

**SUMMARY OF CHANGES  
INCLUDED IN THE FULL VERSION PROTOCOL AMENDMENT OF**

**MTN-032**

**Assessment of ASPIRE and HOPE Adherence**

**DAIDS Protocol #12058**

**A Non-IND Study**

**THE AMENDED PROTOCOL IS IDENTIFIED AS: Version 2.0/ September 5, 2017**

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**Information/Instructions to Study Sites**

The information contained in this protocol amendment impacts the MTN-032 study and must be forwarded to your Institutional Review Board (IRB)/Ethics Committee (EC) as soon as possible for their information and review. IRB approval is required before implementation of the modifications contained in this amendment. All IRB requirements must be followed.

Please file this Summary of Changes, Version 2.0 of the protocol and all associated IRB correspondence in your essential documents files for MTN-032.

**Summary of Revisions**

A summary of revisions is provided below:

1. Expansion of Phase 2 sample size and composition to include all HOPE participants, not just those that completed Phase 1, and to add a subset of focus group discussion (FGD) participants – Protocol Summary, Section 4 (Study Design), Section 5 (Study Population), Section 7 (Study Procedures), Section 10 (Analytical Considerations), Appendix II (Screening and Enrollment Sample Informed Consent Form [SIC]-Phase 2 (HOPE) Participants)
  - Changed sample size description from “Approximately 84 HOPE participants” or similar language to “Up to 156 HOPE participants” or similar language – Protocol Summary, Section 5.1 (Selection of Study Population), Section 7.2 (Phase 2: HOPE participants), Section 10.4 (Participant Selection), Appendix II (SIC-Phase 2 (HOPE) Participants)
  - Changed Phase 2 accrual duration from “Approximately 4-6 months” to “Approximately 9-12 months” – Protocol Summary, Section 4.3 (Time to Complete Accrual)
  - Added “an additional 2-3 months for Phase 2 FGD recruitment, if needed, once HOPE results are released” or similar language to sample size descriptions – Protocol Summary, Section 4.3 (Time to Complete Accrual), Section 10.4 (Participant Selection)

- Deleted “completed Phase 1 of MTN-032” eligibility criterion – Section 5.3.2 (Phase 2: HOPE Participants), Section 7.2 (Phase 2: HOPE Participants), Appendix II (SIC-Phase 2 (HOPE) Participants)
  - Changed descriptions of Phase 1 study activities from present tense to past tense given Phase 1 is already completed – Section 7.1 (Phase 1), Section 10.2 (Study Endpoints), Section 10.3.1 (ASPIRE (Phase 1) participants)
  - Modified language related to Phase 2 IDI sample selection and added language related to Phase 2 FGD sample selection to Section 7.2 (Phase 2: HOPE Participants)
  - Added FGD study visit procedure – Section 7.2 (Phase 2: HOPE Participants), Section 7.2.1 (Screening and Enrollment (HOPE participants) – Administrative, Behavioral and Regulatory Procedures), Section 10.2 (Study Endpoints)
  - Added Section 10.3.2 (HOPE (Phase 2) participants) describing sample size and composition specific to the Phase 2 HOPE participant study population
  - Modified Appendix II (SIC – Phase 2 (HOPE) Participants) to reflect the expanded Phase 2 sample size and composition as well as the addition of FGDs to the Phase 2 visit procedures
2. Expansion of Phase 2 sample size and composition to include male partners of HOPE participants who consented to allow their male partners to be contacted – Protocol Summary, Section 2 (Introduction), Section 4 (Study Design), Section 5 (Study Population), Section 7 (Study Procedures), Section 8 (Assessment of Safety), Section 10 (Analytical Considerations), Section 13 (Human Subjects Protection), Appendix III (SIC-HOPE Participants’ Male Partners), and Appendix IV (Permission to Contact Form)
- Added “up to 120 male partners of randomly selected HOPE participants who consented to have their male partners contacted” or similar language to sample size descriptions – Protocol Summary, Section 5.1 (Selection of Study Population), Section 10.4 (Participant Selection)
  - Added Section 2.5 (Role of Male Partners in Study Product Use and Trial Participation) providing background information on the role of male partners in women’s use of HIV prevention products
  - Added “Although studies show that male partners play an important role in women’s adherence to microbicides, more research is needed to understand how this manifests in the context of women’s uptake of the dapivirine VR” to Section 2.6 (Rationale for Study Design)
  - Added “including the role played by their male partners” to Section 4.1 (Identification of Study Design)
  - Added “male partners of HOPE participants who meet eligibility criteria” to Section 4.2 (Description of Study Population)
  - Added Section 5.3.3 (Phase 2: Male partners of HOPE participants) describing eligibility criteria for Phase 2 male partners
  - Added descriptions of sample selection and study procedures for Phase 2 male partners – Section 7.3 (Phase 2: Male partners of HOPE participants), Section 7.3.1 (Screening and Enrollment (Male partners of HOPE participants) – Administrative, Behavioral and Regulatory Procedures)
  - Added “from the perspective of both the participants and their male partners” or similar language to Section 7.4 (Behavioral Evaluations)

- Added description of permission to contact process to informed consent procedures – Section 8.2 (Social Harms Reporting), Section 13.4.1 (Risks), Section 13.5 (Informed Consent Process)
  - Added Section 10.3.3 (Male partners (Phase 2)) describing sample size and composition specific to the Phase 2 male partner study population
  - Added Appendix III (SIC-HOPE Participants' Male Partners) to consent HOPE participant male partners recruited for Phase 2
  - Added Appendix IV (Permission to Contact Form) to consent HOPE participants to allow study staff to contact their male partners for Phase 2 recruitment
3. Additions and modifications to Phase 2 research objectives in response to the expansion of Phase 2 sample size and composition – Protocol Summary, Section 2 (Introduction), Section 3 (Objectives), Section 7 (Study Procedures), Section 10 (Analytical Considerations)
- Primary Objectives – Protocol Summary, Section 2.6 (Rationale for Study Design), Section 3.1 (Primary Objectives), Section 10.1 (Overview and Summary of Design), Section 10.2 (Study Endpoints)
    - i. Added new objective “To explore male partner attitudes towards and experiences with the DPV VR, and their perspective of their female partner’s attitudes and experiences”
  - Secondary Objectives – Protocol Summary, Section 3.2 (Secondary Objectives), Section 10.1 (Overview and Summary of Design), Section 10.2 (Study Endpoints)
    - i. Modified existing “HIV risk and perceptions of HIV risk” objective to include “male partner support (or lack thereof) of participants’ product use in HOPE”
    - ii. Modified existing “understanding of ASPIRE results and ring efficacy” objective to include “male partner support (or lack thereof) of participants’ trial participation and product use in HOPE”
  - Exploratory Objectives – Protocol Summary, Section 2.6 (Rationale for Study Design), Section 3.3 (Exploratory Objectives), Section 7.2 (Phase 2: HOPE Participants), Section 7.4 (Behavioral Evaluations), Section 10.2 (Study Endpoints)
    - i. Modified existing “preference regarding drug delivery modalities” objective
    - ii. Added new objective “To explore how male partners and men should and could be engaged in scale up of ring demonstration projects and licensure in the future”
    - iii. Added new objective “To explore participants’ perspectives on marketing aspects of ring in scale up activities, e.g. most suitable target audiences and marketing approaches, support services needed, ideal access points, etc.”
    - iv. Added new objective “To explore key unexpected and/or important findings of HOPE trial results”
4. Updates to dapivirine VR safety, adherence, and/or acceptability background information, including recent results from ASPIRE, The Ring Study, MTN-024, and IB Version 11.0 – Section 2.3 (Dapivirine Vaginal Ring)
5. Updates to protocol language to better reflect study procedures as implemented during Phase 1
- Updated data analysis and management procedures – Section 10.5 (Data and Study Monitoring Procedures), Section 10.6 (Data Analysis)

- Added “and tools” and description of tools to Phase 2 visit procedure for administration of behavioral questionnaire – Section 7.2.1 (Screening and Enrollment (HOPE participants) – Administrative, Behavioral and Regulatory Procedures), Section 7.3.1 (Screening and Enrollment (Male partners of HOPE participants) – Administrative, Behavioral and Regulatory Procedures), Section 7.4.1 (Behavioral Questionnaires and Tools)
6. Updates to protocol to reflect recently added requirements for DAIDS-approved protocol documents
- Modified Investigator Signature Page
  - Modified protocol formatting, including within-text hyperlinks and page numbering

Also, please note that the protocol roster has been updated, DAIDS documentation web links in Sections 11.2, 11.3 and 13.5 have been updated, and that the changes made with the LoA (changed 2-step translation/ transcription process to 1-step process) and CM (changed eligibility criteria language from “completed HOPE” to “participated in HOPE”, and reduced redundancy between O32 and HOPE qualitative components) have also been included in v2.0.



**MTN-032**

**Assessment of ASPIRE and HOPE Adherence**

**Microbicide Trials Network**

**Funding Agencies:**

**Division of AIDS, US National Institute of Allergy and Infectious Diseases  
US Eunice Kennedy Shriver National Institute of  
Child Health and Human Development  
US National Institute of Mental Health  
US National Institutes of Health**

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**DAIDS Protocol ID: 12058**

**A Non-IND Study**

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**Version 2.0**

**September 5, 2017**

Assessment of ASPIRE and HOPE Adherence

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## MTN-032

### Assessment of ASPIRE and HOPE Adherence

#### LIST OF ABBREVIATIONS AND ACRONYMS

ACASI	Audio Computer-Assisted Self-Interviewing
AIDS	Acquired Immunodeficiency Syndrome
ARV	antiretroviral
BRWG	Behavioral Research Working Group
CAPRISA	Centre for the AIDS Programme of Research in South Africa
CAB	community advisory board
CFR	Code of Federal Regulations
CRF	case report form
CRS	clinical research site
CSPRO	Census and Survey Processing System
CWG	Community Working Group
DAIDS	Division of AIDS
DLV	Delavirdine
EC	Ethics Committee
EFV	Efavirenz
FGD	focus group discussion
FHCRC	Fred Hutchinson Cancer Research Center
FTC	Emtricitabine
FTP	File Transfer Protocol
GCP	Good Clinical Practices
HIV	human immunodeficiency virus
IB	Investigator's Brochure
ICF	informed consent form
IDI	in-depth interview
IND	investigational new drug
IoR	Investigator of Record
IPM	International Partnership for Microbicides
IPV	intimate partner violence
IRB	Institutional Review Board
LOC	Leadership and Operations Center
MTD	maximum tolerated dose
MTN	Microbicide Trials Network
MO	Medical Officer
NIH	National Institutes of Health
NIAID	National Institute of Allergy and Infectious Diseases
NICHD	National Institute of Child Health and Human Development
NIMH	National Institute of Mental Health
NNRTI	non-nucleoside reverse transcriptase inhibitor
NVP	Nevirapine
OHRP	Office for Human Research Protections
PK	pharmacokinetics
PrEP	pre-exposure prophylaxis
PRO	Protocol Registration Office
PTID	Participant Identification
QC	quality control

RSC	Regulatory Support Center
RTI	Research Triangle Institute
SCHARP	Statistical Center for HIV/AIDS Research & Prevention
SDMC	Statistical Data Management Center
SMC	Study Monitoring Committee
SOP	standard operating procedure
SSP	study specific procedures
STI	sexually transmitted infection
TDF	Tenofovir Disoproxil Fumarate
UNAIDS	Joint United Nations Programme on HIV/AIDS
US	United States
VR	vaginal ring

**MTN-032**

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**MTN-032**

**Assessment of ASPIRE and HOPE Adherence**

**INVESTIGATOR SIGNATURE FORM**

Version 2.0; September 5, 2017  
A Study of the Microbicide Trials Network

**Funded by:**

Division of AIDS (DAIDS), US National Institute of Allergy and Infectious Diseases  
US Eunice Kennedy Shriver National Institute of Child Health and Human Development  
US National Institute of Mental Health  
US National Institutes of Health (NIH)

**IND Sponsor:**

A Non-IND Study (DAIDS Protocol ID: 12058)

I, the Investigator of Record (IoR), agree to conduct this study in full accordance with the provisions of this protocol and all applicable protocol-related documents. I agree to conduct this study in compliance with United States (US) Health and Human Service regulations (45 CFR 46); applicable U.S. Food and Drug Administration (FDA) regulations; standards of the International Conference for Harmonization Guideline for Good Clinical Practice (E6); Institutional Review Board/Ethics Committee determinations; all applicable in-country, state, and local laws and regulations; and other applicable requirements (e.g., NIH, DAIDS) and institutional policies.

I agree to maintain all study documentation for a minimum of three years after submission of the site's final Financial Status Report to DAIDS, unless otherwise specified by DAIDS or the Microbicide Trials Network (MTN) Leadership and Operations Center (LOC). These documents should be retained for a longer period, however, if required by the applicable regulatory requirements or by an agreement with the sponsor. DAIDS will inform the investigator/institution as to when these documents no longer need to be retained.

I have read and understand the information in this protocol and will ensure that all associates, colleagues, and employees assisting in the conduct of the study are informed about the obligations incurred by their contribution to the study.

\_\_\_\_\_  
Name of Investigator of Record (print)

\_\_\_\_\_  
Signature of Investigator of Record

\_\_\_\_\_  
Date

## MTN-032

### Assessment of ASPIRE and HOPE Adherence

#### PROTOCOL SUMMARY

<b>Short Title:</b>	Assessment of ASPIRE and HOPE Adherence
<b>Funders:</b>	Division of AIDS, NIAID, NIMH, NICHD, US NIH
<b>Protocol Chair:</b>	Elizabeth Montgomery, PhD, MHS
<b>Protocol Co-Chairs:</b>	Sarita Naidoo, PhD Jonathan Stadler, PhD, MA (Phase 1 only)
<b>Sample Size:</b>	Phase 1: Up to 224 former ASPIRE participants Phase 2: Up to 156 HOPE participants and up to 120 male partners of HOPE participants
<b>Study Population:</b>	Former ASPIRE and HOPE participants Male partners of HOPE participants
<b>Study Sites:</b>	ASPIRE and HOPE site(s) selected by the MTN Executive Committee
<b>Study Design:</b>	Exploratory sub-study of the ASPIRE and HOPE trials that will utilize qualitative In-Depth Interviews (IDIs) and Focus-Group Discussions (FGDs)
<b>Study Duration:</b>	Approximately 4-6 months for recruitment and enrolment for Phase 1 and 9-12 months for Phase 2 at each site, and an additional 2-3 months for Phase 2 FGD recruitment, if needed, once HOPE results are released

#### Primary Objectives:

- To explore socio-contextual and trial specific issues which affected participants' adherence to the dapivirine vaginal ring (VR)
- To explore male partner attitudes towards and experiences with the dapivirine VR, and their perspective of their female partner's attitudes and experiences

#### Secondary Objectives:

- To explore participants' and their male partners' HIV risk and perceptions of HIV risk, in general and specific to:
  - motivation to participate in ASPIRE and/or HOPE
  - product use (or lack of) in ASPIRE and/or HOPE
  - male partner support (or lack thereof) of participants' product use in HOPE

- To explore factors influencing product initiation and patterns of use during ASPIRE and/or HOPE
- To explore participants' perceptions of various adherence support interventions and engagement activities implemented (or not implemented) during ASPIRE and/or HOPE
- To explore participants' and their male partners' understanding of the ASPIRE results and ring efficacy, and the impact of this understanding on
  - participants' intention and/or ability to join HOPE and continue in follow-up
  - adherence to the dapivirine VR as part of an open label extension trial as compared to adherence in a Phase 3 safety and effectiveness trial
  - male partner support (or lack thereof) of participants' trial participation and product use in HOPE

**Exploratory Objectives:**

- To explore participants' and their male partners' preference regarding drug delivery modalities and attributes that might encourage end-user uptake
- To explore how male partners and men should and could be engaged in scale up of ring demonstration projects and licensure in the future
- To explore participants' perspectives on marketing aspects of ring in scale up activities, e.g. most suitable target audiences and marketing approaches, support services needed, ideal access points, etc.
- To explore key unexpected and/or important findings of HOPE trial results

# 1 KEY ROLES

## 1.1 Protocol Identification

Protocol Title: Assessment of ASPIRE and HOPE Adherence

Protocol Number: MTN-032

Date: September 5, 2017

## 1.2 Sponsor and Monitor Identification

Funding Agencies: US Division of AIDS (DAIDS)/National Institute of Allergy and Infectious Diseases (NIAID)  
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## 2 INTRODUCTION

### 2.1 Microbicides and Human Immunodeficiency Virus (HIV) Prevention

In 2012, 2.3 million people became newly infected with HIV and 1.6 million people lost their lives to acquired immunodeficiency syndrome (AIDS). Every 60 seconds, a young woman is infected with HIV.<sup>1</sup> According to the Joint United Nations Programme on Human Immunodeficiency Virus (HIV)/AIDS (UNAIDS) Global Report, the estimated number of individuals living with HIV is 35.3 million globally. Women and girls continue to be disproportionately affected by HIV in sub-Saharan Africa, where women account for approximately 60% of people living with HIV. Given the high rates of HIV infection among women, female controlled prevention options remain a global priority. The ongoing development of safe and effective HIV prevention technologies that can be made easily accessible to developing countries remains a public health priority.

Unprotected heterosexual intercourse is currently the leading mode of HIV acquisition among women. Condoms, as the most widely available HIV prevention methods require the consent of the male partner. Correct and consistent use of latex condoms is one proven method of preventing HIV acquisition; however, condoms are widely regarded as inadequate prevention options for women, because many women are unable to negotiate condom use with their partners. Thus, developing HIV prevention options that women can use remains a global concern. Vaginal microbicides, which are self-initiated and controlled, offer women a critically needed biomedical prevention tool that will complement existing HIV prevention strategies as well as future products that are being developed.

With successful proof-of-concept that antiretroviral (ARV)-based microbicides reduce the risk of HIV-1 acquisition, confirmatory work and further trials involving different ARV compounds, of various formulations and differing dosing strategies are required to provide further options to end-users.

### 2.2 HIV Prevention Product Adherence

Results from VOICE, a multi-site randomized placebo-controlled trial of three different formulations of tenofovir among women in sub-Saharan Africa, indicated that drug was detected in less than a third of blood samples from participants assigned to the Truvada and oral tenofovir arms, and in less than a quarter of samples from participants assigned to the tenofovir gel arm.<sup>2</sup> If trial participants do not consistently use products, demonstration of effectiveness is undermined even if the product is efficacious. The link between product adherence and the likelihood of infection has been demonstrated in several microbicide trials. The CAPRISA 004 trial of tenofovir gel indicated that: 1) HIV incidence was significantly higher among participants who used the product less frequently, and 2) greater protection was conferred with higher drug concentration in the cervico-vaginal fluids of participants who received the active gel.<sup>3</sup> Similarly in the iPrEx trial of oral prophylaxis with Truvada, the odds of infection among men and transgender women were substantially lower among those with detectable drug level, a biomarker of adherence to product use.<sup>4</sup> Partners PrEP, which tested both daily dosing of tenofovir and Truvada, found that the estimated protective effect of pre-exposure prophylaxis (PrEP) against HIV, based on concentrations of tenofovir consistent with daily dosing, was 88% for individuals receiving Tenofovir Disoproxil Fumarate (TDF) and 91% for individuals receiving emtricitabine (FTC)/TDF.<sup>5</sup>

Adherence to a trial product is required to determine a product's effectiveness, and accurate measurement of product adherence is critical to help explain why a product may or may not be

effective. It is unknown what level of participant adherence is needed in order to achieve sufficient levels of drug to provide efficacy. Even with adherence levels as high as 60%, the effectiveness of a product can be reduced to less than half of its true biological efficacy, resulting in a significant decrease in a trial's ability to detect efficacy.<sup>6</sup> Accurate measurement also plays an important role in estimating product effectiveness. If participants' actual use of a product does not match what is measured through self-report or other methods, a trial will be unable to determine whether lack of effectiveness is due to inefficacy of the drug or simply lack of use by participants.<sup>7</sup>

For a microbicide to be effective, it is essential that it is used correctly and consistently, and importantly, is acceptable to the user. In addition, a product used independently of sex could be more convenient for women and provide long-term protection during anticipated and unanticipated sexual intercourse. Higher adherence to a product may translate into higher effectiveness of the product. It is likely that products that can be applied less frequently or products that can remain *in situ* for an extended duration will be more acceptable and will achieve better adherence. Vaginal rings (VRs) that need to be replaced monthly may have benefits over dosage forms that need to be used more frequently.

## **2.3 Dapivirine Vaginal Ring**

### **2.3.1 Description**

Dapivirine, a non-nucleoside reverse-transcriptase inhibitor (NNRTI), is a substituted di-amino-pyrimidine (DAPY) derivative with potent antiviral activity against HIV-1. Dapivirine is chemically described as 4-[[4-[(2,4,6-trimethylphenyl)amino]-2-pyrimidinyl]amino]benzotrile.<sup>8</sup> The dapivirine matrix VR is a flexible ring containing 25 mg of drug substance dispersed in a platinum-catalyzed cured silicone matrix. When delivered via VR, dapivirine has demonstrated favorable safety and pharmacokinetic profiles as described in [Section 2.3.2](#).

Dapivirine was originally developed by Janssen Research and Development (formerly Tibotec Pharmaceuticals Ltd.), a subsidiary of Johnson & Johnson, as an oral ARV compound for treatment of HIV/AIDS and was tested in Phase 1 and 2 clinical trials in more than 200 participants.<sup>9</sup> However, dapivirine is also a promising topical microbicide candidate due to its proven *in vitro* and *in vivo* efficacy and favorable safety profile as well as its physical and chemical properties. Dapivirine has potent activity against wild-type HIV-1 strains and strains harboring different resistance-inducing mutations. Dapivirine's ARV profile is superior to that of several other NNRTI drugs, including nevirapine (NVP), delavirdine (DLV), and efavirenz (EFV). Like other NNRTIs, *in vitro* tests have also shown that dapivirine is not active against HIV-2 and has little or no activity against common sexually transmitted infections (STI), therefore, it is not intended for use against HIV-2 or other STIs. Dapivirine does not have any contraceptive properties.<sup>10</sup> Detailed information on dapivirine is available in the Dapivirine VR Investigator's Brochure (IB).<sup>11</sup>

The International Partnership for Microbicides (IPM) has investigated a wide range of dosage forms for the development of topical microbicide products, including vaginal gels, rings, films, tablets and soft gel capsules. The vaginal gel was the initial dosage form chosen for a dapivirine-based microbicide because the majority of previous microbicides to have entered clinical trials were also vaginal gels and therefore a wealth of information was available on that dosage form. However, the dapivirine silicone elastomer VR has now been prioritized over all other dosage forms for the following reasons:

- Clinical trials have demonstrated sustained delivery of high levels of dapivirine throughout the cervicovaginal vault for up to 1 month;
- Since the ring is able to deliver drug for at least 1 month, the burden of user-dependent adherence is lower than for once daily products;
- Product acceptability studies and the experience gained from marketed VR products have established a high level of acceptance and adherence from women using VR with similar physical characteristics;
- The overall cost for the VR is relatively low;
- Minimal storage space is required for the VR when compared with once daily products

Summaries of the safety and tolerability of dapivirine delivered orally and vaginally as evaluated in clinical studies by IPM and Tibotec Pharmaceuticals can be found in the following section.

### **2.3.2 Clinical Studies**

Multiple clinical trials have evaluated the safety of dapivirine in VRs, gels and oral formulation. These clinical trials support the favorable safety profile and tolerability of dapivirine in general and specifically in vaginal delivery formulations.

To date, 29 Phase 1 and Phase 1/2 clinical trials of dapivirine have been conducted, with all but two completed:<sup>11</sup>

- Eight trials of dapivirine VRs (containing 25 mg and 200 mg loads) in which 298 participants were assigned to receive dapivirine VRs
- Eight trials of dapivirine vaginal gel in which 491 participants were assigned to receive dapivirine vaginal gel
- Eleven trials of oral dapivirine in which 211 participants were assigned to receive oral dapivirine
- And, two trials of dapivirine vaginal film in which 71 participants were assigned to receive dapivirine vaginal film.

Additionally, two recently completed Phase 3 trials, MTN-020 (ASPIRE) and IPM 027 (The Ring Study), evaluated long-term safety and efficacy of the 25 mg dapivirine vaginal Ring-004, in which the VR was replaced with a new VR after approximately 28 days of use. A total of 4588 participants were enrolled between the two studies, with 2620 assigned to receive dapivirine VRs.<sup>12, 13</sup>

#### ***Clinical Pharmacokinetics of Dapivirine Vaginal Rings***

In all clinical trials of dapivirine VRs and gels to date, dapivirine concentrations in plasma have been very low (less than 2 ng/mL) or undetectable after up to 84 days exposure. Plasma levels of dapivirine after vaginal exposure in clinical trials are 1000-fold lower than maximum plasma concentrations after oral administration of dapivirine (e.g.,  $C_{max}$  after 300 mg b.i.d. for 14 days was 2286 ng/mL).<sup>11</sup>

The clinical pharmacokinetic profile of Ring-004 in IPM 013 showed a rapid increase in plasma and vaginal fluid concentrations of dapivirine after ring insertion, resulting in maximum concentrations in plasma by Day 7 and in vaginal fluids between Day 1 and Day 14, after which concentrations decreased steadily over the remainder of a 28-day or 35-day ring use period. Plasma dapivirine concentrations did not exceed 1 ng/mL, and were therefore well below

concentrations at the maximum tolerated dose (MTD) for multiple oral doses (300 mg b.i.d. for 14 days; plasma C<sub>max</sub> of 2286 ng/mL). For dapivirine in vaginal fluids, the highest concentration was observed in the area where the ring was placed, followed by the cervix, with the lowest concentrations near the introitus.<sup>11</sup>

Data from post-use analysis of residual levels of dapivirine in Ring-004 (IPM 015, in which a ring was inserted once every 28 days over a 12-week period) indicate that, on average, 4 mg of dapivirine were released over approximately one month of ring use. The mean amounts of dapivirine remaining in the used rings were similar for Weeks 4, 8 and 12 (post-insertion), at 21.09 mg, 21.54 mg and 21.84 mg, respectively. No clear relationship (neither linear nor exponential) was observed between the residual amount of dapivirine and corresponding plasma concentrations (i.e., at scheduled ring removal). It would appear that plasma concentrations below approximately 200 pg/mL were generally associated with above-average ring residual amounts, while the residual amounts appeared relatively constant (at levels between approximately 20 and 22 mg) for plasma concentrations above this value (200 pg/mL).<sup>11</sup>

### Safety of Dapivirine Vaginal Rings

**Table 1: Clinical Phase I/II Trials of Dapivirine Vaginal Rings**

Trial Details			Number of Participants				
Trial Number	Description	Country	Ring-001 reservoir (200 mg)	Ring-002 reservoir (25 mg)	Ring-003 matrix* (25 mg)	Ring-004 matrix** (25 mg)	Placebo Ring
IPM 001	Safety and pharmacokinetics (PK) in women; 7 days	Belgium	12	--	--	--	12 (crossover)
IPM 008	Safety and PK in women; 7 days	Belgium	--	10	--	--	3
IPM 013	Safety and PK in women; 56/57 days	Belgium	--	--	--	36	12
IPM 015	Safety and PK in women; 84 days	Multiple Countries in Sub-Saharan Africa	--	--	--	140	140
IPM 018	Safety and PK in women; 28 days	Belgium	--	8	8	--	8
IPM 024	Safety and PK in women; 28 days	Belgium	--	--	--	8	8
MTN-013/IPM 026***	Safety and PK in women	United States	--	--	--	12	12
IPM 028	Drug-drug Interaction (miconazole nitrate); 28 days	Belgium				36	0

Trial Details			Number of Participants				
Trial Number	Description	Country	Ring-001 reservoir (200 mg)	Ring-002 reservoir (25 mg)	Ring-003 matrix* (25 mg)	Ring-004 matrix** (25 mg)	Placebo Ring
IPM 034	Safety and PK in women; 7, 14, 28, 56, or 84 days	Belgium				40	0
<b>TOTAL</b>			<b>12</b>	<b>18</b>	<b>8</b>	<b>272</b>	<b>195</b>

\*Tin-catalyzed matrix ring.

\*\*Platinum-catalyzed matrix ring

\*\*\*MTN-013/ IPM 026 was the first in human clinical trial of a VR containing maraviroc alone, dapivirine alone or a combination of the two (dapivirine/maraviroc) compared to placebo. The dapivirine VR arm included 12 participants. It should be noted, however, that the dapivirine VR was similar to Ring-004, but of slightly different composition.

Across all clinical trials with multiple ring configurations in healthy participants, the dapivirine VR was generally safe and well-tolerated.<sup>11</sup>

### ***Extended Safety and Efficacy of Dapivirine Vaginal Rings***

IPM 027 was a randomized, double-blind, placebo-controlled efficacy and long-term safety study that enrolled 1959 healthy, HIV-uninfected women, ages 18-45. Approximately 1762 women in South Africa and 197 in Uganda were randomized in a 2:1 ratio to receive either a dapivirine ring or a placebo ring to use every four weeks over approximately two years. The main goals of The Ring Study were to evaluate the long-term safety and efficacy of the dapivirine ring for the prevention of HIV-1 as compared to a placebo ring, when used by healthy, HIV-negative women over a two-year period. Additional goals included measuring the incidence of curable STIs, HIV-2 and pregnancy; monitoring ring acceptability and adherence as reported by the study participants; and tracking the development of any HIV-1 drug resistance in participants who become HIV positive during the study. Results were presented at the February 2016 Conference on Retroviruses and Opportunistic Infections (CROI) and published later that year in the New England Journal of Medicine.<sup>13, 14</sup>

The median age at enrollment was 25 years, and 91% were unmarried. At the data cut-off point, the total number of person years of follow-up was 2805, and 761 women had completed the two year follow-up period. A total of 133 post-randomization HIV-1 infections occurred: 77 among women assigned to dapivirine ring (incidence 4.08 per 100 person-years) and 56 among women assigned to placebo (incidence 6.10 per 100 person-years). The dapivirine VR reduced the risk of HIV-1 infection by 30.7% (95% CI: 0.90-51.5%; p=0.0401) relative to placebo. A 37.5% (95% CI: 3.5-59.5%) reduction in HIV-1 infection was observed in a subgroup analysis of women older than 21 years.<sup>13, 14</sup>

No clinically significant differences in the frequency of treatment emergent adverse events were detected between the dapivirine and placebo treatment groups, and the majority (>80%) were assessed as moderate (Grade 2) or mild (Grade 1) in severity as per the current Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events or Female Genital Grading Table for use in Microbicide Studies at the time of diagnosis. Product-related adverse events in both treatment groups included metrorrhagia, menometrorrhagia, pelvic discomfort/pain, suprapubic pain and application site pain, and all were assessed as mild (Grade 1) in severity by the Investigator. There were no statistically significant differences in the frequency of the primary safety endpoints between the study arms. Further, there was no overall difference between NNRTI resistance profiles.<sup>13, 14</sup>

MTN-020, A Study to Prevent Infection with a Ring for Extended Use (ASPIRE), was a Phase 3 clinical trial designed to assess the efficacy and safety of a ring containing 25 mg of dapivirine for the prevention of HIV-1 acquisition in women. The double-blind, randomized controlled trial enrolled HIV-uninfected women, between the ages 18 – 45. A total of 2629 women from Malawi, South Africa, Uganda, and Zimbabwe enrolled in the trial. Participants replaced the ring monthly for a minimum of one year. MTN-020 aimed to determine the safety and efficacy of the dapivirine ring in preventing HIV-1 infection among healthy sexually active HIV-uninfected women when inserted vaginally once every 4 weeks. Additional goals of MTN-020 included the assessment of participant acceptability and adherence to the investigational product, HIV-1 drug resistance mutations among participants who acquire HIV-1 infection and establishing steady state drug concentrations in the study population. Results were presented at the February 2016 CROI and published that same month in the New England Journal of Medicine.<sup>12</sup>

A total of 168 HIV-1 infections occurred: 71 among those assigned the dapivirine VR and 97 among those assigned the placebo ring (incidence 3.3 and 4.5 per 100 person-years, respectively). Dapivirine ring resulted in a 27% (95% CI: 1-46%, p=0.046) relative reduction in HIV-1 incidence overall and a 37% (95% CI: 12-56%, p=0.007) reduction in an analysis defined early in the study excluding data from two study sites with lower retention and adherence. In pre-defined as-randomized subgroup analyses, HIV protection differed significantly by age, with a 61% reduced risk of HIV for women  $\geq 25$  years [CI: 32%, 77%] p<0.001, and 10% reduced risk for women < 25 years (CI: -41%, 43%) p=0.64. A post-hoc analysis was conducted to further explore this result, which indicated a 56% (95% CI: 31-71%, p<0.001) reduced risk of HIV among women older than 21 years of age, and no HIV-1 protection for women aged 18-21, with objective markers of adherence lower in this subgroup compared to women older than 21.<sup>12</sup>

There were no statistically significant differences in the frequency of the primary safety endpoints between the study arms or in other AEs commonly detected in the study population. Incident STIs occurred at a similar rate in the two study arms. Product-related AEs included pelvic pain, application site pain, pelvic inflammatory disease (PID), cervix erythema, cervix edema, cervicitis, urinary tract infection (UTI), urinary incontinence, dyspareunia, headache, decreased neutrophil count, abnormal weight loss, and dysmenorrhea, and all were assessed as moderate (Grade 2) in severity as per the current DAIDS Table for Grading the Severity of Adult and Pediatric Adverse Events or Female Genital Grading Table for use in Microbicide Studies at the time of diagnosis. Finally, among those acquiring HIV-1, detection of NNRTI mutations did not differ by study arm (8/68 assigned dapivirine and 10/96 assigned placebo, p=0.80).<sup>11, 12</sup>

MTN-025, the HIV Open-label Prevention Extension (HOPE) trial, is a multi-site, open-label, randomized, Phase 3B trial currently being implemented in the MTN-020 (ASPIRE) trial research sites. Eligible HIV-uninfected ASPIRE participants will receive the same VR used in MTN-020, a silicone elastomer VR containing 25 mg of dapivirine, to be replaced monthly, for a total period of 12 months of use. Study follow-up visits will occur monthly for the first 3 months and quarterly thereafter, reflecting a transition to a more real-world type of follow-up (versus a clinical trial approach). The study will evaluate the safety of and participant adherence to the dapivirine (25 mg) VR in the context of an open-label extension trial, reflecting a transition to a more real-world type of product use where the participants know they are getting an active product that has been shown to be safe and effective when used as indicated. The HOPE sample size will be contingent upon how many former ASPIRE participants are interested in enrolling, are HIV-negative and otherwise eligible to enroll.

IPM 032, the Dapivirine Ring Extended Access and Monitoring (DREAM) study, is a multi-site, open-label follow-on trial to The Ring Study currently being implemented in six of the IPM 027 sites. Approximately 1700 eligible HIV-uninfected former Ring Study participants, as well as ring-naïve women aged 18-25, will receive the same VR used in The Ring Study. Similar to the HOPE study, DREAM study participants will be asked to use the VR for a total period of 12 months, replacing it monthly, and to attend monthly study follow-up visits for the first 3 months and quarterly thereafter. In addition to offering former Ring Study participants access to the VR and evaluating the safety of and participant adherence to the dapivirine VR in the context of an open-label extension trial, the DREAM study will also explore when, how and why young women use the ring, as well as how adherence may affect the VR's efficacy and ways to support effective VR use.

### **2.3.3 Behavioral Studies**

#### ***Acceptability of Dapivirine VR***

IPM 011 assessed the acceptability of the placebo VR in 170 women. The trial was conducted across multiple sites in Tanzania and South Africa. The study participants found the ring to be very comfortable (95%), very easy to insert (94%) and remove (92%), and rarely were the rings felt during daily activities. All questionnaire respondents, when asked if they would be willing to use the VR if shown to be effective for HIV prevention, replied that they would use the VR.<sup>15</sup>

In IPM 015, at Week 12, 97% of African women reported that the dapivirine VR was comfortable and that they were willing to use the VR if it was found to be effective. Women preferred to wear the VR every day (97%) and reported that the ring did not interfere with their daily activities (89%). In terms of the male partner acceptability, 63% of women reported that their partner did not feel the ring during sex. Of those participants who reported that their partner felt the ring, only 1% reported that this might be or definitely was a problem.<sup>16</sup>

In MTN-020, participant acceptability of the dapivirine VR was evaluated qualitatively in 214 women.<sup>17</sup> This subset of women participated in single in-depth interviews (IDI), serial IDIs, or focus group discussions (FGD) at six of the fifteen ASPIRE sites. Interview guides focused on motivations to join the trial, HIV risk perception, trial experiences, attitudes of the participant and her male partner(s) toward the ring, effect of the ring on sex and use of the ring. The following dimensions of acceptability were evaluated: use attributes, product characteristics, drug formulation and dosing regimen, effect on sex, product-related norms and perceived partner acceptability. Ease of ring insertion and lack of interference in daily activities were common themes, and women appreciated the monthly regimen and discreetness of the ring. Early during ring use, concerns about ring safety and fears of ring expulsions were common, though these were mostly overcome with actual ring use experience and staff and peer support. The ring was most often reported as soft, flexible and comfortable after participants actually used it, and using the ring made the women feel like they were contributing to the common good. Women differed on whether and how ring use impacted their sexual experience, and most women agreed that disclosure of ring use to partners was important to prevent relationship problems. The actual or perceived dynamics of participants' male partner relationship(s) were the most consistently described influence, both negative and positive, on participants' acceptability of the ring.

MTN-024/IPM 031 was a multi-center, two-arm, randomized, double blind, placebo-controlled Phase 2a trial that enrolled 96 healthy, HIV-uninfected, post-menopausal females 45-65 (inclusive) years of age in the United States. Participants were randomized in a 3:1 ratio to use dapivirine (25 mg) or placebo VR for approximately 12 weeks. Over three months of use, almost



all study participants found the VR easy to use (99%), felt comfortable with the ring inside every day (97%), and liked the ring (93%). Most study participants felt the VR was easy to insert (85%) and easy to remove (80%). Over one third (36%) of study participants reported some change in their vagina over three months of use, with the majority of those not feeling bothered by those changes. Two thirds (65%) of study participants preferred the VR over condoms, and most participant worries about ring use decreased significantly after three months of use. Overall, the VR was very acceptable to study participants.<sup>18</sup>

### ***Adherence to Dapivirine VR***

MTN-013/IPM 026 assessed adherence to the dapivirine VR, the maraviroc VR, the dapivirine-maraviroc combination VR, and the placebo VR in 48 women aged 18-40. The trial was conducted at two sites in the United States, and adherence was assessed by self-report. Despite restrictions including abstinence from sexual activities for the duration of the study, almost all women (94%) were fully adherent with 28 days of VR use by self-report. Residual VR drug levels supported these data. Mean residual dapivirine concentrations were 20.6 mg (SD 0.8, n=8) and 21.6 mg (SD 1.6, n=8) in the dapivirine and dapivirine-maraviroc arms, respectively, representing 82% and 86% of the loaded doses. These residual drug levels are comparable to a previous study conducted by IPM that also found approximately 4 mg dapivirine released from the VRs over 28 days, thus the rings were likely used as instructed.

IPM 011 assessed adherence to the placebo VR in 170 women. 11% of the participants enrolled in the study experienced expulsions/removal, with the most common reason being 'menses related'. In the majority of cases (64%), the VR was washed and re-inserted.<sup>15</sup>

In IPM 015, perfect adherence, defined as never having the VR out for more than an entire day, was reported by 92% of the female participants. Of the women who reported that the ring was out, the most common activity for expulsion was urination/defecation. The most common reason reported by participants for VR removal was cleaning. As the study progressed, more women reported removing the VR prior to sexual intercourse, 17% at week 2 and 36% by week 12.<sup>16</sup>

In MTN-020, participant adherence was objectively measured using plasma drug levels collected quarterly, and after the first year of the trial, using residual drug levels in rings returned monthly.<sup>12</sup> Women were defined as being adherent if their plasma dapivirine levels were more than 95 pg/mL, which meant continuous ring use for at least 8 hours prior to plasma collection; women were also defined as being adherent if their returned rings contained less than 23.5 mg of dapivirine, which meant that at least 1.5 mg had been released. In the dapivirine group (n = 1313), 82% of plasma samples showed adherent levels of dapivirine. Drug detection appeared to increase after the first months of use and become stable after the first year, which may indicate that some time was needed for participants to become comfortable with the ring. In the sample with available returned ring data, 84% of returned rings showed adherent levels of residual drug. In general, dapivirine levels in plasma and returned rings were correlated. However, the adherence definitions used in MTN-020 could have led to an overestimation of adherence because participants were categorized as being adherent even though they may have used the ring for only a portion of the month (and possibly only for a few hours before a clinic visit).

In MTN-020, adherence to the dapivirine VR was also evaluated qualitatively in 214 women.<sup>17</sup> Adherence to ring use was assessed by examining narratives related to initial uptake (initiation), consistent use and descriptions of ring expulsions; removals and use-related barriers and

motivators. In general, participants described themselves as correct, consistent ring users. Staff and peer support activities were seen as important platforms for motivating adherence, helping participants overcome concerns about ring use and trial participation, receiving feedback on their ring use experiences and fostering a sense of a shared goal. Participants described voluntarily removing the ring because of their male partners' wishes or due to menses or perceived side effects; involuntary expulsions were rare and were mostly due to sexual activity or using the toilet. Many women spoke of how participants' individual ring use translated more broadly to study objectives and HIV prevention for other women in their communities, and that this was a source of pride and motivation for continuous ring use. The actual or perceived dynamics of participants' male partner relationship(s) were the most consistently described influence, both negative and positive, on participants' use of the ring. Subgroup analyses of residual ring data suggest that the majority of women inconsistently used the ring throughout their trial duration, yet narratives of nonadherence downplayed this trend, particularly among younger women.

In MTN-024/IPM 031, most participants (81%) kept the VR inside every day except for protocol-instructed removals, and this was confirmed by objective adherence markers. Median dapivirine concentrations in plasma and vaginal fluid showed no significant change over 12 weeks. The median residual drug level for returned VRs across all visits was 21.1 mg, consistent with adherence to VR use. Overall, most participants were able to use the VR consistently.<sup>18</sup>

## **2.4 HIV Risk Perception and Motivation for Trial Participation**

One possible factor that may contribute to low adherence is participants' varying perceptions of HIV risk, as well as reasons for joining the trial. A woman's perception of HIV risk is influenced by her individual level behaviors, such as engagement in high-risk sex, as well as the social-cultural context in which she lives. This perception of risk has often been linked to willingness to participate in hypothetical HIV prevention trials<sup>19-30</sup> and occasionally to interest in and acceptance of an HIV prevention product.<sup>31</sup>

Despite these linkages, the question remains: how does one's perception of HIV risk contribute to product adherence once enrolled in a trial? One might expect that a higher perception of risk would lead to more consistent product use due to a greater desire for protection. However, a recent study in India found that contrary to this hypothesis, increased HIV risk perception was negatively associated with consistent gel use. Indeed, women who perceive themselves at higher risk may be less able to adhere to product use for a host of contextual reasons.<sup>32</sup> Further, it is not well understood how regular (e.g., monthly) HIV testing may change individual risk perception and adherence behavior over time. By investigating how the socio-cultural environment influences perception of risk and ultimately product use among ASPIRE and HOPE participants, this study hopes to contribute to a greater understanding of the relationship between these issues.

Other motivations for joining an HIV prevention trial, such as increased access to quality health care and altruism, and their contribution to product adherence will also be explored.

## **2.5 Role of Male Partners in Study Product Use and Trial Participation**

Another possible factor that may contribute to low (or high) VR adherence is male partners' attitudes about HIV prevention studies, HIV prevention products, intravaginal products, and/or the dapivirine VR. Secondary data (both qualitative and quantitative) from the ASPIRE, VOICE, CAPRISA 008, and other trials, as well as a review of primary and secondary analyses of data

from six qualitative studies implemented in conjunction with microbicide trials (in South Africa, Kenya, and Tanzania), showed that for some women, microbicide use improved communication with partners, reinforcing product adherence.<sup>33</sup> However, it increased partner conflicts and the risk of intimate partner violence (IPV) for others.

Microbicides were designed to give women an HIV prevention tool they could use without a male partner's involvement, but research suggests that the approval or support of male partners is often desired, or even required, to enable women to use microbicides. By investigating the role that male partners had in HOPE participants' use of the VR, this study hopes to contribute to a greater understanding of this important component of adherence in the context of a large, open-label HIV-prevention microbicide trial, including possible ways to mitigate opposition and cultivate support among men and communities for HIV prevention research, HIV prevention products, and microbicide use.

## **2.6 Rationale for Study Design**

MTN-032, an exploratory study, is primarily designed to identify factors that may have affected participant adherence to study product in ASPIRE and HOPE. MTN-032 will also elicit perceptions about various participant engagement and adherence promotion interventions implemented in ASPIRE and may also explore the potential use of incentives to promote adherence to VR use as well as suitable approaches to market the study product. There are few published studies investigating whether adherence interventions facilitate or maintain microbicide use in general and dapivirine VR use in particular. Although studies show that male partners play an important role in women's adherence to microbicides<sup>33</sup>, more research is needed to understand how this manifests in the context of women's uptake of the dapivirine VR. Therefore, perceptions of the dapivirine VR will also be elicited from male partners of HOPE participants.

There is little known about what works to encourage uptake and sustain product use in microbicide trials. MTN-032 will use study product adherence results from ASPIRE and HOPE, qualitative IDI and FGD to explore study product adherence behaviors and strategies used to overcome adherence challenges. An in-depth understanding of the various socio-behavioral factors that contribute to product use adherence, including male partner attitudes towards the VR, may assist in the interpretation of past and ongoing study results and inform implementation of future studies.

In the absence of a "gold standard," it is recommended that HIV prevention trials use multiple measures to capture adherence.<sup>34</sup> However, the use of multiple adherence measures often results in some level of discrepancy between measures.<sup>35</sup> Any potential difference in reported adherence across measures raises questions around true levels of product adherence as well as the measures themselves. It is for these reasons that the adherence measures utilized in this study will be derived from biological, objective markers of adherence.<sup>36</sup>

This study will examine the role of the contextual environment on adherence. Generally, trials attempt to discourage behaviors that may have a detrimental effect on outcomes through participant-focused counseling. For example, they may provide guidance and support to participants to maintain high levels of product use. However, despite a trial's best efforts to support adherence and/or discourage sexual behaviors that may contribute to dilution of efficacy, the socio-cultural context,<sup>37</sup> including the trial context, organization of the participant's social environment (i.e., living arrangements, importance and role of partners, family members, and the larger social network), and individual beliefs and attitudes about HIV risk and/or the trial

may influence these behaviors. Furthermore, a trial's efforts to discourage non-adherence to study product through ongoing counseling and messaging may promote social desirability bias in participant responses about these behaviors. MTN-032 will explore the impact of adherence support interventions, including the potential effects of this support on the dynamic between trial participants and trial staff and between trial participants and their male partners.

### **3 OBJECTIVES**

#### **3.1 Primary Objectives**

- To explore socio-contextual and trial specific issues which affected participants' adherence to the dapivirine VR
- To explore male partner attitudes towards and experiences with the dapivirine VR, and their perspective of their female partner's attitudes and experiences

#### **3.2 Secondary Objectives**

- To explore participants' and their male partners' HIV risk and perceptions of HIV risk, in general and specific to:
  - motivation to participate in ASPIRE and/or HOPE
  - product use (or lack of) in ASPIRE and/or HOPE
  - male partner support (or lack thereof) of participants' product use in HOPE
- To explore factors influencing product initiation and patterns of use during ASPIRE and/or HOPE
- To explore participants' perceptions of various adherence support interventions and engagement activities implemented (or not implemented) during ASPIRE and/or HOPE
- To explore participants' and their male partners' understanding of the ASPIRE results and ring efficacy, and the impact of this understanding on
  - participants' intention and/or ability to join HOPE and continue in follow-up
  - adherence to the dapivirine VR as part of an open label extension trial as compared to adherence in a Phase 3 safety and effectiveness trial
  - male partner support (or lack thereof) of participants' trial participation and product use in HOPE

#### **3.3 Exploratory Objectives**

- To explore participants' and their male partners' preference regarding drug delivery modalities and attributes that might encourage end-user uptake
- To explore how male partners and men should and could be engaged in scale up of ring demonstration projects and licensure in the future
- To explore participants' perspectives on marketing aspects of ring in scale up activities, e.g. most suitable target audiences and marketing approaches, support services needed, ideal access points, etc.

- To explore key unexpected and/or important findings of HOPE trial results

## 4 STUDY DESIGN

### 4.1 Identification of Study Design

The MTN-032 trial is a two-phase exploratory sub-study of the ASPIRE and HOPE trials. MTN-032 will utilize qualitative IDIs and FGDs to explore the socio-contextual and trial specific issues which affected ASPIRE and HOPE trial participants' adherence to the dapivirine VR, including the role played by their male partners.

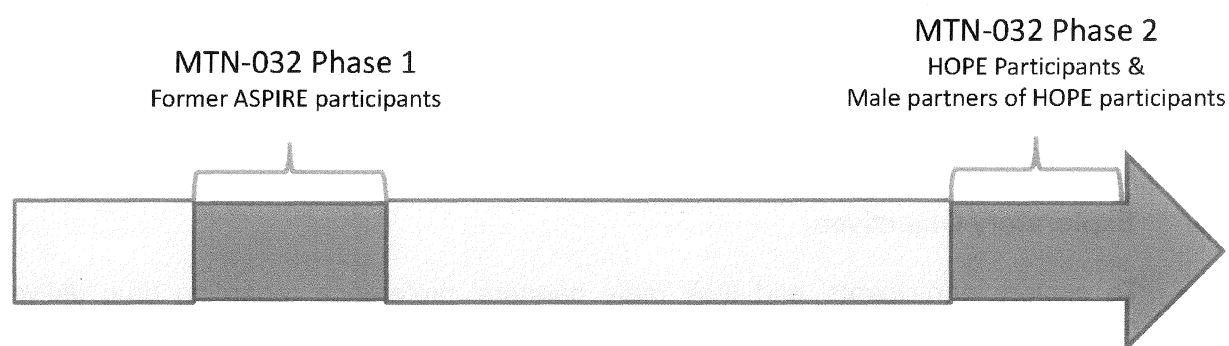
### 4.2 Description of Study Population

- Phase 1: The MTN-032 study population will consist of former ASPIRE participants who meet eligibility criteria as described in Sections [5.3.1](#) and [5.4](#).
- Phase 2: The MTN-032 study population will consist of HOPE participants who meet eligibility criteria as described in Sections [5.3.2](#) and [5.4](#), and male partners of HOPE participants who meet eligibility criteria as described in Sections [5.3.3](#) and [5.4](#).

### 4.3 Time to Complete Accrual

- Phase 1: Approximately 4-6 months for recruitment and enrolment at each site. See [Section 10.4](#) for additional details.
- Phase 2: Approximately 9-12 months for recruitment and enrolment at each site, and an additional 2-3 months for FGD recruitment, if needed, once HOPE results are released. See [Section 10.4](#) for additional details.

Figure 1: MTN-032 Study Timeline in Relation to the ASPIRE and HOPE Timelines



### 4.4 Expected Duration of Participation

The total duration of study participation for each participant is not anticipated to exceed 6 hours for each phase, including administrative and data collection procedures. However, the duration

of participation is dependent upon the scheduling of IDIs or FGDs. Each IDI is not anticipated to exceed 2 hours and each FGD is expected to take up to 4 hours. Multiple visits may be conducted to complete all required procedures, if necessary.

#### **4.5 Sites**

MTN-032 participants will be recruited from former ASPIRE and current HOPE clinical research sites (CRS) selected by the MTN Executive Committee.

## **5 STUDY POPULATION**

### **5.1 Selection of the Study Population**

A sample of up to 224 women who participated in ASPIRE will be selected for participation in Phase 1 of this study. A sample of up to 156 HOPE participants will be selected for participation in Phase 2. In addition, a sample of up to 120 male partners of HOPE participants who provided consent to have their male partners contacted will be selected for participation in Phase 2. Inclusion and Exclusion Criteria, Sections 5.3 and 5.4, respectively, are used to ensure the appropriate selection of study participants for MTN-032.

### **5.2 Recruitment**

Participants will be recruited from ASPIRE and HOPE study sites in Africa. Recruitment materials will be approved by site Institutional Review Boards/Ethics Committees (IRBs/ECs) prior to use. Site community representatives should advise on these materials before they are submitted to the IRB/EC for review. Community education strategies, including group sessions, may be employed as part of participant/partner outreach.

### **5.3 Inclusion Criteria**

#### **5.3.1 Phase 1: Former ASPIRE participants**

Potential participants must meet all of the following criteria to be eligible for inclusion in the study:

1. Participated in the ASPIRE protocol, randomized to active product and informed of their randomization assignment.
2. Able and willing to provide written informed consent in one of the study languages.
3. Able and willing to complete the required study procedures.

For participants who did not acquire an HIV infection while taking part in ASPIRE:

4. Evidence of study product dispensation at a minimum of three consecutive ASPIRE scheduled clinic visits.
5. Have a minimum of three ASPIRE PK data measurement points available.

For participants who acquired HIV infection while taking part in ASPIRE:

6. Evidence of study product dispensation in the month prior to the participant's acquisition of HIV infection.
7. Have a minimum of one ASPIRE PK data measurement available.

### **5.3.2 Phase 2: HOPE participants**

Potential participants must meet all of the following criteria to be eligible for inclusion in the study:

1. Participated in the HOPE protocol.
2. Able and willing to provide written informed consent in one of the study languages.
3. Able and willing to complete the required study procedures.

For participants who did not acquire an HIV infection while taking part in HOPE:

4. Evidence of study product dispensation for a minimum of three consecutive months.

For participants who acquired an HIV infection while taking part in HOPE:

5. Evidence of study product dispensation in the month prior to the participant's acquisition of an HIV infection.

### **5.3.3 Phase 2: Male partners of HOPE participants**

Potential participants must meet all of the following criteria to be eligible for inclusion in the study:

1. Identifies as a male sexual partner of a HOPE participant for whom the HOPE participant has given permission to contact.
2. Was a male sexual partner of a HOPE participant during her participation in HOPE (regardless of whether she used the ring or not).
3. Able and willing to provide written informed consent in one of the study languages.
4. Able and willing to complete the required study procedures.
5. Is above the age of 18 at the time of study participation.

### **5.4 Exclusion Criteria: Phase 1 & 2**

Potential participants who meet the following criteria will be excluded from both phases of the study:

1. Has any significant medical condition or other condition that, in the opinion of the Investigator of Record (IoR)/designee, would preclude informed consent, make study participation unsafe, complicate interpretation of study outcome data, or otherwise interfere with achieving the study objectives.

## 6 STUDY PRODUCT

MTN-032 will not involve the administration of any study product.

## 7 STUDY PROCEDURES

### 7.1 Phase 1

In Phase 1 of the MTN-032 study, 189 ASPIRE participants who had varying levels of adherence to the dapivirine VR were enrolled (see [Section 10.3.1](#) for sample composition details). Based upon objective measures of adherence, participants were pre-designated into two groups and then randomly selected and approached for study participation. Final group designation was dependent on adequate sample size and ability to determine level and pattern of adherence, and resembled the following:

- Low adherence
- High adherence

*Note: Specific information regarding group designation is specified in the MTN-032 study-specific procedures (SSP) Manual, available at <http://www.mtnstopshiv.org/studies>.*

After having their ASPIRE adherence results presented and explained to them, enrolled participants were asked to complete a single IDI or a FGD (with other participants in the same adherence group) where factors influencing adherence, as well as strategies used to overcome adherence challenges, were explored. Intermittent and strategic use of the ring around study visits was also discussed.

#### 7.1.1 Screening and Enrollment – Administrative, Behavioral and Regulatory Procedures

Table 2: Screening and Enrollment Procedures

Screening and Enrollment	
Component	Procedures
Administrative and Regulatory	<ul style="list-style-type: none"> <li>• Confirm eligibility</li> <li>• Obtain written informed consent for screening and enrollment</li> <li>• Assign a unique Participant Identification (PTID) Number</li> <li>• Collect demographic data</li> <li>• Collect locator information</li> <li>• Provide reimbursement for study visit</li> </ul>
Behavioral	<ul style="list-style-type: none"> <li>• Administer behavioral questionnaire(s)</li> </ul>



	<ul style="list-style-type: none"> <li>• Conduct in-depth interview (IDI) or Focus Group Discussion (FGD)</li> </ul>
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Multiple visits may be conducted to complete all required procedures, if necessary.

## 7.2 Phase 2: HOPE participants

Up to 156 HOPE participants will be enrolled into Phase 2 (see [Section 10.3.2](#) for sample composition details). Prior to being invited to enroll in Phase 2, IDI participants will be designated into groups of interest (e.g., adherence levels during ASPIRE and/or HOPE), and randomly pre-selected for recruitment into Phase 2. FGD participants will be selected through a purposive and random selection process depending on key characteristics of interest, (e.g. randomly selected from among participants meeting specified age and adherence criteria).

The second phase will examine the effect of known VR efficacy on adherence to study product in HOPE. In particular, this phase will focus on:

- Motivations for participants with varying levels of adherence in ASPIRE to enroll into HOPE
- What effect, if any, knowledge of the ring’s efficacy had on adherence behavior
- Motivation for continued study participation among those participants who were inconsistently or not adherent
- VR uptake, marketing and other product roll-out issues
- Exploration of key unexpected and/or important findings from HOPE study results

A single IDI or a FGD will be conducted with each enrolled participant.

### 7.2.1 Screening and Enrollment (HOPE participants) – Administrative, Behavioral and Regulatory Procedures

**Table 3: Screening and Enrollment Procedures – HOPE participants**

Screening and Enrollment – HOPE participants	
Component	Procedures
<b>Administrative and Regulatory</b>	<ul style="list-style-type: none"> <li>• Confirm eligibility</li> <li>• Obtain written informed consent for Phase 2 screening and enrollment</li> <li>• Collect demographic data</li> <li>• Collect locator information</li> <li>• Provide reimbursement for study visit</li> </ul>
<b>Behavioral</b>	<ul style="list-style-type: none"> <li>• Administer behavioral questionnaire(s) and tools</li> <li>• Conduct IDI or FGD</li> </ul>

Multiple visits may be conducted to complete all required procedures, if necessary.

## 7.3 Phase 2: Male partners of HOPE participants

Up to 120 male partners of HOPE participants will be enrolled into Phase 2 (see [Section 10.3.3](#) for sample composition details). Sites will receive a list of randomly selected HOPE participants, and will identify which HOPE participants from this list provided permission to contact their male partners. Male partners will then be systematically contacted for participation in order, from

among those who the study team has been given permission to contact (see [Section 13.5](#) for details on the contact permission consenting process).

The second phase will examine the role male partners may have had on study product adherence for HOPE participants. In particular, this phase will focus on male partners' views on:

- HIV risk and perceptions of HIV risk, and how this impacted their support of HOPE participants' use of the dapivirine VR.
- ASPIRE results and ring efficacy, and how their understanding of these impacted their support of HOPE participants' trial participation and use of the dapivirine VR.
- Preferred drug delivery modalities and attributes that might encourage end-user uptake.
- How other men in their social networks and communities would view the VR.
- How they should and could be engaged in scale up of VR demonstration projects and licensure in the future.
- Physical sensation of women's VR use during sex.

A single IDI or FGD will be conducted with each enrolled male partner participant.

### 7.3.1 Screening and Enrollment (Male partners of HOPE participants) – Administrative, Behavioral and Regulatory Procedures

**Table 4: Screening and Enrollment Procedures – Male partners of HOPE participants**

Screening and Enrollment – Male partners of HOPE participants	
Component	Procedures
<b>Administrative and Regulatory</b>	<ul style="list-style-type: none"> <li>• Confirm eligibility</li> <li>• Obtain written informed consent for Phase 2 screening and enrollment</li> <li>• Assign a unique Participant Identification (PTID) Number</li> <li>• Collect demographic data</li> <li>• Collect locator information</li> <li>• Provide reimbursement for study visit</li> </ul>
<b>Behavioral</b>	<ul style="list-style-type: none"> <li>• Administer behavioral questionnaire(s) and tools</li> <li>• Conduct IDI or FGD</li> </ul>

Multiple visits may be conducted to complete all required procedures, if necessary.

### 7.4 Behavioral Evaluations

The study will address questions related to the primary and secondary objectives of product adherence facilitators and challenges experienced by ASPIRE and HOPE participants, from the perspective of both the participants and their male partners. The study will also explore participants' and their male partners' views on acceptable approaches to support study product adherence (e.g., financial incentives) and to market the study product. These questions will be assessed via behavioral questionnaires and either IDIs or FGDs conducted by trained interviewers/facilitators. In addition, the study aims to gain further insight on:

- Attitudes and understanding of VR efficacy and the concept of partial efficacy
- Product storage and use, including facilitators and barriers
- Motivations to join the trial

- Socio-cultural context of risk behaviors and risk perceptions over time
- Perceived feasibility of continued study product use with and without adherence support interventions
- Attitudes towards other types of adherence support interventions (e.g., financial incentives)

Additional questions and probes will be designed to delve further into the social and cultural norms that may play a role more broadly in adherence to product use.

#### **7.4.1 Behavioral Questionnaires and Tools**

Behavioral questionnaires will be used to inform different dimensions of data collected during the IDIs and FGDs. Adherence trajectory tools and individual-level drug level tools will be used to facilitate discussion of product use.

#### **7.4.2 In-Depth Interviews (IDIs) and Focus Group Discussions (FGDs)**

Both IDIs and FGDs will include, but not be limited to, topics such as:

- Reactions to and explanation of longitudinal adherence data
- Descriptions of ring use practices (e.g., unorthodox use, sharing, disposal, removal, etc.)
- Main challenge(s) encountered with ring use
- Other reasons for nonuse or removal (e.g., wanting to get pregnant, menses, etc.)
- Main facilitator(s) to ring use
- Participant engagement activities influencing ring use patterns (e.g., ring uptake, sustained use) during ASPIRE and/or HOPE
- Other factors (e.g., situational, relationship, trial-specific, social/cultural/economic, sex and menstruation related, etc.) influencing ring use patterns (e.g., ring uptake, sustained use) during ASPIRE and/or HOPE
- Understanding of (partial) efficacy and simultaneous use of various methods of prevention (e.g., ring, condoms, contraceptives)
- Recommendations for “real world” implementation (e.g., overcoming financial barriers, marketing of study product)
- Factors that affect decision to join HOPE (e.g., situational, relationship, trial-specific, social/cultural/economic, sex and menstruation related, fertility intentions, etc.)

IDI and FGD guides will be developed by qualified social scientists and administered by qualified interviewers. Guides will contain key research questions relating to the main topics of interest and suggested probes. Interviews and discussion sessions will be audio-recorded and transcribed into English (using a 1-step translation/transcription process).

Various tools will be used to facilitate interviews and discussion of sensitive topics with both IDI and FGD participants. These may include, but not be limited to, visual displays of objective adherence marker data/results and drug use patterns over time, study visit timelines, show-cards listing topics and themes previously elicited in other studies, and newspaper clippings of other study results when appropriate.

## 8 ASSESSMENT OF SAFETY

MTN-032 is a minimum-risk research study. It does not involve a study product nor involve clinical, laboratory or other procedures associated with significant risk to participants. Therefore, few safety concerns are expected as a result of study participation, see [Section 13.4.1](#) for expected risks of trial participation. The study site IoR is responsible for continuous monitoring of all study participants and for alerting the protocol team if unexpected safety events arise. Study sites will have written procedures for ensuring prompt reporting to the IRB/EC, of any unanticipated problem involving risks to subjects or others. No safety events will be captured in the study database.

### 8.1 Safety Monitoring

Site IoRs are responsible for continuous close safety monitoring of all study participants, and for alerting the protocol team if unexpected concerns arise. Since the safety risks are minimal in this study, if any such unexpected concerns arise, site study staff must make the site IoR aware. The site IoR will provide follow-up guidance to the appropriate on-site staff member (e.g., site clinician, counselor, nurse, etc.).

The Manual for Expedited Reporting of Adverse Events to DAIDS will not be used for this study for the following reasons: 1) this study does not involve a study drug and is non-invasive; and, 2) adverse events are not primary or secondary objectives of the study. Untoward clinical or medical occurrences reported by study participants to have been experienced during study participation will be recorded in participant file notes.

### 8.2 Social Harms Reporting

Although study sites will make every effort to protect participant privacy and confidentiality, it is possible that participants' involvement in the study could become known to others and that social harms – non-medical adverse consequences – may result. For example, participants could be treated unfairly, or could have problems being accepted by their families, partners and/or communities. Social harms that are judged by the IoR/designee to be related to study participation will be reported to the DAIDS Medical Officer (MO), Protocol Chairs, and responsible site ECs/IRBs according to their individual requirements beginning at the time of enrollment (i.e., after a participant signs the informed consent and eligibility is confirmed) until study participation is complete. In the event that a participant reports social harm, every effort will be made by study staff to provide appropriate care and counseling to the participant, and/or referral to appropriate resources for the safety of the participant as needed. Each site will provide such care and counseling in accordance with standardized guidance provided in the MTN-032 SSP Manual. To mitigate one possible source of social harms, each site will work with those HOPE participants who have given permission to contact their male partners to carefully explain the potential consequences of allowing their male partners to be contacted for Phase 2 participation (e.g., disclosure of study involvement and/or ring use) prior to contacting the male partners (see [Section 13.5](#) for additional details on the contact permission consenting process). While maintaining participant confidentiality, study sites may engage their community advisory boards (CABs) in exploring the social context surrounding instances of social harm. Additionally, a Standard Operating Procedure (SOP) for emergency procedures will be developed for the MTN-032 site staff to be used in situations of social harm and when situations that require immediate attention are identified, including domestic violence, and suicidal ideation

or behavior. The SOP will provide clear guidelines for site staff to refer participants in these situations to the relevant institution/body and to provide feedback to the protocol team.

## **9 CLINICAL MANAGEMENT**

There are no additional clinical management considerations for participants enrolled in this study. Participants who express concerns with social, psychological or clinical issues will be referred for appropriate care to services available at the CRS, or at nearby partnering facilities.

### **9.1 Criteria for Early Termination of Study Participation**

Participants may voluntarily withdraw from the study for any reason at any time. The IoR also may withdraw participants from the study to protect their safety and/or if they are unwilling or unable to comply with required study procedures. Participants also may be withdrawn if the study sponsors, government or regulatory authorities, including the Office for Human Research Protections (OHRP), or site IRBs/ECs terminate the study prior to its planned end date. Study staff members will record the reason(s) for all withdrawals in participants' study records. In the event that participants who voluntarily withdraw from the study wish to re-join the study, they may do so if the accrual target has not yet been met for that Phase.

## **10 ANALYTICAL CONSIDERATIONS**

### **10.1 Overview and Summary of Design**

MTN-032 is an exploratory sub-study of the ASPIRE and HOPE trials that will utilize qualitative research methods, specifically IDIs and FGDs.

One main goal of the study is to explore the socio-contextual and trial specific issues which affected ASPIRE and HOPE participants' adherence to the dapivirine VR as captured via objective marker data. Another main goal of the study is to explore male partner attitudes towards and experiences with the dapivirine VR, and their perspective of their female partner's attitudes and experiences with the dapivirine VR.

Secondary objectives of the study include:

- To explore participants' and their male partners' HIV risk and perceptions of HIV risk, in general and specific to participants' motivation to take part in ASPIRE and/or HOPE, participants' product use (or lack of) during ASPIRE and/or HOPE, and male partners' support (or lack thereof) of participants' product use in HOPE
- To explore factors influencing product initiation and patterns of use during ASPIRE and/or HOPE
- To explore participants' perceptions of various adherence support interventions and engagement activities implemented (or not implemented) during ASPIRE and/or HOPE
- To explore participants' and their male partners' understanding of the ASPIRE results and ring efficacy, and the impact of this understanding on participants' intention and/or ability to join HOPE and continue in follow-up, participants' adherence to the dapivirine

VR as part of an open label extension trial as compared to adherence in a Phase 3 safety and effectiveness trial, and male partners' support (or lack thereof) of participants' trial participation and product use in HOPE

## 10.2 Study Endpoints

After being presented and explained their ASPIRE adherence results, Phase 1 participants were asked to complete a single IDI or FGD (with other participants in the same designated adherence group) to explore:

- Factors influencing adherence
- Strategies used to overcome adherence challenges
- Intermittent and strategic use around study visits

Phase 2 will examine the effect of known ring efficacy level on adherence in participants who take part in HOPE, an open label extension trial to ASPIRE. A single IDI or FGD will be conducted with each HOPE participant enrolled in Phase 2. In particular, this phase will focus on:

- Motivations for participant enrollment into HOPE among participants with varying levels of adherence in ASPIRE
- What effect, if any, knowledge of the ring's efficacy had on adherence behavior
- Motivation for continued study participation among those participants who were inconsistently or not adherent
- VR uptake, marketing and other product roll-out issues
- Key unexpected and/or important findings of HOPE trial results

Phase 2 will also examine the role male partners may have had on study product adherence for HOPE participants. A single IDI or FGD will be conducted with each male partner enrolled in Phase 2. In particular, this phase will focus on:

- HIV risk and perceptions of HIV risk, and how this impacted their support of HOPE participants' use of the dapivirine VR
- ASPIRE results and ring efficacy, and how their understanding of these impacted their support of HOPE participants' trial participation and use of the dapivirine VR
- Preferred drug delivery modalities and attributes that might encourage end-user uptake
- How other men in their social networks and communities would view the VR
- How they should and could be engaged in scale up of VR demonstration projects and licensure in the future
- Physical sensation of women's VR use during sex

## 10.3 Sample Size and Composition

### 10.3.1 ASPIRE (Phase 1) participants

Originally, a sample size of up to 224 ASPIRE participants was targeted for Phase 1 of the study, and approximately 84 Phase 1 participants who then enrolled in HOPE were to be selected to take part in Phase 2. Two items thought to be of significance were factored into the Phase 1 sample size: the number of sites and the required number of participants for Phase 2 of MTN-032. First, it was important to have at least one site from each country represented, with at

least three sites from South Africa in order to have a somewhat representative country sample. Therefore, seven (7) sites were thought to be ideal. Second, a minimum of twelve (12) participants per site were thought to be necessary in order to achieve a meaningful sample size for Phase 2 of the study. Thus, given loss-to-follow-up between Phase 1 and 2 and other issues that may have surfaced, a sample size of up to 224 ASPIRE participants (in order to re-interview 84 who later went on to enroll in HOPE) was thought to be necessary.

In Phase 1, 189 ASPIRE participants who had varying levels of adherence to the dapivirine VR were ultimately enrolled. Based upon participants' ASPIRE objective adherence marker results, participants were pre-selected for study participation in Phase 1. Phase 1 participants were categorized into one of the following groups (final group designation was dependent on adequate sample size and ability to determine pattern of product use):

- Low adherence
- High adherence

While the number of participants in each group at a given site is relatively small, we anticipated they would still be sufficient to reach theoretical saturation.<sup>38</sup> Furthermore, it was anticipated that participants would be representative of the overall ASPIRE trial by enrolling participants from each of the participating ASPIRE countries.

### **10.3.2 HOPE (Phase 2) participants**

A sample size of up to 156 HOPE participants will be selected to take part in Phase 2 of the study. **Note: Phase 2 participants need not have taken part in Phase 1.** Two items thought to be of significance were factored into the Phase 2 sample size: the number of sites and the desired number of IDIs and FGDs per site. First, seven (7) sites are taking part in MTN-032, with two sites from the same Clinical Trials Unit (CTU) pooling their accrual numbers due to similarities in their participant characteristics, thus giving a total of six (6) sites/CTUs. Second, a maximum of 26 participants per site/CTU were thought to be necessary in order to achieve a large enough sample size to conduct approximately 10 IDIs and up to two FGDs (with up to eight participants per FGD) at each site/CTU. Thus, a sample size of up to 156 HOPE participants was thought to be necessary.

Similar to Phase 1, HOPE participants who had varying levels of adherence to the dapivirine VR will be identified and enrolled in Phase 2. Categorization of Phase 2 participants into an adherence group will be dependent on adequate sample size and ability to determine pattern of product use.

### **10.3.3 Male partners (Phase 2)**

A sample size of up to 120 male partners of HOPE participants who consented to have their male partners contacted will be identified from a list of randomly selected HOPE participants and invited to take part in Phase 2 of the study. Two items thought to be of significance were factored into the male partner sample size: the number of sites and the desired number of IDIs and FGDs per site. First, seven (7) sites are taking part in MTN-032, with two sites from the same CTU pooling their accrual numbers due to similarities in their participant characteristics, thus giving a total of six (6) CTUs. Second, a maximum of twenty (20) participants per CTU were thought to be necessary in order to achieve a large enough sample size to conduct up to four IDIs and up to two FGDs (with approximately 4-8 participants per FGD) at each CTU. Thus,

a sample size of up to 120 male partners of HOPE participants was thought to be necessary.

## **10.4 Participant Selection**

Selection of former ASPIRE and HOPE participants will be based upon objective measures of adherence in ASPIRE and HOPE (see Sections [7.1-7.3](#) and [10.3](#) for likely group categorization parameters). The pre-determined method for group designation (i.e., non-adherent or adherent in Phase 1; to be determined in Phase 2) is available in the MTN-032 SSP Manual.

Male partners of HOPE participants will be recruited from a list of randomly selected HOPE participants. Selection of male partners will be determined by identifying HOPE participants from that list who consented to have their partners contacted and systematically inviting them to take part in the study.

An additional 2-3 months may be needed for recruitment of HOPE FGD participants after HOPE study results are released. The MTN-032 Protocol Team will review the HOPE results at that time and make a determination on whether collecting qualitative data from that cohort would help clarify or expand upon unexpected or important findings from the HOPE trial. For example, if adherence rates are clearly and consistently higher in HOPE than ASPIRE across all sites, exploring the differences in adherence counseling and support activities between both studies, and how these differences influenced the participants' attitudes and behaviors, could inform future marketing and messaging approaches that might facilitate product roll-out in an open-label non-research context.

## **10.5 Data and Study Monitoring Procedures**

Demographic and behavioral data will be captured by case report form (CRF) and entered in an electronic database (e.g., Redcap). Qualitative data will be audio-recorded, processed (i.e., translated and transcribed in English), and coded for thematic analyses using Dedoose or a similar qualitative software. Research Triangle Institute (RTI) International will function as the overall data coordinating center for quantitative and qualitative data and will lead all analyses.

No Study Monitoring Committee (SMC) review will be performed for MTN-032 given the short study timeline and the nature of the study. Protocol team members from MTN, including RTI International and FHI 360, will provide oversight of study operations and ensure the study is implemented in accordance with MTN standards, as defined in the MTN Manual of Operating Procedures.

## **10.6 Data Analysis**

### **10.6.1 Quantitative Analysis**

Demographic and behavioral data will be captured by CRF and entered in an electronic database (e.g., Redcap). We will use the following descriptive statistics to assess the characteristics of MTN-032 participants: the number and percent in each category for categorical variables (e.g., marital status, employment, adherence group, self-reported product use and sexual practices, etc.), and the mean or median and range for continuous variables (e.g., age, number of children, etc.).



## 10.6.2 Qualitative Analysis

### *Data Sources*

The qualitative data from MTN-032 will include three main data sources:

- Original handwritten notes of IDIs and FGDs
- Debrief report summaries of IDIs and FGDs
- Audio-recorded IDIs and FGDs

Qualitative data will be audio-recorded, processed, and coded for thematic analyses using Dedoose or a similar qualitative software. RTI International will function as the overall data coordinating center for quantitative and qualitative data and will lead all analyses.

### *Qualitative Analysis Overview*

The following section provides a brief overview of the analysis process; however, a more detailed description of the qualitative analysis will be presented in the study analysis plan.

Qualitative analyses from the MTN-032 study will use a variety of techniques to provide an in-depth characterization of the contextual factors that affected participants' actual product use, as well as participants' reactions to adherence support interventions. The primary source of qualitative data used in the MTN-032 analysis will consist of raw textual data. Qualitative data will be audio-recorded, processed, and coded for qualitative analyses using Dedoose or a similar qualitative software. Data coding will be used as a primary analytical approach for data reduction, that is, to summarize, extract meaning, and condense the data.<sup>39, 40</sup> MTN-032 transcripts will be coded first through descriptive coding for key themes and topics, using a preliminary codebook (see [Section 10.6.3](#)).<sup>41</sup> Additional codes will be identified through an iterative process of reading the textual data to identify emergent themes, and the codebook will be modified accordingly. In addition to descriptive codes, pattern codes, which achieve a greater level of abstraction, will be used to start linking themes and topics together in order to explore the relationship between socio-contextual factors and adherence, as well as between adherence support interventions and adherence.<sup>39</sup> Whenever possible, we will also compare study sites and explore differences or similarities related to product use adherence facilitators and challenges and participating in adherence support interventions due to different socioeconomic, cultural and geographical contexts. The analysis will be done by the investigative team, working interactively through emails, and regular phone or face-to-face meetings. The findings and interpretations of the data will be critically discussed until there is group consensus on the dominant themes and meanings contained in the data.<sup>42</sup> Whenever possible, site staff will be involved to corroborate findings from the analysis team.

## 10.6.3 Codebook Development and Coding Process<sup>43</sup>

Coding is an essential process for data reduction necessary for the management and interpretation of large amounts of qualitative data. Staff at RTI International will develop a codebook and study procedures for coding and analysis of all of the qualitative data. Each code will be operationally-defined and refined in an iterative way, as needed. Transcripts will be coded using a qualitative software package such as Dedoose.

During the study development stage, a set of preliminary codes will be developed based on the research questions of this study. The analysis coding structure will be hierarchical, and will

reflect the topics/themes covered in the interview guides. After the first 2-3 interviews are completed, each member (analyst) of the coding group will apply this initial set of thematic codes to a common transcript, discuss their coding experiences (via email, a meeting, or conference call), and agree on expanding and modifying code names and definitions when necessary. The coding team will generate substantive and conceptual categories through an iterative process of reading the data, and generating codes based on the data and on key themes or topics identified *a priori*, applying the codes to the data, and refining these as coding progresses. Thus, codes will be centered on the main topics of interest (e.g., product use adherence: facilitators influencing product initiation, persistence and implementation and challenges associated with product use) and the hypothesized contextual spheres of influence. However, by nature, the qualitative research process is iterative, and the Dedoose software allows for the generation of new codes for emergent themes that were not identified *a priori* by the research team. The software also allows for coders to insert descriptive comments and memos to themselves and others as they are working, and to code for concepts not spelled out in verbatim text, such as “contradiction,” when a participant contradicts herself.

Once finalized, the codebook will be used for coding of all of the transcripts. Comprehensive listings of all coded quotations for every code (as well as “families” of related codes) will be generated in Dedoose. The coding team will consider the coded dataset in its entirety, and “stratify” the coded quotations by the site, reported opinions of adherence facilitators/challenges, reported opinions of adherence support interventions, and group assignment (e.g., low vs. inconsistent vs. high product use) when applicable. Depending on findings from the analysis of these data clusters, the team may conduct additional grouping and stratifications of the data.

The coding process will involve a core group of at least 2-3 analysts who will frequently communicate (via email, phone or in person meetings) and discuss their use of the codebook and application of the codes during the coding process. A pre-selected proportion of inter-rater reliability tests using Dedoose or other coding software functions will be assessed with all coders. Following this process, the coding team will discuss (in person or via teleconference) the coding discrepancies, which will ultimately be resolved through consensus. Sufficient inter-rater reliability is defined as above .65 pooled kappa. Regular discussions among the coding team will ensure that coding remains standardized and reliable.

## **11 DATA HANDLING AND RECORDKEEPING**

### **11.1 Data Management Responsibilities**

Study CRFs will be developed by RTI International in conjunction with the protocol team and will be manually double-entered in an electronic database. Quality control (QC) reports and queries routinely will be generated and distributed by RTI International to the study sites for verification and resolution. As part of the study activation process, each study site must identify all CRFs to be used as source documents.

IDI and FGD guides will be developed by RTI International in conjunction with the protocol team and, where required, will receive IRB/EC approval. Interview and group discussion files generated in the field will be electronically transferred to RTI International using a secure File Transfer Protocol (FTP) site, where they will be uploaded and managed using a qualitative software package. RTI International will act as a hub, and manage all data for the study. A

convention for file naming will be developed, and all data will be labeled according to this process. Transcripts will be transferred to RTI International as they are completed. RTI International will save all versions of all files on a secure, password-protected server.

## **11.2 Source Documents and Access to Source Data/Documents**

All study sites will maintain source data/documents in accordance with Requirements for Source Documentation in DAIDS Funded and/or Sponsored Clinical Trials (<https://www.niaid.nih.gov/sites/default/files/daids-sourcedocpolicy.pdf>) and the relevant appendix regarding source documentation (<https://www.niaid.nih.gov/sites/default/files/sourcedocappndx.pdf>).

For MTN-032, source documentation may include recruitment logs, enrollment records, visit checklists, CRFs, interview data, participant file notes, and electronic audio files. Essential documentation for the study also includes all versions of the protocol, informed consent forms, operating procedures and key communication with the protocol team. In accordance with U.S regulations, each IoR/designee will maintain, and store securely, complete, accurate and current study records throughout the study.

Study records must be maintained on site for the entire period of study implementation. Thereafter, instructions for record storage will be provided by DAIDS. No study records may be moved to an off-site location or destroyed prior to receiving approval from DAIDS.

## **11.3 Quality Control and Quality Assurance**

At the field level, designated staff will check the quality of the transcripts and translations to ensure that they reflect the content of the interview, and then send each transcript to RTI International for additional QC. CRFs will be reviewed at the site and transmitted to RTI International where they will be reviewed and queried. All queries will be resolved through a standardized QC reporting mechanism.

All study sites will conduct QC and quality assurance procedures in accordance with Requirements for Clinical Quality Management Plans at DAIDS Funded and/or Supported CRS (<https://www.niaid.nih.gov/sites/default/files/qmppolicy.pdf>).

## **12 CLINICAL SITE MONITORING**

FHI 360 staff or designee will review study records during the course of the study, however no formal clinical monitoring will be conducted. FHI 360 staff or designee will do the following:

- Review informed consent forms, procedures, and documentation
- Assess compliance with the study protocol, Good Clinical Practices (GCP) guidelines, and applicable regulatory requirements (US and non-US), including US Code of Federal Regulations (CFR) Title 45 Part 46 and Title 21 Parts 50, 56, and 312
- Perform source document verification to ensure the accuracy and completeness of study data
- Assess implementation and documentation of internal site quality management procedures

The IoR/designee will allow inspection of study facilities and documentation (e.g., informed consent forms, clinic records, other source documents, CRFs), as well as observation of study procedures. The IoR/designee also will allow inspection of all study-related documentation by authorized representatives of the US OHRP, NIH, NIAID, and/or contractors of the NIH, and other local or US regulatory authorities, and representatives of the MTN, as needed. A site visit log will be maintained at the study site to document all visits.

## **13 HUMAN SUBJECTS PROTECTIONS**

### **13.1 Institutional Review Boards/Ethics Committees**

Site investigators will make every effort to minimize risks to participants. Participants and study staff members will take part in a thorough informed consent process. Before beginning the study, the IoR will have obtained IRB/EC approval. The IoR will permit audits by the NIH, local authorities, site IRBs/ECs, the MTN, OHRP, or any of their appointed agents.

Each participating institution is responsible for assuring that this protocol, the associated site-specific informed consent form, and study-related documents as required, are reviewed by an IRB/EC responsible for oversight of research conducted at the study site. Any amendments to the protocol must be approved by the responsible IRBs/ECs prior to implementation.

Each IoR/designee will make progress reports to the IRBs/ECs within three months after study termination or completion, unless specified otherwise by their IRBs/ECs. These reports will include the total number of participants enrolled in the study, the number of participants who completed the study, all changes in the research activity, and all unanticipated problems involving risks to human subjects or others. More real-time or frequent reporting of one or more of these or other items may need to be furnished if so specified by their IRBs/ECs. Study sites will submit documentation of continuing review to the DAIDS Protocol Registration Office (DAIDS PRO) in accordance with the most current DAIDS policies at the time of registration.

### **13.2 Protocol Registration**

Prior to implementation of this protocol, and any subsequent full version amendments, each site must have the protocol and the protocol consent forms approved, as appropriate, by their local IRB/ EC and any other applicable regulatory entity. Upon receiving final approval, sites will submit all required protocol registration documents to the DAIDS PRO at the Regulatory Support Center (RSC). The DAIDS PRO will review the submitted protocol registration packet to ensure that all of the required documents have been received.

Site-specific informed consent forms (ICFs) *will not* be reviewed or approved by the DAIDS PRO, and sites will receive an Initial Registration Notification when the DAIDS PRO receives a complete registration packet. Receipt of an Initial Registration Notification indicates successful completion of the protocol registration process. Sites will not receive any additional notifications from the DAIDS PRO for the initial protocol registration. A copy of the Initial Registration Notification should be retained in the site's regulatory files.

Upon receiving final IRB/EC and any other applicable RE approval(s) for an amendment, sites should implement the amendment immediately. Sites are required to submit an amendment registration packet to the DAIDS PRO at the RSC. The DAIDS PRO will review the submitted protocol registration packet to ensure that all the required documents have been received. Site-specific ICF(s) *will not* be reviewed and approved by the DAIDS PRO and sites will receive an Amendment Registration Notification when the DAIDS PRO receives a complete registration packet. A copy of the Amendment Registration Notification should be retained in the site's regulatory files.

For additional information on the protocol registration process and specific documents required for initial and amendment registrations, refer to the current version of the DAIDS Protocol Registration Manual.

### **13.3 Study Coordination**

Close coordination between protocol team members is necessary to track study progress, respond to queries about proper study implementation, and address other issues in a timely manner.

Study implementation will be directed by this protocol, which may not be amended without prior written approval from the Protocol Chair and DAIDS MO. Study implementation will be guided by a common SSP manual that provides further instructions and operational guidance on conducting study procedures and associated data processing. Standardized study-specific training will be provided to all sites by FHI 360, RTI International, and other designated members of the Protocol Team.

### **13.4 Risk Benefit Statement**

#### **13.4.1 Risks**

It is not expected that this trial will expose human subjects to unreasonable risk. Participation in research includes the risks of loss of confidentiality and discomfort with the personal nature of questions when discussing sexual behaviors and VR use.

#### ***Psychological Harms***

MTN-032 will ask questions that may cause individuals discomfort given their personal nature. Stress and feelings of guilt or embarrassment may arise simply from thinking or talking about one's own behavior or attitudes on sensitive topics. This could result in undesired changes in thought and emotion.

While the risk of psychological harm is anticipated to be minimal, and study staff will inform participants that they can choose not to answer questions at any time, study staff will collect information on participants who report a change in mood as a result of study participation. In addition, study staff will ensure that participants have access to proper clinical resources to address psychological harms.

All FGD participants will be asked and strongly encouraged to respect each other's confidentiality, but participants who take part in the FGDs may still disclose what other participants said during the group discussion. Furthermore, all FGD participants will be asked to

use pseudonyms for themselves and for anyone they may talk about during the course of the FGD.

### **Social Harms**

Although study sites make every effort to protect participant privacy and confidentiality, it is possible that participants' involvement in the study could become known to others, and that social harms may result (i.e., because participants could become known as HIV-positive or at "high risk" for HIV infection). For example, participants could be treated unfairly or discriminated against, or could have problems being accepted by their families and/or communities. To mitigate one possible source of social harms, each site will work with those HOPE participants who have given permission to contact their male partners to carefully explain the potential consequences of allowing their male partners to be contacted for Phase 2 participation (e.g., disclosure of study involvement and/or ring use) prior to contacting the male partners.

Data on the occurrence of potential social harms will be collected from all participants. These data will be captured via CRF and analyzed on an ongoing basis. The protocol team will monitor, evaluate and adjust operations to reduce the potential for such occurrences.

#### **13.4.2 Benefits**

There are no direct benefits to participating in this study. However, participants and others may benefit in the future from information learned from this study. Specifically, information learned in this study may help to understand issues important for broader implementation of the dapivirine ring. Participants may also appreciate the opportunity to contribute to the field of HIV prevention research.

Lastly, the information that participants provide may help health professionals develop better ways to improve communication and understanding between researchers and participants in HIV prevention studies.

### **13.5 Informed Consent Process**

Each study participant will provide written informed consent prior to completing any study procedures. In obtaining and documenting informed consent, the IoR and their designees will comply with applicable local and US regulatory requirements and will adhere to GCP and to the ethical principles that have their origin in the Declaration of Helsinki. Study staff must document the informed consent process in accordance with the Requirements for Source Documentation in DAIDS Funded and/or Sponsored Clinical Trials (<https://www.niaid.nih.gov/sites/default/files/daids-sourcedocpolicy.pdf>). Participants will be provided with copies of the informed consent forms if they are willing to receive them.

In addition to informed consent forms, the Protocol Team will work with study staff and community representatives to develop appropriate materials about the study and a standardized approach to the informed consent process to be implemented at all study sites, which will be detailed in the MTN-032 SSP manual. Furthermore, participants who consent to have their male partners contacted while in HOPE will be asked to provide written consent at the HOPE PUEV for MTN-032 study staff to contact their male partners for recruitment into MTN-032. Only those HOPE participants who read and sign an additional "Permission to Contact" form will have their male partners invited to enroll in Phase 2. This form will explain that the participant gives the study staff permission to contact her male partner with the understanding that her male

partner will be invited to discuss the research and her experiences using the ring, which means her male partner will be aware of her study involvement, potential use of the ring, and that the ring contains ARV and is for HIV prevention.

The informed consent process will cover all elements of informed consent required by research regulations. In addition, the process will specifically address the following topics of importance to this study:

- The purpose of the study
- The potential social harms associated with study participation (and what to do if such harms are experienced)
- There is no benefits to taking part in this study
- The right to withdraw from the study at any time

### **13.6 Participant Confidentiality**

All study procedures will be conducted in a location agreed upon by the participant, and every effort will be made to protect participant privacy and confidentiality. Each study site will implement confidentiality protections that reflect the local study implementation plan and the input of study staff and community representatives to identify potential confidentiality issues and strategies to address them. In addition to local considerations, the protections described below will be implemented at all sites.

All study-related information will be stored securely at the study site. All participant information will be stored in locked areas with access limited to study staff. All study data collection and administrative forms will be identified solely by PTID number to maintain participant confidentiality. All records that contain names or other personal identifiers, such as informed consent forms, will be stored securely. All local databases will be secured with password protected access systems. Forms, lists, logbooks, appointment books, and any other listings that link PTID numbers to identifying information will be stored in a locked file in an area with limited access. All digital audio files will be stored on password-protected computers. Audio files will be transcribed in English (using a 1-step translation/transcription process) and securely stored. Please see MTN-032 SSP Manual for guidance. Participants' study information will not be released without their written permission, except as necessary for review, monitoring, and/or auditing by the following:

- Representatives of the US Federal Government, including the US OHRP, NIH, and/or contractors of the NIH, and other local and US regulatory authorities
- Study staff
- Site IRBs/ ECs

### **13.7 Special Populations**

#### **13.7.1 Pregnant Women**

Pregnancy is not exclusionary. Due to the nonclinical nature of this study, no pregnancy-related risks are anticipated in MTN-032.

#### **13.7.2 Children**

MTN-032 will enroll former ASPIRE and HOPE participants who were age 18 through 45 years (inclusive) at the time of screening for ASPIRE, as verified per site SOPs, thus children will not

be considered eligible for this trial.

### **13.8 Compensation**

Pending IRB/EC approval, participants will be compensated for time and effort in this study, and/or be reimbursed for travel to study visits and time away from work. Site-specific reimbursement amounts will be specified in the study informed consent forms.

### **13.9 Study Discontinuation**

This study may be discontinued at any time by NIH, the MTN, the US OHRP, other government or regulatory authorities, or site IRBs/ECs.

## **14 PUBLICATION POLICY**

DAIDS/NIAID and MTN policies will govern publication of the results of this study.

## **15 APPENDICES**



**APPENDIX I: SCREENING AND ENROLLMENT SAMPLE INFORMED  
CONSENT FORM - PHASE I (ASPIRE) PARTICIPANTS**

**SAMPLE INFORMED CONSENT FORM  
DIVISION OF AIDS, NIAID, NIH**

**MTN-032**

**Assessment of ASPIRE and HOPE Adherence**

**Version 1.0**

**PHASE I (ASPIRE) PARTICIPANTS**

**August 20, 2015**

**PRINCIPAL INVESTIGATOR: [Site to insert]**

**PHONE: [Site to insert]**

**Short Title for the Study: Assessment of ASPIRE and HOPE Adherence**

**INFORMED CONSENT**

You are being asked to take part in this research study because you are a woman who took part in the MTN-020 (ASPIRE) trial and received the dapivirine vaginal ring during your trial participation. Up to 224 women will take part in the first study phase of this study at multiple ASPIRE research sites in Africa. This Microbicide Trials Network (MTN) study is sponsored by the US National Institutes of Health (NIH). At this site, the person in charge of this study is **[INSERT NAME OF PRINCIPAL INVESTIGATOR]**.

Before you decide if you want to join this study, we want you to learn more about it. This consent form gives you information about the study. Study staff will talk with you and answer any questions you may have. Once you read and understand the study and its requirements, you can decide if you want to join. If you do decide to take part in the trial, you will sign your name or make your mark on this form. A copy of this document will be offered to you.

Your eligibility to participate in this study will then be assessed, and once confirmed, you will be considered enrolled in the MTN-032 study.

It is important to know that your participation in this research is your decision and taking part in this study is completely voluntary (see Your Rights as a Research Participant/Volunteer for more information).

**WHAT IS THE PURPOSE OF THIS STUDY?**

You are being asked today to take part in Phase 1 of MTN-032. The main goal of the first phase of this study is to better understand ASPIRE participants' use of study product (vaginal rings) when they were in the ASPIRE trial. If you are eligible for and

complete Phase 1, and afterwards decide to enroll and participate in the HOPE trial, you then may be eligible to participate in MTN-032 Phase 2.

Some Phase 1 participants will be asked to participate in an in-depth interview (IDI), and some will be asked to participate in a focus group discussion (FGD) with other participants. Participants will be asked questions individually or in a group setting. Study staff will tell you if you are going to take part in an IDI or FGD.

To obtain information about your participation in ASPIRE, the MTN-032 study team will need to review your ASPIRE research records. By signing this form, you are giving the MTN-032 study team permission to access your research records.

### **STUDY PRODUCTS**

There are no study products (investigational drugs or other products) involved in this research study.

### **STUDY PROCEDURES**

Phase 1 of the MTN-032 study consists of one study visit, including the Screening/Enrollment Visit which is taking place today after you sign this informed consent form. Additional visit(s) may be conducted to complete all required procedures, if necessary. Visit(s) will take place here at this study clinic or at a place agreed upon by you and the study staff, which may be your home or another convenient location **[SITE TO INCLUDE ALTERNATE LOCATION]**.

The procedures done at this visit will take about **[SITE TO INSERT TIME]**.

- Study staff will ask you where you live and other questions about you, and your understanding of the study requirements.
- You will complete one or more questionnaires that will help researchers better understand your interview responses.
- You may be asked to have an in-depth interview (IDI). If asked to complete an IDI:
  - You will have an IDI in the presence of one or two MTN-032 research staff members. The IDI will take approximately **[SITE TO INSERT TIME]**. Clinic staff will make every effort to ensure your privacy and confidentiality.
  - Before the IDI begins, the interviewer will talk with you about your ASPIRE adherence results.
    - Adherence refers to whether ASPIRE participants correctly used the dapivirine vaginal ring as instructed by trial staff.
    - In ASPIRE, a participant's adherence levels were measured by the amount of study drug (dapivirine) that remained in returned vaginal rings, the amount of study drug in your blood, and adherence was discussed during counseling and interview sessions.
  - The interviewer will then ask more questions, and may take notes and will audio-record your conversation. Interviews will be audio-recorded to make sure we record your words exactly how you said them.
  - You will be asked some general questions, such as your age, education,

- living situation, relationship status, and health.
- The interviewer will also ask you questions about:
  - Your experience with ring use and ASPIRE trial participation.
  - Your understanding of the results of the ASPIRE trial.
  - Your perception of your sexual health risk, how this understanding may have affected your decision to use vaginal rings, and what impact it may have on your use of HIV prevention products that may become available in the future.
- You may be asked to participate in a focus group discussion (FGD). If you're asked to join a FGD:
  - The FGD will take approximately **[SITE TO INSERT TIME]**. Study interviewers/facilitators will lead the discussion, fully explain the process, and answer any questions you have.
  - Before the FGD begins, the interviewer will talk with you in private about your ASPIRE adherence results.
    - Adherence refers to whether ASPIRE participants correctly used the dapivirine vaginal ring as instructed by trial staff.
    - In ASPIRE, a participant's adherence levels were measured by the amount of study drug (dapivirine) that remained in returned vaginal rings, the amount of study drug in your blood, and adherence was discussed during counseling and interview sessions.
  - In a small group setting with other study participants, an interviewer will encourage discussion of various topics similar to those discussed during the IDIs.
  - Like the IDIs, FGDs will be audio-recorded and later transcribed.
  - A study staff member will take notes during the discussion as a backup to the audio-recording.
  - You will be asked to use fake names for yourself and anyone you talk about.
- If you have either an IDI or FGD, study staff will also:
  - Inform you about other services, if needed
  - Schedule your next visit, if necessary
  - Reimburse you for your visit(s)

## **RISKS AND/OR DISCOMFORTS**

During the interview or focus group discussion, you may be asked some questions that cause you to feel embarrassed or uncomfortable. You may become embarrassed and/or worried when discussing sexual practices or your use of the vaginal ring. Trained study interviewers will help you deal with any feelings or questions you have. You can choose not to answer questions in the interview at any time.

Another possible risk of this study is loss of confidentiality of the information you give. Every effort will be made to protect your confidential information, but this cannot be guaranteed. To reduce this risk, IDIs will take place in private, and the information recorded during your interview will be strictly protected. The audio recording, notes, and analyses from these materials will be kept confidential and will only use study numbers

or fake names. This means that no one other than the MTN-032 interview team will be able to link your responses to you personally. The information that links you to the research materials will be kept in a secure location that will be accessed only by members of the MTN-032 study team for the purposes of this research. Your voice recordings will also be kept in a secure location and only people involved with the study will have access to these recordings. Study leaders will make sure this happens.

If you participate in a focus group discussion, other participants will hear what you say. Although we will not reveal your full name to other participants, it is possible that others may know you from previous interactions. We will also ask every participant not to tell anyone outside of the group what any person said during the FGD. While it is not at all likely that your discussion will be made public, we cannot guarantee that everyone will keep the discussion private.

However, it is possible that others may learn of your participation here and, because of this, may treat you unfairly or discriminate against you. For example, you could have problems getting or keeping a job, or being accepted by your family or community. If you have any problems, study counselors will talk with you and/or your partner to try to help resolve them.

## **BENEFITS**

There are no direct benefits to participating in this study. However, you and others may benefit in the future from information learned in this study. Participants in this study may also appreciate the opportunity to contribute to HIV prevention research efforts. Information participants provide may help researchers improve counseling materials about product use and sexual behavior. Lastly, the information provided in this study may help health professionals develop ways to improve communication and understanding between researchers and participants in HIV prevention studies.

Medical care for HIV infection and other health conditions will not be part of this study. This study cannot provide you with general medical care, but study staff will refer you to other available sources of care, if needed.

## **NEW INFORMATION**

You will be told of any new information learned during this study that might affect your willingness to stay in the study. You will also be told when study results may be available, and how to learn about them.

## **WHY YOU MAY BE WITHDRAWN FROM THE STUDY WITHOUT YOUR CONSENT**

You may be removed from the study early without your permission if:

- The study is cancelled by the US NIH, the US Office for Human Research Protections (OHRP), MTN, the local government or regulatory agency, or the Institutional Review Board (IRB) or Ethics Committee (EC). An IRB is a committee that watches over the safety and rights of research participants
- You are unwilling or unable to comply with required study procedures, including study visit attendance.

- Other reasons that may prevent you from completing the study successfully

## **COSTS TO YOU**

There is no cost to you for study related visits.

## **REIMBURSEMENT**

**[SITES TO INSERT INFORMATION ABOUT LOCAL REIMBURSEMENT:]** You will receive **[SITES TO INSERT AMOUNT \$XX]** for your time, effort, and travel to and from the clinic at each scheduled visit.

## **CONFIDENTIALITY**

Efforts will be made to keep your information confidential. However, it is not possible to guarantee confidentiality. Your personal information may be disclosed if required by law. The study staff may use your personal information to verify that you are not in any other research studies. This includes studies conducted by other researchers that study staff may know about. Any publication of this study will not use your name or identify you personally.

Your records may be reviewed by:

- The Research Triangle Institute
- Site IRBs/ECs
- FHI 360
- Representatives of the US Federal Government, including the US OHRP, NIH and/or contractors of NIH, and other local and US regulatory authorities
- Study monitors
- Study staff

The researchers will do everything they can to protect your privacy.

## **RESEARCH-RELATED INJURY**

**[SITE TO SPECIFY INSTITUTIONAL POLICY]:** It is unlikely that you will be injured as a result of study participation. If you are injured, the **[INSTITUTION]** will give you immediate necessary treatment for your injuries. You **[WILL/WILL NOT]** have to pay for this treatment. You will be told where you can receive additional treatment for your injuries. The U.S. NIH does not have a mechanism to pay money or give other forms of compensation for research related injuries. You do not give up any legal rights by signing this consent form.

## **YOUR RIGHTS AS A RESEARCH PARTICIPANT/VOLUNTEER**

**[SITE TO SPECIFY INSTITUTIONAL POLICY]:** Taking part in this study is completely voluntary. You may choose not to take part in this study or leave this study at any time. If you choose not to participate or to leave the study, you will not lose the benefit of services to which you would otherwise be entitled at this clinic. If you want the results of the study after the study is over, let the study staff members know.

## **PROBLEMS OR QUESTIONS**

If you ever have any questions about the study, or if you have a research-related injury, you should contact ***[INSERT NAME OF THE INVESTIGATOR OR OTHER STUDY STAFF]*** at ***[INSERT TELEPHONE NUMBER AND/OR PHYSICAL ADDRESS]***.

If you have questions about your rights as a research participant, you should contact ***[INSERT NAME OR TITLE OF PERSON ON THE IRB/EC OR OTHER ORGANIZATION APPROPRIATE FOR THE SITE]*** at ***[INSERT PHYSICAL ADDRESS AND TELEPHONE NUMBER]***.

**SIGNATURES- VOLUNTARY CONSENT**

***[INSERT SIGNATURE BLOCKS AS REQUIRED BY THE LOCAL IRB/EC]:***

***If you have read this consent form (or had it read and explained to you) and if you understand the information and voluntarily agree to take part in the study, please sign your name or make your mark below.***

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Participant Name (print)	Participant Signature/Mark	Date
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Study Staff Conducting Consent Discussion (print)	Study Staff Signature	Date
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Witness Name (print)	Witness Signature	Date
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**APPENDIX II: SCREENING AND ENROLLMENT SAMPLE INFORMED  
CONSENT FORM - PHASE 2 (HOPE) PARTICIPANTS**

**SAMPLE INFORMED CONSENT FORM  
DIVISION OF AIDS, NIAID, NIH**

**MTN-032**

**Assessment of ASPIRE and HOPE Adherence**

**Version 2.0**

**PHASE 2 (HOPE) PARTICIPANTS**

**September 5, 2017**

**PRINCIPAL INVESTIGATOR: [Site to insert]**

**PHONE: [Site to insert]**

**Short Title for the Study: Assessment of ASPIRE and HOPE Adherence**

**INFORMED CONSENT**

You are being asked to take part in this phase of the research study because you are a woman who participated in the MTN-025 (HOPE) trial and received the dapivirine vaginal ring during your trial participation. Up to 156 women will participate in this second study phase at multiple HOPE research sites in Africa. This Microbicide Trials Network (MTN) study is sponsored by the US National Institutes of Health (NIH). At this site, the person in charge of this study is **[INSERT NAME OF PRINCIPAL INVESTIGATOR]**.

Before you decide if you want to continue in this study, we want you to learn more about Phase 2 of the MTN-032 study. This consent form gives you information about Phase 2 of this study. Study staff will talk with you and answer any questions you may have. Once you read and understand Phase 2 and its requirements, you can decide if you want to take part in the second phase of this trial. If you do decide to continue in this study and take part in Phase 2, you will sign your name or make your mark on this form. A copy of this document will be offered to you.

Your eligibility to participate in Phase 2 of this study will then be assessed, and once confirmed, you will be considered enrolled in Phase 2 of the MTN-032 study.

It is important to know that your participation in this research is your decision and taking part in this study is completely voluntary (see Your Rights as a Research Participant/Volunteer for more information).



## **WHAT IS THE PURPOSE OF THIS STUDY?**

You are being asked today to take part in Phase 2 of MTN-032. The main goal of the second phase of this study is to better understand HOPE participants' use of study product (vaginal rings) while participating in both the ASPIRE and HOPE trials. Women who completed the HOPE trial may be eligible to participate in MTN-032 Phase 2.

Some Phase 2 participants will be asked to participate in an in-depth interview (IDI), and some will be asked to participate in a focus group discussion (FGD) with other participants. Participants will be asked questions individually or in a group setting. Study staff will tell you if you are going to take part in an IDI or FGD.

To obtain information about your participation in ASPIRE or HOPE, the MTN-032 study team will need to review your ASPIRE and/or HOPE research records. By signing this form, you are giving the MTN-032 study team permission to access your research records.

## **STUDY PRODUCTS**

There are no study products (investigational drugs or other products) involved in this research study.

## **STUDY PROCEDURES**

Phase 2 of the MTN-032 study consists of one study visit, including the Screening/Enrollment Visit which is taking place today after you sign this informed consent form. Additional visit(s) may be conducted to complete all required procedures, if necessary. Visits will take place here at this study clinic or at a place agreed upon by you and the study staff, which may be your home or another convenient location ***[SITE TO INCLUDE ALTERNATE LOCATION]***.

The procedures done at this visit will take about ***[SITE TO INSERT TIME]***.

- Study staff will ask you where you live and other questions about you, and your understanding of the study requirements.
- You will complete one or more questionnaires that will help researchers better understand your interview responses.
- You may be asked to have an in-depth interview (IDI):
  - You will have an IDI in the presence of one or two MTN-032 research staff members. The IDI will take approximately ***[SITE TO INSERT TIME]***. Clinic staff will make every effort to ensure your privacy and confidentiality.
  - During the IDI, the interviewer will talk with you about your HOPE adherence results.
    - Adherence refers to whether HOPE study participants used the dapivirine vaginal ring as instructed by trial staff.
    - In HOPE, a participant's adherence levels were measured by the amount of study drug (dapivirine) that remained in returned vaginal rings, and adherence was discussed during counseling and interview sessions.

- The interviewer will then ask more questions, and may take notes and will audio-record your conversation. Interviews will be audio-recorded to make sure we record your words exactly how you said them.
- You will be asked some general questions, such as your age, education, living situation, relationship status, and health.
- The interviewer will also ask you questions about:
  - Your experience with ring use and HOPE trial participation.
  - Your motivations for participating in HOPE.
- You may be asked to participate in a focus group discussion (FGD). If you're asked to join a FGD:
  - The FGD will take approximately **[SITE TO INSERT TIME]**. Study interviewers/facilitators will lead the discussion, fully explain the process, and answer any questions you have.
  - Before the FGD begins, the interviewer will talk with you in private about your HOPE adherence results.
    - Adherence refers to whether HOPE participants correctly used the dapivirine vaginal ring as instructed by trial staff.
    - In HOPE, a participant's adherence levels were measured by the amount of study drug (dapivirine) that remained in returned vaginal rings, and adherence was discussed during counseling and interview sessions.
  - In a small group setting with other study participants, an interviewer will encourage discussion of various topics similar to those discussed during the IDIs. The interviewer will also encourage discussion about the results of the HOPE trial and about possible educational and marketing approaches to promote ring use.
  - Like the IDIs, FGDs will be audio-recorded and later transcribed.
  - A study staff member will take notes during the discussion as a backup to the audio-recording.
  - You will be asked to use fake names for yourself and anyone you talk about.
- Study staff will also:
  - Inform you about other services, if needed.
  - Schedule your next visit, if necessary.
  - Reimburse you for your visit(s).

## **RISKS AND/OR DISCOMFORTS**

During the interview or focus group discussion, you may be asked some questions that cause you to feel embarrassed or uncomfortable. You may become embarrassed and/or worried when discussing sexual practices or your use of the vaginal rings. Trained study interviewers will help you deal with any feelings or questions you have. You can choose not to answer questions during the interview at any time.

Another possible risk of this study is loss of confidentiality of the information you give. Every effort will be made to protect your confidential information, but this cannot be guaranteed. To reduce this risk, IDIs will take place in private, and the information

recorded during your interview will be strictly protected. The audio recording, notes, and analyses from these materials will be kept confidential and will only use study numbers or fake names. This means that no one other than the MTN-032 interview team will be able to link your responses to you personally. The information that links you to the research materials will be kept in a secure location that will be accessed only by members of the MTN-032 study team for the purposes of this research. Your voice recordings will also be kept in a secure location and only people involved with the study will have access to these recordings. Study leaders will make sure this happens.

If you participate in a focus group discussion, other participants will hear what you say. Although we will not reveal your full name to other participants, it is possible that others may know you from previous interactions. We will also ask every participant not to tell anyone outside of the group what any person said during the FGD. While it is not at all likely that your discussion will be made public, we cannot guarantee that everyone will keep the discussion private.

However, it is possible that others may learn of your participation here and, because of this, may treat you unfairly or discriminate against you. For example, you could have problems getting or keeping a job, or being accepted by your family or community. If you have any problems, study counselors will talk with you and/or your partner to try to help resolve them.

## **BENEFITS**

There are no direct benefits to participating in this study. However, you and others may benefit in the future from information learned in this study. Participants in this study may also appreciate the opportunity to contribute to HIV prevention research efforts. Information participants provide may help researchers improve counseling materials about product use and sexual behavior. Lastly, the information provided in this study may help health professionals develop ways to improve communication and understanding between researchers and participants in HIV prevention studies.

Medical care for HIV infection and other health conditions will not be part of this study. This study cannot provide you with general medical care, but study staff will refer you to other available sources of care, if needed.

## **NEW INFORMATION**

You will be told of any new information learned during this study that might affect your willingness to stay in the study. You will also be told when study results may be available, and how to learn about them.

## **WHY YOU MAY BE WITHDRAWN FROM THE STUDY WITHOUT YOUR CONSENT**

You may be removed from the study early without your permission if:

- The study is cancelled by the US NIH, the US Office for Human Research Protections (OHRP), MTN, the local government or regulatory agency, or the Institutional Review Board (IRB) or Ethics Committee (EC). An IRB is a committee that watches over the safety and rights of research participants

- You are unwilling or unable to comply with required study procedures, including study visit attendance.
- Other reasons that may prevent you from completing the study successfully

### **COSTS TO YOU**

There is no cost to you for study related visits.

### **REIMBURSEMENT**

**[SITE TO INSERT INFORMATION ABOUT LOCAL REIMBURSEMENT]:** You will receive **[SITE TO INSERT AMOUNT \$XX]** for your time, effort, and travel to and from the clinic at each scheduled visit.

### **CONFIDENTIALITY**

Efforts will be made to keep your information confidential. However, it is not possible to guarantee confidentiality. Your personal information may be disclosed if required by law. The study staff may use your personal information to verify that you are not in any other research studies. This includes studies conducted by other researchers that study staff may know about. Any publication of this study will not use your name or identify you personally.

Your records may be reviewed by:

- The Research Triangle Institute
- Site IRBs/ECs
- FHI 360
- Representatives of the US Federal Government, including the US OHRP, NIH and/or contractors of NIH, and other local and US regulatory authorities
- Study monitors
- Study staff

The researchers will do everything they can to protect your privacy.

### **RESEARCH-RELATED INJURY**

**[SITE TO SPECIFY INSTITUTIONAL POLICY]:** It is unlikely that you will be injured as a result of study participation. If you are injured, the **[INSTITUTION]** will give you immediate necessary treatment for your injuries. You **[WILL/WILL NOT]** have to pay for this treatment. You will be told where you can receive additional treatment for your injuries. The U.S. NIH does not have a mechanism to pay money or give other forms of compensation for research related injuries. You do not give up any legal rights by signing this consent form.

### **YOUR RIGHTS AS A RESEARCH PARTICIPANT/VOLUNTEER**

Taking part in this study is completely voluntary. You may choose not to take part in this study or leave this study at any time. If you choose not to participate or to leave the study, you will not lose the benefit of services to which you would otherwise be entitled at this clinic. If you want the results of the study after the study is over, let the study staff members know.

## **PROBLEMS OR QUESTIONS**

If you ever have any questions about the study, or if you have a research-related injury, you should contact ***[INSERT NAME OF THE INVESTIGATOR OR OTHER STUDY STAFF]*** at ***[INSERT TELEPHONE NUMBER AND/OR PHYSICAL ADDRESS]***.

If you have questions about your rights as a research participant, you should contact: ***[INSERT NAME OR TITLE OF PERSON ON THE IRB/EC OR OTHER ORGANIZATION APPROPRIATE FOR THE SITE]*** at ***[INSERT PHYSICAL ADDRESS AND TELEPHONE NUMBER]***.

**SIGNATURES- VOLUNTARY CONSENT**

***[INSERT SIGNATURE BLOCKS AS REQUIRED BY THE LOCAL IRB/EC]:***

***If you have read this consent form (or had it read and explained to you) and if you understand the information and voluntarily agree to take part in the study, please sign your name or make your mark below.***

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Participant Name (print)	Participant Signature/Mark	Date
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Study Staff Conducting Consent Discussion (print)	Study Staff Signature	Date
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Witness Name (print)	Witness Signature	Date
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**APPENDIX III: SCREENING AND ENROLLMENT SAMPLE INFORMED  
CONSENT FORM – HOPE PARTICIPANTS’ MALE PARTNERS**

**SAMPLE INFORMED CONSENT FORM  
DIVISION OF AIDS, NIAID, NIH**

**MTN-032**

**Assessment of ASPIRE and HOPE Adherence**

**Version 2.0**

**HOPE PARTICIPANTS’ MALE PARTNERS**

**September 5, 2017**

**PRINCIPAL INVESTIGATOR: *[Site to insert]***

**PHONE: *[Site to insert]***

**Short Title for the Study: Assessment of ASPIRE and HOPE Adherence**

**INFORMED CONSENT**

You are being asked to take part in this research study because you are a male partner of a woman who participated in the MTN-025 (HOPE) trial and she gave us permission to contact you. Up to 120 men will participate in this study at multiple HOPE research sites in Africa. This Microbicide Trials Network (MTN) study is sponsored by the US National Institutes of Health (NIH). At this site, the person in charge of this study is ***[INSERT NAME OF PRINCIPAL INVESTIGATOR]***.

Before you decide if you want to be in this study, we want you to learn more about the MTN-032 study. This consent form gives you information about this study. Study staff will talk with you and answer any questions you may have. Once you read and understand this study and its requirements, you can decide if you want to take part in the trial. If you do decide to take part in this study, you will sign your name or make your mark on this form. A copy of this document will be offered to you.

Your eligibility to participate in this study will then be assessed, and once confirmed, you will be considered enrolled in the MTN-032 study.

It is important to know that your participation in this research is your decision and taking part in this study is completely voluntary (see Your Rights as a Research Participant/Volunteer for more information).

**WHAT IS THE PURPOSE OF THIS STUDY?**

You are being asked today to take part in MTN-032. The main goal of this study is to better understand HOPE participants’ use of study product (vaginal rings) while

participating in the HOPE trial as well as their male partner's thoughts and feelings about the ring.

Some MTN-032 participants will be asked to participate in an in-depth interview (IDI), and some will be asked to participate in a focus group discussion (FGD) with other participants. Participants will be asked questions individually or in a group setting. Study staff will tell you if you are going to take part in an IDI or FGD.

## **STUDY PRODUCTS**

There are no study products (investigational drugs or other products) involved in this research study.

## **STUDY PROCEDURES**

The MTN-032 study consists of one study visit, including the Screening/Enrollment Visit which is taking place today after you sign this informed consent form. Additional visit(s) may be conducted to complete all required procedures, if necessary. Visits will take place here at this study clinic or at a place agreed upon by you and the study staff, which may be your home or another convenient location ***[SITE TO INCLUDE ALTERNATE LOCATION]***.

The procedures done at this visit will take about ***[SITE TO INSERT TIME]***.

- Study staff will ask you where you live and other questions about you, and your understanding of the study requirements.
- You will complete one or more questionnaires that will help researchers better understand your interview responses.
- You may be asked to have an in-depth interview (IDI). If you are selected to take part in an IDI:
  - You will have an IDI in the presence of one or two MTN-032 research staff members. The IDI will take approximately ***[SITE TO INSERT TIME]***. Clinic staff will make every effort to ensure your privacy and confidentiality.
  - Before the IDI begins, the interviewer will talk with you about the HOPE study and the vaginal rings used during that study.
  - The interviewer may take notes and will audio-record your conversation. Interviews will be audio-recorded to make sure we record your words exactly how you said them.
  - You will be asked some general questions, such as your age, education, living situation, relationship status, and health.
  - The interviewer will also ask you questions about:
    - Your experience with your partner's ring use and her participation in the HOPE trial.
    - Your understanding of the results of the ASPIRE trial and how those results effected your support for your partner's participation in HOPE.
    - Your perception of your sexual health risk, how this understanding may have affected your decision to support your partner's use of the vaginal rings, and what impact it may have on your support for



her use of HIV prevention products that may become available in the future.

- You may be asked to join a focus group discussion (FGD). If you are selected to take part in a FGD:
  - You will join around 4-8 other men in a private room in **[SITE TO INSERT location]** to take part in a discussion in the presence of one or two MTN-032 research staff members. The FGD will take approximately **[SITE TO INSERT TIME]**.
  - One of the staff members may take notes during the discussion. Staff will make every effort to ensure your privacy and confidentiality.
  - Interviews will be audio-recorded to make sure we record your words exactly how you said them. If you do not want to be audio recorded, you will not be able to participate in the group discussion.
  - You will be asked some general questions, such as your age, education, living situation, relationship status, and health.
  - The interviewer will also ask you questions about:
    - Your experience with the vaginal ring while your partner was participating in the study.
    - Your understanding of the results of the ASPIRE trial and how this may have affected your attitude toward your female partner's use of the ring and participation in HOPE
    - Your perception of your sexual health risk and how this understanding may have affected your thoughts about your partner's use of the vaginal ring, and what impact it may have on your partner's use of HIV prevention products that may become available in the future.
- Study staff will also:
  - Inform you about other services, if needed.
  - Schedule your next visit, if necessary.
  - Reimburse you for your visit(s).

## **RISKS AND/OR DISCOMFORTS**

During the interview or focus group discussion, you may be asked some questions that cause you to feel embarrassed or uncomfortable. You may become embarrassed and/or worried when discussing sexual practices or your partner's use of the vaginal rings. Trained study interviewers will help you deal with any feelings or questions you have. You can choose not to answer questions during the interview at any time.

Another possible risk of this study is loss of confidentiality of the information you give. Every effort will be made to protect your confidential information, but this cannot be guaranteed. To reduce this risk, IDIs will take place in private, and the information recorded during your interview will be strictly protected. The audio recording, notes, and analyses from these materials will be kept confidential and will only use study numbers or fake names. This means that no one other than the MTN-032 interview team will be able to link your responses to you personally. The information that links you to the research materials will be kept in a secure location that will be accessed only by

members of the MTN-032 study team for the purposes of this research. Your voice recordings will also be kept in a secure location and only people involved with the study will have access to these recordings. Study leaders will make sure this happens.

If you participate in a focus group discussion, other participants will hear what you say. Although we will not reveal your full name to other participants, it is possible that others may know you from previous interactions. We will also ask every participant not to tell anyone outside of the group what any person said during the FGD. While it is not at all likely that your discussion will be made public, we cannot guarantee that everyone will keep the discussion private.

However, it is possible that others may learn of your participation here and, because of this, may treat you unfairly or discriminate against you. For example, you could have problems getting or keeping a job, or being accepted by your family or community. If you have any problems, study counselors will talk with you and/or your partner to try to help resolve them.

## **BENEFITS**

There are no direct benefits to participating in this study. However, you and others may benefit in the future from information learned in this study. Participants in this study may also appreciate the opportunity to contribute to HIV prevention research efforts. Information participants provide may help researchers improve counseling materials about product use and sexual behavior. Lastly, the information provided in this study may help health professionals develop ways to improve communication and understanding between researchers and participants in HIV prevention studies.

Medical care for HIV infection and other health conditions will not be part of this study. This study cannot provide you with general medical care, but study staff will refer you to other available sources of care, if needed.

## **NEW INFORMATION**

You will be told of any new information learned during this study that might affect your willingness to stay in the study. You will also be told when study results may be available, and how to learn about them.

## **WHY YOU MAY BE WITHDRAWN FROM THE STUDY WITHOUT YOUR CONSENT**

You may be removed from the study early without your permission if:

- The study is cancelled by the US NIH, the US Office for Human Research Protections (OHRP), MTN, the local government or regulatory agency, or the Institutional Review Board (IRB) or Ethics Committee (EC). An IRB is a committee that watches over the safety and rights of research participants.
- You are unwilling or unable to comply with required study procedures, including study visit attendance.
- Other reasons that may prevent you from completing the study successfully.

## **COSTS TO YOU**

There is no cost to you for study related visits.

## **REIMBURSEMENT**

**[SITE TO INSERT INFORMATION ABOUT LOCAL REIMBURSEMENT]:** You will receive **[SITE TO INSERT AMOUNT \$XX]** for your time, effort, and travel to and from the clinic at each scheduled visit.

## **CONFIDENTIALITY**

Efforts will be made to keep your information confidential. However, it is not possible to guarantee confidentiality. Your personal information may be disclosed if required by law. The study staff may use your personal information to verify that you are not in any other research studies. This includes studies conducted by other researchers that study staff may know about. Any publication of this study will not use your name or identify you personally.

Your records may be reviewed by:

- The Research Triangle Institute
- Site IRBs/ECs
- FHI 360
- Representatives of the US Federal Government, including the US OHRP, NIH and/or contractors of NIH, and other local and US regulatory authorities
- Study monitors
- Study staff

The researchers will do everything they can to protect your privacy.

## **RESEARCH-RELATED INJURY**

**[SITE TO SPECIFY INSTITUTIONAL POLICY]:** It is unlikely that you will be injured as a result of study participation. If you are injured, the **[INSTITUTION]** will give you immediate necessary treatment for your injuries. You **[WILL/WILL NOT]** have to pay for this treatment. You will be told where you can receive additional treatment for your injuries. The U.S. NIH does not have a mechanism to pay money or give other forms of compensation for research related injuries. You do not give up any legal rights by signing this consent form.

## **YOUR RIGHTS AS A RESEARCH PARTICIPANT/VOLUNTEER**

Taking part in this study is completely voluntary. You may choose not to take part in this study or leave this study at any time. If you choose not to participate or to leave the study, you will not lose the benefit of services to which you would otherwise be entitled at this clinic. If you want the results of the study after the study is over, let the study staff members know.

## **PROBLEMS OR QUESTIONS**

If you ever have any questions about the study, or if you have a research-related injury, you should contact ***[INSERT NAME OF THE INVESTIGATOR OR OTHER STUDY STAFF]*** at ***[INSERT TELEPHONE NUMBER AND/OR PHYSICAL ADDRESS]***.

If you have questions about your rights as a research participant, you should contact: ***[INSERT NAME OR TITLE OF PERSON ON THE IRB/EC OR OTHER ORGANIZATION APPROPRIATE FOR THE SITE]*** at ***[INSERT PHYSICAL ADDRESS AND TELEPHONE NUMBER]***.

**SIGNATURES- VOLUNTARY CONSENT**

***[INSERT SIGNATURE BLOCKS AS REQUIRED BY THE LOCAL IRB/EC]:***

***If you have read this consent form (or had it read and explained to you) and if you understand the information and voluntarily agree to take part in the study, please sign your name or make your mark below.***

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Participant Name (print)	Participant Signature/Mark	Date
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Study Staff Conducting Consent Discussion (print)	Study Staff Signature	Date
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Witness Name (print)	Witness Signature	Date
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## APPENDIX IV: PERMISSION TO CONTACT FORM

**Instructions:** This form is to be completed for each HOPE participant prior to contacting her male partner for MTN-032 participation.

You are being asked to provide us permission to contact your male partner to take part in MTN-032. The aim of this research study is to better understand HOPE participants' use of study product (vaginal rings) while participating in both the ASPIRE and HOPE trials as well as their male partner's thoughts and feelings about the ring. MTN-032 male participants will be asked to participate in either an in-depth interview (IDI) or in a focus group discussion (FGD), where we will discuss his perceptions of, and invite his feedback on, the ring and HOPE.

It is important to know that if you agree for us to contact your male partner, he will find out that you participated in the HOPE study, that you used the vaginal ring, and that the ring is intended for HIV prevention. It is also important to know that your permission to allow us to contact your partner to join the MTN-032 study is your decision and is completely voluntary. Up to 20 male partners of HOPE participants from this area will be involved in the study. They will be randomly selected from a list of all the HOPE participants who provide permission to contact their partners. Even if you give us permission to contact your partner, we may not invite him to participate in MTN-032 if he is not randomly selected.

<b>Permission</b>	<p><i>If he is randomly selected, I agree to allow MTN-032 staff to contact my male partner for participation in the MTN-032 study, per the contact information and method(s) specified below.</i></p> <p>Yes <input type="checkbox"/>                  No <input type="checkbox"/></p> <p>Participant's Signature _____ Date: _____</p> <p>Participant's Name (print) _____</p>																
<b>Name of Partner</b>	First Name: _____ Surname: _____ Nickname: _____																
<b>Partner Type:</b>																	
<b>Cell Number:</b>																	
<b>Home Address:</b>																	
<b>Home Phone Number:</b>																	
<b>Work Address or NA:</b>																	
<b>Work Phone Number or NA:</b>																	
<b>Permissions:</b> (place X in "Yes" boxes for all methods of contact the participant provides permission for)	<table style="width: 100%; border: none;"> <tr> <td>Home visit?</td> <td><input type="checkbox"/> Yes</td> <td><input type="checkbox"/> No</td> </tr> <tr> <td>Work visit?</td> <td><input type="checkbox"/> Yes</td> <td><input type="checkbox"/> No</td> </tr> <tr> <td>Phone call?*</td> <td><input type="checkbox"/> Yes</td> <td><input type="checkbox"/> No</td> </tr> <tr> <td>Mail?*</td> <td><input type="checkbox"/> Yes</td> <td><input type="checkbox"/> No</td> </tr> <tr> <td>OK to mention HOPE / vaginal ring?*</td> <td><input type="checkbox"/> Yes</td> <td><input type="checkbox"/> No</td> </tr> </table>		Home visit?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	Work visit?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	Phone call?*	<input type="checkbox"/> Yes	<input type="checkbox"/> No	Mail?*	<input type="checkbox"/> Yes	<input type="checkbox"/> No	OK to mention HOPE / vaginal ring?*	<input type="checkbox"/> Yes	<input type="checkbox"/> No
Home visit?	<input type="checkbox"/> Yes	<input type="checkbox"/> No															
Work visit?	<input type="checkbox"/> Yes	<input type="checkbox"/> No															
Phone call?*	<input type="checkbox"/> Yes	<input type="checkbox"/> No															
Mail?*	<input type="checkbox"/> Yes	<input type="checkbox"/> No															
OK to mention HOPE / vaginal ring?*	<input type="checkbox"/> Yes	<input type="checkbox"/> No															

<b>Best way to contact partner:</b>	<input type="checkbox"/> Cell phone <input type="checkbox"/> Landline <input type="checkbox"/> Home Visit	<input type="checkbox"/> Work Visit <input type="checkbox"/> Posted letter home <input type="checkbox"/> Other: _____
<b>Comments:</b>		
Staff's Signature _____ Date: _____ Staff's Name (print) _____		

*\*Specify in comments section if these permissions apply to only work, only home, etc., or any other special circumstances.*

## REFERENCES

1. UNAIDS, Joint United Nations Programme on HIV/AIDS. UNAIDS Report on the Global AIDS Epidemic 2013. [http://www.unaids.org/en/media/unaids/contentassets/documents/epidemiology/2013/gr2013/UNAIDS\\_Global\\_Report\\_2013\\_en.pdf](http://www.unaids.org/en/media/unaids/contentassets/documents/epidemiology/2013/gr2013/UNAIDS_Global_Report_2013_en.pdf) accessed 30 May 2014. 2012.
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