

**CAPRISA 104**

**CAPRISA 104 Microbicide Case Control Study to Evaluate Behavioral Patterns of Risk and Gel Use in a Phase 2b Trial**

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## INTRODUCTION

Determining the effectiveness of experimental microbicides is complicated by difficulties in obtaining accurate measures of microbicide use. HIV prevention rates among women in the treatment arm(s) of a trial reflect the combined effects of the underlying efficacy of the microbicide and variability in the patterns of microbicide use. The importance of behavioral variability is increased for antiretroviral-based microbicides, which may have a larger window for effective use and/or may require re-application during an extended post-coital timeframe. The ability to identify potentially effective combinations of behaviors from a complex array of possibilities could significantly improve planning for expanded phase 3 or 4 trials or pilot programs of promising microbicides. The evaluation of innovative behavioral measurement strategies in the context of current phase 2 and 3 trials may also lead to better research designs that can directly assess the contribution of behavioral variability to microbicide effectiveness.

The CAPRISA 004 Tenofovir Microbicide Trial seeks to assess the safety and effectiveness of tenofovir gel, a candidate vaginal microbicide, in sexually active women at risk for human immunodeficiency virus (HIV) infection in South Africa. The trial has been approved by the South African Medicines Control Council, the University of KwaZulu-Natal Biomedical Research Ethics Committee, and the Family Health International Protection of Human Subjects Committee. This is a Phase IIb, two-arm, double-blind, randomized, controlled trial comparing 1% tenofovir gel with a placebo gel that will enroll 980 sexually active, HIV-uninfected women aged 18 to 40 years at two study sites: the CAPRISA Vulindlela Clinical Research Site, KwaZulu-Natal, and the CAPRISA eThekweni Clinical Research Site, Durban. Participants will be provided with a supply of single-use, pre-filled applicators according to their randomization. While in the study, participants will be asked to apply a first dose of the assigned study product, 1% tenofovir gel or placebo gel, within 12 hours prior to coitus and insert a second dose as soon as possible within 12 hours after coitus. They will be advised to use only two doses of gel in a 24-hour period.

The complexity of the gel-use message for the trial creates challenges for accurately measuring compliance and, hence, evaluating the potential contribution of behavioral variability to the effectiveness outcome. The trial protocol includes behavioral and gel use assessments at monthly and quarterly follow-up visits. The most detailed data is collected on gel use, condom use and coital acts on the day of the last sex act at each monthly visit. While it is anticipated that this data will identify important behavioral correlates of seroconversion, the extent to which the detailed data reflect use-patterns directly associated with seroconversion will be unknown. For example, it is possible that women will be more likely to use gel and condoms in the days before a study visit.

It may be possible to enhance the validity of self-report data on sexual behavior and gel use for longer time frames by using more intensive interview strategies that include techniques to reduce bias. However, the costs of collecting such data from all trial participants would be prohibitive and it is also unlikely that women in the trial would be willing to expend the additional effort needed to provide the data on a monthly or even

quarterly basis, given the other requirements of the trial. An optimal compromise with regard to cost and effort may be to conduct intensive interviews with a random sample of women in the trial. However, the number of anticipated incident HIV infections during the trial is small (projected n=68). It is unlikely that a completely random sample will capture enough of the women with incident infections to support any analysis of sexual behaviors and gel use patterns that may be contributing to the effectiveness outcome.

As an important step toward addressing this quandary we will conduct a case-control study in parallel with the Tenofovir Microbicide trial. Data collection will center on in-depth interviews with seroconverters (cases) matched 1:3 to a random sample of uninfected controls. Both qualitative and quantitative data will be collected. Formative research will be conducted to ensure enrollment strategies will be sensitive and ethically appropriate. Strategies to reduce bias in self-reported data will be incorporated, for example, cognitive framing techniques and multiple measures. The interviews will focus on behavior related to gel use, sexual behavior, and partners since enrollment or in the previous three months, whichever is less.

## **STUDY OBJECTIVES**

The objectives of the study are to:

- (1) Statistically model the relative risk of HIV infection for women in the experimental arm of the trial compared to those in the placebo arm, controlling for behavioral variability in gel use patterns.
- (2) Qualitatively evaluate patterns of gel use behavior among participants, and the extent to which those patterns vary by infection status and study arm.

## **STUDY DESIGN**

This nested case-control study is an innovative approach to assess the role of sexual behavior and product adherence in HIV infection in the Tenofovir Microbicide trial; therefore, one of the goals of the study is to evaluate the design's utility for untangling behavioral factors from gel efficacy in the overall measurement of effectiveness.

The study design is a 1:3 case-control study, where cases are women with incident HIV infections enrolled in a randomized controlled trial of a microbicide and controls are selected randomly from among uninfected women enrolled in the same trial.

The design integrates qualitative and quantitative data collection and analysis. Psychological measures of stress are included in order to evaluate the potential impact of HIV infection status on recall of gel use and sexual behavior. Source documents for the Tenofovir Microbicide trial will also be reviewed and gel counseling and adherence information abstracted.

## **STUDY SETTING**

This study will be conducted at two Clinical Research Sites in KwaZulu-Natal, South Africa and will enroll women at high risk of HIV infection in Durban and Vulindlela. All participants, with the exception of some of those participating in the formative research component, will be actively enrolled in the Tenofovir Microbicide gel study. English and Zulu are the primary languages spoken. From past experience at these CAPRISA sites, at least one of these two languages is spoken by almost all those in the target population.

The Vulindlela Clinical Research Site is situated in a rural community with approximately 400,000 residents in the KwaZulu-Natal midlands, about 150 km north-west of Durban. Primary Health Care (PHC) services are provided through seven clinics in the district. These nurse-managed services provide antenatal care, family planning, childhood immunization, STI treatment, minor ailment care, tuberculosis treatment and HIV Voluntary Counseling and Testing (VCT). The closest referral hospitals are Grey's and Edendale. The CAPRISA Clinical Research Site in Vulindlela adjoins the Mafakathini PHC Clinic. The prevalence of HIV infection in pregnant women in Vulindlela has increased from 32.4% (95% CI 27.6-37.6%) in 2001 to 42.7% (95% CI 38.4-46.8%) in 2004. In 2004, the age specific prevalence among ANC attendees was 54.7% among 20-24 year old women and 66.3% among 25-29 year old women. An increase from 31.2% (2001) to 42.9% (2002) to 66.0% (2003) was demonstrated in the 25-29 year old women. These data underscore the high and growing HIV prevalence and incidence rates in young, sexually active women under the age of 30 in this community.

The CAPRISA eThekweni Clinical Research site is located adjacent to the Prince Cyril Zulu Communicable Disease Centre (CDC), a designated PHC of the Durban City Health Department, for the diagnosis and treatment of STIs and tuberculosis. The clinic is conveniently situated in the Warwick triangle in the metropolitan region of Durban which serves as the nucleus of the public transportation with the central bus, "minibus" taxi station and rail station all within a 500 metre radius of the clinic building. This clinic is readily accessible in terms of the transport infrastructure. This clinic provides free STI and tuberculosis treatment. Annually, approximately 40 000 cases of STIs are treated at this clinic, approximately 36 000 of which are new cases. The majority of the STI patients accessing these facilities are self-referred either symptomatic with genital ulceration and/or vaginal discharge syndrome or as contacts of patients with a diagnosis of a STI and include both males and females. Given the high prevalence of HIV infection in South Africa and the strong association between STIs and HIV acquisition, these patients are at an increased risk of acquiring and transmitting HIV through sex. Between July and December 2005, as part of a provider initiated HIV testing programme CAPRISA tested 1190 women for HIV infection. The HIV prevalence was 54.7% with the highest prevalence in the 30-34 and 35-39 age groups

## **PARTICIPANT SELECTION**

Participants for this study will be recruited from the 980 women aged 18 to 40 years enrolled in the Tenofovir Microbicide Trial. All women identified as HIV-positive

following enrollment into the trial will be invited to participate. The trial is designed to continue follow-up until 68 incident infections are observed, hence the total targeted number of cases to be recruited will be 68. Three times as many controls (204) will be recruited to achieve a 1:3 case:control ratio. Thus, total targeted recruitment is 272 women. Refusals to participate by some seroconverters may reduce the total number of cases enrolled but will not affect the targeted recruitment for controls. Controls will be randomly selected without replacement from among women identified as HIV-negative at their monthly visits; enrollment will target approximately 8 women as controls each month or about one woman per week at each of the two trial sites. The procedures for randomly selecting controls will be developed in consultation with the Tenofovir Microbicide trial study directors at the two sites and will ensure proportionate representation from the trial participants at each site.

According to the Tenofovir Microbicide Trial protocol, participants will be tested for HIV with two rapid HIV tests at each monthly visit. Participants with two negative rapid tests will continue follow-up in the trial. If either or both of the rapid tests are positive or indeterminate, then RNA PCR testing will be performed to confirm HIV status and a follow-up visit will be scheduled for a week later. If the RNA PCR test is positive, a second blood sample will be drawn to confirm HIV status using RNA PCR during the scheduled visit a week later and another follow-up visit will be scheduled for a week thereafter to present results. The primary HIV endpoint of HIV infection is defined as two positive PCR tests from independent samples. Participants will continue using gel product until HIV serostatus is confirmed.

The participant flow differs at the two trial sites. At the eThekwini clinic in Durban, pre-test counseling is provided by a counselor; a nurse then collects the specimen for the HIV rapid test. The participant continues with other study procedures while awaiting results from the HIV antibody test and post-test counseling. At the Vulindlela clinic, pre-test counseling, specimen collection, HIV rapid testing, and post-test counseling are all done by the same person in the same room. The participant remains in the counseling room and observes the result of the rapid test with the counselor.

As described in more detail below, we will employ interviewing strategies that are designed to minimize recall bias for self-reported behavior. However, there is also the possibility that stress related to HIV testing status may affect the responses of cases. In order to evaluate the potential impact of such bias on the overall results, we will seek to minimize the potential for biased reporting between cases and controls at the eThekwini site by attempting initial recruitment of both cases and controls after rapid HIV test results are known but before women receive post-test counseling for the results.

- Women at eThekwini will be asked if they would be willing to participate in an immediate in-depth interview which would mean they would delay completion of the study procedures for their current follow-up visit, including post-test counseling, until after the one hour interview. If they are not willing to do an immediate interview, they will be asked if they would be willing to consider doing an interview at some other time. If yes, they will be asked to set up an interview appointment (see eThekwini recruitment script in Appendix B).

- Cases who do not express immediate interest in the study will be provided a card with the contact information for the Case Control Study, should they decide they would like to learn more. If RNA PCR test results are positive when they return for the first RNA PCR test the following week, they will be reminded about the Case Control Study and again invited to participate. If they still are not interested, a final effort at referral to the Case Control Study will be made when she returns for her second RNA PCR test, when she is also referred for enrollment into other studies for Tenofovir Microbicide trial seroconverters.
- Controls who do not express immediate interest in the study will also be provided a card with the contact information for the Case Control Study, should they decide they want to learn more about the study. If they have not enrolled prior to the time they return for their next monthly follow-up visit they will be reminded about the Case Control Study and again invited to participate.
- If the interviewer is unable to approach the targeted participant for recruitment prior to post-test counseling, she will consult with the Case Control study coordinator to identify other opportunities to do so. The study coordinator will work with the Tenofovir Microbicide Trial staff to identify appropriate opportunities.

At the eThekwini site, the interviewer will have a 10 minute window within which to approach the trial participant for enrollment in the case control study before HIV post-test counseling commences by default. If post-test counseling is delayed more than 10 minutes due to other factors unrelated to the Case Control Study (e.g., a backlog in trial procedures) the Case Control Study interviewer can approach the trial participant for recruitment at any point during that delay so long as it does not further delay trial procedures.

At Vulindlela, recruitment of cases will initially occur following post-test counseling, with referral to the Case Control Study occurring as part of other standard procedures for trial participants who seroconvert. The process will be similar to that followed at the eThekwini clinic for cases who decline to be interviewed prior to post-test counseling. The process for recruiting controls at Vulindlela will similarly occur following post-test counseling. A recruitment script for participants in Vulindlela is included in Appendix B.

At both eThekwini and Vulindlela, participants must be interviewed for the Case Control Study within 6 weeks from the date of the rapid test when recruitment was initiated, in order to remain eligible for the study. Rates of refusal among cases and controls will be evaluated to determine whether uncontrolled enrollment bias may be present.

For both scientific and confidentiality reasons, the interviewers for the Case Control study will be blinded to the HIV infection status of the participant. The Case Control study coordinators are CAPRISA staff who are also Tenofovir Microbicide trial staff. At both eThekwini and Vulindlela the Case Control Study coordinators will coordinate with the appropriate Tenofovir Microbicide Trial study staff to facilitate recruitment of both cases and controls. They will inform the Case Control Study interviewers who should be recruited and when, but they will not provide any information on HIV test results. The

Case Control Study interviewers will not be members of the Tenofovir Microbicide Trial staff and will not have access to any Tenofovir Microbicide Trial participant files or attend Tenofovir Microbicide Trial staff meetings where participant details are discussed.

At both eThekweni and Vulindlela, the recruitment process will be carefully monitored by the Case Control Study coordinators who will work with the Tenofovir Microbicide Trial counselors and other trial staff as appropriate to ensure that seroconverters in particular are not unduly stressed by efforts at recruitment. Since the number of Case Control Study participants recruited at each site will be one to two per week, this level of monitoring and oversight is practical and manageable.

Efforts to enroll the first 10 cases will be carefully evaluated and changes will be made in the recruitment process if problems are identified. We will work closely with the clinical trial staff conducting HIV counseling and testing to ensure that recruitment for this study is respectful of participants and minimizes any potential burdens on the clinical trial.

### **SAMPLE SIZE JUSTIFICATION**

The sample size for this study is the minimum necessary to allow for the possibility of a comprehensive case control analysis. If the trial shows overall moderate to no gel effectiveness, we anticipate that infection events in the treatment arm will be on the order of 20 (moderate effectiveness) to 33 (no effectiveness). Under these conditions a case control analysis of participants in the tenofovir gel arm of the trial would have 70% or more power to identify common behavioral patterns demonstrating very high associations with HIV incidence (odds ratios > 4.0). Under conditions of moderate effectiveness, such results could identify critical behavioral patterns. Under conditions of low effectiveness, such results could indicate whether poor compliance could have been a major contributing factor to the trial outcome. If the trial demonstrates high rates of gel effectiveness, then infection events in the treatment arm will be too few for meaningful statistical analysis, however, the qualitative results will be highly informative for developing gel use counseling messages. It is anticipated that there will be an additional 30-50 seroconversion events in the placebo arm, which will provide additional statistical power for analysis of gel use compliance.

### **FORMATIVE RESEARCH AND PILOTING**

The Tenofovir Microbicide Trial is currently scheduled to begin screening participants for enrollment in mid-May 2007, with initial enrollment to be slow. In order to avoid interference with trial procedures during the critical start-up period, enrollment for this study is targeted to begin in August 2007, when trial enrollment targets increase substantially.

Prior to beginning enrollment for the Case Control Study we will pilot the data collection strategy. Up to 10 one-on-one pilot interviews will be held with women who have been enrolled in the trial for at least one month to evaluate the interview guide and procedures, using a “think aloud” strategy (Edwards, Thomsen, & Toroitich-Ruto, 2005). The “think

aloud” approach is a form of cognitive testing where a participant is asked to verbalize what she is thinking as she answers the researcher’s questions. When used concurrently, i.e., as the participant attempts to answer questions, the method is useful for uncovering problems associated with comprehension and event recall. Changes may be made in wording, sequencing of questions, and elicitation strategy based on the pilot results. We do not anticipate any substantive changes to the content of the interviews; if substantive changes are needed we will submit a protocol amendment prior to implementing data collection.

We will pilot the recruitment process at the two sites among women participating in other CAPRISA studies that include HIV antibody testing. Only women participating in CAPRISA studies where the informed consent form states that they may be asked to participate in other studies will be approached. The women participating in the pilot recruitment process will be administered a shortened version of the Case Control study interview guide that includes some of the generic open-ended questions and the psychological stress measures (see Appendix D). These interviews will not be tape-recorded or analyzed.

We will conduct additional formative research to inform recruitment and interviewing procedures in the early weeks of the Case Control Study. Some formative research may overlap with active recruitment for the study. Given the planned recruitment of one-to-two participants per week, the combined experience of the formative research and evaluation of the initial interviews in the first few weeks of the study will be mutually informing.

In-depth interviews with up to 5 HIV testing counselors and up to 5 women living with HIV at the two research locales (eThekweni and Vulindlela) will be conducted to ensure that the proposed recruitment procedures are implemented in ways that are psychologically and culturally sensitive (see Appendix E and F). Up to 4 focus groups will be held with trial participants or women drawn from the same populations as the trial participants to explore cultural concepts of time, time-keeping, and calendars, and to identify strategies for eliciting accurate and detailed information on sexual behavior (see Appendix G). For example, object probes are material objects that are used explicitly to generate verbal responses, and may include photographs or other images as well as physical objects (de Leon & Cohen, 2005). We will explore the utility of using study-related items such as gel applicators and condoms as well as non-study objects that could prompt memory. For example, newspaper clippings or souvenirs reflective of local events for which the date and time are known may serve as useful time anchors for participants. Other object probes could include photographs of things that are part of important local cycles of activity, e.g., local transportation, a church, a school, a market. These and other objects could be displayed and the participant encouraged to use them to orient her thoughts, explain the sequencing of events, etc. We will explore the cultural utility of a wide range of such object probes to improve recall during the interview process.

## **DATA COLLECTION**

The interview guide will be translated into Zulu and back-translated to assure accuracy. The CAPRISA Standard Operations Procedures for translation will be followed.

We will collect self-reported data on sexual behavior and gel use for the previous 3 months. For those women who are interviewed after post-test counseling for an HIV+ test result, there may be effects on recall and self-reported behaviors. We will use several psychometric scales to assess the likelihood that stress related to HIV testing status may be affecting the responses of cases. We also include measures that assess study-related procedures recall, by comparing self-report experience in the trial with what is recorded in the participant's study file, and measures that assess systematic behavioral recall bias by re-administering selected behavioral and gel use questions from the trial data collection forms.

Interviews will take approximately 1 hour and will be the same for cases and controls. The interview will include both quantitative and qualitative components, as follows. A draft of the interview guide is included with this protocol.

1. Background (approximately 5 minutes): To build rapport and obtain background information on sociodemographic factors that may be related to gel use, the interview will begin with a series of open-ended questions about the participant. Systematic sociodemographic data will not be collected as this information will already be available from the clinical trial.
2. Perceived Stress Scale (PSS) (approximately 5 minutes): The PSS measures the degree to which life situations are perceived to be stressful. The scale items measure the degree to which life is perceived as unpredictable, uncontrollable, and overloading---three components that are central to the experience of stress (Cohen, Kamarck, & Mermelstein, 1983). Since the scale items are not linked to a specific event, the PSS will provide a measure of overall background stress for participants in the Case Control study.
3. Study-related procedures recall (<5 minutes): A number of studies have suggested that life event stress has a negative impact on different types of memory (Klein & Boals, 2001; Harvey & Bryant, 2000; Jones, Griffiths, Humphris, & Skirrow, 2001). To evaluate the potential for recall bias resulting from the impact of seroconversion-related stress on memory, we will include several questions about study-related procedures that the participant may have undergone in the past 2 months, e.g., treatment for STIs. Responses to questions about actual study procedures will be verified against the participant's study file; these will serve as one set of gold standards for assessing systematic recall bias. We will also include one or two fictive procedures that are not part of the study.
4. Impact of Event Scale (IES) (approximately 5 minutes): The IES is a widely used measure of subjective stress following traumatic events, and has excellent psychometric properties (Horowitz, Wilner, & Alvarez, 1979; Sundin & Horowitz, 2002; Joseph, 2000). It has been successfully used to measure health-related stress impacts, including HIV diagnosis (Lutgendorf et al., 1997). The IES references a specific event, which for this study will be the most recent HIV test. We will use the IES to evaluate the extent to which stress linked to HIV testing in

- general and seroconversion in particular is experienced by participants, and the potential impact of such stress on self-reported behavior.
5. Systematic behavioral recall bias (<5 minutes): Selected behavioral and gel use questions from the Tenofovir Microbicide data collection forms will be re-administered during this interview to assess differential recall among cases and controls. These items will serve as another set of gold standards for assessing recall bias.
  6. Drug and alcohol use (approximately 5 minutes): There is increasing concern that risk behavior in the target populations may be significantly related to drug and alcohol use. Concerns are also emerging that injecting drug use may be or may become a factor in HIV transmission. If even a small proportion of trial participants are injecting drugs it could have implications for evaluating the effectiveness of the tenofovir gel microbicide. For these reasons we will collect data on substance use.
  7. Timeline Followback (TLFB) for gel use and sexual activity (approximately 20 minutes): The TLFB was originally developed to assess alcohol use but has been shown to be valid for use in HIV behavioral research as well (Carey, Carey, Maisto, Gordon, & Weinhardt, 2001). The TLFB combines findings from cognitive psychology about the value of memory aids to facilitate recall with open-ended interviewing techniques to facilitate collection of detailed behavior patterns over extended time intervals. The study by Carey et al. (2001) found that the structural features of the TLFB facilitated recall of sexual behaviors that occurred up to 90 days earlier; this timeframe encompasses the period during which infection would be most likely to occur for cases. TLFB strategies that may be incorporated into the interview include:
    - Use of “special days” that are generally meaningful, e.g., holidays, pay days, travel away from home
    - Menstrual cycles
    - “Anchor days” defined by the participant rather than the interviewer
    - Visual aids (see discussion of object probes in the section on Interview Development and Piloting)

Although the TLFB appears on paper to be complex and lengthy, it is in fact quite straightforward and efficient when properly implemented. Data collection will include questions on sex partners including each the partner may be HIV-positive, has been circumcised, and knows that the participant is in the Tenofovir Microbicide Trial.

8. Product and Trial Acceptability (approximately 10 minutes): The interview will conclude with a set of open-ended questions about product use, study participation, and access to needed services/care.

In addition to the data collected via interview, the Tenofovir Microbicide Trial source documents will be reviewed for all Case Control Study participants and descriptive data on gel counseling and adherence will be abstracted. The Tenofovir Microbicide Trial includes a structured Adherence Support Program (ASP) that includes individualized counseling for each trial participant and comprehensive notes on gel adherence successes and challenges. Data from the ASP notes will not be included in the trial data base. By

abstracting these notes from the trial source documents and including them as part of the qualitative data base for the Case Control Study we will be able to describe evolving patterns of gel use and risk behavior and evaluate their potential relationship to seroconversion. Data abstraction from the trial source documents will be conducted by the Case Control Study coordinators; interviewers will not have access to the participants' Tenofovir Microbicide trial files for confidentiality reasons.

The data collected specifically for the Case Control Study will be linked to data collected as part of the Tenofovir Microbicide Trial. A participant log that links the Case Control Study ID to the Tenofovir Microbicide Trial participant ID will be maintained by the Case Control Study coordinators in a secure location. Tenofovir Microbicide Trial counselors and nurses and Case Control Study interviewers will not have access to the linked participant log.

## **DATA MANAGEMENT**

All interviews will be audio taped. The Background, Timeline Followback, and Product and Trial Acceptability components will be transcribed verbatim and translated into English for qualitative analysis. The interviewer will use standard tools to record the TLFB data during the interview and will use the recorded information to complete a standardized data collection form that will summarize sexual behavior and gel use during the 3 month data collection timeframe. As needed, the audiotape will be reviewed to facilitate completion of the standardized form. The first 10 interviews with controls and the first 5 with cases will be carefully reviewed by the Case Control study investigators and study coordinators to identify problematic areas and make changes or reinforce training points as needed. At random intervals throughout the study, a sample of audiotapes will be independently reviewed and compared with transcripts and data collection forms by the CAPRISA lead investigator, who is a native Zulu speaker.

ASP notes abstracted from the Tenofovir Microbicide trial source documents will be typed into computer text files identified only with the Case Control Study participant ID number. No identifying information will be abstracted. The ASP text files will be analyzed as part of the qualitative data base.

Participant files will be managed using systems developed at FHI for other qualitative and mixed-methods research projects (Mack, Woodson, MacQueen, Guest, & Brelsford, 2005). A pre-numbered log book will be used to assign unique codes to each interview event. The assigned code will be placed on all materials associated with the interview event, including interview or focus group guides, tapes, hand-written notes, consent forms, transcriptions, etc. A data collection event summary sheet will be completed, and all materials are then placed in a sturdy Tyvek envelope. Whenever materials are removed or replaced from the envelope it will be noted on the envelope with the date, purpose, and name of the person removing the item listed. The assigned code will be incorporated into all computer files associated with the interview event as well. The Tyvek envelopes with the 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. Transcription of the qualitative data will be done according to a standardized protocol to facilitate data management and analysis (McLellan, MacQueen, & Neidig, 2003). Quality checks for accuracy of the transcripts will be conducted by CAPRISA team members and checks for completeness of transcripts will be conducted by FHI team members.

Quantitative data will be entered by CAPRISA Case Control study staff; all quantitative data will be double entered to ensure accuracy. Any discrepancies will be resolved by reviewing the original questionnaire and, if necessary, the audio taped interview. CAPRISA staff will clean the data by checking for missing responses and inconsistent and out-of-range responses. A copy of the clean database will be transmitted to FHI via email for data standardization and analysis. Original forms and surveys will be kept in locked files at CAPRISA throughout the duration of the data analysis and report writing, to be made available to FHI study monitors upon request.

All local staff will be trained in maintaining participant confidentiality and rigorous data management procedures. A study-specific manual will be developed outlining data management procedures and containing templates for data management forms. Additionally, FHI staff will regularly monitor the study sites, using a systematic monitoring procedure. Data will also be reviewed for accuracy as it arrives at FHI and feedback provided as needed.

## **DATA ANALYSIS**

### *Statistical Analysis*

We will compare self-reported data on gel use and risk behavior obtained from all participants enrolled in the case-control study via in-depth interview with data obtained from the same participants using the monthly Tenofovir Microbicide trial data collection forms. We will conduct a case-control and cluster analyses using only trial data, and a similar analysis using comparable quantified data from the in-depth interviews to see if results vary based on timing of the data collection strategies relative to HIV testing. These analyses will indicate potential strengths and weaknesses of the different data collection approaches.

We will use psychological measures of stress that are known to correlate with memory-affected states to assess the potential for systematic memory bias due to the stress of a positive or potentially positive HIV diagnosis.

Based on the foregoing results we will assess the potential for systematic bias in self-reported data from cases versus controls. If these analyses suggest that no systematic bias is occurring, and provided sufficient statistical power exists, we will conduct a comprehensive case-control analysis to evaluate the relative risk of specific behavioral and gel use patterns for HIV infection.

A detailed analysis plan for the case-control study will be written prior to unblinding the study. In brief, we will use multiple logistic regression techniques (Rothman and

Greenland, 1998) to evaluate whether gel use patterns are associated with risk of HIV. For each evaluated gel use ‘exposure’ (e.g. perfect adherence to BAT24 regimen in the three months prior to seroconversion) we will fit a model that includes effects for age, time since enrollment, treatment group, exposure status, and the interaction between exposure and treatment group. The interaction effect will be evaluated at the two-sided .05 significance level to assess whether gel use patterns are differentially associated with HIV risk in the experimental arm compared to the placebo arm. Exploratory regression models will similarly be used to evaluate the effects of other participant characteristics and behaviours on the risk of HIV.

### *Qualitative Analysis*

Qualitative data analysis will be used to evaluate clustering of gel use behaviors by infection status. Even with very small numbers, such analysis may provide insight into the contribution of behavioral variability to effectiveness measures. If the trial shows moderate to high effectiveness, the qualitative analysis could be used to develop improved guidance for gel use counseling in subsequent trials or pilot programs.

The transcribed text data will be managed using a well-established systematic process (McLellan et al., 2003). Thematic analysis will be performed on the text data using qualitative data analysis software that can support team-based multisite analyses. To discover emerging themes, team members will read through transcripts and use common exploratory techniques used by anthropologists, sociologists, and other qualitative researchers (Dey, 1993; Strauss & Corbin, 1990; Ryan & Bernard, 2003). Using a standardized iterative process, a codebook will be developed (MacQueen, McLellan, Kay, & Milstein, 1998) and a minimum of two individuals will independently code text segments. Inter-coder agreement will be assessed at various points in the analysis process using percent agreement and kappa scores, as appropriate (Carey, Morgan, & Oxtoby, 1996). Coding discrepancies (e.g., code applications that receive initial kappa scores of less than 0.8) will be discussed by the analysis team, the codebook revised accordingly, and recoding performed when necessary to ensure consistent application of codes. To identify key themes, saliency reports based on Boolean minimization logic applied to co-occurrence measure of codes (Ragin, 1987), and code frequency reports will be generated.

Identifying patterns among codes and across respondents in large, multidimensional qualitative data sets is difficult. For this reason, cluster analysis will be performed on code configurations as a form of data reduction. Binary matrices will be generated and code-by-code matrices run through complete linkage cluster analysis to identify lateral and hierarchical relationships between codes (Guest & McLellan, 2003). Clusters formed will be assessed for reliability and validity using both substantive and statistical criteria. Thematic content will then be compared across cases and controls to assess similarities and differences in responses. Comparisons will be made with respect to code frequencies and salience (i.e., the number of combinations in which a code co-occurs) and configuration of code co-occurrences. References to verbatim text will frequently be made explicit to aid in the interpretation of thematic relationships and to provide

additional explanation to patterns observed (Guest & McLellan, 2003). Cronbach's alpha will be calculated to assess the internal reliability of themes included in cluster formation.

## **PROTECTION OF HUMAN SUBJECTS**

Before initiating the study, the protocol and consent process must be approved in writing by the University of KwaZulu-Natal Biomedical Research Ethics Committee (BREC) and the Family Health International Protection of Human Subjects Committee (PHSC).

### *Privacy and Confidentiality*

Interviews will be conducted in a private location where they cannot be overheard. All participant study materials, including audiotapes, interview guides, data collection forms, and transcripts will be labeled with a study-specific ID code. This code will be linked via a master list to the participant's identifying information. A separate document will link study-specific ID codes to the participant's Tenofovir Microbicide identification code, to facilitate linkage of participant data for analysis. Both documents will be kept in a separate, locked file from the study materials and the study materials will contain no personally identifying information.

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 her consent. Research facility records may be audited by FHI staff or other individuals authorized to audit the study.

### *Risks and their Reduction*

There is a risk that those who have recently been informed that they are or may be HIV-infected may experience psychological distress when being interviewed about their sexual behavior and gel and condom use. If any questions clearly upset the participant, she will be asked if she wishes to stop. If she wishes to continue, she will be asked if she would like to skip the upsetting questions. Trained counselors will be available to help participants who become worried or anxious while waiting for their HIV test results or after receiving HIV-positive test results. Women who are experiencing distress will not be approached for enrollment in this study until (and unless) their distress is appropriately managed.

### *Benefits to Participants*

There are no direct benefits to participants in this study. Some women may find that talking about their sexual practices may help them better understand their personal risks for HIV or other sexually transmitted infections. There may be long term benefits to society. The study results may help improve the design of future HIV prevention trials. They may also provide important information on how to counsel women about using tenofovir gel if the gel proves to be effective.

### *Informed Consent*

Staff will explain the study and its associated procedures, risks, and benefits. They will then ask an eligible participant to sign an informed consent form if she wishes to

participate. The consent form will be translated into Zulu and back-translated to assure accuracy. The CAPRISA Standard Operations Procedures for translation will be followed. Participants will be provided with copies of the consent forms. An impartial witness is required for the entire informed consent process for any participant who is illiterate or whose literacy is limited.

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.

*Compensation*

All participants will be compensated R100-00 for their time.

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## **APPENDIX A: INFORMED CONSENT FORMS**

**CAPRISA 104**  
**Microbicide Case Control Study**  
**Version 1.0**  
**27 September 2007**

**INFORMED CONSENT FORM FOR ENROLMENT**

**PRINCIPAL INVESTIGATORS:**

Mr. Francois van Loggerenberg  
Professor Quarraisha Abdool Karim  
2nd Floor Doris Duke Medical Research Institute  
Nelson R Mandela School of Medicine  
Private Bag 7, Congella 4013  
Durban, South Africa  
PHONE: 031-260 4550

Dr. Kathleen MacQueen  
Family Health International  
PO Box 13950  
Research Triangle Park, NC 27709  
USA  
PHONE: 919-544-7040 ext 587

**Introduction**

You are being asked to volunteer in the research study named above. The purpose of this research study is to understand how women in the Tenofovir Microbicide Trial are using the study gel. We want to understand what makes it easy or hard to use the study gel. This Microbicide Case Control Study is for women who are enrolled in the Tenofovir Microbicide Trial. It is being conducted jointly by the Center for the AIDS Programme of Research in South Africa (CAPRISA) and Family Health International (FHI) in the USA.

**Your participation is voluntary**

In order to be sure that you are informed about being in this research, we are asking you to read (or have read to you) this Consent Form in the language of your choice. You will be asked to sign this Consent Form (or make your mark in front of a witness). If you decide to participate, we will give you a copy of this form to keep.

This Consent Form might contain some words that are unfamiliar to you. Please ask us to explain anything you may not understand. Before you learn about the study, it is important that you know the following:

- o Your participation is entirely voluntary.
- o You may decide not to take part or to withdraw from the study at any time. You will not lose the benefits of your routine medical care at this site.
- o If you decide to not take part in this research study, you can still take part in the Tenofovir Microbicide Trial or another research study, if one is available and you meet the study requirements.

**PURPOSE OF THE STUDY**

The purpose of the Microbicide Case Control research study is to understand how women in the Tenofovir Microbicide Trial are using the study gel. We also want to understand what makes it easy or hard to use the study gel. This study is for women who are enrolled in the Tenofovir Microbicide Trial.

About 275 women from Vulindlela and Durban will take part in this research study.

## **PROCEDURES**

If you agree to take part in the study, here is what you will do. You will be asked questions about your sexual practices, condom use, and Tenofovir Microbicide Trial gel use during the past 3 months. Some of these questions are like ones you have already been asked in the Tenofovir Microbicide Trial. The questions for this study will be more detailed. You will be asked some questions about alcohol and drug use. For questions on drug use you should know that information on illegal activities gathered by researchers is not privileged in law and that you may refuse to answer. You will also be asked some questions about your feelings and thoughts in the past month and your experiences with the Tenofovir Microbicide Trial. The interview will take about one hour.

The interview will be tape recorded so we can make an exact record of what you said. Your name will not be written on the tape and we will destroy the tape when the research is completed. Some of your responses will also be recorded on paper; your name will not be written on the paper.

None of the information you tell me during this interview will go into your Tenofovir Microbicide Trial record or be shown to the counselors or nurses in the Tenofovir Microbicide Trial. Your Tenofovir Microbicide Trial identification number will not be written on the tape or interview papers.

I will interview you for this Case Control study. I am not a counselor or nurse for the Tenofovir Microbicide Trial. I do not know what is in your Tenofovir Microbicide Trial file and I am not allowed to look in your file. I have not been told the results of any of your HIV tests.

The Case control study coordinator is a member of the Tenofovir Microbicide Trial. He/she will link your file records from the Microbicide Trial with this study. However, trial counselors, nurses and I will have no access to these linked records.

## **RISKS AND/OR DISCOMFORTS**

You may become embarrassed, worried, or anxious when talking about your sexual practices and gel use. You may refuse to answer questions that make you uncomfortable. If you are interviewed while you are waiting for your HIV test results, you may become worried or anxious while waiting for those results. A trained counselor will be available to help you deal with any feelings or questions you have.

We will make every effort to protect your privacy and confidentiality while you are in this study. Your interview here will take place in private. However, it is possible that others may learn of your participation in this study, and think that you are infected with HIV, or at “high risk” for HIV. Because of this, others may treat you unfairly or discriminate against you. For example, you could have problems getting or keeping a job. You also could have problems being accepted by your family or community.

## **BENEFITS**

You may get no direct benefit from being in this study. But you may get some personal satisfaction from being part of a research study on HIV prevention. Talking about your sexual practices may help you better understand your personal risks for HIV or other sexually transmitted infections. You or others may benefit in the future from information learned in this study.

## **NEW FINDINGS**

At the end of the study, you will be told when the study results may be available and how to learn about them.

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

You may be removed from the study without your consent for the following reasons:

- o The investigator decides that continuing in the study would be harmful to you.
- o The study is cancelled by the Ethics Committee.
- o Other administrative reasons.

## **COSTS TO YOU**

There is no cost to you for taking part in this study.

## **COMPENSATION**

You will be compensated R100-00 for your time.

## **CONFIDENTIALITY**

If, in the course of this study, we find you are encountering harm, require medical or non-medical care, or are posing a risk/harm to others, we may be obliged to share this information with relevant authorities. Otherwise all information you share with us will be kept confidential.

You will be identified by a unique code. Personal information from your records will not be released without your written permission. We will not write your name on the audiotape used to record your interview or on anything else that might let someone know what you said. We will make a written record from the audiotape but we will not write down any information that might identify you or others. For example, if you mention the names of family or friends we will not write those names down. The interview tapes and notes will be stored in a locked cabinet and only the staff working on this research will be able to use them. We will destroy the tapes when the research is completed.

None of the information you tell us as part of this interview will go into your Tenofovir Microbicide Trial record or be shown to the counselors or nurses in the Tenofovir Microbicide Trial.

After the Tenofovir Microbicide Trial is over we will combine information from the Tenofovir Microbicide Trial with information from this Case Control research study. This will include Tenofovir Microbicide Trial information about whether you were given the

gel with tenofovir or the gel without tenofovir, and whether you became infected with HIV. It will also include information you provided about your sexual behavior and gel use. We will combine this information by using a special identification code; your name will not be included with any of this information.

You will not be personally identified in any publication about this study. However, your records may be reviewed by the University of KwaZulu-Natal Biomedical Research Ethics Committee, FHI Protection of Human Subjects Committee, study monitors, and study sponsors. These agencies are government or sponsor appointed regulatory oversight or monitoring bodies. They are responsible for ensuring that this study follows the study protocol and international and local guidelines for doing research with people.

**PROBLEMS OR QUESTIONS**

If you ever have any questions about the your participation in this study you should contact Mr. Francois van Loggerenberg or Professor Quarraisha Abdool Karim at 031-260 4550, CAPRISA, Second Floor Doris Duke Medical Research Institute, Durban or Dr Janet Frohlich at 031-260 6851, CAPRISA Vulindlela Clinical Research Site, Mafakathini or Dr Ayesha Kharsany at 031-260 4558 at the eThekwini Site. If you have questions about your rights as a research participant, you should contact Chairperson of the Biomedical Research Ethics Committee of the University of KwaZulu-Natal at 031-260 4604/4495 in Durban or David Borasky at FHI in the USA at +091-919-544-7040 ext. 295.

**SIGNATURE:**

If you have read the informed consent (or if you have had it read to you) and understand the information, and you voluntarily agree to join this study, and have your interview tape recorded, please sign your name below.

_____	_____	_____
Volunteer's name (print)	Volunteer's signature	Date

_____	_____	_____
Name of staff member who administered consent (print)	Staff member's signature	Date

_____	_____	_____
Witness' name (print)	Witness' signature	Date

If the volunteer cannot read, this form must be read to the volunteer exactly as written, in the volunteer's native language, and a witness must sign this form to confirm that the correct information was given to the volunteer and that the volunteer freely consents to be in this study and have their interview tape recorded.

## **CAPRISA 104**

### **Microbicide Case Control Study: Formative Research Think-Aloud Interview**

**Version 1.0**

**27 September 2007**

## **INFORMED CONSENT FORM FOR ENROLMENT**

### **PRINCIPAL INVESTIGATORS:**

Mr. Francois van Loggerenberg  
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2nd Floor Doris Duke Medical Research Institute  
Nelson R Mandela School of Medicine  
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Dr. Kathleen MacQueen  
Family Health International  
PO Box 13950  
Research Triangle Park, NC 27709  
USA  
PHONE: 919-544-7040 ext 587

### **Introduction**

You are being asked to volunteer in the research study named above. The purpose of this research study is to understand how women in the Tenofovir Microbicide Trial are using the study gel. We want to understand what makes it easy or hard to use the study gel. This Microbicide Case Control Study is for women who are enrolled in the Tenofovir Microbicide Trial. It is being conducted jointly by the Center for the AIDS Programme of Research in South Africa (CAPRISA) and Family Health International (FHI) in the USA.

### **Your participation is voluntary**

In order to be sure that you are informed about being in this research, we are asking you to read (or have read to you) this Consent Form in the language of your choice. You will be asked to sign this Consent Form (or make your mark in front of a witness). If you decide to participate, we will give you a copy of this form to keep.

This Consent Form might contain some words that are unfamiliar to you. Please ask us to explain anything you may not understand. Before you learn about the study, it is important that you know the following:

- o Your participation is entirely voluntary.
- o You may decide not to take part or to withdraw from the study at any time. You will not lose the benefits of your routine medical care at this site.
- o If you decide to not take part in this research study, you can still take part in the Tenofovir Microbicide Trial or another research study, if one is available and you meet the study requirements.

### **PURPOSE OF THE STUDY**

The purpose of the Microbicide Case Control formative research study is to find the most respectful way to ask women to be in the Microbicide Case Control study. We also want to make sure that the questions we ask in the Microbicide Case Control study are clear

and easy to understand. About 50 people from Vulindlela and Durban will take part in this formative research study.

## **PROCEDURES**

If you agree to take part in the study, here is what you will do. You will be asked questions about your sexual practices, condom use, and Tenofovir Microbicide Trial gel use during the past 3 months. Some of these questions are like ones you have already been asked in the Tenofovir Microbicide Trial. The questions for this study will be more detailed. You will be asked some questions about alcohol and drug use. For questions on drug use you should know that information on illegal activities gathered by researchers is not privileged in law and that you may refuse to answer. You will also be asked some questions about your feelings and thoughts in the past month and your experiences with the Tenofovir Microbicide Trial.

After each question we will ask you to think aloud about how you would answer the question and why. We will ask you if you think there might be a better way to ask the question to make it easier to understand or to answer. We will ask you if you think women in the trial will be able and willing to give an accurate answer to each question.

The interview will take about one and a half hours. The interview will be tape recorded so we can make an exact record of what you said. Your name will not be written on the tape and we will destroy the tape when the research is completed. Some of your responses will also be recorded on paper; your name will not be written on the paper.

None of the information you tell me during this interview will go into your Tenofovir Microbicide Trial record or be shown to the counselors or nurses in the Tenofovir Microbicide Trial. Your Tenofovir Microbicide Trial identification number will not be written on the tape or interview papers.

I will interview you for this Case Control study. I am not a counselor or nurse for the Tenofovir Microbicide Trial. I do not know what is in your Tenofovir Microbicide Trial file and I am not allowed to look in your file. I have not been told the results of any of your HIV tests.

## **RISKS AND/OR DISCOMFORTS**

You may become embarrassed, worried, or anxious when talking about your sexual practices and gel use. You may refuse to answer questions that make you uncomfortable. A trained counselor will help you deal with any feelings or questions you have.

We will make every effort to protect your privacy and confidentiality while you are in this study. Your interview here will take place in private. However, it is possible that others may learn of your participation in this study, and think that you are infected with HIV, or at “high risk” for HIV. Because of this, others may treat you unfairly or discriminate against you. For example, you could have problems getting or keeping a job. You also could have problems being accepted by your family or community.

## **BENEFITS**

You may get no direct benefit from being in this study. But you may get some personal satisfaction from being part of a research study on HIV prevention. Talking about your sexual practices may help you better understand your personal risks for HIV or other sexually transmitted infections. You or others may benefit in the future from information learned in this study.

## **NEW FINDINGS**

At the end of the study, you will be told when the study results may be available and how to learn about them.

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

You may be removed from the study without your consent for the following reasons:

- o The investigator decides that continuing in the study would be harmful to you.
- o The study is cancelled by the Ethics Committee.
- o Other administrative reasons.

## **COSTS TO YOU**

There is no cost to you for taking part in this study.

## **COMPENSATION**

You will be compensated R100-00 for your time.

## **CONFIDENTIALITY**

If, in the course of this study, we find you are encountering harm, require medical or non-medical care, or are posing a risk/harm to others, we may be obliged to share this information with relevant authorities. Otherwise all information you share with us will be kept confidential.

You will be identified by a unique code. Personal information from your records will not be released without your written permission. We will not write your name on the audiotape used to record your interview or on anything else that might let someone know what you said. We will make a written record from the audiotape but we will not write down any information that might identify you or others. For example, if you mention the names of family or friends we will not write those names down. The interview tapes and notes will be stored in a locked cabinet and only the staff working on this research will be able to use them. We will destroy the tapes when the research is completed.

None of the information you tell us as part of this interview will go into your Tenofovir Microbicide Trial record or be shown to the counselors or nurses in the Tenofovir Microbicide Trial.

You will not be personally identified in any publication about this study. However, your records may be reviewed by the University of KwaZulu-Natal Biomedical Research Ethics Committee, FHI Protection of Human Subjects Committee, study monitors, and

study sponsors. These agencies are government or sponsor appointed regulatory oversight or monitoring bodies. They are responsible for ensuring that this study follows the study protocol and international and local guidelines for doing research with people.

**PROBLEMS OR QUESTIONS**

If you ever have any questions about the your participation in this study you should contact Mr. Francois van Loggerenberg or Professor Q Abdool Karim at 031-260 4550, CAPRISA, Second Floor Doris Duke Medical Research Institute, Durban or Dr Janet Frohlich at 031-260 6851, CAPRISA Vulindlela Clinical Research Site, Mafakathini or Dr Ayesha Kharsany at 031-260 4558 at the eThekwini Site. If you have questions about your rights as a research participant, you should contact Chairperson of the Biomedical Research Ethics Committee of the University of KwaZulu-Natal at 031-260 4604/4495 in Durban or David Borasky at FHI in the USA at +091-919-544-7040 ext. 295.

**SIGNATURE:**

If you have read the informed consent (or if you have had it read to you) and understand the information, and you voluntarily agree to join this study, and have your interview tape recorded, please sign your name below.

Volunteer's name (print)	Volunteer's signature	Date
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Name of staff member who administered consent (print)	Staff member's signature	Date
-------------------------------------------------------	--------------------------	------

Witness' name (print)	Witness' signature	Date
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If the volunteer cannot read, this form must be read to the volunteer exactly as written, in the volunteer's native language, and a witness must sign this form to confirm that the correct information was given to the volunteer and that the volunteer freely consents to be in this study and have their interview tape recorded.

**CAPRISA 104**  
**Microbicide Case Control Study: Formative Research Focus Group**

**Version 1.0**  
**27 September 2007**

**INFORMED CONSENT FORM FOR ENROLMENT**

**PRINCIPAL INVESTIGATORS:**

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2nd Floor Doris Duke Medical Research Institute  
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Dr. Kathleen MacQueen  
Family Health International  
PO Box 13950  
Research Triangle Park, NC 27709  
USA  
PHONE: 919-544-7040 ext 587

**Introduction**

You are being asked to volunteer in the research study named above. The purpose of this research study is to understand how women in the Tenofovir Microbicide Trial are using the study gel. We want to understand what makes it easy or hard to use the study gel. This Case Control formative research study is for people who live in the areas where the Tenofovir Microbicide Trial is being done and for women participating in the gel study. It is being conducted jointly by the Center for the AIDS Programme of Research in South Africa (CAPRISA) and Family Health International (FHI) in the USA.

**Your participation is voluntary**

In order to be sure that you are informed about being in this research, we are asking you to read (or have read to you) this Consent Form in the language of your choice. You will be asked to sign this Consent Form (or make your mark in front of a witness). If you decide to participate, we will give you a copy of this form to keep.

This Consent Form might contain some words that are unfamiliar to you. Please ask us to explain anything you may not understand. Before you learn about the study, it is important that you know the following:

- o Your participation is entirely voluntary.
- o You may decide not to take part or to withdraw from the study at any time. You will not lose the benefits of your routine medical care at this site.
- o If you decide to not take part in this research study, you can still take part in another research study, if one is available and you meet the study requirements.

**PURPOSE OF THE STUDY**

The purpose of the Case Control formative research study is to find the most respectful way to ask women to be in the Case Control study. We also want to make sure that the questions we ask in the Case Control study are clear and easy to understand. About 50 people from Vulindlela and Durban will take part in this formative research study.

## **PROCEDURES**

If you agree to take part in the study, here is what you will do. You will be asked to participate in a focus group with about 10 other people. You will be asked questions about the way people in your community think about time, time-keeping, and calendars. You will be asked about how we can help women in research studies to feel comfortable talking about their sexual behavior. You will not be asked any questions about your personal sexual behavior.

The focus group will take about one and a half hours. The focus group discussion will be tape recorded so we can make an exact record of what everyone said. Your name will not be written on the tape and we will destroy the tape when the research is completed. Some of your responses will also be recorded on paper; your name will not be written on the paper.

If you are a Tenofovir Microbicide Trial participant, none of the information you tell us during this focus group will go into your Tenofovir Microbicide Trial record or be shown to the counselors or nurses in the Tenofovir Microbicide Trial. Your Tenofovir Microbicide Trial study number will not be written on the tape or interview papers. The people who will conduct the focus group for this Case Control study are not counselors or nurses for the Tenofovir Microbicide Trial. They do not know what is in your Tenofovir Microbicide Trial file and are not allowed to look in your file. They do not know the results of any of your HIV tests.

## **RISKS AND/OR DISCOMFORTS**

You may become embarrassed, worried, or anxious when talking about sexual practices. You do not have to answer any questions that make you uncomfortable or you don't want to answer. You may leave the focus group at any time for any reason.

We will make every effort to protect your confidentiality, but other people in the group will hear what you have to say and might tell others about it. We will ask all participants to not tell others about what they hear in the focus group.

The focus group will take place in private. However, it is possible that others may learn of your participation in this study, and think that you are infected with HIV, or at "high risk" for HIV. Because of this, others may treat you unfairly or discriminate against you. For example, you could have problems getting or keeping a job. You also could have problems being accepted by your family or community.

## **BENEFITS**

You may get no direct benefit from being in this study. But you may get some personal satisfaction from being part of a research study on HIV prevention. You or others may benefit in the future from information learned in this study.

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

You may be removed from the study without your consent for the following reasons:

- o The investigator decides that continuing in the study would be harmful to you.
- o The study is cancelled by the Ethics Committee.
- o Other administrative reasons.

### **COSTS TO YOU**

There is no cost to you for taking part in this study.

### **COMPENSATION**

You will be compensated R100-00 for your time.

### **CONFIDENTIALITY**

If, in the course of this study, we find you are encountering harm, require medical or non-medical care, or are posing a risk/harm to others, we may be obliged to share this information with relevant authorities. Otherwise all information you share with us will be kept confidential.

You will be identified by a unique code. Personal information from your records will not be released without your written permission. We will not write your name on the audiotape used to record the focus group or on anything else that might let someone know what you said. We will make a written record from the audiotape but we will not write down any information that might identify you or others. For example, if you mention the names of family or friends we will not write those names down. The interview tapes and notes will be stored in a locked cabinet and only the staff working on this research will be able to use them. We will destroy the tapes when the research is completed.

None of the information you tell us as part of this interview will go into your Tenofovir Microbicide Trial record or be shown to the counselors or nurses in the Tenofovir Microbicide Trial.

You will not be personally identified in any publication about this study. However, your records may be reviewed by the University of KwaZulu-Natal Biomedical Research Ethics Committee, FHI Protection of Human Subjects Committee, study monitors, and study sponsors. These agencies are government or sponsor appointed regulatory oversight or monitoring bodies. They are responsible for ensuring that this study follows the study protocol and international and local guidelines for doing research with people.

### **PROBLEMS OR QUESTIONS**

If you ever have any questions about your participation in this study you should contact Mr. Francois van Loggerenberg or Professor Q Abdool Karim at 031-260 4550, CAPRISA, Second Floor Doris Duke Medical Research Institute, Durban or Dr Janet Frohlich at 031-260 6851, CAPRISA Vulindlela Clinical Research Site, Mafakathini or Dr Ayesha Kharsany at 031-260 4558 at the eThekweni Site. If you have questions about your rights as a research participant, you should contact Chairperson of the Biomedical

Research Ethics Committee of the University of KwaZulu-Natal at 031-260 4604/4495 in Durban or David Borasky at FHI in the USA at +091-919-544-7040 ext. 295.

**SIGNATURE:**

If you have read the informed consent (or if you have had it read to you) and understand the information, and you voluntarily agree to join this study, and have your interview tape recorded, please sign your name below.

Volunteer's name (print)	Volunteer's signature	Date
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Name of staff member who administered consent (print)	Staff member's signature	Date
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Witness' name (print)	Witness' signature	Date
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If the volunteer cannot read, this form must be read to the volunteer exactly as written, in the volunteer's native language, and a witness must sign this form to confirm that the correct information was given to the volunteer and that the volunteer freely consents to be in this study and have their interview tape recorded.

**CAPRISA 104**  
**Microbicide Case Control Study: Formative Research Interview**

**Version 1.0**  
**27 September 2007**

**INFORMED CONSENT FORM FOR ENROLMENT**

**PRINCIPAL INVESTIGATORS:**

Mr. Francois van Loggerenberg  
Professor Quarraisha Abdool Karim  
2nd Floor Doris Duke Medical Research Institute  
Nelson R Mandela School of Medicine  
Private Bag 7, Congella 4013  
Durban, South Africa  
PHONE: 031-260 4550

Dr. Kathleen MacQueen  
Family Health International  
PO Box 13950  
Research Triangle Park, NC 27709  
USA  
PHONE: 919-544-7040 ext 587

**Introduction**

You are being asked to volunteer in the research study named above. The purpose of this formative research study is to understand how women in the Tenofovir Microbicide Trial are using the study gel. We want to understand what makes it easy or hard to use the study gel. This Microbicide Case Control formative research study is for people who live in the areas where the Tenofovir Microbicide Trial is being done and for women participating in the Tenofovir Microbicide Trial. It is being conducted jointly by the Center for the AIDS Programme of Research in South Africa (CAPRISA) and Family Health International (FHI) in the USA.

**Your participation is voluntary**

In order to be sure that you are informed about being in this research, we are asking you to read (or have read to you) this Consent Form in the language of your choice. You will be asked to sign this Consent Form (or make your mark in front of a witness). If you decide to participate, we will give you a copy of this form to keep.

This Consent Form might contain some words that are unfamiliar to you. Please ask us to explain anything you may not understand. Before you learn about the study, it is important that you know the following:

- o Your participation is entirely voluntary.
- o You may decide not to take part or to withdraw from the study at any time. You will not lose the benefits of your routine medical care at this site.
- o If you decide to not take part in this research study, you can still take part in another research study, if one is available and you meet the study requirements.

**PURPOSE OF THE STUDY**

The purpose of the Microbicide Case Control formative research study is to find the most respectful way to ask women to be in the Case Control study. We also want to make sure that the questions we ask in the Microbicide Case Control study are clear and easy to

understand. About 50 people from Vulindlela and Durban will take part in this formative research study.

## **PROCEDURES**

If you agree to take part in the study, here is what you will do. You will be asked to participate in an interview. You will be asked questions about your experience with HIV counseling and testing. Some questions will be about what it is like to wait for HIV test results. We will also ask questions about how people think and feel after they are told their test results. Some of the people we will interview have provided HIV counseling and testing to others. Some of the people will have had HIV counseling and testing done for them.

The interview will take about an hour. The interview will be tape recorded so we can make an exact record of what you said. Your name will not be written on the tape and we will destroy the tape when the research is completed. Some of your responses will also be recorded on paper; your name will not be written on the paper.

## **RISKS AND/OR DISCOMFORTS**

You may become worried or anxious when talking about your experience with HIV counseling and testing. You do not have to answer any questions that make you uncomfortable or you don't want to answer.

We will make every effort to protect your privacy and confidentiality while you are in this study. Your interview here will take place in private. However, it is possible that others may learn of your participation in this study, and think that you are infected with HIV, or at "high risk" for HIV. Because of this, others may treat you unfairly or discriminate against you. For example, you could have problems getting or keeping a job. You also could have problems being accepted by your family or community.

## **BENEFITS**

You may get no direct benefit from being in this study. But you may get some personal satisfaction from being part of a research study on HIV prevention. You or others may benefit in the future from information learned in this study.

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

You may be removed from the study without your consent for the following reasons:

- o The investigator decides that continuing in the study would be harmful to you.
- o The study is cancelled by the Ethics Committee.
- o Other administrative reasons.

## **COSTS TO YOU**

There is no cost to you for taking part in this study.

## **COMPENSATION**

You will be compensated R100-00 for your time.

**CONFIDENTIALITY**

If, in the course of this study, we find you are encountering harm, require medical or non-medical care, or are posing a risk/harm to others, we may be obliged to share this information with relevant authorities. Otherwise all information you share with us will be kept confidential.

You will be identified by a unique code. Personal information from your records will not be released without your written permission. We will not write your name on the audiotape used to record your interview or on anything else that might let someone know what you said. We will make a written record from the audiotape but we will not write down any information that might identify you or others. For example, if you mention the names of family or friends we will not write those names down. The interview tapes and notes will be stored in a locked cabinet and only the staff working on this research will be able to use them. We will destroy the tapes when the research is completed.

You will not be personally identified in any publication about this study. However, your records may be reviewed by the University of KwaZulu-Natal Biomedical Research Ethics Committee, FHI Protection of Human Subjects Committee, study monitors, and study sponsors. These agencies are government or sponsor appointed regulatory oversight or monitoring bodies. They are responsible for ensuring that this study follows the study protocol and international and local guidelines for doing research with people.

**PROBLEMS OR QUESTIONS**

If you ever have any questions about the your participation in this study you should contact Mr. Francois van Loggerenberg or Professor Q Abdool Karim at 031-260 4550, CAPRISA, Second Floor Doris Duke Medical Research Institute, Durban or Dr Janet Frohlich at 031-260 6851, CAPRISA Vulindlela Clinical Research Site, Mafakathini or Dr Ayesha Kharsany at 031-260 4558 at the eThekwinini Site. If you have questions about your rights as a research participant, you should contact Chairperson of the Biomedical Research Ethics Committee of the University of KwaZulu-Natal at 031-260 4604/4495 in Durban or David Borasky at FHI in the USA at +091-919-544-7040 ext. 295.

**SIGNATURE:**

If you have read the informed consent (or if you have had it read to you) and understand the information, and you voluntarily agree to join this study, and have your interview tape recorded, please sign your name below.

\_\_\_\_\_  
Volunteer's name (print)      Volunteer's signature      Date

Name of staff member who administered consent (print)	Staff member's signature	Date
-------------------------------------------------------	--------------------------	------

Witness' name (print)	Witness' signature	Date
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If the volunteer cannot read, this form must be read to the volunteer exactly as written, in the volunteer's native language, and a witness must sign this form to confirm that the correct information was given to the volunteer and that the volunteer freely consents to be in this study and have their interview tape recorded.

## **CAPRISA 104**

### **Microbicide Case Control Study: Formative Research Pilot Recruitment Interview Version 1.0**

**27 September 2007**

## **INFORMED CONSENT FORM FOR ENROLMENT**

### **PRINCIPAL INVESTIGATORS:**

Mr. Francois van Loggerenberg  
Professor Quarraisha Abdool Karim  
2nd Floor Doris Duke Medical Research Institute  
Nelson R Mandela School of Medicine  
Private Bag 7, Congella 4013  
Durban, South Africa  
PHONE: 031-260 4550

Dr. Kathleen MacQueen  
Family Health International  
PO Box 13950  
Research Triangle Park, NC 27709  
USA  
PHONE: 919-544-7040 ext 587

### **Introduction**

You are being asked to volunteer in the research study named above. The purpose of this formative research study is to understand how women in the Tenofovir Microbicide Trial are using the study gel. This Microbicide Case Control formative research study is for people who live in the areas where the Tenofovir Microbicide Trial is being done and for women participating in the Tenofovir Microbicide Trial. It is being conducted jointly by the Center for the AIDS Programme of Research in South Africa (CAPRISA) and Family Health International (FHI) in the USA.

### **Your participation is voluntary**

In order to be sure that you are informed about being in this research, we are asking you to read (or have read to you) this Consent Form in the language of your choice. You will be asked to sign this Consent Form (or make your mark in front of a witness). If you decide to participate, we will give you a copy of this form to keep.

This Consent Form might contain some words that are unfamiliar to you. Please ask us to explain anything you may not understand. Before you learn about the study, it is important that you know the following:

- o Your participation is entirely voluntary.
- o You may decide not to take part or to withdraw from the study at any time. You will not lose the benefits of your routine medical care at this site.
- o If you decide to not take part in this research study, you can still take part in the Tenofovir Microbicide Trial or another research study, if one is available and you meet the study requirements.

### **PURPOSE OF THE STUDY**

The purpose of this formative research study is to see if women are willing to be recruited for research while they are waiting for HIV test results. About 10 women from Vulindlela and Durban will take part in this formative research study.

## **PROCEDURES**

If you agree to take part in the study, here is what you will do. You will be asked questions about yourself such as where you are from, what you do for a living, and whether you travel. You will also be asked some questions about your feelings and thoughts in the past month and your experiences with HIV testing. The interview will take about a half hour. Your responses will also be recorded on paper; your name will not be written on the paper.

I will interview you for this study. I am not a counselor or nurse and I have not been told the results of any of your HIV tests.

## **RISKS AND/OR DISCOMFORTS**

You do not have to answer any questions that make you uncomfortable or you don't want to answer. You may become worried or anxious while you are waiting for your HIV test results. A trained counselor will be available to help you deal with any feelings or questions you have.

We will make every effort to protect your privacy and confidentiality while you are in this study. Your interview here will take place in private. However, it is possible that others may learn of your participation in this study, and think that you are infected with HIV, or at "high risk" for HIV. Because of this, others may treat you unfairly or discriminate against you. For example, you could have problems getting or keeping a job. You also could have problems being accepted by your family or community.

## **BENEFITS**

You may get no direct benefit from being in this study. But you may get some personal satisfaction from being part of a research study on HIV prevention. You or others may benefit in the future from information learned in this study.

## **NEW FINDINGS**

At the end of the study, you will be told when the study results may be available and how to learn about them.

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

You may be removed from the study without your consent for the following reasons:

- o The investigator decides that continuing in the study would be harmful to you.
- o The study is cancelled by the Ethics Committee.
- o Other administrative reasons.

## **COSTS TO YOU**

There is no cost to you for taking part in this study.

## **COMPENSATION**

You will be compensated R100-00 for your time.

**CONFIDENTIALITY**

If, in the course of this study, we find you are encountering harm, require medical or non-medical care, or are posing a risk/harm to others, we may be obliged to share this information with relevant authorities. Otherwise all information you share with us will be kept confidential.

You will be identified by a unique code. Personal information from your records will not be released without your written permission. We will not write your name on the paper where we write your answers or on anything else that might let someone know what you said.

You will not be personally identified in any publication about this study. However, your records may be reviewed by the University of KwaZulu-Natal Biomedical Research Ethics Committee, FHI Protection of Human Subjects Committee, study monitors, and study sponsors. These agencies are government or sponsor appointed regulatory oversight or monitoring bodies. They are responsible for ensuring that this study follows the study protocol and international and local guidelines for doing research with people.

**PROBLEMS OR QUESTIONS**

If you ever have any questions about the your participation in this study you should contact Mr. Francois van Loggerenberg or Professor Quarraisha Abdool Karim at 031-260 4550, CAPRISA, Second Floor Doris Duke Medical Research Institute, Durban or Dr Janet Frohlich at 031-260 6851, CAPRISA Vulindlela Clinical Research Site, Mafakathini or Dr Ayesha Kharsany at 031-260 4558 at the eThekwini Site. If you have questions about your rights as a research participant, you should contact Chairperson of the Biomedical Research Ethics Committee of the University of KwaZulu-Natal at 031-260 4604/4495 in Durban or David Borasky at FHI in the USA at +091-919-544-7040 ext. 295.

**SIGNATURE:**

If you have read the informed consent (or if you have had it read to you) and understand the information, and you voluntarily agree to join this study, and have your interview tape recorded, please sign your name below.

Volunteer's name (print)	Volunteer's signature	Date

Name of staff member who administered consent (print)	Staff member's signature	Date

---

Witness' name (print)

Witness' signature

Date

If the volunteer cannot read, this form must be read to the volunteer exactly as written, in the volunteer's native language, and a witness must sign this form to confirm that the correct information was given to the volunteer and that the volunteer freely consents to be in this study and have their interview tape recorded.