



CENTRE FOR THE AIDS PROGRAMME OF RESEARCH  
IN SOUTH AFRICA

## PROTOCOL

### HIV Incidence Rates in Vulindlela and Durban: A Prevention Preparedness Study<sup>1</sup>

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## **LIST OF ABBREVIATIONS AND ACRONYMS**

AIDS	Acquired Immunodeficiency Syndrome
BV	bacterial vaginosis
CAPRISA	Centre for the AIDS Programme of Research in South Africa
CDC	Sexually Transmitted Diseases clinic, Prince Cyril Zulu Communicable Diseases Centre
EC	ethics committee
EIA	enzyme immunoassay
HIV	Human Immunodeficiency Syndrome
HSV-2	Herpes simplex virus type 2
LDMS	Laboratory Data Management System
PCR	polymerase chain reaction
RNA	ribonucleic acid
SDA	strand displacement assay
STD	sexually transmitted disease
TB	tuberculosis
UNAIDS	Joint United Nations Programme on HIV/AIDS
WB	Western blot
WHO	World Health Organization

## **SCHEMA**

**Purpose:** To prepare for the implementation of a proposed Phase II safety and effectiveness study of the vaginal microbicide PRO 2000/5 Gel (P) (CAPRISA 052) for the prevention of HIV infection in women

**Design:** Prospective cohort study with a 12-month accrual period and 12-24 months of follow-up for each enrolled participant

**Study Population:**

Sexually active HIV uninfected women utilizing the Family Planning and Antenatal Clinics at the Vulindlela Primary Health Care Facilities and Sexually Transmitted Disease clinic attendees utilizing the Prince Cyril Zulu Communicable Diseases Center (CDC) in Durban

**Study Size:** 600 participants

**Study Duration:**

Accrual will require 12 months. Each participant will be maintained in follow-up for a minimum of 12 months and a maximum of 24 months. The duration of follow-up will depend on the timing of initiation of the proposed Phase II PRO 2000/5 microbicide trial

**Primary Objective:**

To estimate rates of HIV seroincidence among women targeted for inclusion in a proposed Phase II PRO 2000/5 microbicide trial

**Secondary Objectives:**

- i. To develop and describe the accrual process and estimate rates of accrual into a standardized HIV related research study among women targeted for inclusion in the proposed Phase II PRO 2000/5 microbicide trial
- ii. To estimate rates of retention in a standardized HIV-related research study among women targeted for inclusion in the proposed Phase II PRO 2000/5 microbicide trial
- iii. To describe the demographic characteristics and HIV risk behaviors of women targeted for inclusion in the proposed

Phase II PRO 2000/5 microbicide trial

- iv. To characterise and describe understanding of the informed consent process of women targeted for inclusion in the proposed Phase II PRO 2000/5 microbicide trial.
- v. To estimate prevalence and incidence rates of the following among women targeted for inclusion in the Phase II PRO 2000/5 microbicide trial
  - Deep cervico-vaginal epithelial disruption
  - Genital ulcer disease
  - Other genital signs and symptoms
  - Bacterial vaginosis (BV)
  - Clinical Candidiasis
  - HPV
- x. To assess the role of vaginal epithelial disruption in acquisition of HIV and other STIs.

Study Sites: CAPRISA Vulindlela Research Facility

Sexually Transmitted Diseases Clinic-Prince Cyril Zulu Communicable Diseases Centre (CDC)

# **1. INTRODUCTION**

## **1.1. Background**

HIV/AIDS continues to exact a devastating toll on the health, economic and political infrastructure, and social fabric of communities worldwide. The Joint United Nations Programme on HIV/AIDS (UNAIDS) estimates that 40 million adults and children were living with HIV/AIDS at the end of 2001, and that about 14,000 new infections are occurring each day. Over 95 percent of new infections are occurring in developing countries where there is little access to the treatments that have prolonged life in industrialized countries.

It has been stated that a safe and effective vaccine remains the best hope for ending the HIV/AIDS pandemic, however the timeline for developing and making available a safe and effective HIV/AIDS vaccine to communities affected by the pandemic remains unclear. While the search for an HIV/AIDS vaccine continues, additional research must be conducted to develop and test non-vaccine strategies to prevent the spread of HIV.

Microbicides, represent one such strategy. They are designed for vaginal and/or rectal use to prevent sexual transmission of HIV.

## **1.2. HIV Infection in South Africa**

South Africa is experiencing one of the largest and fastest growing HIV epidemics in Sub-Saharan Africa and the world (UNAIDS, 2001). About 5.3 million people are living with HIV/AIDS in South Africa (Department of Health, Republic of South Africa, 2002). There are many factors that contribute to the unprecedented, explosive spread of HIV in South Africa. The economically motivated population migration with its associated disruption of conjugal stability and family units is a key factor driving the epidemic in Southern Africa (Lurie et al, 1997). During the first six months of 2000, approximately 320,000 South Africans were infected, contributing to half of all new infections in sub-Saharan Africa (UNAIDS, 2001). Sixty percent of all infected adults acquire their infection before age 25, and young women between the ages of 20-24 years have the highest HIV prevalence and incidence rates (Abdool Karim et al, 1999). HIV prevalence among antenatal clinic



attendees in one rural district of the KwaZulu-Natal province increased from 4.2% in 1992 to 34.0% in 1999 (Wilkinson et al, 1999).

A cross-sectional survey (Colvin et al, 2001) of HIV prevalence and AIDS related diseases of 507 patients in the medical wards at King Edward VIII hospital in Durban demonstrated that HIV positive individuals occupied 54% of the beds, 84% of whom met the WHO AIDS case criteria. Patients with HIV infection were significantly younger than the uninfected (34.9 vs 47.1), had a higher risk of oral candidiasis (RR=18.6), generalized lymphadenopathy (RR=7.1), unexplained fever (RR =7), chronic diarrhoea (RR=6.2) and pulmonary TB (RR=3.2). Fifty six per cent of those with HIV presented with TB, which was also present in 59% of the deaths. The case fatality rate in HIV infected patients was 22% compared to 9% in the uninfected group.

### **1.3.HIV infection in Vulindlela**

#### **1.3.1. The Vulindlela community**

Vulindlela, is a rural community with approximately 400,000 residents in the Natal midlands, about 150 km west of Durban. Since 1996 there have been several initiatives to improve the living conditions in the area through development of roads and other services. Many residents have access to water and electricity.

Vulindlela is under the authority of two tribal chiefs, and is administered through both tribal and democratically elected structures. There are several organizations in the area representing a variety of civic interests such as youth, women, religion, politics, and housing.

Employment opportunities exist within Vulindlela through extensive forestry projects. In addition, men seek employment in Pietermaritzburg, Howick or neighboring cities. These men usually live in the city during the week and return home over the weekend. Women are also employed by the forestry projects and engage in communal income generating activities such as gardening and sewing to a more limited extent. There are 12 primary schools and four high schools in the area and school attendance is high for both boys and girls.

Primary Health Care services are provided through seven clinics in the district. These are nurse-managed services that provide care for antenatal, family

planning, childhood immunization, sexually transmitted infection, minor ailments, tuberculosis and VCT. The closest referral hospitals are Grey's and Edendale that are about twenty minutes away.

### **1.3.2. Community Participation in Research**

The presence of the research team in this community is by invitation by the two traditional chiefs, Nkosi Sondelani Zondi and Nkosi Nsikayezwe Zondi, motivated by their growing concern about the unfolding AIDS epidemic in Vulindlela and to complement their current efforts in the community. The community-based organizations are also actively involved in addressing the challenges being posed by the HIV epidemic to their constituencies. The partnership between the community and researchers is growing. Several consultative meetings have been held with key stakeholders in this community and feedback has been provided on the research that has been completed to date. A formal mechanism for interacting with key stakeholders including health service providers, traditional leaders and community structures has been established in the form of a Community Advisory Board.

### **1.3.3. CAPRISA Research Facility in Vulindlela**

The CAPRISA research facility in Vulindlela adjoins the Mafakathini Primary Care Clinic, with a shared entrance, security and waiting area. The research facility has four clinical examination rooms with offices for nurses/clinicians, three counselling rooms, a training/meeting room, a laboratory and specimen preparation room, four offices, a dispensary, archives/record rooms, and a reception area and is equipped to undertake studies at good clinical practice (GCP) standards. It has Internet connectivity and full Information Technology (IT) support from the University of Natal, Pietermaritzburg. Transport systems to get specimens from Vulindlela to the laboratories in Durban are in place. These facilities are equipped with computers, telephones and a fax machine.

### **1.3.4. HIV infection in Vulindlela**

#### **1.3.4.1 Antenatal HIV surveys**

Three anonymous, HIV sero-surveys have been conducted among first-visit antenatal clinic attendees utilizing the seven primary health care clinics in

Vulindlela from 2001-2002. The prevalence of HIV infection has increased from 26% in May-June 2001 to 34% in September-October 2002. The age-specific prevalence for the most recent survey is presented in Table 1. Of significance is that 39% of the ANC attendees were younger than 19 years with the youngest being 12 years of age and the HIV prevalence in this age group was an alarming 25.8%.

**Table 1: Age-specific prevalence of HIV infection amongst antenatal clinic attendees in Vulindlela – 2002**

<b>Age (years)</b>	<b>N</b>	<b>Prevalence (%) (95% CI)</b>
≤ 19	159	25.8 (19.0 – 32.6)
20–24	107	45.8 (36.4 – 55.2)
25–29	84	42.9 (32.3 – 35.8)
30– 4	36	22.2 (8.6 – 35.8)
≥ 35	23	26.1 (8.1 – 44.0)
Total	409	34.1

#### **1.3.4.2. Family Planning HIV survey**

During September to November 2002, family planning clinic (FPC) attendees were offered HIV testing in the context of pre- and post-test counselling at two primary care clinics in Vulindlela. There was a 92% uptake of HIV testing. The overall prevalence of HIV infections was 45.5% in this group. HIV prevalence by age is presented in Table 2. About a third of the Family Planning Clinic users are under 20 years of age and about one in four are already infected with HIV.

**Table 2: Age-specific prevalence of HIV infection amongst select family planning clinic attendees in Vulindlela - 2002**

Age (years)	N	Prevalence (%) (95% CI)
≤ 19	80	27.5 (17.7 - 37.3)
20-24	86	54.7 (44.1 - 65.2)
25-29	65	58.5 (46.5 – 70.4)
30-34	29	44.8 (26.7 – 62.9)
≥ 35	17	11.8 (2.4 – 41.8)
Total	277	45.5

#### **1.3.4.3. Aetiology of STIs in Vulindlela**

During September to November 2002 a preliminary survey of the aetiological distribution of sexually transmitted infections (STIs) among women utilizing two Vulindlela primary health care clinics for ANC, family planning or STI services was assessed among consenting clinic users. The uptake of STI screening was 92%. A total of 272 women were recruited into the pilot study as follows: 224 family planning clients; and 48 antenatal clinic attendees. Vulvo-vaginal swabs were collected for screening for *Neisseriae gonorrhoea*, *Chlamydia trachomatis* and *Trichomonas vaginalis* using DNA amplification methods and Nugents gram staining method for the diagnosis of bacterial vaginosis. A specimen of peripheral blood was collected for syphilis testing using the RPR card test and TPHA tests.

The prevalence of genital tract infections amongst both the ANC and FPC group of women was high, with about 60% of these clinic attendees having least one infection, and 17.9% and 14.5% from the family planning and antenatal clinics respectively having two recognized infections present. The prevalence of selected STIs is presented in Table 3.

**Table 3: Aetiology of STIs amongst select antenatal and family planning clinic attendees in Vulindlela –2002**

	Antenatal Clinic (N=48)	Family Planning Clinic (N=224)
I	Prevalence(%)	Prevalence (%)
Bacterial vaginosis	46.3	58.8
<i>Trichomonas vaginalis</i>	22.2	24.3
<i>Neisseriae gonorrhoeae</i>	4.2	6.7
<i>Chlamydia trachomatis</i>	8.3	8.9
<i>Treponema pallidum</i>	2.6	2.3

#### 1.3.4.4. AIDS related mortality in Vulindlela

In Vulindlela, as in many rural communities in South Africa, no accurate mortality statistics exist. As the HIV/AIDS epidemic matures in Kwazulu-Natal there are reports of increasing morbidity and mortality. In September 2002, a cross-sectional study was undertaken in the Mafakathini ward of Vulindlela to explore the feasibility of establishing AIDS-related mortality in this community. All households where a death had occurred in the previous 3 months were visited and interviewed using a semi-structured questionnaire that included items such as demographic details of deceased, cause of death. If death resulted from illness, signs and symptoms and duration of illness were obtained. Community Health workers and traditional leaders in the area were also interviewed using the same instrument. A total of 89 deaths had occurred. A random sample of 30 households where deaths had occurred during this period were visited. The verbal autopsy identified that 23 of deaths in the 30 households could possibly be AIDS-related. In terms of gender breakdown of the possible AIDS related deaths, 15 were female and 8 male and all were under the age of 40 years. Pulmonary TB was the most common reported cause of death (11 cases). Fever, cough, loss of weight, painful feet and oral thrush were other frequently mentioned symptoms. There was a 100% correlation on cause of death between Community Health workers and Heads of Households.

The high HIV prevalence, in Vulindlela, together with the high burden of other STI's makes Vulindlela an ideal study population for Phase III HIV prevention

and treatment trials and to assess the impact of the introduction of new HIV/AIDS interventions and programmes.

### **1.3. (b) Prince Cyril Zulu Communicable Diseases Centre**

The clinic is situated in the Warwick triangle in the metropolitan region of Durban . This triangle is the nucleus of the public transportation with the central bus, “minibus” taxi station and rail station all within 500 meter radius of the clinic building. This clinic is readily accessible in terms of the transport infrastructure rather than the clinics located in the area of residence. The clinic is designated for the diagnosis and treatment of STDs and provides free treatment, Voluntary counseling and testing for HIV, HIV testing and free male condoms predominantly to the local indigent Black population. Majority of 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 sexually transmitted infection. Surveillance studies conducted at the clinic has shown that trichomoniasis (15%), gonorrhoeae (26%) and chlamydial infections (18%) are the commonest causes of discharge syndrome among women. Mixed infections with all three infections are equally high and the prevalence of HIV infections was 61%. These studies clearly show that women attending this clinic are most vulnerable for HIV infection. It is proposed that HIV negative STD clinic attenders who are at high risk of acquiring HIV infection will participate in the HIV / STI seroincidence study (CAPRISA 050) and form a potential cohort for future microbicide studies (CAPRISA 052).

#### **1.3.1(b) HIV infection at CDC**

Over a three week period approximately 800 STI clients attended the clinic either as patients with symptoms or as contact of patients diagnosed with an STD. On a daily basis a health educator informed the clients of the benefits of an HIV test and due to the limited number of counselors available, 87 clients could be counseled over this period. Of these 69 (79%) were tested. The median age of those tested was 26 years. Forty nine (56%) were attending the clinic for the first time whilst 39

clients attended for a repeat visit. Of those agreeing for an HIV test 45 (65%) tested HIV positive and 23 (33%) tested negative. Only one client refused testing after counseling

#### 1.4. Rationale

Previous prevention trial planning efforts have indicated that Phase II/III studies of HIV prevention interventions will require the participation of large numbers (several hundred to several thousands) of persons at high risk for HIV infection. In addition to accruing large numbers of participants, research sites conducting Phase III HIV prevention studies must retain participants in extended periods of follow-up — from several months to several years — in order to preserve the statistical power of the study as well as avoid potentially biased results that may not accurately reflect the impact of the intervention in the target population.

The design of Phase II/III HIV prevention trials will depend on the efficacy or effectiveness of the intervention being studied as well as the interplay of the four parameters referred to above ie the number of participants enrolled, the HIV incidence rate among enrollees, the duration of follow-up, and the number of participants retained in follow-up. The potential impact of these parameters is illustrated in the table below, which present the number of study participants required to adequately power a two-arm placebo controlled phase III HIV prevention study assuming various levels of intervention efficacy (E), annual HIV incidence rates (I), durations of participant follow-up (D), and semiannual retention rates (R).

**Table 4: Sample size calculation based on intervention efficacy, annual HIV incidence rates, duration of participant follow-up and semi-annual retention rates**

		R=85%								
		I=2%			I=5%			I=8%		
		D=12	D=18	D=24	D=12	D=18	D=24	D=12	D=18	D=24
E=25%	S=515	34,604	25,020	20,287	14,016	10,191	8307	8869	6485	5314
E=50%	S=95	7408	5354	4340	2996	2177	1772	1894	1382	1131

E=75%	S=29	2742	1981	1605	1108	804	654	700	510	417
E=90%	S=16	1675	1210	981	677	491	400	427	311	254

S=number of seroconversions observed. Power=90% , Type 1 error=5%

As indicated above, dramatically different study designs may be required depending on the ability of the site to recruit study participants and the rate of HIV incidence observed in study populations. As such, in order to realistically plan for future Phase II/III studies, information must be obtained to characterize these parameters at sites. Sites also need to develop strategies to achieve high rates of participant retention throughout the duration of a prospective study.

The proposed Phase II trial of Pro2000/5 Gel (CAPRISA 052) has been designed to determine whether it is at least 33 percent effective in preventing HIV infection. In order to determine effectiveness within a period of two years, this trial will need to accrue 600 women at high risk for HIV infection within 12 months. The study also requires high rates of participant retention for 12-24 months of follow-up and an average HIV sero-incidence rate of 5-6 percent among enrolled participants.

This would require the sites designated to conduct CAPRISA 052 to have established effective standard operating procedures to recruit and retain high-risk populations in research studies, and have characterized HIV incidence rates in these populations. This HIV incidence study for HIV Prevention Preparedness serves this purpose.

## **2. STUDY OBJECTIVES**

### **2.1. Primary Objective**

The primary objective of this study is to estimate rates of HIV sero-incidence among women targeted for inclusion in the proposed CAPRISA 052 trial.

### **2.2. Secondary Objectives**

The secondary objectives of this study are to:

- i. Develop and describe the accrual process and estimate rates of accrual into a standardized HIV-related research study among women targeted for inclusion in the proposed CAPRISA 052 trial.
- ii. Estimate rates of retention in a standardized HIV-related research



study among women targeted for inclusion in the proposed CAPRISA 052 trial.

- iii. Describe the demographic characteristics and HIV risk behaviors of women targeted for inclusion in the proposed CAPRISA 052 trial.
- iv. To characterise and describe understanding of the informed consent process of women targeted for inclusion in the proposed Phase II PRO 2000/5 microbicide trial.
- v. Estimate prevalence and incidence rates of the following among women targeted for inclusion in the proposed CAPRISA 052 trial
  - Deep cervico-vaginal epithelial disruption
  - Genital ulcer disease
  - Other genital signs and symptoms
  - Bacterial vaginosis (BV)
  - Clinical Candidiasis
  - HPV
- vi. To assess the role of vaginal epithelial disruption in acquisition of HIV and other STIs.

### **3. STUDY DESIGN**

#### **3.1. Overview of the Study Design**

This is a prospective cohort study to be conducted at the CAPRISA Vulindlela Research Facility and at the STD clinic. Prince Cyril Zulu Communicable Disease Centre (CDC). The study design and visit/procedures schedule are summarized in the Schema and in Appendix I. All procedures are consistent with those specified for implementation in the proposed CAPRISA 052 trial.

The study site will target enrollment of 600 study participants over the course of a ~~twelve-~~ twenty four month accrual period, according to the following schedule of monthly enrollment targets:

Study month 1:	20 participants
Study month 2:	30 participants
Study month 3:	25 participants
Study month 4:	25 participants
Study month 5:	25 participants
Study month 6:	25 participants

Study month 7:	25 participants
Study month 8:	25 participants
Study month 9:	25 participants
Study month 10:	25 participants
Study month 11:	25 participants
Study month 12:	25 participants.
Study month 13:	25 participants.
Study month 14:	25 participants.
Study month 15:	25 participants.
Study month 16:	25 participants.
Study month 17:	25 participants.
Study month 18:	25 participants.
Study month 19:	25 participants.
Study month 20:	25 participants.
Study month 21:	25 participants.
Study month 22:	25 participants.
Study month 23:	25 participants.
Study month 24:	25 participants.

The study follow-up period then will extend for at least twelve months, and up to a maximum of 24 months, from the end of the accrual period. It is expected that the study site will be activated to implement CAPRISA 052 by the end of the 12-month follow-up period, ~~however if this is not the case, the follow-up period may be extended for up to another 12 months, pending activation of CAPRISA 052.~~ Possible reasons for a delay in activation of CAPRISA 052 include delays in finalizing the CAPRISA 052 protocol and implementation plans, delays in manufacturing and packaging the investigational product for CAPRISA 052, delays in obtaining ethical review and approval of the CAPRISA 052 protocol, and indication based on performance in this study that additional preparedness work is required prior to transitioning to CAPRISA 052. Upon activation of CAPRISA 052, this study will be terminated and participants will be invited to screen for CAPRISA 052.

As described more fully in Section 3.3, potential study participants will be screened for eligibility and enrolled in the study over the course of up to 30 days, and over the course of at least one Screening Visit and one Enrollment Visit.

Enrolled participants then will complete monthly follow-up assessments throughout the duration of their participation. At each visit, participants will

complete an interval medical/menstrual history and undergo pregnancy testing. Participants will receive HIV/STD pre-test, risk reduction, and post-test counseling. Sexually transmitted disease (STD) risk-reduction counseling messages will be reinforced as needed and condoms and other prevention supplies will be distributed. Participants who have symptoms and/or signs of STIs will be treated syndromically in accordance with the National Department of Health Guidelines.

Further, each quarter, participants will undergo a structured interview to ascertain HIV risk behaviors. Participants will also undergo pelvic exams. Vulvo-vaginal swabs will be collected for HPV.

If genital symptoms are found during an unscheduled visit, the participant will be instructed to report to the CAPRISA Research Facility as soon as possible for a pelvic exam. Other participant-initiated interim visits may occur at any time during follow-up, for example to obtain additional HIV counseling and testing.

All HIV and STD testing will be performed in the context of pre-test, risk-reduction and post-test counseling. This counseling will be provided in accordance with accepted standards of practice as outlined by the Department of Health counseling policies and procedures and documented prior to study implementation for purposes of staff training, quality assurance, and study monitoring. In accordance with CAPRISA policies, study participants must receive their HIV test results in order to remain eligible for study participation.

Participants who test HIV antibody negative will have a qualitative PCR performed. Participants who test HIV positive on screening will be counseled and referred to other sources of support and/care including the CAPPRISA AIDS Treatment Project in Vulindlela and Durban. Participants who are found to have an STD or other reproductive tract infection will be provided counseling, treatment, and follow-up care in accordance with Department of Health guidelines for STI management, free-of-charge. Such participants will be encouraged to refer their partners for STD diagnosis and treatment if applicable. Participants who become pregnant during the study will be maintained in follow-up until the initiation of CAPRISA 052. Participants who become infected with HIV will be counseled and have the option of remaining in this study or referred to the CAPRISA Acute

Infection Study and available sources of medical and psychosocial care and support, as well as to any other available research studies for HIV-infected persons.

### **3.2. Study Population**

This study will be conducted at the Vulindlela Research Facility and at the STD Clinic Prince Cyril Zulu Communicable Disease Centre (CDC), among women who meet the eligibility criteria listed in Sections 3.1, 3.2, and 3.4 below.

Participants will be screened and enrolled in the study as described in Section 3.3. Information related to participant retention and withdrawal from the study is provided in Sections 3.5 and 3.6, respectively.

### **3.3. Inclusion Criteria**

Women who meet all of the following criteria are eligible for inclusion in this study:

- \* Able to provide independent informed consent per National Ethics guidelines
- \* Between the ages of 14 – 30 years  
In order to accrue a study population at highest risk of HIV infection, the upper and lower age limit for participants is based on available information about the epidemiology of HIV infection in Vulindlela and among STD clients at the Prince Cyril Zulu Communicable Disease Centre (CDC).
- \* Able and willing to provide written informed consent to be screened for, and to take part in the study.
- \* Able and willing to provide adequate locator information for study retention purposes, as defined by local standard operating procedures.
- \* Sexually active (defined as having had vaginal intercourse at least once in the three months prior to screening).
- \* HIV seronegative

### **3.4. Exclusion Criteria**

Women who meet any of the following criteria will be excluded from this study:

\* At screening:

- Plans to travel away from the study site for more than three consecutive months in the next 12 months.
- Plans to relocate away from the study site in the next 12 months.
- Plans to become pregnant in the next 12 months.

\* At screening or enrollment:

- Is enrolled in any other study of a vaginally-applied product.

\* At enrollment, has any other condition that, in the opinion of the Principal Investigator or designee, would preclude provision of informed consent, make participation in the study unsafe, complicate interpretation of study outcome data, or otherwise interfere with achieving the study objectives.

### **3.5. Screening and Enrollment Process**

Eligibility for the study will be assessed in a step-wise manner at the study Screening and Enrollment Visits. Although all required procedures may be completed in one Screening Visit and one Enrollment Visit, additional visits may be conducted if needed. For example, a participant may want more time to consider whether to participate in the study, may require treatment for an STD or other reproductive tract infection, or may not be able to undergo a pelvic exam due to menstruation. Regardless of the number of visits required, all screening and enrollment procedures will be completed within a 30-day period, beginning on the day the participant provides informed consent for screening. If a participant is not enrolled within 30 days after providing informed consent for screening, the screening process will be repeated.

After providing written informed consent for screening, potential study participants will be assigned an ID number and asked to provide demographic information, behavioral eligibility information, and locator information. They will undergo urine pregnancy testing and HIV and STD counseling and testing. Presumptively eligible participants will be scheduled to return for their Enrollment Visits approximately 7-14 days later, when all screening test results are expected

to be available.

For study screening purposes HIV infection status will be ascertained using two different rapid antibody assays; in the event that results from the two tests are discordant, a third test will be performed (either an Enzyme Linked Immunosorbent Assay (EIA) and/or qualitative Polymerase Chain Reaction test to detect presence of HIV). Once a participant has enrolled in the study, follow-up HIV testing will be performed according to the algorithm in Appendix II.

At their Enrollment Visits, potential participants will be informed of their screening test results, in the context of post-test counseling, and again undergo testing for pregnancy. Those who test negative will undergo a pelvic exam with Pap smears including HPV typing will be performed and appropriate follow-up care to participants with abnormal results will be provided as per the Department of Health guidelines.

Potential participants diagnosed with infection(s) requiring treatment per Department of Health guidelines will be offered treatment and enrolled in the study provided they meet all other eligibility criteria.

Similarly, potential participants with pelvic exam findings involving deep epithelial disruption observed on pelvic exam at the Enrollment Visit will be enrolled, provided that they meet all other eligibility criteria.

Women who meet all the study eligibility criteria will be asked to provide written informed consent to take part in the study. Those who provide informed consent will be enrolled and scheduled for their first three follow-up assessments. They will complete a baseline behavioral risk assessment and will be given instructions to contact study staff to ask questions about the study, report STD symptoms, and/or request additional HIV/STD counseling and testing between scheduled visits.

### **3.6. Co-Enrollment Guidelines**

Participants in this study may not take part in other concurrent research studies, except for the following:

- Participants in this study may take part in microbicide acceptability studies (not involving application of vaginal products) and other

ancillary studies approved by the Principal Investigator.

- Participants who become infected with HIV and who wish to remain in this study may continue in this study and take part in HIV natural history studies or HIV treatment trials.

### **3.7. Participant Retention**

Once a participant enrolls in this study, the study site will make every effort to retain her in follow-up to minimize possible bias associated with loss-to-follow-up. Participant retention procedures will be established such that loss-to-follow-up rates do not exceed the 10-12 percent average annual HIV seroincidence rate expected to be observed in the control groups of CAPRISA 052. As such, annual retention rates of 90 percent are targeted. Standard operating procedures will be developed to achieve this goal. Components of such procedures include:

- \* Thorough explanation of the study visit schedule and procedural requirements during the informed consent process, and re-emphasis at each study visit.
- \* Collection of detailed locator information at the study Screening Visit, and active review and updating of this information at each subsequent visit.
- \* Use of mapping techniques to establish the location of participant residences and other locator venues.
- \* Use of appropriate and timely visit reminder mechanisms.
- \* Immediate and multifaceted follow-up on missed visits.
- \* Mobilization of trained outreach workers or “tracers” to complete in-person contact with participants at their homes and/or other community locations.
- \* Regular communication with the study community at large to increase awareness of HIV/AIDS and explain the purpose of HIV prevention research and the importance of completing research study visits.

The CAPRISA Data Management Core will provide the study site with a participant tracking database to facilitate visit scheduling and timely identification and follow-up on missed visits and will generate weekly reports on the number and

percentage of participants completing quarterly follow-up assessments. The Protocol Team as well as the CAPRISA Study Monitoring Committee will track retention rates closely and work with study site staff as needed to take any required action to address below-target retention rates.

### **3.8. Participant Withdrawal**

Regardless of the participant retention methods just described, participants may voluntarily withdraw from the study for any reason at any time. The Principal Investigator also may withdraw participants from the study in order to protect their safety and/or if they are unwilling or unable to comply with required study procedures, after consultation with the Protocol Statistician and Site Manager. Study participation may also be terminated if regulatory authorities terminate the study prior to its planned end date. Study staff will record the reason(s) for all withdrawals in participants' study records.

## **4. STUDY PROCEDURES**

See also Appendix I. Detailed instructions to guide and standardize all study procedures will be provided in the study-specific procedures manual. Unless otherwise specified, the laboratory procedures listed below are performed at the CAPRISA laboratories or the Department of Virology, University of Cape Town Microbiology, Nelson R Mandela School of Medicine.

### **4.1. Pre-Screening**

Study staff may pre-screen potential study participants either on site or at off-site locations. During these interactions, study staff may explain the study to participants and ascertain presumptive eligibility, to be confirmed at an on-site Screening Visit (see Section 4.2). Pre-screening data may be recorded and stored at the study site in the absence of written informed consent from potential participants, provided the information is collected in such a manner that it cannot be linked to participant identifiers.

### **4.2. Screening Visit (up to day -30)**

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

Written informed consent for screening will be obtained before any



screening procedures are initiated. For potential participants who do not meet the study eligibility criteria, the screening process will be discontinued when ineligibility is determined.

#### **4.2.1. Administrative, Behavioral, and Regulatory Procedures**

Informed consent for screening.

Demographic information.

Locator information.

HIV/STD counseling, condoms, other HIV prevention supplies.

Understanding of rights of research participants

#### **4.2.2. Clinical Procedures**

Urine collection.

Vulvo-vaginal specimen collection

Blood collection.

Test results disclosure.

Treatment for STD symptoms; offer of STD testing and treatment for partner(s).

#### **4.2.3. Laboratory Procedures**

Urine pregnancy test.

~~SDA for chlamydia and gonorrhea.~~

~~Gram stain for BV and candidiasis~~

~~PCR for trichomoniasis and HSV-2~~

Dipstick urinalysis if clinically indicated; urine culture if dipstick is positive for leukocytes or nitrites.

HIV serology.

### **4.3. Enrollment Visit (day 0)**

Multiple visits may be conducted to complete all required procedures if necessary. Written informed consent for study participation will be obtained before any “on-study” procedures are initiated. For potential participants whose eligibility is not confirmed at this visit, the screening and enrollment process will be discontinued when ineligibility is determined.

#### **4.3.1. Administrative, Behavioral, and Regulatory Procedures**

HIV/STD counseling, condoms, other HIV prevention supplies.

Informed consent for study.

Informed consent for specimen storage.

Locator information.

Behavioral risk assessment.

Assessment of understanding of informed consent

#### **4.3.2. Clinical Procedures**

Urine collection.

Vulvo-vaginal specimen collection

Blood collection.

Focused medical history and ascertainment of current medications.

Physical exam.

Pelvic exam with:

colposcopy

ecto- and endocervical cytobrush for Pap smear

Test results disclosure.

Treatment for STDs and other infections (except asymptomatic candidiasis), when clinically indicated; offer of STD testing and treatment for partner(s).

#### **4.3.3 Laboratory Procedures**

Urine pregnancy test.

Dipstick urinalysis if clinically indicated; urine culture if dipstick is positive for leukocytes or nitrites.

Pap smear interpretation

Plasma archive (For participants who do not consent to long-term specimen storage and possible future research testing, archived plasma will be discarded after all protocol-required and quality assurance testing has been completed (see also Section 8.3).

#### **4.4. Follow-up Visits**

Monthly follow-up visits are scheduled throughout the study follow-up period

on the monthly anniversary dates of participants' study enrollment dates. For example, for a participant enrolled on September 15, follow-up visits will be targeted to take place on October 15, November 15, December 15, etc. For participants enrolled on the last day of a month with 31 days, follow-up visits will be targeted to take place on the last day of all subsequent months (e.g., February 28, April 30, June 30, September 30, November 30). Acknowledging that it will not always be possible to complete follow-up visits on the targeted dates, visits may be completed within a two-week window around the target date (i.e.,  $\pm$  1 week from the target date).

For participants who do not complete scheduled visits within the allowable window, the visit will be considered "missed" and relevant case report forms will be completed to document the missed visit. However, for participants who miss visits scheduled to take place in study months 3, 6, 9, and 12, the pelvic exam and HIV counseling and testing procedures specified to take place at these visits will be conducted at the participants' next visit. If this is not possible, an interim on-site visit in which the pelvic exam and HIV counseling and testing procedures are performed will be conducted as soon as possible after the off-site visit.

Participants who become pregnant or infected with HIV during follow-up may be maintained in this study until the initiation of CAPRISA 052. For participants who become pregnant, follow-up procedures may be modified according to guidelines specified in the study-specific procedures manual. For example, after 24 weeks of pregnancy, quarterly pelvic exams may be discontinued and blood collection may be limited to fingersticks for HIV serology only. For participants who become infected with HIV, HIV serology will be discontinued and counseling will be tailored to primary and secondary HIV/STD prevention for infected women.

#### **4.4.1 Administrative, Behavioral, and Regulatory Procedures**

\* Ongoing informed consent:

-As needed at all visits.

\* Locator information:

-At all visits and contacts.

\* Behavioral risk assessment:

-Quarterly.

\* HIV/STD counseling, condoms, other prevention supplies:

- Monthly

-Additionally when needed/requested.

\* Assessment of understanding of informed consent process

- 6 monthly

#### **4.4.2 Clinical Procedures**

\* Interval (i.e., since last visit) medical and menstrual history and concomitant medication review:

-At all visits.

\* Pelvic exam with:

vulvo-vaginal specimen collection

-Additionally when clinically indicated.

\* Urine collection:

-At all visits.

\* Blood collection:

- Monthly

-Additionally when clinically indicated.

\* Test results disclosure:

-As needed at all visits and contacts.

\* Treatment for STDs and other infections; offer of STD testing and treatment for partner(s):

-When clinically indicated.

#### **4.4.3 Laboratory Procedures**

Urine pregnancy test:

-At all visits.

Dipstick urinalysis; urine culture if dipstick is positive for leukocytes or nitrites:

-When clinically indicated.

HIV testing:

- Monthly
- Additionally when clinically indicated.

2 rapid HIV Antibody tests

Qualitative HIV PCR on Negatives

Plasma archive:

- When phlebotomy is performed for confirmatory HIV testing (i.e. when “sample 2” in Appendix II is obtained).
- At study exit.

For participants who do not consent to long-term specimen storage and possible future research testing, archived plasma will be discarded after all protocol-required and quality assurance testing has been completed (see also Section 8.3).

#### **4.5. Interim Contacts and Visits**

Interim visits may be performed at any time during the study. Depending on the type of visit, site capacity, and site and participant preferences, interim visits may take place at the study site or at community-based locations. Interim visits may occur:

For administrative reasons, e.g., the participant may have questions for study staff or may need to re-schedule a follow-up visit. For interim STD counseling and testing in response to STD symptoms. For interim HIV counseling and testing in response to presumed exposure to HIV.

To provide participants with the results of confirmatory HIV test results, per the algorithm in Appendix II. In the event that a participant presents to the study site after having missed a scheduled visit (e.g., in response to locator/tracing efforts) on a day that does not fall within a scheduled visit window.

To complete pelvic exam and HIV counseling and testing procedures after a missed quarterly visit.

For other reasons at participant request.

All interim contacts and visits will be documented in participants' study records and on applicable case report forms.

#### **4.6. Final Contact**

As indicated above, the results of laboratory tests performed at study visits will be provided to participants at their next monthly visit. Depending upon when the transition from this study to CAPRISA 052 occurs, some participants will not have received the results of tests performed at their last visit prior to the transition. In such cases, study staff will contact participants with pending test results and deliver their results and appropriate treatment in a timely manner.

#### **4.7. Project Management**

##### **4.7.1 Overall Management Responsibility**

The project will be managed by the PI, Dr. Quarraisha Abdool Karim and by Dr J Frohlich as site Coordinator at Vulindlela and by Dr Ayesha Kharsany as site coordinator at CDC . Dr. Abdool Karim will be responsible for overall quality of the study, adherence to the study protocol, analysis of study data, scientific integrity of the study results, interpretation of the study results and dissemination of the study findings. Dr. Abdool Karim will also oversee the overall financial management of the project and will coordinate the transfer, and quality control of the study data.

##### **4.7.2 Management Responsibilities at Vulindlela**

Drs Frohlich and Mashego and Ms Mlotshwa will be the on-site study coordinators and oversee the implementation of the project in accordance with the protocol. Dr. Frohlich and Ms Mlotshwa will be responsible for logistical aspects of the study including cohort recruitment and retention strategies and community outreach activities. Dr Mashego will oversee the visit procedures and clinical aspects of study. Ms Makhaya will oversee the data collection for the demographic and HIV risk behaviors and assist with community liaison. She will also work closely with Dr Frohlich to refine the recruitment and cohort management strategies and the development of the community liaison plan. Co-ordination and management all the laboratory aspects of the study including specimen collection, laboratory tests, and getting results to the clinical staff will be performed by designated person appointed. A designated person will conduct quality checks on

the case record forms (CRFs) to ensure completeness of the form, thereafter the forms will be datafaxed on a daily basis to the CAPRISA Central Data Management Division in Durban.

#### **4.7.3 Management Responsibilities at Prince Cyril Zulu Communicable Disease Centre (CDC)**

Dr Kharsany will be the on-site study co-ordinator and oversee the implementation of the project in accordance with the protocol. Dr. Kharsany will be responsible for logistical aspects of the study including cohort recruitment and retention strategies and community outreach activities. Dr Busisiwe Ncama ~~An appointed clinician~~ will oversee the visit procedures and clinical aspects of study. Personnel specifically appointed will oversee the data collection for the demographic and HIV risk behaviors and assist with community liaison. All appointed staff will work closely with Dr Kharsany to refine the recruitment and cohort management strategies and the development of the community liaison plan. Co-ordination and management all the laboratory aspects of the study including specimen collection, laboratory tests, and getting results to the clinical staff will be performed by designated person appointed. A designated person will conduct quality checks on the case record forms (CRFs) to ensure completeness of the form, thereafter ~~after which~~ the forms will be datafaxed on a daily basis to the CAPRISA Central Data Management Centre in Durban.

#### **4.7.4 Management responsibilities at CAPRISA (CENTRAL)**

The data capturing system has been set up using the DataFax system. This system is linked via a radiolink to the research site in Vulindlela and to the CAPRISA eThekweni Research Facility at the Prince Cyril Zulu Centre for Disease Control. The system is fully functional at both research sites. Presently all the data forms are captured by faxing on a daily basis and verified by central data capturers. Mr Jayraj Ramota, a data manager from the CAPRISA Data Management Centre will oversee the data capture systems and the data capturers for completion of data entry and will also undertake quality assurance checks on

the data capture forms. Mr Carrara will provide statistical support for this project. Dr S Abdool Karim will advise on study design. Drs Sturm and Moodley will advise and provide ~~laboratory~~ oversight on the STI components of the study.

Fortnightly meetings will be established between Drs. Q Abdool Karim, Frohlich, Mashego, Kharsany, Ncama ~~Moodley~~, and Ms Makhaya, Mlotshwa and Mr Ramota and Carrara ~~van Middelkoop~~ to discuss progress and problems that arise.

## **5. SAFETY MONITORING AND ADVERSE EVENT REPORTING**

The Principal Investigator will be responsible for continuous close safety monitoring of all study participants, and for alerting the protocol team if unexpected concerns arise. The protocol team will meet every two to four weeks during the period of study implementation, and additional ad hoc meetings will be convened if required. Since this is an observational study in which participants will not receive any investigational agents, no adverse event reporting will be undertaken.

## **6. STATISTICAL CONSIDERATIONS**

### **6.1. Review of Study Design**

This is a prospective cohort study. Accrual of 600 participants will be completed over the course of twenty four ~~twelve~~ months. Each participant will complete a minimum of six and a maximum of 12 scheduled monthly follow-up assessments. The total length of the study will be 12-24 months.

### **6.2. Endpoints**

#### **6.2.1. Primary Endpoints**

Consistent with the primary study objective, HIV seroconversions observed during the study follow-up period will be assessed as primary endpoints.

#### **6.2.1. Secondary Endpoints**

Consistent with the secondary study objectives, the following will be assessed as secondary endpoints:

- \* Potential participants screened for the study, and the screening outcome for each screenee.



- \* Participants enrolled in the study.
- \* Participants retained in the study until the site-specific study end date.
- \* Demographic characteristics of women screened for and/or enrolled in the study, including:
  - Age
  - Race/ethnicity
  - Educational level
  - Employment status
  - Income level
  - HIV risk behaviors reported by women enrolled in the study, including:
    - Number of sex partners
    - Frequency of vaginal intercourse
    - Frequency of unprotected vaginal intercourse
    - Frequency of anal intercourse
    - Frequency of unprotected anal intercourse
- \* Prevalent (i.e., at screening/enrollment) and incident (i.e., during follow-up) occurrences of the following:
  - Deep cervico-vaginal epithelial disruption
  - Genital ulcer disease
  - Other genital signs and symptoms
  - Bacterial vaginosis
  - Clinical Candidiasis

### **6.3. Accrual, Follow-up, and Sample Size**

600 study participants will be accrued within the twenty four-month accrual period, with the monthly enrollment targets presented in Section 2.2. Retention of 95 percent of enrolled participants annually (or 97.5 percent semi-annually) will be the target.

As will be described in Section 6.4.2, assessment of the study outcomes related to accrual and retention will not require statistical analysis. However the

precision of study estimates of HIV and STD incidence depends on the number of participants enrolled and retained in the study, as well as the “true” seroincidence rate. Shown in Tables 1 and 2 below are the widths of exact 95% confidence intervals around specific incidence rates, assuming the accrual schedule presented in Section 2.2 and retention of 97.5 percent of participants semi-annually, with either a 12-month (Table 1) or 24-month (Table 2) follow-up period.

**Table 5: 95% Exact Confidence Intervals for Infection Rates Observed in a 12-Month Follow-up Period**

<b>No. of Infections Observed</b>	<b>Observed Infection Rate</b>	<b>95% Exact Confidence Interval</b>
2	1.7%	0.2-6.2%
4	3.4%	0.9-8.8%
6	5.1%	1.8-11.2%
8	6.8%	2.9-13.5%
10	8.5%	4.0-15.7%
12	10.3%	5.3-17.9%

**Table 6: 95% Exact Confidence Intervals for Infection Rates Observed in a 24-month Follow-up Period**

No. of Infections Observed	Observed Infection Rate	95% Exact Confidence Interval
4	1.7%	0.4-4.4%
8	3.4%	1.4-6.7%
12	5.1%	2.6-9.0%
16	6.8%	3.9-11.1%
20	8.5%	5.2-13.2%
24	10.3%	6.5-15.3%

## 6.4. Data Analysis

### 6.4.1. Primary Analysis

Corresponding to the primary study objective, an HIV seroincidence rate will be computed, as the total number of confirmed HIV sero-conversions divided by the total number of woman-years of follow-up. Confidence intervals will be calculated based on Poisson distribution assumptions.

### 6.4.2. Secondary Analyses

Corresponding to the secondary study objectives, the following secondary analyses will be performed:

- The study accrual process will be described by tabulating the number and rate of potential participants screened for and enrolled in the study, overall and by month during the accrual period. Actual accrual rate will be compared to the target rates, and reasons for ineligibility for the study will be tabulated.
- The number of enrolled participants retained in the study will be tabulated for the entire follow-up period as well as for each quarter in the follow-up period. Retention rates also will be calculated. The denominator for these calculations will be the total number of participants enrolled in the study. The numerator will include all participants who complete a scheduled visit during the interval and/or are known to have died during a previous interval. Retention rates will be compared to the annual target of 95 percent.
- The demographic characteristics of persons screened for and/or

enrolled in the study will be described. At a minimum, the characteristics listed in Section 6.2 will be tabulated.

- The HIV risk behaviors of persons enrolled in the study will be described. At a minimum, the frequency of each of the outcomes listed in Section 6.2 will be tabulated.
- The baseline prevalence for each of the genital signs and symptoms and infections listed in Section 6.2 will be computed for the enrolled study population, as the total number of endpoints observed among enrollees divided by the number of participants enrolled. Appropriate 95% confidence intervals also will be computed. An incidence rate for each of the genital signs and symptoms and infections listed in Section 6.2 also will be computed, as the total number of endpoints observed divided by the total number of person-years of follow-up. Confidence intervals will be calculated based on Poisson distribution assumptions.

### **6.5. Data Management and Quality Control**

Data will be primarily managed by the data entry and management team coordinated by Mr Ramota ~~Ms van Middelkoop~~.

**Baseline and Follow-up visit data:** Data will be collected manually on standardized Case Report Forms that will be datafaxed to the CAPRISA Data Management Centre in Durban and captured electronically in a dedicated study database. ~~paper forms and entered, using double entry methods, into a standardized database.~~ A database management system will be developed to provide confidential and secure databases. Protection against loss of data will be provided by maintaining copies of data files in two computer systems. Backup diskettes will be produced daily with weekly back-up onto magnetic tapes. The study requires a data system that can successfully handle several priorities including: 1) maintenance and review of data; 2) editing and flagging logical inconsistencies; 3) identification and notification of missed visits; 4) linkage among longitudinal data for analyses; and 5) linkage among cross-sectional data for analyses. We will use SPSS and SAS software for data ~~entry, management and~~

analysis. We will develop a system to monitor verification, including field range limits and logical checks to help identify and eliminate data entry errors. All data collection forms will be checked by the Study Coordinators and data quality assurance manager to assure completeness and accuracy.

## **7. HUMAN SUBJECTS CONSIDERATIONS**

### **7.1. Ethical Review**

The protocol, informed consent forms, participant education and recruitment materials, and other requested documents — and any subsequent modifications — will be reviewed and approved by the Nelson R Mandela School of Medicine Biomedical Research Ethics Committee (EC). Subsequent to initial review and approval, the EC will review the study at least annually. The PI will make safety and progress reports to the EC at least annually, and within three months after termination or study completion. These reports will include the total number of participants enrolled in the study, the number of participants who completed the study, all changes in the research activity, and all unanticipated problems involving risks to human subjects or others.

### **7.2. Informed Consent**

Written informed consent will be obtained from each study participant prior to both screening and enrollment. Written informed consent also will be obtained for long-term specimen storage and possible future testing, however consent for specimen storage is not required for study participation. Participants will be provided with a copy of their informed consent forms if they are willing to receive them.

In addition this study specifically seeks to characterise and describe understanding of the informed consent process of women targeted for inclusion in the proposed Phase II PRO 2000/5 microbicide trial. A structured questionnaire will be used to assess participants understanding of rights of research participants and informed consent prior to enrolment, at enrolment and 6 monthly thereafter. This data will be used to refine the informed consent procedure for the proposed Phase II Pro 2000/5 microbicide trial.

### **7.3. Risks**

Study participants may experience discomfort when having pelvic exams and/or undergoing phlebotomy for this study. During phlebotomy, participants may feel dizzy or faint, and/or develop a bruise, swelling, or infection where the needle is inserted.

Participants may become embarrassed, worried, or anxious when completing their HIV-related interviews and/or receiving HIV/STD counseling. They also may become worried or anxious while waiting for their HIV test results or after receiving HIV-positive test results. Trained counselors will be available to help participants deal with these feelings.

Although every effort will be made to protect participant privacy and confidentiality, it is possible that participants' involvement in the study could become known to others, and that social harms may result (i.e., because participants could become known as HIV-infected or at "high risk" for HIV infection). For example, participants could be treated unfairly or discriminated against, or could have problems being accepted by their families and/or communities. A 24 hour telephone counseling crisis line has been established at the CAPRISA Vulindlela Research Facility. Counselling services are offered through Open Door at the Prince Cyril Zulu Communicable Disease Centre (CDC)

### **7.4. Benefits**

There may be no direct benefits to participants in this study. However, participants and others may benefit in the future from information learned from this study.

Study participants will receive HIV and STD counseling and testing, a physical exam, and pelvic exams. They will be provided STD treatment in accordance with DOH guidelines free-of-charge, and will be offered STD testing and treatment for their partners. For other medical conditions identified as part of the study screening and/or follow-up procedures, participants will be referred to other sources care available in their community.

## **7.5. Access to HIV-Related Care**

### **7.5.1 HIV Counseling and Testing**

HIV pre-test, risk reduction, and post-test counseling will be provided to all potential study participants who consent to undergo HIV screening to determine their eligibility for this study, and to all enrolled participants at each follow-up HIV testing timepoint. Counseling will be provided in accordance with accepted standards of practice. Counseling policies and procedures will be documented prior to study implementation for purposes of staff training, quality assurance, and study monitoring. In addition to testing for the presence of antibodies to HIV, those who test negative on the two on-site rapid assays will additionally be tested for the presence of HIV. Final HIV diagnosis will be based on the combined results of the antibody and virus tests.

In accordance with CAPRISA policies, participants must receive their HIV test results in order to take part in this study.

Condoms and other HIV prevention supplies will be provided to participants throughout the duration of their participation.

### **7.5.2. Care for Participants Identified as HIV-Infected**

This study will identify persons who are infected with HIV, either as part of the study screening process or during follow-up of enrolled participants. Study staff will provide participants with their HIV test results in the context of post-test counseling. They will also refer persons found to be HIV-infected to available sources of medical and psychosocial care and support, as well as to any available research studies for HIV-infected persons. Participants will also be referred to CAPRISA AIDS treatment (CAT) project for further assessment and eligibility for treatment.

## **7.6 Confidentiality**

All study procedures will be conducted in private. All study-related information will be stored securely at the study site. All participant information will be stored in locked file cabinets in areas with access limited to study staff. Data collection process, administrative forms, colposcopic images, laboratory

specimens, and other reports will be identified by a coded number only to maintain participant confidentiality. All records that contain names or other personal identifiers, such as locator forms and informed consent forms, will be stored separately from study records identified by code number. All local databases will be secured with password-protected access systems. Forms, lists, logbooks, appointment books, and any other listings that link participant ID numbers to other identifying information will be stored in a separate, locked file in an area with limited access.

Participants' study information will not be released without their written permission, except as necessary for monitoring by the sponsors and/or its contractors; or local government authorities.

#### **7.7. Incentives**

Participants will not be compensated for their time and effort in this study. They will only be reimbursed for costs associated with travel to study visits. Supervised child-care facilities will be provided at the Vulindlela Research facility.

#### **7.8. Communicable Disease Reporting Requirements**

Study staff will comply with all applicable requirements to report communicable diseases identified among study participants to local health authorities. Participants will be made aware of all reporting requirements during the study informed consent process.

#### **7.9. Study Discontinuation**

The study may be discontinued at any time by local regulatory authorities.

### **8. LABORATORY CONSIDERATIONS**

#### **8.1. Laboratory Specimens**

The following types of specimens will be collected for laboratory testing:

- Blood for HIV ~~and syphilis serology.~~
- Blood for plasma archive
- Urine for pregnancy testing
- Vulvo-Vaginal swab specimens for BV
- Ecto- and endocervical specimens for Pap smear

The laboratory will adhere to standards of good laboratory practice; the



study-specific procedures manual; standard operating procedures for proper collection, processing, labeling, transport, and storage of specimens. Specimen collection, testing, and storage will be documented using the Laboratory Data Management System (LDMS) as described in the study-specific procedures manual.

In addition, plasma will be sent to the NICD for quality assurance HIV testing.

## **8.2. Specimen Storage and Possible Future Research Testing**

Plasma collected from each study participant at the time of study entry, seroconversion (if applicable), and study exit will be stored. In addition, study participants will be asked to provide written informed consent for their plasma specimens to be stored after the end of the study for possible future research testing. Any residual specimens of participants who do not consent to long-term storage and additional testing will be destroyed at the end of the study, after all protocol-required and quality assurance testing has been completed.

## **8.3 Biohazard Containment**

As the transmission of HIV and other blood-borne pathogens can occur through contact with contaminated needles, blood, and blood products, appropriate blood and secretion precautions will be employed by all personnel in the drawing of blood and shipping and handling of all specimens for this study, as currently recommended by South African guidelines on biohazard containment.

# **9. ADMINISTRATIVE PROCEDURES**

## **9.1. Study Coordination**

Study implementation will be directed by this protocol as well as a study-specific procedures manual. This manual will outline procedures for conducting study visits, collecting and submitting study data, collecting and shipping specimens, and other study operations. Study case report forms will be developed by the protocol team. The Principal Investigator will identify all case report forms to be used as source documents. Data will be transferred to the CAPRISA Data Management Core Team in Durban and entered using the DataFax data management system. Quality control reports and queries routinely will be

generated and distributed to the study sites for verification and resolution.

Close cooperation between protocol team members will be necessary to track study progress, respond to queries about proper study implementation, address issues in a timely manner, and assure consistent participant management, documentation, and information sharing. Rates of accrual, follow-up, and protocol compliance will be monitored closely by the study team and the CAPRISA Study Monitoring Committee.

### **9.2. Protocol Compliance**

The study will be conducted in full compliance with the protocol. The protocol will not be amended without prior approval by the Principal Investigator. All protocol amendments will be submitted to and approved by the EC prior to implementing the amendment.

### **9.3. Investigator's Records**

The Principal Investigator will maintain and store in a secure manner complete, accurate, and current study records throughout the study. The PI will retain all study records for at least three years after submission of the final report. Study records include administrative documentation — including all reports and correspondence relating to the study — as well as documentation related to each participant screened for and/or enrolled in the study — including informed consent forms, locator forms, case report forms, notations of all contacts with the participant, and all other source documents.

### **9.5. Use of Information and Publications**

Presentation and publication of the results of this study will be governed by CAPRISA policies. Any presentation, abstract, or manuscript will be made available by the protocol team to the CAPRISA Manuscript Review Committee for review prior to submission.

## **10. References**

Abdool Karim Q, Abdool Karim SS. Epidemiology of HIV infection in South Africa. *AIDS* 1999; 13: S4-S7 (Reprinted from the International AIDS Society Newsletter).

- Abdool Karim Q, Abdool Karim SS. South Africa: host to a new and emerging HIV epidemic (editorial). *Sex Transm Inf* 1999; 75: 139-140.
- Colvin M, Dawood S, Kleinschmidt I, Mullick S, Lalloo U. Prevalence of HIV and HIV-related disease on the adult medical wards of a tertiary hospital in Durban, South Africa. *Int J STD and AIDS*, 2001; 12: 386-389.
- Department of Health, RSA. Summary report: National HIV and syphilis antenatal sero-prevalence survey in South Africa. Pretoria, 2002.
- UNAIDS. AIDS epidemic update – sub-Saharan Africa. December 2001. UNAIDS/01.74E-WHO/CDS/CSR/NCS/2002 Geneva Switzerland.
- Mayer KH, Abdool Karim S, Kelly C, Maslankowski L, Rees H, Profy A, Day J, Welch J, Rosenberg Z, for the HPTN 020 Protocol team. Safety and tolerability of vaginal PRO 2000 gel in sexually active HIV-uninfected and abstinent HIV infected women. *AIDS* 2003; 17: 221-229.

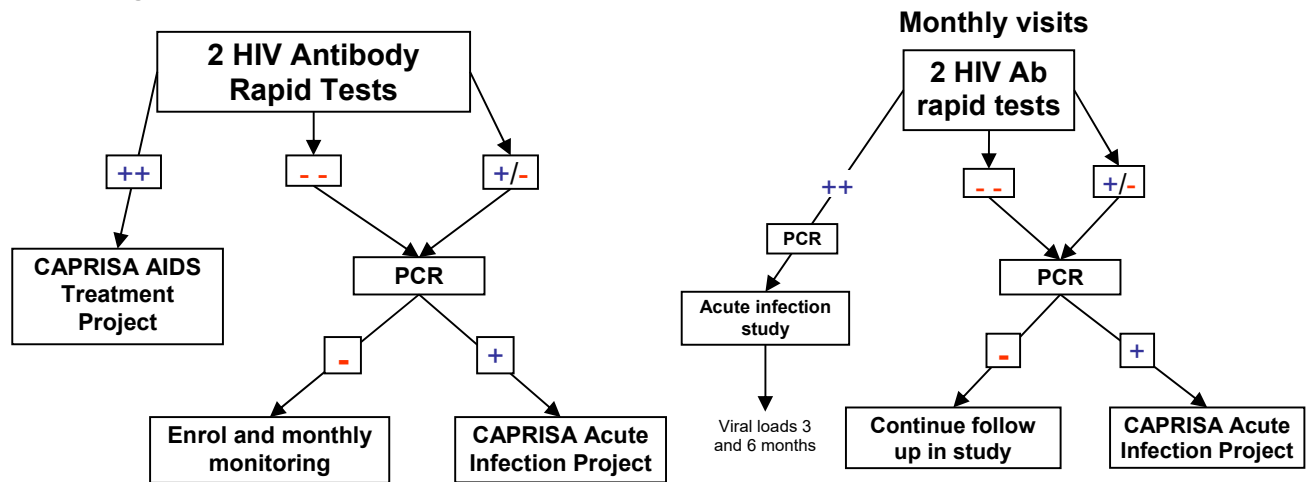
## Appendix I : Schedule of Study Visits and Procedures

	Screening (up to -30 days)	Enrollment (day/month 0)	Monthly Follow-up mos 1,2,4,5,7,8,10,11	Quarterly Follow-up mos 3,6,9,12
Obtain informed consent	X	X		
Obtain demographic information	X			
Obtain/update locator information	X	X	X	X
Administer behavioral eligibility checklist	X			
Administer behavioral risk assessment		X		
Provide HIV/STD pre-test counseling	X		[X]	X
Provide HIV/STD risk reduction counseling	X		[X]	X
Provide HIV/STD post-test counseling	X	X	[X]	X
Obtain medical/menstrual history		X	X	X
Perform physical exam		X		
Perform pelvic exam:				
-naked eye exam of external genitalia		X	[X]	X
-speculum exam of vagina and cervix		X	[X]	X
-VVS smear for Gram staining (BV and candidiasis)		X	[X]	X
-ecto- and endocervical cytobrush for Pap smear		X		
<del>-genital ulcer swab for PCR</del>			<del>[X]</del>	<del>[X]</del>
Perform laboratory evaluations:				
-urine pregnancy test	X	X	X	X
- Quantitative PCR to detect HIV	X	X	X	X
-HIV serology	X		[X]	X
-Pap smear interpretation		X		
-plasma archive		X	[X]	X
Provide test results	X	X	X	X
Provide STD treatment	[X]	[X]	[X]	[X]

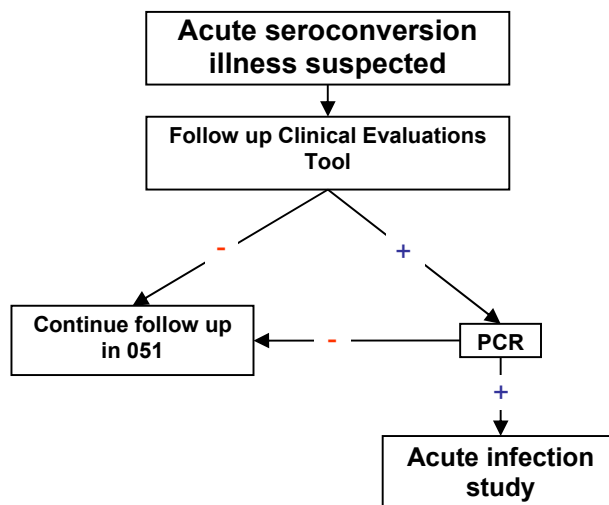
[x] = if clinically indicated.

## Appendix II : HIV Testing Algorithm

### Screening



### HIV antibody testing algorithm for suspected acute illness



**Appendix III : Informed Consent Form for Screening  
HIV and STI Incidence rates in Vulindlela and Durban : A Prevention  
Preparedness Study**

**SCREENING ONLY**

PRINCIPAL INVESTIGATOR: Professor Quarraisha Abdool Karim

PHONE: 031-2604208

**INFORMED CONSENT**

You are being asked to volunteer for screening tests to find out if you are eligible for the research study named above. The research study is for women who could get HIV or are already infected with HIV or other STIs. HIV is the virus that causes AIDS. The screening tests include interview questions, urine and blood tests, a physical exam, and an exam of your vagina.

Before you decide whether to have the screening tests, we would like to explain the purpose of the screening tests, the risks and benefits to you, and what is expected of you.

**YOUR PARTICIPATION IS VOLUNTARY**

This consent form gives information about the screening tests that will be discussed with you. Once you understand the screening tests, and if you agree to take part, you will be asked to sign your name or make your mark on this form. You will be offered a copy to keep.

Before you learn about the screening tests, it is important that you know the following:

- Your participation is entirely voluntary.
- You may decide not to have the screening tests, or to withdraw from the screening tests at any time, without losing the benefits of your routine medical care.
- If you decide not to have the screening tests, you can still join another research study later, if one is available and you qualify.

You are only being asked to have the screening tests at this time. Even if you agree to have the screening tests, you do not have to join the research study.

## **PURPOSE OF THE SCREENING TESTS**

The purpose of the screening tests is to find out if you are eligible for a research study. The purpose of the research study is to set up a system at the CAPRISA Vulindlela Research facility and at CDC for doing research with this group. Specifically, this study will help us to prepare for another study that may begin within the next year to find out if a gel can protect women from getting HIV during sex. If you choose not to join the research study we would like to ask you a few questions to understand why you are choosing not to participate and assess your understanding of your rights as a research participant.

Some people may not be able to join the research study because of information found during the screening tests.

## **PROCEDURES**

If you agree to have the screening tests, you will have 2 visits here over about 1-2 weeks. Depending on your screening test results, more visits may be needed, as described below. All screening tests must be done within 30 days. If all tests are not done within 30 days, and you still want to find out if you are eligible for the research study, you will have to start the screening tests over from the beginning.

### ***Visit 1:***

Your first visit will continue today, after you read, discuss, and sign this form. The visit will take about 1 hour. The study staff will ask you where you live and other questions about you, your health, and your sexual practices.

If your answers to the questions show that you may be eligible for the study, you will give urine for a pregnancy test. If you are pregnant, you will still be eligible for the research study. In addition, the study staff will refer you to available sources of medical care and other services you may need.

Regardless of your pregnancy status, you will have counseling about HIV and other infections passed during sex. These infections are called syphilis,

gonorrhoea, genital herpes and chlamydia. If you are having health problems that may be due to these infections, the study staff will give you medicine to treat them. The study staff will talk with you about the HIV test and tests for other infections passed during sex. You will talk about what it may mean to know the results of these tests, and whether you are prepared to receive the test results. You will talk about ways to avoid these infections.

If you are prepared to have an HIV test, study staff will draw about 1 teaspoon of blood from your arm with a needle. They will test your blood for HIV. It will take about 15-20 minutes to get your test result. You will be told your result as soon as it is available, on the same day you give blood and have the test. You will talk with the study staff about the meaning of your result and how you feel about it. If the HIV tests done by the study staff are negative, we will draw your blood again and send your it to the laboratory to confirm the tests result with new tests that are now available.

Sometimes HIV tests are not clearly positive but also not negative. In that case, we will draw your blood again and repeat the tests until we know the result for sure. You must receive your HIV test results to be in the research study. If the test shows that you have HIV, you will not be eligible for this research study. Study staff will tell you about other studies you may be eligible for, if any. They will also refer you to available sources of medical care and other services you may need.

These tests take 1-2 weeks. You will be asked to come back for another visit when your results are available.

***Visit 2:***

This visit will take about 90 minutes. The study staff will tell you your test results from Visit 1, and what they mean. They will talk with you again about HIV and other infections passed during sex, and how to avoid these.

You will give urine for a pregnancy test. If you are pregnant, you will still be eligible for this research study. If indicated the study staff will also refer you to available sources of medical care and other services you may need. Regardless of your pregnancy status, you will talk with the study staff about your health. You will have a physical exam, including an exam of your genital area and inside your



vagina. The study staff will collect fluid from your vagina with a swab to test for infections. These infections are called trichomoniasis, candidiasis, bacterial vaginosis, gonorrhoeae, chlamydia and genital herpes. If you have these infections, we will tell you about them and give you medicine to treat them, if needed. If you have an infection that your partner may also have, you can bring him here for testing and treatment that he may need too. The study staff will also collect samples from your cervix to test for abnormalities that could mean you have cervical cancer, or that could lead to cervical cancer. This test is called a “Pap smear.” It takes about 2 weeks before Pap smear results are available. We will give you the results as soon as they are available.

On completion of these procedures you will be eligible for this research study. The study staff will fully explain the study to you and answer any questions you have. If you decide to take part in the research study, you will be asked to sign another consent form. If you choose not to participate you will be asked a few questions to understand why you are choosing not to participate and your understanding of your rights as a research participant will be assessed.

If you have a sore seen during the exam of your vagina, you will be given medicine to treat it, if needed, and asked to come back here after several days for another exam.

### **RISKS AND/OR DISCOMFORTS**

You may feel discomfort or pain when your blood is drawn. You may feel dizzy or faint. You may have a bruise, swelling, or infection where the needle goes into your arm. You may feel discomfort during the exam of your vagina.

You may become embarrassed, worried, or anxious when discussing your sexual practices, ways to protect against HIV and other infections passed during sex, and your test results. You may become worried or anxious while waiting for your test results. If you have HIV or other infections, knowing this could make you worried or anxious. 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 having the screening tests. Your visits here will take place in private.

However, it is possible that others may learn of your participation here, and think you have HIV, or are 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, or being accepted by your family or community.

### **BENEFITS**

You may get no direct benefit from the screening tests. However, you will have a physical exam and a genital exam. You will get counseling and testing for HIV. You will get free condoms. If you are infected with HIV, you will be referred for medical care, counseling, and other services available to you. You will get counseling and testing for other infections. If you have these infections, you will get medicine to treat them, if needed. You can bring your partner here for tests and treatment for these infections if he needs them. If your Pap smear result is abnormal, you will be referred for treatment at Gray’s Hospital.

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

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

- The research study is stopped or canceled.
- The study staff feel that having the screening tests would be harmful to you.
- You are not willing to find out your HIV test result.
- You are not able to attend clinic visits or complete the screening tests.
- Other administrative reasons.

### **COSTS TO YOU**

There is no cost to you for the screening tests. You will be reimbursed for your travel costs for each scheduled screening visit. Childcare facilities will be available to you at no cost during your scheduled study.

### **CONFIDENTIALITY**

The records of your screening tests, including the pictures of your vagina, will be confidential to the extent permitted by law. You will be identified by a code.

Personal information from your records will not be released without your written permission. You will not be personally identified in any publication about this study. However, your records may be reviewed, under the guidelines of the study monitors, and the Nelson R Mandela Faculty of Medicine Ethics and Professional Standards Committee.

### **RESEARCH-RELATED INJURY**

It is unlikely that you will be injured as a result of having the screening tests. If you are injured, the study staff will give you immediate necessary treatment for your injuries. You will not have to pay for this treatment. You will be told where you can get additional treatment for your injuries. There is no program for monetary compensation or other forms of compensation for such injuries. You do not give up any legal rights by signing this consent form.

### **PROBLEMS OR QUESTIONS**

#### **At Vulindlela**

If you ever have any questions about the screening tests, or if you have a research-related injury, you should contact Professor Q Abdool Karim at 031-2604208, CAPRISA, Second Floor Doris Duke Medical Research Institute, Durban or Dr Janet Frohlich or Ms M Mlotshwa at 033-2606851 ~~033-9974425~~, CAPRISA Vulindlela Research Facility, Mafakathini.

#### **At STD clinic, CDC, Durban**

If you ever have any questions about the screening tests, or if you have a research-related injury, you should contact Professor Q Abdool Karim at 031-2604208, CAPRISA, Second Floor Doris Duke Medical Research Institute, Durban or Dr Ayesha Kharsany or Dr B Ncama at 031-2601919 ~~4558~~, CAPRISA, Durban offices.

If you have questions about your rights as a research participant, you should contact Professor A Dhali, the Chairperson of the Nelson R Mandela School of Medicine Biomedical Research Ethics Committee at 031-260 4604 at 719 Umbilo Road, Durban.

## SIGNATURES

If you have read this consent form, or had it read and explained to you, and you understand the information, and you voluntarily agree to have the study tests, please sign your name or make your mark below.

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Participant Name (print)	Participant Signature	Date
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Study Staff Conducting Consent Discussion (print)	Study Staff Signature	Date
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Witness Name (print)	Witness Signature	Date
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## **Appendix IV: Informed Consent Form for Enrollment**

### **INFORMED CONSENT FORM**

#### **HIV and STI Incidence Rates in Vulindlela and Durban: A Prevention Preparedness Study**

#### **ENROLLMENT**

PRINCIPAL INVESTIGATOR: Professor Quarraisha Abdool Karim

PHONE: 031-2604208

#### **INFORMED CONSENT**

You are being asked to volunteer for the research study named above. This is a study for women who already have or could get HIV or other sexually transmitted infections. HIV is the virus that causes AIDS. Before you decide whether to take part in the study, we would like to explain the purpose of the study, the risks and benefits to you, and what is expected of you.

#### **YOUR PARTICIPATION IS VOLUNTARY**

This consent form gives information about the study that will be discussed with you. Once you understand the study, and if you agree to take part, you will be asked to sign your name or make your mark on this form. You will be offered a copy to keep.

Before you learn about the study, it is important that you know the following:

- Your participation is entirely voluntary.
- You may decide not to take part in the study, or to withdraw from the study at any time, without losing the benefits of your routine medical care.
- If you decide not to take part in the study, you can still join another study later, if one is available and you qualify.

## **PURPOSE OF THE STUDY**

The Centre for the AIDS Programme of Research (CAPRISA) is undertaking research on ways to prevent HIV infection. One purpose of this study is to set up a system at the CAPRISA Vulindlela Research Facility and the STD Clinic CDC for undertaking research in this community. This study will help CAPRISA prepare for another study that may begin in the next year to find out if a gel can protect women from getting HIV during sex. A second purpose is to find out about how likely people living in Vulindlela are to become infected with HIV and other infections passed during sex. A total of 600 women will be in this study. The whole study will take 18-30 months to finish. Each woman will be in the study for about 12 –24 months.

## **STUDY PROCEDURES**

If you decide to take part in the study, your first visit will continue today, after you read, discuss, and sign this form. You will answer interview questions about your sexual practices and you may be asked questions relating to your experiences and understanding of being a research participant. You will give 2 teaspoons of blood that the study staff will keep frozen at the CAPRISA laboratories in Durban while you are in the study. If needed, they will test this blood later in the study to help check on your health. This will help us make sure we are doing the best possible HIV testing here. After today, you will be in the study for 12-24 months, depending on when you join. You will have a study visit every month while you are in the study. These visits will take 30-60 minutes. All study visits will take place at the CAPRISA Vulindlela Research Facility or the CAPRISA eThekweni Research Facility. You will have a genital exam and testing for HIV and other infections passed during sex every month.

Every month, you will:

- Tell the study staff if you had any health problems since your last visit.
- Give urine for a pregnancy test.
- Get condoms.
- Get the results of tests done at the visit and at the previous visit.

- Get treatment for infections passed during sex if you need it.
- Get referrals for medical care and other services if you need them.
- Have an exam of your genital area and inside your vagina. The study staff will collect fluid from your vagina with a swab to test for infections (trichomoniasis, candidiasis, bacterial vaginosis, gonorrhoeae and chlamydia). These are infections passed during sex.
- Answer interview questions about your sexual practices and about your understanding of the research and your experience of being a research participant.
- Talk with study staff about ways to avoid HIV and other infections passed during sex.
- Talk with study staff about the HIV test and give about 2 teaspoons of blood from your arm for the test. When we do HIV testing for this study, we first do a test that gives results in 15-20 minutes. You will get the result of that test when it is available, on the same day you give blood and have the test. If you the tests are negative we will do another different test to confirm this result. This test takes about 1-2 weeks, so you will have to come back here at that time to get the results. You will talk with the study staff about the meaning of your results and how you feel about them.

Sometimes HIV tests are not clearly positive but also not negative. In that case, we will draw your blood again and repeat the tests until we know the result for sure. You must receive your HIV test results to stay in the study.

At any time in the study, if you are having health problems that may be caused by infections passed during sex, you will:

- Have an exam of your genital area and inside your vagina.
- Give blood to test for infections passed during sex.
- Get treatment for infections passed during sex if you need it.

You are asked to tell the study staff about medical problems you have

during the study, especially genital problems. You can also contact the study staff between regular visits to report these problems. The study staff will examine you as needed. They will either provide or refer you for medical care that you may need.

If you become pregnant during the study, you can stay in the study if you wish. The study staff will refer you to available sources of medical care and other services you or your baby may need.

If you are found to have an infection that is passed during sex, the study staff will give you medicine to treat it, if needed. If you have an infection that your partner also may have, you can bring him here for testing and treatment that he may need too.

You can have extra counseling and testing for HIV if needed between regular visits. If you wish, your partner can have counseling with you. If you become infected with HIV, you can stay in the study if you wish or you will be referred to other CAPRISA studies for follow-up. The study staff will give you counseling and refer you to available sources of medical care and other services you may need.

At each study visit, the study staff will update information on where you live and how to keep in contact with you. They will use this information to remind you of scheduled visits. If you miss a visit, the study staff will try to contact you. They also may visit your home to find you. They will try to reach you through the contact people that you list. If they talk to these people, they will not tell them why they are trying to reach you.

Other blood tests: At your last study visit, blood that is left over from your HIV test will be kept frozen here at the clinic. Leftover blood also will be kept if you become infected with HIV.

The study staff also would like to draw blood from you to keep after the study is over. You will be asked to sign a separate consent form to give permission for that. Even if you do not give permission to store your blood after the study, you can still be in the study.



## **RISKS AND/OR DISCOMFORTS**

You may feel discomfort or pain when your blood is drawn. You may feel dizzy or faint. You may have a bruise, swelling, or infection where the needle goes into your arm. You may feel discomfort during the exam of your vagina. You may become embarrassed, worried, or anxious when discussing your sexual practices, ways to protect against HIV and other infections passed during sex, and your test results. You may become worried or anxious while waiting for your test results. If you have HIV or other infections passed during sex, knowing this could make you worried or anxious. 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 the study. Your visits here will take place in private. However, it is possible that others may learn of your participation here, and think you have HIV, or are 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, or being accepted by your family or community.

## **BENEFITS**

You may get no direct benefit from being in this study. You or others may benefit in the future from information learned in this study. You may get some personal satisfaction from being part of research on HIV. You will have exams of your vagina and tests for infections passed during sex. If you have these infections, you will get medicine to treat them, if needed.

You will have pregnancy tests. If these tests show that you are pregnant, you will be referred for medical care and other services that you and your baby may need.

You will get counseling and testing for HIV. You will get free condoms. You can bring your partner here for counseling, tests for infections passed during sex, and treatment for these infections. If you become infected with HIV, you will be referred for medical care, counseling, and other services available to you.

## **NEW FINDINGS**

You will be told any new information learned during this study that might

cause you to change your mind about staying in the study. You will be told when the results of the study 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:

- The study is stopped or canceled.
- The study staff feel that staying in the study would be harmful to you.
- You are not willing to find out your HIV test results.
- You are not able to attend study visits or complete the study procedures.
- Other administrative reasons.

### **ALTERNATIVES TO PARTICIPATION**

There may be other HIV research studies going on here or in the community that you may be eligible for. If you wish, we will tell you about other studies that we know about. There also may be other places where you can go for HIV counseling and testing. We will tell you about those places if you wish.

### **COSTS TO YOU**

There is no cost to you for being in the study. You will be reimbursed for your travel costs for your scheduled study visits and child care facilities will be available to you.

### **CONFIDENTIALITY**

Your study records, including the pictures of your vagina will be confidential to the extent permitted by law. You will be identified by a code. Personal information from your records will not be released without your written permission. You will not be personally identified in any publication about this study. However, your records may be reviewed, under the guidelines of the South African Medicine Control Council.

### **RESEARCH-RELATED INJURY**

It is unlikely that you will be injured as a result of having the screening tests. If you are injured, the study staff will give you immediate necessary treatment for

your injuries. You will not have to pay for this treatment. You will be told where you can get additional treatment for your injuries. There is no program for monetary compensation or other forms of compensation for such injuries. You do not give up any legal rights by signing this consent form.

## **PROBLEMS OR QUESTIONS**

### **At Vulindlela**

If you ever have any questions about the study tests, or if you have a research-related injury, you should contact Professor Q Abdool Karim at 031-2604208, CAPRISA, Second Floor Doris Duke Medical research Institute, Durban or Dr Janet Frohlich or Ms M Mlotshwa at 033-260 6851 ~~9971425~~, CAPRISA Vulindlela Research Facility, Mafakathini.

### **At STD clinic, CDC, Durban**

If you ever have any questions about the study tests, or if you have a research-related injury, you should contact Professor Q Abdool Karim at 031-2604208, CAPRISA, Second Floor Doris Duke Medical research Institute, Durban or Dr Ayesha Kharsany or Dr B Ncama at 031-260 1919, CAPRISA, Durban

If you have questions about your rights as a research participant, you should contact Professor A Dhali, the Chairperson of the Nelson R Mandela School of Medicine Biomedical Research Ethics Committee at 031-260 4604 at 719 Umbilo Road, Durban.

## **SIGNATURES**

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

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Participant Name (print)	Participant Signature	Date
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Study Staff Conducting Study Consent Discussion (print)	Staff Signature	Date
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Witness Name (print)	Witness Signature	Date
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## **Appendix V : Informed Consent Form for Specimen Storage and Possible Future Research Testing**

### **INFORMED CONSENT FORM**

#### **HIV and STI Incidence Rates in Vulindlela and Durban: A Prevention Preparedness Study**

#### **SPECIMEN STORAGE**

##### **INTRODUCTION**

You have decided to take part in a CAPRISA research study. While you are in this research study, there may be some blood taken from you that might be useful for future research. You are being asked to agree to the storage of this blood. This consent form gives you information about the collection, storage, and use of your blood. The study staff will talk with you about this information. Please ask if you have any questions. If you agree to the storage of your blood, you will be asked to sign this consent form. You will get a copy to keep.

##### **HOW WILL YOU GET THE BLOOD FROM ME?**

The researchers and doctors want to take blood from you at your first study visit and your last study visit for storage. If you agree to this, you will have you will have about 2 teaspoons of blood drawn at each of these visits. This blood will be kept and used for future research.

##### **HOW WILL YOU USE MY BLOOD?**

Your blood will only be used to look for additional evidence of infection with HIV or other agents, damage caused by infection, or your body's response to infection (such as examining cells, proteins, and other chemicals in your body). Tests may also include examining your genes (DNA), since they might affect your response to disease in important ways. Your genes might make you more or less susceptible to becoming infected, your responses to infection or to treatment stronger or weaker, or make HIV progress more rapidly or slowly. No other kinds of genetic test will be done by anyone on your stored blood without first explaining

the test to you and obtaining your permission.

The researchers do not plan to contact you or your regular doctor with any results from tests done on your stored blood. This is because research tests are often done with experimental procedures, so the results from one research study are generally not useful for making decisions on managing your health. Should a rare situation come up where the researchers decide that a specific test result would provide important information for your health, the researchers notify your study doctor and your study doctor will try to contact you. If you wish to be contacted with this type of test result, you must give the study doctor or nurse any change to your address and/or phone number. If you want your regular doctor to be told about this type of test result, you must provide the study doctor or nurse with your regular doctor's name, address, and phone number. Your blood will not be sold or used directly to produce commercial products. Research studies using your samples will be reviewed by the CAPRISA Scientific Review Committee and a special committee at the Nelson R Mandela School of Medicine Ethics and Professional Standards Committee.

### **HOW LONG WILL YOU KEEP MY BLOOD?**

There is no time limit on how long your blood will be stored.

### **HOW WILL MY BLOOD BE STORED?**

Your blood will be stored at special facilities that are designed to store blood samples safely and securely. The storage facilities are designed so that only approved researchers will have access to the blood samples. Some employees of the storage facilities will need to have access to your blood samples in order to store them and to keep track of where they are, but these people will not have information that directly identifies you. An Institutional Review board will oversee the storage facilities to protect you and other research volunteers from harm.

### **DOES STORAGE OF MY BLOOD BENEFIT ME?**

There are no direct benefits to you. The benefit of doing research on stored blood includes learning more about HIV infection.

### **WHAT ARE THE RISKS?**

There are few risks related to storing your blood. When tests are done on

the stored blood, there is a small but possible risk to your privacy. It is possible that if others found out information about you that is learned from tests (such as information about your genes), it could cause you problems with your family (having a family member learn about a disease that may be passed on in families or learning who is the true parent of a child) or problems getting a job or insurance.

### **WHAT ABOUT CONFIDENTIALITY?**

In order to keep your information private, your blood will be labelled with a code that can only be traced back to your research clinic. Your personal information (name, address, phone number) will be protected by the research clinic. When researchers are given your stored blood to study, they will not be given your personal information. The results of future tests will not be included in your health records. Every effort will be made to keep your personal information confidential, but we cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law.

### **WHAT ARE MY RIGHTS?**

Allowing your blood to be stored is completely voluntary. You may decide not to have any blood stored other than what is needed to complete this study and still be in this research study or any future study.

If you decide now that your blood can be stored for future research, you may change your mind at any time. You must contact your study doctor or nurse and let them know that you do not want your samples used for future research. Your blood will then not be used.

### **WHAT DO I DO IF I HAVE QUESTIONS?**

#### **At Vulindlela**

If you ever have any questions about the study tests, or if you have a research-related injury, you should contact Professor Q Abdool Karim at 031-2604208, CAPRISA, Second Floor Doris Duke Medical research Institute, Durban or Dr Janet Frohlich or Ms M Mlotshwa at 2606851 ~~033-9971425~~, CAPRISA Vulindlela Research Facility, Mafakathini.

**At STD clinic, CDC, Durban**

If you ever have any questions about the study tests, or if you have a research-related injury, you should contact Professor Q Abdool Karim at 031-2604208, CAPRISA, Second Floor Doris Duke Medical research Institute, Durban or Dr Ayesha Kharsany or Dr B Ncama at 031-2601919 4558, CAPRISA eThekweni Research Facility, Durban

If you have questions about your rights as a research participant, you should contact Professor A Dhai, the Chairperson of the Nelson R Mandela School of Medicine Biomedical Research Ethics Committee at 031-260 4604 at 719 Umbilo Road, Durban.

**SIGNATURES**

Please carefully read the statements below and think about your choice. No matter what you decide it will not affect your care. I agree to have blood taken for the purpose of storage and testing for future research related to HIV infection.

\_\_\_\_\_ Yes

\_\_\_\_\_ No

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Participant Name (print)	Participant Signature	Date
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Study Staff Conducting Consent Discussion (print)	Staff Signature	Date
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Witness Name (print)	Witness Signature	Date
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