

**CAPRISA 106 Tenofovir Gel Social and Health Systems Research Study**  
(CAP 106 TFV-SHSR study)

Protocol Version 1.1  
Study #388030-1  
Date: 01 February 2013

**Funded by:** USAID

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## STUDY SUMMARY

- Title:** CAPRISA 106 Tenofovir Gel Social and Health Systems Research Study
- Study #:** 388030-1
- Purpose:** The overall goal of this study is to inform 1% tenofovir (TFV) gel program implementation through examining gel acceptability, adherence, compliance and continuation, health systems delivery issues, and costing associated with open-label TFV gel use during the CAPRISA 008 study.
- Design:** Descriptive, exploratory study using a mixed methods design (qualitative and quantitative data collection and analysis)
- Study Population:** CAPRISA 008 participants; male partners of CAPRISA 008 participants; men in communities where CAPRISA 008 is being implemented; and CAPRISA 008 providers and research staff.
- Sample Size:** Up to 300
- Study Duration:** 15 months
- Objectives:**
1. To explore the interface between social context and user experience with TFV gel use, specifically:
    - a. The social acceptability of coitally-related use of TFV gel among women and men;
    - b. The influence of gender dynamics on TFV gel use disclosure, adherence, and continuation; and
    - c. The social barriers and facilitators to compliance with medical requirements associated with TFV gel use.
  2. To explore the CAPRISA 008 experience with implementing the Health System Strengthening/Quality Improvement (HSS/QI) approach for integrated family planning (FP)/TFV gel service provision, specifically:
    - a. To assess fidelity of the HSS/QI approach applied;
    - b. To describe perceptions of the HSS/QI approach, implementation process, and service delivery experience among CAPRISA 008 providers, research staff and participants;
    - c. To describe the resources used for, and estimate the cost of, the HSS/QI approach for FP/TFV gel service provision; and
    - d. To describe changes in service delivery indicators over time.
- Study Sites:** KwaZulu-Natal, South Africa

## ABBREVIATIONS AND ACRONYMS

A2C2 –	Acceptability, Adherence, Compliance and Continuation
ARV –	Antiretroviral
BAT 24 –	<b>B</b> efore sex, <b>A</b> fter sex, no more than <b>T</b> wo doses in <b>24</b> hours
BREC –	Biomedical Research Ethics Committee
CAPRISA –	Centre for the AIDS Programme of Research in South Africa
CAPVL –	CAPRISA Vulindlela Research Clinic
CAPTK –	CAPRISA eThekweni Research Clinic
CRF –	Case Report Forms
DAIDS –	Division of Acquired Immunodeficiency Syndrome
EC –	Ethics Committee
FACTS –	Follow-on African Consortium for Tenofovir Studies
FGD –	Focus Group Discussions
FP –	Family Planning
FPVL –	Neighboring FP clinic in Vulindlela subdistrict
FPTK –	Neighboring FP clinic in eThekweni municipality
HIV –	Human Immunodeficiency Virus
HSS –	Health Systems Strengthening
IDI –	In-depth Interview
IRB –	Institutional Review Board
MTN –	Microbicide Trials Network
NIAID –	National Institute of Allergy and Infectious Diseases
PDSA –	Plan-Do-Study-Act
PHSC –	Protection of Human Subjects Committee
PMTCT –	Prevention of Mother-to-Child Transmission of HIV
PrEP –	Pre-exposure Prophylaxis
QDA –	Qualitative Data Analysis
QI –	Quality Improvement
TFV –	1% Tenofovir
UKZN –	University of KwaZulu-Natal
VOICE –	Vaginal and Oral Interventions to Control the Epidemic

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## BACKGROUND

The CAPRISA 106 Tenofovir Gel Social and Health Systems Research Study is an ancillary study to the CAPRISA 008 study, a two-arm, open-label randomized controlled trial assessing the implementation effectiveness and safety of 1% tenofovir (TFV) gel provision through family planning (FP) services in KwaZulu-Natal, South Africa. The CAPRISA 008 control arm is conducted in CAPRISA research clinics with monthly provision and monitoring of TFV gel, while the intervention arm is conducted at neighboring FP clinics with 2-3 monthly provision and monitoring of TFV gel, combined with a health systems strengthening/quality improvement (HSS/QI) approach to promote reliable service delivery.

In July 2010, the CAPRISA 004 trial presented findings which demonstrated that TFV gel reduced risk of HIV acquisition by 39% compared to placebo when used before and after sexual intercourse among trial participants in KwaZulu-Natal, South Africa (95% CI 6-60).<sup>1</sup> A pre- and post-coital dosing strategy, also referred to as BAT 24, was used. Study participants were counseled and supported throughout the study to apply the first dose of the assigned study gel within 12 hours before anticipated sex; a second dose as soon as possible but within 12 hours after sex and to apply no more than two gel doses in 24 hours. These results provided the first proof of concept that a topically applied antiretroviral (ARV) could prevent HIV infection among women living in communities with high rates of HIV infection. TFV gel efficacy is currently being assessed in two other trials. The Vaginal and Oral Interventions to Control the Epidemic (VOICE) trial, sponsored by the Microbicides Trial Network (MTN), included daily insertion of a single dose of TFV gel versus placebo gel as one of the comparison arms. In November 2011 VOICE discontinued the daily gel arms early when they found no difference in the number of HIV infections for women using daily TFV gel versus placebo gel among trial participants in South Africa, Zimbabwe and Uganda. No safety concerns were identified and a full analysis of the VOICE trial is pending.<sup>2</sup> A third trial, Follow-on African Consortium for Tenofovir Studies (FACTS) 001, is presently being conducted in South Africa and was designed to replicate the CAPRISA 004 study. FACTS 001 is evaluating the same coitally-based TFV gel dosing regimen (BAT 24) as CAPRISA 004, with results anticipated in 2014.<sup>3</sup> If FACTS 001 confirms the CAPRISA 004 trial findings it may provide the information needed to support licensure of TFV gel for HIV prevention.

### *CAPRISA 008 TFV Gel Adherence Support*

The CAPRISA 008 study is an open-label follow-on study to CAPRISA 004. The study randomizes women who have previously participated in an HIV prevention trial to receive open-label TFV gel through the CAPRISA research clinics with monthly study visits (control arm) or through neighboring FP clinics with 2-3 monthly study visits in conjunction with routine FP provision (intervention arm). CAPRISA 004 demonstrated that effectiveness of TFV gel is linked to adherence. The CAPRISA 008 adherence support counseling is theory-based and customized to meet individual participant needs. The aim is to understand the factors that affect adherence to TFV gel use and thus assist participants to preempt situations that may lead to non-adherence and set goals to achieve optimal gel adherence. A motivational interviewing-based approach which focuses on participant's barriers to gel use and/or study participation and self-initiated solutions to overcoming these barriers will be used in both study arms. This is a participant-centered and interviewer-driven technique based on the rationale that participants are more likely to act upon a self-motivating statement. Once enrolled in the study, potential barriers to TFV gel use will be discussed and solutions explored, followed by a discussion on how to integrate gel use into the participant's schedule. Instructions will be in the form of a one-on-one

verbal counseling session with designated trained staff. The enrollment session will also include on-site use of TFV gel (directly or indirectly observed) to establish correct mechanics of TFV gel use as counseled. During follow-up visits each participant will receive additional individualized product use adherence support by designated, trained staff. Sessions will be customized based on individual participant needs and self-efficacy level achieved for correct use of product in terms of dose and timing, as well as any other participant identified barriers to gel use or study participation.

### **CAPRISA 008 HSS/QI Approach**

Along with TFV gel provision and adherence counseling, the CAPRISA 008 study applies an HSS/QI approach to strengthen the reliability of health service delivery in the neighboring FP clinics. It also provides research infrastructure support for integrated FP/TFV gel delivery to CAPRISA 008 participants in the FP clinics through study-specific training for the staff involved, clinical support and mentorship provided by CAPRISA staff, the use of standard operating procedures and visit checklists, TFV gel supply management, and other supports related to research activities in the FP clinics. These research infrastructure supports are required to ensure safety and accountability with TFV gel product use, since TFV gel is currently an unlicensed investigational new drug. The CAPRISA 008 study will evaluate whether similar levels of product adherence and safety can be achieved among study participants in the FP clinics (intervention arm) using the HSS/QI approach for integrated FP/TFV gel delivery as those achieved among study participants in the CAPRISA research clinics (control arm).

### **CAPRISA 106 Ancillary Study**

With implementation of the CAPRISA 008 open label TFV gel study underway, an opportunity now exists to conduct ancillary research among women using TFV gel in a non-placebo-controlled study. The provision of open-label TFV gel removes a key element of uncertainty in women's decision-making about product use and also provides a unique opportunity to conduct formative health systems research on TFV gel provision in a family planning context, closer to that found in real-world settings.

Factors influencing women's decision-making: Findings from multiple ARV-based HIV prevention trials, including trials of TFV gel, underscore the critical importance of individual behavior for maximizing product effectiveness. Four key interrelated behavioral components, referred to here as A2C2, need to be maximized and coordinated. Each component has important social dimensions that have been minimally addressed in ARV-based HIV prevention trials and microbicide trials more generally. Moreover, what is currently known about these components has been learned in the context of blinded, placebo-controlled trials where participants are told that it is not known if the product is effective and that they will not know if they received the product or a placebo until after the study has ended. Each component has implications for the design and implementation of successful TFV gel intervention programs and research is needed to fully support TFV gel effectiveness in a context of known efficacy. In the CAPRISA 106 study we will explore these components:

- **Acceptability** focuses on the extent to which women are willing and able to use an efficacious TFV gel product. This includes the potential influence of male partners. Acceptability informs social marketing and is informed by epidemiologic questions.
- **Adherence** focuses on the ability of women to use an efficacious TFV gel product correctly and consistently. The relationship between adherence and prevention effectiveness is sufficiently established, and the current priority is to improve adherence in order to improve effectiveness.

Social support, including but not limited to partner support, has been generally shown to improve adherence to medical regimens.

- **Compliance** focuses on the extent to which women accept and comply with all of the aspects of an efficacious TFV gel HIV prevention program that go beyond adherence to the prescribed regimen. For example, this would include compliance with required frequency of HIV and other medical tests, use of additional tools such as condoms and partner reduction to reduce HIV risk, and constraints on vaginal cleansing practices. Here, social support is likely to impact compliance.
- **Continuation** focuses on the extent to which women who take up efficacious TFV gel as a means of HIV prevention continue to use the gel while at increased risk for HIV infection. Lessons learned from contraception again indicate that social factors, such as family and relationship dynamics, can have considerable impact on continuation rates.

TFV gel provision in a service delivery context: Important information on each of these components can be gleaned from completed and ongoing clinical trials of TFV gel; however, many questions cannot be fully explored in the context of clinical equipoise. Further, we know from experience with the roll out of new contraceptive technologies, female condoms, medical male circumcision, PMTCT, and HIV treatment programs that health systems need to be prepared to meet new challenges in the development and implementation of programs designed to roll out new products such as TFV gel.

The CAPRISA 008 study addresses the need for health system preparation through the use of a HSS/QI approach to integrated FP/TFV gel delivery. The HSS/QI approach is a multifaceted adaptive intervention. Structural components include staff (QI Advisor, QI Mentor, and FP clinic improvement teams), training, structured QI activities (e.g. process mapping, root cause analyses, change packages and Plan-Do-Study-Act [PDSA] rapid work cycles), and documentation of these processes and outcomes with standardized tracking tools (e.g. reports, performance indicator data and run charts).<sup>4,5</sup> The actual change packages/interventions and performance measures used are not predetermined, but evolve out of the QI process over time. Typical areas targeted for performance improvement include clinic flow, quality of care, supply chain management, and changes in the way data is used for local systems improvement. Key components that reflect fidelity to the QI approach include: (i) establishing a local improvement team, (ii) regular team meetings, (iii) understanding and executing PDSA cycles, and (iv) using locally-derived data to implement changes at rapid intervals.

The primary impact (effectiveness) of the HSS/QI intervention for integrated FP/TFV gel provision will be evaluated within the CAPRISA 008 implementation study by measuring the mean number of returned used applicators as a proxy measure for product adherence. In addition, the CAPRISA 008 study will measure self-reported service acceptability among study participants through the use of a standardized interviewer-administered questionnaire. However, more in-depth exploratory research on the HSS/QI approach used in CAPRISA 008 is important and needed to better understand the health systems issues relevant to microbicide introduction and to inform the design of structural interventions to support future product roll-out.

Most evidence-based recommendations for bio-behavioral interventions, such as TFV gel, are derived from highly-controlled efficacy trials. However, the highly-controlled nature of efficacy trials can limit the external relevance and practicality of those recommendations in clinical practice. Feasibility studies are used to fill this gap by exploring what health services modifications may be needed to make a new

intervention more relevant and sustainable when introduced in a real-world setting. For this ancillary study, we will consider four constructs with relevance for clinical feasibility:

- **Fidelity:** The extent to which the CAPRISA 008 HSS/QI approach was implemented as intended.
- **Implementation:** Perceptions of the HSS/QI approach, its implementation, and service delivery experience from the perspective of providers and clients.
- **Resources:** The resources required and costs associated with implementing and maintaining the HSS/QI approach for FP/TFV gel service provision.
- **Program Efficacy:** The extent to which the QI approach can be linked to improvements in service delivery performance. While we will not be able to demonstrate program efficacy in this study, we can assess the extent to which changes in performance indicators over time provide supportive evidence for QI-driven improvements in system performance.

### Previous Research

**Objective 1** of the CAPRISA 106 study builds on findings related to the social dynamics of gel use from the CAPRISA 104 Case-Control Study, an ancillary study conducted in real time with the CAPRISA 004 study. In the CAPRISA 104 Case-Control Study, we conducted in-depth interviews with 277 study participants (72 seroconverting cases, 205 randomly selected non-seroconverting controls).<sup>6,7</sup> Of the 277 women interviewed for the Case-Control Study, 165 discussed the issue of gel use disclosure (75% of cases, 76% of controls). Of the 113 women who said they disclosed to at least one partner, few reported gel use difficulties (n=7) and most said they received supportive or neutral reactions from their partners (n=74). For women who disclosed, we found that many were comfortable inserting gel in presence of a partner, that partners may facilitate or provide reminders, and that they were able to use gel for unexpected partner visits. Of the 52 women who said they did not disclose gel use to any partners, about 1/3 reported gel use difficulties (n=17). They were unable to use gel when the partner was present, found it difficult to use gel for unexpected partner visits, expressed concern that a partner may feel cold or wetness from the gel, and some said it was difficult to hide gel from a partner. A small number of those who did not disclose (n=11) said they were afraid to do so because a partner may be angry or leave, may not want her to use the gel, or may no longer want to use condoms. Additionally, 9 women reported partial disclosure, either disclosing study participation but not gel use or disclosing both participation and gel use but not the fact that the gel was being evaluated for HIV prevention.

These findings are not surprising. We know from other microbicide research<sup>8-14</sup> that these kinds of partner dynamics can influence acceptability and adherence and hence product effectiveness. The apparent importance of adherence for TFV gel effectiveness creates a dilemma for developing implementation strategies, i.e., should TFV gel be specifically targeted to couples on the assumption that this will promote better adherence and, hence, effectiveness? Findings from two HIV prevention trials with discordant couples have shown high effectiveness,<sup>6,15,16</sup> which has led to recommendations that ARV-based interventions should be specifically targeted to discordant couples. While such a strategy could fill an important prevention need, it also runs the risk of leaving out an important group of women at high risk for HIV precisely because they are unable to negotiate prevention with their partners.

**For Objective 2** of the CAPRISA 106 study, we reference the foundation for the CAPRISA 008 HSS/QI approach, which is based on methodology that is grounded in operations research and management science. These are two well-established fields that have, for more than 90 years, combined the

disciplines of statistics, psychology, systems engineering, and iterative learning, to have major impact on systems performance across countries and industries.<sup>17</sup> This approach seeks to design systems for maximum effectiveness, efficiency, and adaptability and to actively disseminate the best models for health service delivery at the most rapid rate possible.<sup>18,19</sup> Specialized, evidenced-based tools aimed at rapid-cycle iterative testing of changes, networked collaborative learning, development of institutional capability for continuous improvement and frameworks to guide large-scale change have been developed to facilitate this process.<sup>20-22</sup> Traditionally this approach is used following policy formulation and where some program implementation experience has already been established. CAPRISA 008 is testing this model through strengthening family planning services as a foundation to introduce a new health technology even prior to licensure and identifying priority impact areas for QI interventions to support TFV gel provision in family planning settings.

## PURPOSE AND OBJECTIVES

The purpose of the CAPRISA 106 study is to describe social and health systems experience with TFV gel in the context of CAPRISA 008, in order to inform the design of potential future TFV gel demonstration projects.

The **objectives** of the CAPRISA 106 study are:

1. To explore the interface between social context and user experience with open label TFV gel use, specifically:
  - a) The social acceptability of coitally-related use of TFV gel among women and men;
  - b) The influence of gender dynamics on gel use disclosure, adherence, and continuation; and
  - c) The social barriers and facilitators to compliance with medical requirements associated with TFV gel use.
2. To explore the CAPRISA 008 experience with implementing the HSS/QI approach for integrated FP/TFV gel service provision, specifically:
  - a) To assess fidelity of the HSS/QI approach applied;
  - b) To describe perceptions of the HSS/QI approach, implementation process, and service delivery experience among CAPRISA 008 providers, research staff and participants;
  - c) To describe the resources used for, and estimate the cost of, the HSS/QI approach for FP/TFV gel service provision; and
  - d) To describe changes in service delivery performance over time.

## STUDY DESIGN

**This is a descriptive, exploratory study using a mixed methods design (qualitative and quantitative data collection and analysis).**

For **objective 1** (exploring the social context and TFV gel user experience) data collection methods center on use of focus group discussions (FGDs) and in-depth interviews (IDIs) to be conducted in real time with implementation of the CAPRISA 008 trial. We will use purposive sampling to identify women who disclose TFV gel use to their partners and those who do not, at each site (urban, rural) and in each

CAPRISA 008 study facility (intervention and control). We will also seek to recruit the male partners to whom women have disclosed as well as men from the community who are not partners of CAPRISA 008 study participants. We will conduct a comparative analysis of the social factors influencing disclosure and, in turn, the way in which disclosure influences A2C2 and where disclosure does not seem to have any notable influence. We will also conduct a comparative analysis to see if these social factors vary in meaningful ways between the rural and urban study sites.

To facilitate analysis of acceptability, adherence, compliance and continuation, the IDIs with CAPRISA 008 participants will be linked to relevant variables from the CAPRISA 008 study case report forms (CRFs) such as baseline demographics, adherence measures, study retention, missed study visits, and social harms.

For **objective 2** (exploring the HSS/QI and integrated FP/TFV gel service provision experience) data collection includes IDIs, use of participant observation techniques, and document review and abstraction at CAPRISA 008 clinics. To assess resources used to implement the HSS/QI approach for FP/TFV gel service provision, we will abstract data using an intervention tracking tool to report on HSS/QI activities and FP/TFV gel service provision in sufficient detail to identify the resources used (such as training, staff time, supplies, physical space, and other resources) and the magnitude of those resources. We will use convenience sampling to recruit CAPRISA 008 providers, research staff, and participants. Documentation of the HSS/QI process and FP/TFV gel service provision will be reviewed and data abstracted to evaluate implementation fidelity, describe impacts on service delivery over time, and assess costs associated with implementation.

## STUDY POPULATION

The research will take place in KwaZulu-Natal, South Africa, and will include women and men aged 18 years and older in the Vulindlela subdistrict and eThekweni municipality where the CAPRISA 008 study is underway. Research participants will include:

- Women participating in the CAPRISA 008 study
- Male partners of women participating in the CAPRISA 008 study
- Men residing in the communities where the CAPRISA 008 study is being implemented
- CAPRISA 008 providers and research staff

The CAPRISA 008 study sites include:

- Control research clinics:
  - CAPRISA Vulindlela research Clinic (CAPVL)
  - CAPRISA eThekweni research Clinic (CAPTK)
- Intervention clinics:
  - Neighboring FP clinic in Vulindlela subdistrict (FPVL)
  - Neighboring FP clinic in eThekweni municipality (FPTK)

### Inclusion Criteria

1. Women participating in the CAPRISA 008 study and not currently on product hold
  - Age 18 years and older who are sexually active, HIV-uninfected, non-pregnant women at the time of enrollment into CAPRISA 008

2. Male partners of women participating in the CAPRISA 008 study
  - Age 18 years and older male partner of a CAPRISA 008 participant to whom the CAPRISA 008 participant has disclosed (a) that she is participating in the CAPRISA 008 study, (b) that as a participant she is using tenofovir gel, and (c) that tenofovir gel is an ARV product designed to reduce her risk of HIV infection
3. Men residing in the communities where the CAPRISA 008 study is being implemented
  - Age 18 years and older who are demographically similar to the CAPRISA 008 male partners described above
4. CAPRISA 008 providers and research staff
  - Age 18 years and older male or female providers and research staff who are (a) providing direct patient care, including FP and/or TFV gel provision, and/or (b) play an integral role in CAPRISA 008 research, QI and service operations

## SAMPLE SIZE

Sample sizes will depend on factors such as the number of eligible candidates at each site and in each clinic setting, as well as the number who are available, willing to participate at the time of recruitment, and ultimately consent to participate. We will attempt to maintain a numeric balance with regard to participant recruitment at the eThekweni and Vulindlela sites. Where applicable, we will also attempt to evenly divide the number of participants between the CAPRISA 008 intervention and control clinics. However, we may adjust the distribution of data collection, for example, if CAPRISA 008 enrollment targets are adjusted at the sites. Any adjustments will reflect the need to maintain a proportional balance for subsequent comparative analyses while taking into account potential variability by type of clinic (intervention, control) and setting (rural, urban). Table 1 summarizes our overall data collection strategy and recruitment targets. Some participants may be asked to participate in more than one data collection activity, e.g., some CAP008 participants may be recruited for both Objective 1 and Objective 2 IDIs. For purposes of estimating total sample size in Table 1 we have assumed only one data collection activity per participant in order to estimate a maximum sample size.

**Table 1. Summary overview of data collection strategies, sample size, and participant recruitment settings at each site (eThekweni and Vulindlela)**

Data collection Activity and Objective	Participant Recruitment Setting at Each Site		
	CAP008 Research Clinics (control sites)	CAP008 Neighboring FP Clinics (intervention sites)	Community
<p><b>Focus groups; objectives 1a., 1c</b></p> <p>Topics: Social &amp; gender dimensions gel acceptability &amp; compliance</p> <p>(6-10 participants per FGD x 14 FGD = up to 140 participants)</p>	<p>CAP008 Participants</p> <ul style="list-style-type: none"> <li>• Disclosers (up to 2 FGD)</li> <li>• Non-disclosers (up to 2 FGD)</li> </ul> <p>Men (up to 2 FGD)</p> <ul style="list-style-type: none"> <li>• CAP008 partners</li> </ul>	<p>CAP008 Participants</p> <ul style="list-style-type: none"> <li>• Disclosers (up to 2 FGD)</li> <li>• Non-disclosers (up to 2 FGD)</li> </ul> <p>Men (up to 2 FGD)</p> <ul style="list-style-type: none"> <li>• CAP008 partners</li> </ul>	<p>Men who are not partners of CAP008 participants but are demographically similar (2 FGD)</p>
<p><b>In-depth interviews; objective 1b</b></p> <p>Topics: Social &amp; gender dimensions of adherence &amp; continuation</p> <p>(up to 72 participants)</p>	<p>CAP008 Participants (n=up to 24)</p> <ul style="list-style-type: none"> <li>• Disclosers</li> <li>• Non-disclosers</li> </ul> <p>Men (n=up to 12)</p> <ul style="list-style-type: none"> <li>• CAP008 partners</li> </ul>	<p>CAP008 Participants (n=up to 24)</p> <ul style="list-style-type: none"> <li>• Disclosers</li> <li>• Non-disclosers</li> </ul> <p>Men (n=up to 12)</p> <ul style="list-style-type: none"> <li>• CAP008 partners</li> </ul>	N/A

Data collection Activity and Objective	Participant Recruitment Setting at Each Site		
	CAP008 Research Clinics (control sites)	CAP008 Neighboring FP Clinics (intervention sites)	Community
<p><b>In-depth interviews; objective 2b</b></p> <p>Topics: Experience with HSS/QI approach, implementation, and service delivery</p> <p>(up to 72 participants)</p>	<p>CAP008 Participants (n=up to 24)</p> <p>CAP008 Providers and Research Staff (n=up to 12)</p>	<p>CAP008 Participants (n=up to 24)</p> <p>CAP008 Providers and Research Staff (n=up to 12)</p>	N/A
<p><b>Participant observations; objectives 2a., 2c, 2d</b></p>	<p>Up to 12 observation events per clinic (up to 4 full-day observations over three different time periods)</p>	<p>Up to 12 observation events per clinic (up to 4 full-day observations over three different time periods)</p>	N/A
<p><b>HSS/QI document review and data abstraction; objectives 2a., 2c., 2d.</b></p>	N/A	<p>Quarterly document review with retrospective data collection back to initiation of HSS/QI activities</p> <p>Intervention tracking tool used to report on resources used for HSS/QI activities and FP/TFV gel service provision</p>	N/A

*Note: The actual sample sizes will depend on factors such as the number of eligible candidates in each category, as well as the number who are available and willing to participate at the time of recruitment.*

## RECRUITMENT

### *Objective 1*

CAPRISA 008 participants will be screened for eligibility into CAPRISA 106 during CAPRISA 008 study visits. A screening tool will be used to (1) assess their interest in learning more about CAPRISA 106; (2) find out whether or not they have fully disclosed TFV gel use to at least one of their partners; (3) if they have disclosed, ask if they are willing to refer their partner; and (4) collect contact information for follow up with the eligible woman.

**Note:** For the purpose of determining eligibility for specific FGDs and IDIs, disclosure of TFV gel use requires that the CAPRISA 008 participant has informed at least one of their sexual partners that they are participating in the CAPRISA 008 study; they have told this partner that as a study participant they are using TFV gel; and that this partner has been informed that TFV gel contains an ARV meant to reduce her risk of HIV infection.

If the CAPRISA 008 participant agrees to learn more about this study, she will be eligible for recruitment to an objective 1 FGD or IDI according to whether or not she has fully disclosed TFV gel use to at least one of her sexual partners. For FGDs we will attempt to recruit enough participants for one focus group per CAPRISA 008 study arm per site in order to maximize the diversity of our sample. It is possible that we will not be able to recruit enough male partners to meet our target enrollment for women who have disclosed to their partners. In this case, we will seek to enroll women who have disclosed regardless of their willingness to refer their partners or their partners willingness to enroll.

Men who are partners of CAPRISA 008 participants and to whom women have fully disclosed TFV gel use will be recruited through the CAPRISA 008 participant; no male partners will be approached for recruitment directly. The referred partners who are also willing to participate in an IDI or FGD may differ in their gender perspectives from other men in the community. To assess whether this is the case, we will conduct FGDs with men who are demographically similar to the partners of CAPRISA 008 participants but who are not in relationships with women enrolled in CAPRISA 008. To recruit for the focus groups with men who are not partners of CAPRISA 008 participants, we will work with local study staff to devise an appropriate recruitment strategy. This may include, but is not limited to, posting or distributing recruitment flyers at social settings often frequented by men such as bars, clubs, or sporting venues. Men who respond to these flyers will be informed about the CAPRISA 008 study and asked whether they know anyone participating in the study. Men who respond that they do not know anyone participating in the CAPRISA 008 study will be recruited for participation in the CAPRISA 106 FGD.

### *Objective 2*

CAPRISA 008 participants will be screened for CAPRISA 106 eligibility for the health system IDIs during CAPRISA 008 study visits. A screening tool will be used to (1) assess their interest in learning more about this study; and (2) collect contact information for follow up with the eligible woman.

To recruit CAPRISA 008 providers and research staff to participate in the health systems research IDIs, we will recruit all available among those staff who (a) provide direct patient care, including FP and TFV gel provision, and/or (b) play an integral role in CAPRISA 008 research, QI and service operations, and (c) agree to participate.

## DATA COLLECTION

All FGD and IDI data collection instruments will be pretested in isiZulu using cognitive techniques such as “think aloud” strategies and/or piloted. If no implementation issues are identified during piloting, the pilot FGD and IDI data will be included as part of the final data analysis; pretesting data will not be included. Up to three pretest/pilot data collection events may be conducted for each instrument.

Social dimensions of TFV gel A2C2 will be explored through FGDs and IDIs with CAPRISA 008 participants, their partners and other men in the community. The health systems research component of this study will also use IDIs with CAPRISA 008 providers, research staff and participants, as well as participant observations using ethnographic techniques and collection of data from documents and other forms of secondary data related to CAPRISA 008, HSS/QI activities and FP/TFV gel service provision.

To enhance participant comfort levels, IDIs and FGDs with CAPRISA 008 participants and men will be conducted by study staff of the same sex as the participant. Participants will have the option to have the IDI conducted at a mutually agreed upon location in the community including the CAPRISA research clinics; this may include the participant’s home if confidentiality and staff safety can be assured. FGDs will take place at recognized community meeting spaces which are easily accessible to study participants, including the CAPRISA research clinics. The privacy of the IDI and FGD participants will be critical when choosing locations to conduct the interviews. For IDIs with CAPRISA 008 providers and research staff, age and status-appropriate study staff will conduct data collection. For CAPRISA 008 providers and research staff, the interview guides and surveys will be conducted in English or isiZulu per participant preference and will be conducted in a private area in or near the research clinic as preferred by the interviewee.

### *Objective 1*

Data collection with CAPRISA 008 research participants, their male partners, and men residing in the community will be documented through audio recordings. The FGDs will primarily focus on exploring the social dimensions of TFV gel acceptability and compliance. The IDIs will primarily focus on exploring the social dimensions of TFV gel adherence and continuation. Specifically, they will inform:

- How gender dynamics influence acceptability, adherence, compliance and continuation of TFV gel use
- How HIV testing and other medical requirements influence acceptability and compliance
- How condom use is negotiated and influenced in the context of a woman-controlled intervention with partial effectiveness
- How women and their partners integrate TFV gel use into their lives
- How social factors create challenges for TFV gel adherence and continuation
- How social factors support TFV gel adherence and continuation
- How the TFV gel delivery context (urban versus rural, research versus family planning setting) influences acceptability, adherence, compliance and continuation

### *Objective 2*

Interviews with CAPRISA 008 providers, research staff and participants will be documented through audio recordings. The health system IDIs will explore perceptions of the HSS/QI approach, implementation process, and service delivery experience among CAPRISA 008 providers, research staff and participants. Specifically, the IDIs will describe:

- How CAPRISA 008 providers and research staff perceive the HSS/QI approach and its implementation, in terms of ease, difficulty, challenges, benefits, and success
- How CAPRISA 008 provider and research staff knowledge, motivation, and experience influence their perception of the HSS/QI approach as implemented
- How CAPRISA 008 participants, providers and research staff perceive the acceptability of FP/TFV service delivery, both in the context of the HSS/QI approach as implemented and in the context of monthly versus 2-3 monthly follow-up
- How CAPRISA 008 participants, providers and research staff perceive the acceptability of other aspects of service delivery (e.g. HIV counseling and testing services, integrated service delivery, clinic flow) in the context of the HSS/QI approach as implemented
- How CAPRISA 008 participants, providers and research staff perceive the involvement of male partners in HIV prevention service delivery for women

Participant observations, including informal conversations, will be documented using field notes, using standard ethnographic techniques.<sup>23</sup> No personally identifying information about individuals will be included in field notes. The observations will be used to document fidelity, implementation issues, and resources used for the HSS/QI approach for FP/TFV gel service provision in the CAPRISA 008 study. The observations will describe:

- To what extent CAPRISA 008 providers and research staff implemented the HSS/QI approach for FP/TFV gel service provision as intended
- To what extent QI supervision was provided as intended
- To what extent the HSS/QI approach is integrated into organizational culture (e.g. changes in the way data is routinely used)
- How challenges to the HSS/QI approach are addressed
- What resources are used to implement the HSS/QI approach for FP/TFV gel service provision

Collection of data from documents and other forms of secondary data related to CAPRISA 008, HSS/QI activities, and FP/TFV gel service provision will be done using data abstraction guides and scanning and/or photocopying source documents, capturing all information as feasible. Source documents may include, but are not limited to: CAPRISA 008 documents, training materials, staffing plans, improvement team notes, performance data, process maps, PDSA worksheets, run charts, data extraction tools, change package worksheets, and administrative reports. An intervention tracking tool will be used to document the process of implementing the HSS/QI approach and the delivery of FP/TFV gel services. The activities described in the intervention tracking tool will be used to develop activity-based pro-forma budgets for each activity. These pro-forma budgets will specify the magnitude of resources required to support HSS/QI activities and FP/TFV gel service delivery and the associated unit cost / value of each resource required. The document analysis will be used to assess fidelity, resources used, and changes in service delivery indicators with the HSS/QI approach, and specifically will describe:

- To what extent CAPRISA 008 providers and research staff implemented the HSS/QI approach for FP/TFV gel service delivery as intended
- To what extent QI supervision was provided as intended
- How well the HSS/QI approach is integrated into organizational culture (e.g. changes in the way data is routinely used)
- How challenges to the HSS/QI approach are addressed

- What resources are used to implement the HSS/QI approach and deliver FP/TFV gel services, including incremental costs for the HSS/QI activities and cost per participant for FP/TFV gel service delivery
- Changes in service delivery indicators over time. The specific indicators to be tracked will be defined in real-time by CAPRISA 008 providers and research staff as part of each change package, but likely examples include:
  - Clinic flow indicators (e.g. wait time, number of steps)
  - Service delivery uptake indicators (e.g. FP uptake and continuation rates)
  - Integrated service delivery indicators (e.g. proportion of FP clients offered HCT)

## DATA MANAGEMENT

Unique identification codes will be assigned to each CAPRISA 106 study participant as well as to each CAPRISA 008 control and intervention site; the identification codes will be entered on the data collection forms. Data collection instruments include: IDI guides, FGD guides, field notes, photographs or scanning of documents, the intervention tracking tool, and data abstraction guides for documents and other forms of secondary data related to CAPRISA 008, HSS/QI activities, and FP/TFV gel service provision.

All IDI and FGD interview guides will be translated to isiZulu and back-translated to ensure accuracy. Prior to conducting study interviews, all participants will be asked permission to have the interview audio recorded. In cases where IDI participants do not wish to have their interview recorded, the interviewer or a designated note-taker will take detailed notes throughout the interview which will later be expanded and translated into English. For IDIs that are audio recorded, permission for recording will be documented on the audio recording by asking the participant to verify permission to record after the recorder has been turned on; instructions for doing this are included on all IDI guides. All FGDs will be audio recorded. Each recorded IDI and FGD will be transcribed and translated from the original language to English, following a transcription protocol.<sup>24</sup> All transcripts and expanded notes will be typed into a word processing program and password-protected; some transcripts may be handwritten first. Transcripts and expanded notes will be stored on password-protected computers at the study sites. Handwritten transcripts and notes will be stored securely in locked file cabinets. Data management logs will be created in order to track and monitor data collection and transcription.

As soon as possible after the IDIs and FGDs are conducted, a sample of transcripts – including the initial transcript from each data collector – will be read carefully by study staff and investigators in order to: (1) ask any questions of the text that may be unclear; (2) point out areas in which interviewing and transcription techniques could be improved; and (3) identify recurrent themes and areas for future probing. As in most qualitative studies, questions may be modified, added to, or deleted from the IDI and FGD question guides during data collection based on information that is learned from conducting and reading the transcripts from the previous interviews or focus group discussions. Grounded in qualitative methodology, this approach allows researchers to explore in more detail themes that emerge during data collection, and improves understanding of the overall issues. These modifications to the interview guides will be made after the original approval from the ethics committees (EC) and/or institutional review boards (IRB) and will not be submitted for approval; however, *only* probes and questions that are related to the overall topics that are described in this protocol and that are similar to the original questions will be added. Any changes made to the question guides that are beyond the

topics described here will be resubmitted for EC/IRB review and approval prior to use. At random intervals throughout the study, a sample of audio recordings will be independently reviewed and compared with transcripts and data collection forms by the on-site study coordinator or designee, who is a native isiZulu speaker.

Qualitative data will be managed using systems developed at FHI 360 for other qualitative and mixed-methods research projects.<sup>25</sup> A pre-numbered log book will be used to assign unique codes to each data collection event. The assigned code will be placed on all materials associated with the data collection event, including interview or focus group guides, tapes, hand-written notes, consent forms, transcriptions, etc. The assigned code will be incorporated into all computer files associated with the data collection event as well. Data management logs will be updated as soon as possible after each data collection event. All original data source materials will be maintained in locked file cabinets that are accessible only to the project research team. Computer files, including back-up files, will be password protected.

Narratives generated from participant observations will follow a semi-structured format, which will include the date and time interval of the observations, name of data collector, location of observations, and detailed notes of what was observed. The semi-structured format of the narratives will also allow for the data collector to offer their impressions/interpretations of the observation in a separate section so as not compromise the validity of the observation. Names of individuals included in the observations will be removed from all field notes and replaced with a general description of their function in the study or clinics. Field notes may initially be handwritten, but all notes will eventually be entered into a word processing program and password-protected. Handwritten field notes will be stored in a locked file cabinet and may be reviewed during monitoring.

Data from documents and other forms of secondary data sources related to CAPRISA 008, HSS/QI activities, and FP/TFV gel service provision will be generated using data abstraction guides and scanning and/or photocopying source documents. Key elements from these data sources will be recorded by CAPRISA 106 study staff in an intervention tracking tool on paper and transferred to an Excel spreadsheet, or a similar data entry software. The intervention tracking tool will document the process used to implement the HSS/QI approach and FP/TFV gel service delivery in the clinics. Collected data will be routinely sent to FHI 360 via the same file sharing platform described earlier and electronically scanned, photocopied or digitally captured source documents will be stored on password protected computers. These documents will be randomly selected for review at regular intervals to ensure accuracy of the data entry.

All local staff will be trained in maintaining participant confidentiality and rigorous data management procedures. A study-specific procedures (SSP) manual that includes standard operating procedures will be developed outlining data management procedures and containing templates for data management forms. Additionally, FHI 360 staff will regularly monitor the study sites, using a systematic monitoring procedure. All electronic files will initially be reviewed by CAPRISA 106 staff and then sent to FHI 360 via a secure file sharing platform (e.g., Leapfile). Data will also be reviewed for completeness and accuracy as it arrives at FHI 360 and feedback provided as needed.

## DATA ANALYSIS

The transcribed text data including expanded field notes will be managed using a well-established systematic process.<sup>24</sup> Data-derived codes developed through inductive coding and retrieving will be used during analysis. A priori codes for retrieving text for key concepts related to the overall objectives may also be applied to the data. Investigators will determine a coding frame to be used based on the question guides and the first few IDIs and FGDs available for analysis. New codes will be added as necessary during transcript analysis. A qualitative data software program (QDA Miner) will be used to organize all qualitative data and prepare the data for analysis. A minimum of two individuals will independently code text segments and procedures will be put into place to check for inter-coding discrepancies. Once all the transcripts have been coded, textual coding reports will be produced. Data reduction techniques will be used to examine codes in detail for sub-themes and patterns across the IDIs and FGDs. Summary reports will be developed identifying the overall themes related to the study objectives.

Analysis of FGD transcripts will focus on themes related to community acceptability of and compliance with TFV gel requirements. In these focus groups we will explore the implications of how TFV gel use is perceived and contextualized in each of the local communities generally and in sexual partnerships specifically. We will assess the extent to which men and women evaluate the acceptability of the gel in similar or dissimilar ways and what makes TFV gel use acceptable or unacceptable for particular women or in specific kinds of relationships. We will also assess the implications of HIV testing and other medical requirements for acceptability, and identify social barriers and facilitators to compliance. A specific area of exploration will be similarities and differences in the way TFV gel use is perceived relative to the use of condoms, and the implications for gel use messaging. We will give particular attention to the potential ways that gender dynamics can be leveraged in a positive way to support women's decisions to use the gel, and where gender dynamics may pose particular challenges to acceptability and compliance.

Analysis of IDI transcripts and interview notes for Objective 1 will focus on identifying themes related to individual adherence and potential continuation of TFV gel. By comparing (a) responses from women who disclose and those who don't, and (b) responses from women who disclose and their partners, we will obtain a better understanding of the way gender and other social dynamics can impact adherence and continuation.

Analysis of IDI transcripts and interview notes for Objective 2 will focus on identifying themes related to perceived ease, difficulty, challenges, benefits, and success of the HSS/QI approach among CAPRISA 008 providers and research staff; knowledge, motivation, and experience with the HSS/QI approach among CAPRISA providers and research staff; and perceived acceptability of FP/TFV gel provision, HIV testing and counseling, and other aspects of service delivery among CAPRISA 008 participants, providers and research staff in the context of both the HSS/QI approach and monthly versus 2-3 monthly follow-up visits. We will also explore CAPRISA 008 participant, provider, and research staff perceptions around male involvement in HIV prevention service delivery for women.

Additionally, for CAPRISA 008 participants recruited to participate in CAPRISA 106 IDIs, demographics and other relevant data collected in the CAPRISA 008 trial will be linked to the CAPRISA 106 data.

The HSS/QI document analysis will include both descriptive analyses of the volume, frequency, and type of activities undertaken, as well as the use of statistical process control and interrupted time series methods, using statistical process control charts, to evaluate quantitative improvements in service delivery performance indicators.<sup>26-29</sup> In addition, we will bring data together from both the document analysis and the qualitative data analysis to generate driver diagrams that visually represent the study's content and process theory.<sup>30</sup>

For the costing analysis, documentation with the intervention tracking tool will be used to identify the magnitude and type of resources utilized to support implementation of the HSS/QI approach and FP/TFV gel service delivery. Appropriate unit costs will be assigned to each resource identified and the multiplication of unit cost by the magnitude of resource used will yield the estimated cost for each resource. The estimated cost of scaling-up the HSS/QI approach and FP/TFV gel service delivery to other settings will be disaggregated into one-time up-front investments of resources (usually associated with initial trainings and team building) and recurrent or ongoing investments that impose a steady infusion of resources to keep the HSS/QI approach for FP/TFV gel service delivery operational on an annual basis.

In addition to the analyses described above, quantitative data analyses will be conducted in SAS. Descriptive analyses (frequencies for categorical data and means, medians, range and standard deviations for continuous data) will be conducted with all quantitative data collected. Bivariate analyses, such as cross-tabulations or comparison of means, or other statistical tests may be employed.

**Note** that for Objective 2, we will integrate certain components of the qualitative and quantitative datasets, using qualitative data where possible to provide a context for and explain patterns observed in the quantitative data.

## STUDY MONITORING

CAPRISA and FHI 360 study investigators will share responsibility for study monitoring. The FHI 360 investigators will be responsible for overall scientific leadership and management of the study. The CAPRISA co-investigator will contribute scientifically and oversee study implementation, particularly ensuring that data collection adheres to the study protocol. CAPRISA and FHI 360 study investigators will be jointly responsible for ensuring that all local approvals are in place, that appropriate interim and annual reports are submitted to IRBs, and that human subjects protection is implemented and documented according to local and institutional IRB standards.

FHI 360 study staff will work closely with CAPRISA investigators to develop and implement appropriate data collection and data management procedures. A study-specific procedures manual will be developed and implemented with standard operating procedures to ensure that field staff comply with the study protocol and human subjects regulations.

Data collection will be routinely monitored by FHI 360 and CAPRISA 106 study staff. FHI 360 and CAPRISA 106 staff will conduct a pre-implementation site visit to ensure readiness for study implementation. Additionally, FHI 360 and CAPRISA 106 study staff will conduct a minimum of three site visits during study implementation to observe data collection. Data collection will also be monitored

through the review of data, weekly data collection reports, participant recruitment logs, and data collection logs. Study documents will be regularly reviewed for completeness and accuracy, including all data collection logs, source documents and processed data. Sites will be routinely monitored for security of data collection and storage.

Study documents will be regularly reviewed to determine whether social, psychological or other harms may be occurring and if so, that they are properly documented and reported. Study investigators will also review study documents to determine if protocol or confidentiality breaches have occurred. Where necessary, corrective actions will be identified and their implementation documented.

Staffing will be monitored and reviewed to ensure that staffing changes are appropriately documented, that confidentiality agreements are signed, and that all necessary trainings have been completed and documented.

## **ETHICAL CONSIDERATIONS**

Before initiating the study, the protocol and consent process must be approved in writing by the University of KwaZulu-Natal (UKZN) Biomedical Research Ethics Committee (BREC), and the FHI 360 Protection of Human Subjects Committee (PHSC). No amendment to the protocol or informed consent forms will be implemented without prior ethics committee (EC) approval. Any violations of the protocol will be reported directly to the local investigator and then to FHI 360's principal investigator. Protocol violations will be reported in writing to all ECs that reviewed and approved the study in accordance with the individual EC's policy.

### **Procedures for Protecting Participant Confidentiality**

Interviews and focus group discussions will be conducted in a private location where they cannot be overheard. All study-related materials will be stored at the CAPRISA clinical research sites, with access limited to CAPRISA 106 study staff. Participant study materials, including audio recordings, interview guides, data collection forms, and transcripts will be labeled with a study-specific ID code and will not contain personally identifying information. Any identifying information inadvertently mentioned during data collection will be cleaned from the text before analysis. The study-specific ID code will be linked via a master list to the participant's identifying information. For CAPRISA 008 participants, a separate document will link study-specific ID codes to the participant's CAPRISA 008 study identification code, to facilitate linkage of participant data for analysis. Similarly, a separate document will link study-specific ID codes for CAPRISA 008 participants and their male partners who participate in FGDs or IDIs. All records that contain names or other personal identifiers, such as informed consent forms, participant master list, and participants' ID codes for the CAPRISA 008 study will be stored separately from participant study materials. These documents will be kept in a separate locked file from the study materials, in an area with limited access.

All electronic data files will be password protected and maintained on the project computer(s) at the field sites, on secure servers, or on back-up disks kept in the locked file cabinet. Transcripts and electronic files will be similarly secured at FHI 360 headquarters in NC.

Participants will not be identified by name in any report or publication resulting from study data, except as required by law, unless the participant gives his/her consent. Research facility records may be audited by FHI 360 staff or other individuals authorized to audit the study. Audio recordings will be destroyed at the end of the study, and all paper-based data will be stored in a secure location for the required time specified by FHI 360's standards of practice.

The study will include the review of documents related to CAPRISA 008 and HSS/QI activities at the CAPRISA 008 study sites. Data will be abstracted from these documents and/or the documents themselves will be scanned, photocopied, or digitally captured for abstraction and analysis. No personally identifying information about clients or CAPRISA 008 participants will be abstracted, and any such information will be redacted from scanned, photocopied, or digitally captured documents.

### **Informed Consent Process**

All informed consent forms will be translated into isiZulu and back-translated to assure accuracy. The CAPRISA Standard Operating Procedures for translation will be followed. Study staff will explain the study and its associated procedures, risks, and benefits to eligible participants. They will then ask an eligible participant to sign an informed consent form if she/he wishes to participate. Participants will be offered copies of their signed consent forms. An impartial witness is required for the entire informed consent process for any participant who is illiterate per CAPRISA guidelines for determining appropriate literacy for research consent.

Written consent will be obtained from all participants. Documentation of the presence of a witness will be achieved through their signature on the informed consent document. Illiterate participants will indicate their consent via use of their mark (finger/thumb print) on the informed consent documents. If a participant decides to withdraw from the study once an IDI has been completed, all data collection materials will be destroyed and a memo added to the participant file indicating this. For FGDs, it will not be possible for participants to withdraw after FGD completion due to the interactive nature of the group data collection.

Before the IDI or FGD is conducted, potential participants will first be asked to provide their informed consent. All IDIs will be conducted either in English or in isiZulu per the participant's preference, will last up to 2 hours, and will be audio recorded when permission is granted by the participant. If the participant prefers not to be recorded then detailed notes will be taken and expanded immediately after the IDI. Where possible, a designated note-taker will assist the interviewer if the participant declines recording of the interview. All FGDs will be in English and/or isiZulu, will last up to 2.5 hours, and will be audio recorded; notes will also be taken to facilitate transcription including distinguishing speakers from each other. Potential FGD participants who do not want to be recorded may decline participation in the FGD.

### **Risks and Benefits to Study Participants**

Participants in this research should face no physical risks. There are also few anticipated social risks associated with participation; however, participants may become embarrassed, worried, or anxious when talking about sexual relationships and gel use, or their experience with service delivery. Participants will be told that they do not have to answer a question that they do not want to and they can terminate the interview or leave the focus group discussion at any time.

We recognize that the recruitment of male partners of CAPRISA 008 participants introduces the potential for violent harm if the CAPRISA 008 participant has not fully disclosed all aspects of study participation and TFV gel use to her partner prior to his being interviewed or joining a focus group. To protect against such harm, we will screen women for the extent of disclosure with their male partner prior to asking any woman if she would be willing to have her partner recruited for the study. Further, all male partners will be recruited through the CAPRISA 008 participant; no male partners will be approached for recruitment directly.

We also recognize that CAPRISA 008 providers and research staff may feel pressured or even coerced to participate in Objective 2, if they believe that participation is a requirement of their work. There may be peer pressure or pressure from higher management to participate, regardless of efforts made by the research team to assure that participation is voluntary. To minimize the potential for coercion, CAPRISA 008 providers and research staff will be given the option to be interviewed away from the research clinic. Further, if they do not wish to participate but are concerned about consequences of non-participation, the interviewer will offer the providers and research staff the opportunity to sit in the interview room for a period of time sufficient to generate the appearance that an interview took place.

Should social harms or any other significant study-related events be reported, staff will be trained to refer participants for appropriate counseling and services within their communities. Social harms will be reported to the relevant ECs or according to their individual requirements. Examples of a social harm event include loss of employment, stigmatization, or physical abuse. Potential risks will be described in the informed consent documents and will be thoroughly discussed with all potential study participants prior to participation.

IDIs and FGDs will be conducted in a private location. Every effort will be made to protect participant confidentiality, but for FGDs, other people in the group will hear what is said and might tell others about it. Each FGD will begin with a discussion of respect for the privacy of the other participants. All FGDs participants will also be asked not to reveal the identity of others who participate in the discussion and to not disclose any information discussed within the group to others outside of the group. Because this cannot be guaranteed, a statement regarding this issue will be included in the consent form.

There are no direct benefits to participants in this study. Some participants may get some personal satisfaction from being part of a research study on HIV prevention and may benefit in the future from information learned in this study.

### **Compensation**

All participants will be compensated for their time and transport with a small stipend in local currency. An appropriate amount will be determined by the site (CAPRISA) and approved by BREC. Refreshments may be served during the IDIs and FGDs.

## **DISSEMINATION AND USE OF FINDINGS**

Study findings will be disseminated via peer review publications and professional meetings, and via stakeholder feedback meetings in KwaZulu-Natal. In combination with interim results from CAPRISA 008, the study findings and stakeholder feedback may be used to design a combined social-structural

intervention to enhance acceptability, adherence, compliance, and continuation of TFV gel as an HIV prevention option for women.

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## APPENDICES

- Appendix A. Informed Consent Form for Formative Social Research: CAPRISA 008 participant focus group discussion on tenofovir gel use
- Appendix B. Informed Consent Form for Formative Social Research: CAPRISA 008 participant in-depth interviews on tenofovir gel use
- Appendix C. Informed Consent Form for Formative Social Research: Male partner in-depth interviews on tenofovir gel use
- Appendix D. Informed Consent Form for Formative Social Research: Male partner focus group discussion on tenofovir gel use
- Appendix E. Informed Consent Form for Formative Social Research: Community men focus group discussion on tenofovir gel use
- Appendix F. Informed Consent Form for Formative Health Systems Research: CAPRISA 008 Participant In-depth Interviews on Clinic Experience
- Appendix G. Informed Consent Form for Formative Health Systems Research: CAPRISA 008 Provider/Research Staff In-depth Interviews on Clinic Experience
- Appendix H. CAPRISA 106 In-depth Interview Guide: CAPRISA 008 Participant In-depth Interview on Social Dimensions of Tenofovir Gel Adherence and Continuation
- Appendix I. CAPRISA 106 In-depth Interview Guide: Male Partner In-depth Interview on Social Dimensions of Tenofovir Gel Adherence and Continuation
- Appendix J. CAPRISA 106 In-depth Interview Guide: CAPRISA 008 Provider/Research Staff Experience with HSS/QI and Clinic Service Delivery
- Appendix K. CAPRISA 106 In-depth Interview Guide: CAPRISA 008 Participant Experience with Clinic Service Delivery
- Appendix L. CAPRISA 106 Focus Group Discussion Guide: CAPRISA 008 Participant Discloser Focus Group Discussion on Social Dimensions of Tenofovir Gel Acceptability and Compliance
- Appendix M. CAPRISA 106 Focus Group Discussions Guide: CAPRISA 008 Participant Non-Discloser Focus Group Discussion on Social Dimensions of Tenofovir Gel Acceptability and Compliance

- Appendix N. CAPRISA 106 Focus Group Discussions Guide: Male Partner Focus Group  
Discussion on Social Dimensions of Tenofovir Gel Acceptability and Compliance
- Appendix O. CAPRISA 106 Focus Group Discussion Guide: Community Men Focus Group  
Discussion on Social Dimensions of Tenofovir Gel Acceptability and Compliance