infected on enrolment indicated with 'α'; PIDs with seroconversion off DVR-004 use indicated with 'β'.

(b) Days since seroconversion (negative values indicate evaluation prior to seroconversion).

(c) Days since first HIV-1 RNA detection.

(d) Visits indicated with a * are not within 14 days of the seroconversion time point.

(e) Reference sequence: HXB2 (accession number K03455-1).

The sequenced region contains RT amino acids 81 – 150, 152 - 212. NGS analyses are considered exploratory.

[Notes to programmer: Amino acids are listed in numeric order (Note e); choose appropriate markers for different populations (Note a).]

Listing 16.2.8.20.2
Next Generation Sequencing: Listing of Detected NNRTI Resistance-associated Mutations
Safety Population

PID (a)	Sample Date	Days (b)	Days (c)	Visit Day	Visit (d)	Number UMI with Consensus	Sample Sensitivity (%)	Number of Mutations	NNRTI RAMs (e)
XXX-XXXXXX	DDMMMYYYY	XX	XX	XXX	Month XX/ Week XX	XXXX	X	X	YxxZ (xx), YxxZ (xx),….
XXX-XXXXXX	DDMMMYYYY	XX	XX	XXX	Month XX/ Week XX	XXXX	X	X	None
XXX-XXXXXX	DDMMMYYYY	XX	XX	XXX	Month XX/ Week XX	XXXX	X	X	No Test

etc.

Table includes PIDS only if NNRTI RAMs were detected in NGS analysis.

(a) PIDs infected on enrolment indicated with 'α'; PIDs with seroconversion off DVR-004 use indicated with 'β'.

(b) Days since seroconversion (negative values indicate evaluation prior to seroconversion).

(c) Days since first HIV-1 RNA detection.

(d) Visits indicated with a * are not within 14 days of the seroconversion time point.

(e) Mutations reported according to Stanford HIVdb algorithm version 8.4 (see SAP).

The sequenced region contains RT amino acids 81 – 150, 152 - 212. NGS analyses should be considered exploratory.

[Notes to programmer: Amino acids are listed in numeric order (Note e); choose appropriate markers for different populations (Note a).]

Listing 16.2.8.20.4
Phenotypic Data: Listing of All Available Data
Safety Population

				DPV		EFV		ETR		NVP		RPV	
PID	Sample Date	NNRTI RAMs	Result ID	IC_{50} (nM)	FC (a)	IC_{50} (nM)	FC (a)	IC_{50} (nM)	FC (a)	IC_{50} (nM)	FC (a)	IC_{50} (nM)	FC (a)
XXX-XXXXXX	DDMMMYYYY	None	1	x.xx (x.xx)		x.xx (x.xx)		x.xx (x.xx)		x.xx (x.xx)		x.xx (x.xx)	
			2	x.xx (x.xx)									
			3	x.xx (x.xx)									
			Avg	x.xx (x.xx)	x.x	x.xx (x.xx)	x.x	x.xx (x.xx)	x.x	x.xx (x.xx)	x.x	x.xx (x.xx)	x.x

etc.

DPV = Dapivirine; EFV = Efavirenz; ETR = Etravirine; FC: Fold change; IC_{50}: 50% Inhibitory concentration; NNRTI: Non-nucleoside reverse transcriptase inhibitor; NVP = Nevirapine; PID: Participant identifier; RAM: Resistance-associated mutation; RPV = Rilpivirine
(a) FC = IC50/IC50CONTROL (Control IC50 [nM] range: DPV: n = X: X.XX - X.XX; EFV: n = X: X.XX - X.XX ; ETR: n = X: X.XX - X.XX; NVP: n = X: X.XX - X.XX; RPV: n = X: X.XX - X.XX). n: number of runs to complete the analysis.
(b) IC50 sample and (IC50 reference virus) are given.

[Note to programmer: Order by PID and then by NNRTI RAMs with 'None' first, then mutations in numeric order. Note the reference virus will be different from that in IPM 027 - a single lab-strain has been used per run.]

Listing 16.2.8.20.5
Genotypic Interpretations with Phenotypic Data: Full Listing for HIV-1 Seroconverters
Safety Population

		NNRTI RAMs			NNRTI Genotypic Susceptibility (Population-based sequencing)	Phenotype	
PID	Sample Date	Population	NGS	NNRTI	(a)	IC_{50} (nM)	FC (b)
XXX-XXXXXX	DDMMMYYYY	None	None	Dapivirine	N/A	X.XX	X.X
				Efavirenz	XX (YYY)	X.XX	X.X
				Etravirine	XX (YYY)	X.XX	X.X
				Nevirapine	XX (YYY)	X.XX	X.X
				Rilpivirine	XX (YYY)	X.XX	X.X
XXX-XXXXXX	DDMMMYYYY	YXXY	YXXY	Dapivirine	N/A	X.XX	X.X
				Efavirenz	XX (YYY)	X.XX	X.X
				Etravirine	XX (YYY)	X.XX	X.X
				Nevirapine	XX (YYY)	X.XX	X.X
				Rilpivirine	XX (YYY)	X.XX	X.X

etc.

HLR = High-level resistant; Interm = Intermediate resistant; LLR = Low-level resistant; N/A = Not applicable; NNRTI = Non-nucleoside Reverse Transcriptase Inhibitor; PLLR = Potential low-level resistant; RAM: Resistance-associated mutation; Sus = Susceptibility.

(a) Stanford HIVdb algorithm version 8.4 drug resistance score (interpretation: Sus, PLLR, LLR, Interm, HLR).

(b) FC = $IC_{50}/IC_{50Control}$ (Control IC50 [nM] range: DPV: n = X: X.XX - X.XX; EFV: n = X: X.XX - X.XX ; ETR: n = X: X.XX - X.XX; NVP: n = X: X.XX - X.XX; RPV: n = X: X.XX - X.XX)

[Note to programmer: Order by PID then by NNRTI RAMs with 'None' first, then mutations in numeric order (as per Phenotype Listing 16.2.8.20.4).]