

**EVALUATION OF HIV-SPECIFIC
IMMUNOLOGICAL AND VIROLOGICAL RESPONSES
OF HIV-1 MULTIPLY-EXPOSED SERONEGATIVE INDIVIDUALS**

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EVALUATION OF HIV-SPECIFIC IMMUNOLOGICAL AND VIROLOGICAL RESPONSES OF HIV-1 MULTIPLY-EXPOSED SERONEGATIVE INDIVIDUALS

PROTOCOL SUMMARY

- Protocol:** Evaluation of HIV-Specific Immunological and Virological Responses of HIV-1 Multiply-Exposed Seronegative Individuals
- Subjects:** Healthy HIV-1 seronegative adult volunteers who have had at least 3 different partners and at least 3 sexually transmitted disease (STD) episodes in the last 3 years.
- Number of Subjects:** 130
- Follow-up period:** 24 months
- Sponsoring Agency:** National Institutes of Health (NIH)
- Collaborating Sites:** CAPRISA, Umbilo Clinical Research Site, DDMRI University of KwaZulu-Natal; CAPRISA eThekweni Clinical Research Site based at the Prince Cyril Zulu Communicable Disease Clinic, Durban, South Africa, CAPRISA Vulindlela Clinical Research Site National Institute for Communicable Diseases (NICD), Johannesburg, and Fred Hutchinson Cancer Research Center/University of Washington HIV Vaccine Trials Unit, Seattle, WA

1.0 Purpose of the Study

1. To identify the presence and perform a detailed analysis of HIV-specific immune responses, both cellular and humoral, that exist in individuals who have experienced multiple exposures to HIV-1 by sexual contact.
2. To examine the expression of certain genetically determined receptors and mediators that may influence HIV-1 disease susceptibility.

The long-term goals of this investigation are to gather evidence to either support or negate the existence of a group of adults who are capable of resisting HIV-1 infection and to define the nature of the immune responses that may be responsible for this resistance.

2.0 Background and Rationale

Since the recognition of AIDS and its etiologic agent, HIV, it has become clear that despite repeated exposure to the virus, some persons do not develop infection. At least two hypotheses may account for these rare occurrences. Some individuals may have resisted infection due to an insufficient or attenuated viral inoculum. Alternatively, some persons may develop an infection initially but manage to control virus replication such that HIV infection is virtually eliminated or at least undetectable by standard methodologies. In either situation, it is conceivable that these individuals have acquired a natural immunity to HIV-1.

An increasing number of investigations now suggest that persons multiply exposed to HIV but uninfected may develop HIV-specific cellular immune responses that may provide some degree of protection. Early proponents of this theory were Clerici and Shearer, who demonstrated that in response to HIV peptides, PBMC from multiply-exposed uninfected adult men produce increased amounts of interleukin-2 in comparison to PBMC from unexposed control donors (Clerici). More definitive data to support this theory have evolved from the examination of cytotoxic T lymphocytes (CTL) responses in HIV-exposed individuals using sensitive methods to amplify CTL precursors. CTL that recognize and lyse target cells expressing the HIV gene products of *gag* or *nef* have been identified in uninfected infants born to HIV-1 infected mothers (Rowland-Jones, Cheynier). In adults, HIV-1 *nef*-specific CTL have been detected in 6 of 6 uninfected heterosexual contacts of HIV-1 infected patients (Langlade-Demoyen). Rowland-Jones *et al* have detected either *nef*-specific or *pol*-specific CTL responses in 3 out of 6 HIV-1/HIV-2 multiply exposed but uninfected female commercial sex workers in Gambia. Pinto and colleagues report that a single exposure to HIV contaminated fluids may induce *env*-specific responses in health care workers.

Other host factors that may provide resistance to HIV infection have been suggested in recent reports. Preliminary data from Plummer and associates (Fowke) indicate that the presence of rare HLA types such as Aw28 and Bw70 may confer resistance among a cohort of female prostitutes in Nairobi, Kenya, who are continuously exposed to HIV-1 but remain persistently seronegative. A factor associated with CD8 cells may render CD4 cells less susceptible to HIV infection (Levy) and its presence has been demonstrated in infected and uninfected individuals. Whether multiply-exposed uninfected persons are more likely to show decreased *in vitro* susceptibility to HIV is unknown.

Thus the proposed study aims to address the following specific questions:

1. Are HIV-1 specific immune responses present in seronegative individuals who are chronically exposed to HIV-1? If so, what epitopes are recognized by antibody or T cells?
2. Are these responses more commonly detected in the genital rather than the systemic compartment?
3. Does the expression or lack of expression of certain genetically determined receptors and mediators which may influence HIV-1 disease susceptibility also influence HIV infectability and the development of HIV-specific immune responses?

3.0 Experimental Design

3.1 Study population

Participants will be recruited from the following CAPRISA sites:

- CAPRISA, Umbilo Clinical Research Site, DDMRI University of KwaZulu-Natal;
- CAPRISA eThekweni Clinical Research Site based the Prince Cyril Zulu Communicable Disease Clinic, Durban, South Africa,
- CAPRISA Vulindlela Clinical Research Site

The Umbilo Site located at the DDMRI was custom designed for the conduct of clinical trials and has the capacity to conduct research at good clinical practice standards. This clinical research facility is currently used for screening, enrolment and follow-up of participants in an NIH funded CIPRA Acute HIV Infection (CAPRISA 002) study. HIV negative participants of this acute infection study who meet the inclusion criteria may be invited to participate in this study.

The Prince Cyril Zulu Communicable Disease Clinic (CDC) is a large local government clinic for the diagnosis and treatment of STIs and TB, for which it provides free treatment. It is based in the busiest part of Durban - in the nucleus of Durban's public transportation system with the central bus terminus, "minibus" taxi station and Durban Central rail station all within a kilometer radius of the clinic building. Most of the STI patients reside within a 10-20 km radius of the clinic. The 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 disease. Annually, approximately 40 000 cases of STIs are treated at this clinic, with an average of about 135 STI patients per day. Given the high HIV prevalence of 63% in this group of STI patients and the strong association between STIs and HIV, these patients are a key risk group for acquiring and transmitting HIV. HIV negative male and female patients seeking STI care at the Prince Cyril Zulu clinic and who meet study eligibility criteria will be invited to participate in this study.

The CAPRISA rural facility in Vulindlela adjoins the Mafakathini Primary Care Clinic with a shared entrance, security and a waiting area. In this setting, adolescents and particularly young women are a vulnerable group at high risk of acquiring HIV. Women acquire HIV infection at a younger age, at least 5-10 years earlier than men. About a quarter of all new infections that occurred globally in 2003 were in young people under the age of 25, highlighting the importance of youth in the pandemic and in South Africa. Adolescents utilising the primary health care services for antenatal, family planning or STI services and who meet all study eligibility criteria will be invited to participate in this study.

3.2 Overview

The study will enroll 130 HIV negative participants who have had at least 3 different partners or at least 2 STD episodes within the last 3 years from the three CAPRISA clinical research sites in an attempt to identify a subset of individuals who, although continuously exposed to HIV-1, have escaped infection by virtue of some type of host response. Intense efforts will be made to rule out HIV infections in any person who has such a response. This is a joint project involving CAPRISA and the University of Washington. Assays will be conducted in Durban, Johannesburg and Seattle.

The evaluation of HIV-specific immune responses will focus on the following analyses:

1. T helper responses: HIV protein or peptide induced lymphoproliferation, IL-2 mRNA expression or secretion
2. CTL responses: presence and specificity of class I MHC-restricted CD8+CTL directed against *env*, *gag*, *nef*, or *pol*
3. B cell antibody production: stimulation with pokeweed mitogen, assessment of anti-HIV *env/gag* IgM, IgA, IgG

The evaluation of HIV-specific receptor and mediator expression will focus on the following:

1. Presence and expression of the HIV-1 co-receptor gene, CCR5's 32-base pair deletion, point mutations and other deletions in CCR5 and the promoter region.

2. Expression of other HIV-1 co-receptor genes CCR1, CCR2, CCR3, CCR4, and CXCR4.
3. Expression of the chemokines SDF-1, RANTES, MIP-1a, MIP-1b, and the dendritic cell-specific C-type lectin, DC-SIGN.

Mucosal Specimens: cervical cytobrush/snostrip, semen, parotid

1. T helper responses: HIV protein or peptide induced lymphoproliferation, IL-2 mRNA expression or secretion
2. CTL responses: presence and specificity of class I MHC-restricted CD8+CTL directed against env, gag, nef, or pol
3. B cell antibody production: stimulation with pokeweed mitogen, assessment of anti-HIV env/gag IgM, IgA, IgG
4. Antibody in secretion: IgM, IgA, IgG

3.3 Collection and processing of specimens;

Participants will be called in for regularly scheduled clinic visits (Table 1), at which point bloods and other biological samples will be collected by clinic staff. Samples will be transported to the CAPRISA laboratory at the Doris Duke Medical Research Institute for processing, distribution and storage in the CAPRISA study repository according to standard operating procedures. Specimens will be shipped from the central CAPRISA repository to the NICD laboratory in Johannesburg and Fred Hutchinson Cancer Research Center in Seattle in compliance with IATA dangerous good packing instructions. Fresh blood specimens will be processed in the central repository and shipped on dry ice, as frozen plasma, sera cells, DNA or culture supernatants for shipment to Johannesburg and Seattle, where the samples will be further processed, catalogued, stored and assayed.

Table 1: Schedule of evaluations for HIV-1 Multiply Exposed Seronegative Individuals

Study Activity	Visit 1 Month 0	Visit 2 Month 3	Visit 3 Month 6	Visit 4 Month 12	Visit 5 Month 15	Visit 6 Month 18	Visit 7 Month 24	Post- Seroconversion Visit ^a
Recruit, enroll, consent	X							
Clinical Evaluation ^b	X	X	X	X	X	X	X	X
HIV testing/ counseling ^c	X	X	X	X	X	X	X	X
Risk reduction counseling	X	X	X	X	X	X	X	X
Questionnaire ^d	Initial	Interval	Interval	Interval	Interval	Interval	Interval	Seroconversion
PBMC cryopreservation for T cell studies	60 cc	60 cc	60 cc	60 cc	60 cc	60 cc	60 cc	60 cc
Sera/Plasma for HIV test confirmation ^e , Ab responses	20 cc	20 cc	20 cc	20 cc	20 cc	20 cc	20 cc	20 cc

^aTo occur for participants who were enrolled as HIV-negative but whom became HIV-positive approximately 1 month after seroconversion

^bIncludes risk assessment, review of symptoms, use of antiretrovirals and/or other medications, and symptom based physical exam.

^cHIV testing will not be done for known HIV-positive participants with the exception of Visit 1

^dAppendix I

^eConfirmation of HIV rapid testing will be performed by standard EIA and plasma will be available for viral loads if volunteers acquire infection (sera from no anticoagulant red-top tube; plasma from ACD tube from PBMC)

3.3 Storage and analysis of specimens

Specimens will be stored at the CAPRISA specimen repository in freezers. Samples will be sent to Dr Clive Gray and Dr Julie McElrath for analysis. The specimen repository will comprise a restricted access laboratory with a courier access window to drop off specimens. Typically, plasma and cell separation will

be performed within a few hours of collection and always within 24 hour of collection. Specimens will be transported from the sites to the repository in biohazard containers. All samples will be accompanied with a study form indicating the clinic code, patient identification number, visit code, sample type, time and date of collection. For long-term storage, plasma, sera, and cell pellets will be stored in – 80°C freezers and PBMCs will be stored at -140°C freezer – these are all electronically monitored.

The processing of blood is well standardised and the collection and processing of mucosal specimens will be according to established SOPs. To ensure uniformity of procedures, these fluids will be processed according to the "Manual for Collection and Processing of Mucosal Specimens".

- **Quality control:**

International laboratories will be employed to assist in assay development and external quality assurance of complex laboratory tests. Procedures for ensuring the quality control of data collection and capturing have also been developed. The Diagnostics division, including the Molecular Diagnostics Unit, at the National Institute for Communicable Diseases has been fully accredited with SANAS (South African National Accreditation Society, SANAS number: M0029) that is internationally recognised. The Molecular Diagnostics Unit participates in external quality assurance programs (National External Quality Assurance Schemes (NEQAS), a UK-based organisation.) for the HIV-1 viral loads and immunophenotyping (CD4 counts). There are also internal quality assurance programs in all sections and bi-annual internal audits for the Diagnostic division including the Molecular Diagnostics Unit. The HLA typing system has been enrolled with the British NEQAS for external quality assurance purposes.

4.0 Eligibility

Inclusion Criteria

- Age: 18-60
- Sex: Male or Female [*For females, negative pregnancy test at the time of entry and assurance that adequate birth control measures will be used for the duration of the study.*]
- Normal history and physical examination
- Higher risk sexual behavior such as at least 3 partners in the last 3 years.
- Negative ELISA and Western Blot for HIV-1
- Able to provide written informed consent to have samples stored
- Availability for follow-up for planned 2 year duration of the study

Exclusion Criteria

- History of immunodeficiency, chronic illness, malignancy, autoimmune disease, or use of immunosuppressive medications. Individuals with a history of cancer are excluded unless there has been surgical excision followed by sufficient observation period to give a reasonable assurance of cure.
- Medical or psychiatric condition or occupational responsibilities, which preclude subject compliance with the protocol.
- Prior receipt of HIV-1 vaccines
- Pregnant or lactating women

5.0 Studies to be performed

5.1 Immunological and Virological Determinants:

Antibody Response

Humoral Ab: HIV-1 *env/gag* antibody subsets (serum, pokeweed mitogen stimulated B cells)

Mucosal Ab: collected from cervical cytobrush, semen and/or parotid secretions
HIV-1 EIA, IgA, IgG, IgM
ECL Western blot

Cellular Responses

CD8+ CTL: stimulation with autologous APC pulsed with HIV-1 peptides or infected with recombinant vectors expressing HIV gene products
CD4+ helper cells: proliferation and cytokine production (mRNA expression or secretions) in response to HIV-1 antigens (*env*, *gag*, *pol*, *nef*)

Other HIV-1 Resistance Factors

Susceptibility of PBMC to in vitro HIV-1 infection (comparison to TCID₅₀ of these persons with low risk seronegatives to NSI and SI clinical isolates)
HLA type
Co-receptor expression
Chemokine expression

Detailed analysis of HIV-1 infection

HIV-1 RNA PCR of plasma, PBMC, semen or cervical swabs

8.0 ACCESS TO HIV RELATED CARE

8.1 HIV Counselling and Testing

HIV pre-test, risk reduction, and post-test counselling 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. Condoms will be provided to participants throughout the duration of their participation.

8.2 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 counselling.

During the study screening process, study staff will refer persons found to be HIV-infected to the CAPRISA AIDS Treatment Programme (which provides comprehensive AIDS care including antiretroviral therapy) or will be referred to the appropriate care facilities for medical and psychosocial care and support. HIV-uninfected study participants who seroconvert during follow-up will be referred to the CAPRISA Acute Infection Study, which provides long-term follow-up, monitoring and access to anti-retroviral therapy. Any participants found to be HIV-infected and pregnant also will be referred to appropriate Health Care Facilities which routinely provide single-dose nevirapine to reduce mother-to-child HIV transmission.

9.0 INFORMED CONSENT PROCEDURES

Participants will be requested to provide written informed consent for participation in the study (Appendix II). In addition, informed consent will be obtained to store specimens (Appendix III). Study staff will store plasma and serum collected from each study participant at the time of study entry, seroconversion (if applicable), and study exit. All such specimens may be required for possible quality assurance testing during and after the study. In addition, study participants will be asked to provide written informed consent for storage of specimens 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.

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Appendix I: Study questionnaire

**Demographics
Form Instructions**

- The Demographics form is completed only at Screening.
- If a data item is not available, draw a line through the response boxes.
- **SEX:**
 - Biological sex is the participant's gender at birth.
 - If the participant is transgender male to female, mark the "male" box.
 - If the participant is transgender female to male, mark the "female" box.
- **RACE:**
 - Mark the box which corresponds with the race the participant identifies with most.
 - If the participant identifies with more than one race, mark the "Other" box and write the races on the specify line.



AIN005 Triple-X (078)

DM (010)

Participant ID

XXX -

Demographics

Screening Date

dd *MMM* *yy*

1. What is the participant's date of birth?
dd *MMM* *yy*

2. What is the participant's biological sex?

male

female

3. Does the participant consider him/herself to be Latino/a or of Hispanic origin? *yes* *no*

4. What is the participant's race? *Mark only one.*

American Indian or Alaska Native

Asian

Black or African American

Native Hawaiian or other Pacific Islander

Australian Aboriginal

White

Other, specify: _____

**Eligibility Checklist
Form Instructions**

- The Eligibility Checklist is completed only at Screening.
- Women who are not of child-bearing potential must have medical documentation indicating this. Otherwise, a pregnancy test is required.
- Note: A complete date of consent is required.



AIN005 Triple-X (078)

EC (020)

Participant ID

XXX -

Eligibility Checklist

Form Completion Date

dd MMM yy

INCLUSION CRITERIA

<i>yes</i>	<i>no</i>	
<input type="checkbox"/>	<input type="checkbox"/>	1. The participant...
<input type="checkbox"/>	<input type="checkbox"/>	1a. has documented negative ELISA and Western Blot for HIV-1 infection ≤ 30 days prior to entry.
<input type="checkbox"/>	<input type="checkbox"/>	1b. is ≥ 18 years old and ≤ 60 years old.
<input type="checkbox"/>	<input type="checkbox"/>	1c. has a normal history and physical examination.
<input type="checkbox"/>	<input type="checkbox"/>	1d. engages in high risk sexual behavior that is classified as: <i>(Mark only one.)</i>
		<input type="checkbox"/> <i>Category A</i> <input type="checkbox"/> <i>Category B</i> <input type="checkbox"/> <i>Category C, specify:</i> _____
<input type="checkbox"/>	<input type="checkbox"/>	1e. is available for 96 weeks of follow-up.
<input type="checkbox"/>	<input type="checkbox"/>	1f. has signed informed consent for study participation.
		1f1. Date consent signed: <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <i>dd MMM yy</i>
<input type="checkbox"/>	<input type="checkbox"/>	1g. Women of child-bearing potential only:
		Participant had a negative pregnancy test ≤ 30 days prior to entry.
		<i>If NO to any of the above, participant is INELIGIBLE; end of form. Complete the Enrollment Assessment.</i>
		<i>To be eligible, all responses must be YES or NOT APPLICABLE. Go to the Exclusion Criteria.</i>

Comments: _____

EXCLUSION CRITERIA

<i>yes</i>	<i>no</i>	
<input type="checkbox"/>	<input type="checkbox"/>	2. The participant...
<input type="checkbox"/>	<input type="checkbox"/>	2a. has a history of immunodeficiency, chronic illness, malignancy, autoimmune disease, or use of immunosuppressive medications.
<input type="checkbox"/>	<input type="checkbox"/>	2b. has medical or psychiatric conditions or occupational responsibilities which preclude participant compliance with the protocol.
<input type="checkbox"/>	<input type="checkbox"/>	2c. has active tuberculosis.
<input type="checkbox"/>	<input type="checkbox"/>	2d. has received HIV-1 vaccination(s).
<input type="checkbox"/>	<input type="checkbox"/>	2e. Women of child-bearing potential only: Participant is pregnant or nursing.
		<i>To be eligible, all responses must be NO or NOT APPLICABLE.</i>
		<i>If YES to any of the above, participant is INELIGIBLE. Complete the Enrollment Assessment.</i>

04-MAY-01

Staff Initials / Date

**Screening Assessment
Form Instructions**

Page 1

- If a data item is not available, draw a line through the response boxes.



AIN005 Triple-X (078)

SRA-1 (030)

Participant ID

XXX - [][][][]

Screening Assessment

Form Completion Date

[][] [][][] [][]
dd MMM yy

QUESTIONS ABOUT SEXUAL BEHAVIOR

We define SEX to include encounters in which either partner's genitals contact the other partner's mouth, tongue, anus, or genitals. We define UNPROTECTED sex as sex without a latex condom or sex during which the condom broke. We define PROTECTED sex as sex using a latex condom which was put on before "penetration" and did not break.

1. In the last 6 months, did you have one regular sex partner? A regular partner is the one person you consider your primary sexual partner. [] yes [] no → If no, go to item 16.

2. Is your regular sex partner male or female? [] male [] female

3. What is his/her HIV status? [] HIV-positive [] HIV-negative and no reason to doubt it [] unknown → If HIV-negative or unknown, go to item 3c.

3a. When did your regular partner first test HIV-positive? [][] dd [][][] MMM [][] yy

3b. Is your regular partner currently taking any anti-retroviral drugs? [] yes [] no [] don't know

3c. MEN ONLY: Have you been circumcised? [] yes [] no

3d. If your regular partner is male, has he been circumcised? [] yes [] no [] N/A

4. In the last 6 months, how often did you have sex with your regular partner? Mark only one.

[] never [] less than 1 day a week [] 1-2 days a week [] 3-6 days a week [] daily
→ If never, go to item 16.

5. When did you most recently have sex with your regular partner? Mark only one.

[] today [] within the last month [] within the last 3 days [] more than 1 month ago [] within the last 2 weeks

[][][x][] 25-JUL-01

Staff Initials / Date

**Screening Assessment
Form Instructions**

Page 2

Sexual Behavior Section

- To the left of items 7–15 are the initials M or M/F, indicating whether the item applies to male participants only (M) or either male or female participants (M/F). There are no female-only items.
- For items 7–15, a response or marking the N/A box is required.
- Mark the N/A box next to each item that does not apply to the participant. For example, if the participant is female, the N/A box should be marked for items 9 and 10.
- If an exact number is not known, ask for the participant's best guess.
- If a data item is not available, draw a line through the response boxes.



AIN005 Triple-X (078)

SRA-2 (031)

Participant ID

XXX - [][][][]

Screening Assessment

6. The last time you had sex with your regular partner, which of the following sexual activities did you have? Mark all that apply.

- active oral sex (your mouth/tongue on your partner's genitals)
receptive oral sex (your partner's mouth/tongue on your genitals)
receptive fisting/insertive rimming
receptive vaginal/anal sex with a condom, as the "bottom"
receptive vaginal/anal sex without a condom, as the "bottom"
insertive vaginal/anal sex with a condom, as the "top" (men only)
insertive vaginal/anal sex without a condom, as the "top" (men only)

SEXUAL BEHAVIOR WITH YOUR REGULAR PARTNER

I am now going to ask you some detailed questions about sex with your regular partner. In the last 6 months...

- 7. how many times did you have unprotected receptive vaginal/anal sex (your partner's penis in your vagina/anus) with your regular partner (male partner only)? [][][] OR []
8. how many times did you have protected receptive vaginal/anal sex (your partner's penis in your vagina/anus) with your regular partner (male partner only)? [][][] OR []
9. how many times did you have unprotected insertive vaginal/anal sex (your penis in your partner's vagina/anus) with your regular partner? [][][] OR []
10. how many times did you have protected insertive vaginal/anal sex (your penis in your partner's vagina/anus) with your regular partner? [][][] OR []
11. how many times did you engage in receptive fisting or insertive rimming with your regular partner? [][][] OR []
12. how many times did you have active oral sex (your mouth on your partner's genitals) with your regular partner where your partner ejaculated or "came" in your mouth without a condom (does not include pre-cum) (male partner only)? [][][] OR []
13. how many times did you have active oral sex (your mouth on your partner's genitals) with your regular partner where you were exposed to his pre-cum (male partner only)? [][][] OR []
14. how many times did you have active oral sex (your mouth on your partner's genitals) with your regular partner where a condom was used OR your partner did NOT ejaculate or "pre-cum" into your mouth (male partner only)? [][][] OR []
15. how many times did you have receptive oral sex (your partner's mouth on your genitals) with your regular partner? [][][] OR []

[] [] [x] [] 25-JUL-01

Staff Initials / Date

**Screening Assessment
Form Instructions**

Page 3

- If an exact number is not known, ask for the participant's best guess.
- For vaginal or anal sex, "unprotected" refers to sex without a latex condom or where the condom broke. "Protected" refers to sex using a latex condom which was put on before penetration and did not break.
- If a data item is not available, draw a line through the response boxes.



AIN005 Triple-X (078)

SRA-3 (032)

Participant ID

XXX -

Screening Assessment

SEXUAL BEHAVIOR WITH HIV-POSITIVE NON-REGULAR SEX PARTNERS

The following section refers to sex partners other than your regular partner.

16. **In the last 6 months**, how many sex partners have you had, other than your regular partner, who were known to be HIV-positive?.....

➔ **If 000, go to item 19.**

Instructions: For items 16a–16f, complete the “yes/no” section first, then obtain the approximate number of times and partners.

ACTIVITY	UNPROTECTED/UNSAFE SEX			PROTECTED/POSSIBLY SAFE SEX				
	yes	no	# of times	# of male partners	# of female partners	# of times	# of male partners	# of female partners
16a. penile-vaginal sex	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/>					
16b. anal receptive sex	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	NOT ASKED	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	NOT ASKED
16c. anal insertive sex (male ppt. only)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/>					
16d. receptive fisting/insertive rimming	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	NOT ASKED	NOT ASKED	NOT ASKED
16e. active oral sex	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/>					
16f. receptive oral sex	<input type="checkbox"/>	<input type="checkbox"/>	NOT ASKED	NOT ASKED	NOT ASKED	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>
16g. Total # of unprotected/unsafe times			<input type="text"/> <input type="text"/> <input type="text"/>			16h. Total # of protected/possibly safe times	<input type="text"/> <input type="text"/> <input type="text"/>	

17. For activities listed under Unprotected/Unsafe Sex above, **in the last 6 months**, what is the total number of different partners involved in all of these activities combined? # of different partners
18. For activities listed under Protected/Possibly Safe Sex above, **in the last 6 months**, what is the total number of different partners involved in all of these activities combined?

**Screening Assessment
Form Instructions**

Page 4

- If an exact number is not known, ask for the participant's best guess.
- For vaginal or anal sex, "unprotected" refers to sex without a latex condom or where the condom broke. "Protected" refers to sex using a latex condom which was put on before penetration and did not break.
- If a data item is not available, draw a line through the response boxes.



AIN005 Triple-X (078)

SRA-4 (033)

Participant ID

XXX -

Screening Assessment

SEXUAL BEHAVIOR WITH HIV-NEGATIVE NON-REGULAR SEX PARTNERS

The following section refers to sex partners other than your regular partner.

19. **In the last 6 months**, how many sex partners have you had, other than your regular partner, who said they were HIV-negative and you had no reason to doubt it?

19a. penile-vaginal sex

→ **If 000, go to item 22.**

Instructions: For items 19a–19f, complete the “yes/no” section first, then obtain the approximate number of times and partners.

ACTIVITY	UNPROTECTED/UNSAFE SEX			PROTECTED/POSSIBLY SAFE SEX				
	yes	no	# of times	# of male partners	# of female partners	# of times	# of male partners	# of female partners
19b. anal receptive sex	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/>					
19c. anal insertive sex	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	NOT ASKED	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	NOT ASKED
(male ppt. only) 19d. receptive fisting/ insertive rimming	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/>					
19e. active oral sex	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	NOT ASKED	NOT ASKED	NOT ASKED
19f. receptive oral sex	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/>					
19g. Total # of	<input type="checkbox"/>	<input type="checkbox"/>	NOT ASKED	NOT ASKED	NOT ASKED	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>
			↓			↓		
			unprotected/unsafe times	<input type="text"/> <input type="text"/> <input type="text"/>		19h. Total # of protected/possibly safe times	<input type="text"/> <input type="text"/> <input type="text"/>	

20. For activities listed under Unprotected/Unsafe Sex above, **in the last 6 months**, what is the total number of different partners involved in all of these activities combined? # of different partners
21. For activities listed under Protected/Possibly Safe Sex above, **in the last 6 months**, what is the total number of different partners involved in all of these activities combined?

**Screening Assessment
Form Instructions**

Page 5

- If an exact number is not known, ask for the participant's best guess.
- For vaginal or anal sex, "unprotected" refers to sex without a latex condom or where the condom broke. "Protected" refers to sex using a latex condom which was put on before penetration and did not break.
- If a data item is not available, draw a line through the response boxes.



AIN005 Triple-X (078)

SRA-5 (034)

Participant ID

XXX -

Screening Assessment

SEXUAL BEHAVIOR WITH HIV-STATUS UNKNOWN NON-REGULAR SEX PARTNERS

The following section refers to sex partners other than your regular partner.

22. **In the last 6 months**, how many sex partners have you had, other than your regular partner, who never told you their HIV status or told you they were negative but you had reason to doubt it?

→ **If 000, go to item 25.**

Instructions: For items 22a–22f, complete the “yes/no” section first, then obtain the approximate number of times and partners.

ACTIVITY	UNPROTECTED/UNSAFE SEX			PROTECTED/POSSIBLY SAFE SEX				
	yes	no	# of times	# of male partners	# of female partners	# of times	# of male partners	# of female partners
22a. penile-vaginal sex	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/>					
22b. anal receptive sex	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	NOT ASKED	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	NOT ASKED
22c. anal insertive sex (male ppt. only)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/>					
22d. receptive fisting/insertive rimming	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	NOT ASKED	NOT ASKED	NOT ASKED
22e. active oral sex	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/>					
22f. receptive oral sex	<input type="checkbox"/>	<input type="checkbox"/>	NOT ASKED	NOT ASKED	NOT ASKED	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>
22g. Total # of unprotected/unsafe times	↓			<input type="text"/> <input type="text"/> <input type="text"/>	22h. Total # of protected/possibly safe times			<input type="text"/> <input type="text"/> <input type="text"/>

23. For activities listed under Unprotected/Unsafe Sex above, **in the last 6 months**, what is the total number of different partners involved in all of these activities combined? # of different partners

24. For activities listed under Protected/Possibly Safe Sex above, **in the last 6 months**, what is the total number of different partners involved in all of these activities combined?

Screening Assessment
Form Instructions

Page 6

- If a data item is not available, draw a line through the response boxes.

Medication Code List

01 AZT (zidovudine; Retrovir)	11 Efavirenz (Sustiva)	21 Lopinavir (ABT-378)/Ritonavir (Kaletra))
02 3TC (Lamivudine; Epivir)	12 Indinavir (Crixivan)	22 ABT-378
03 Combivir (AZT + 3TC)	13 Saquinavir (Invirase; Fortovase)	23 Drug study (unknown or placebo)
04 ddl (didanosine; Videx)	14 Nelfinavir (Viracept)	24 Remune
05 ddC (zalcitabine; HIVID)	15 Ritonavir (Norvir)	25 Trizivir (AZT + 3TC + Abacavir)
06 d4T (Stavudine; Zerit)	16 Amprenavir (Agenerase)	26 Tenofovir
07 Abacavir (Ziagen)	17 Hydroxyurea (Hydrea)	27 T-20
08 Adefovir (Preveon)	18 IL2	99 Other (specify)
09 Nevirapine (Viramune)	19 <i>no longer used</i>	
10 Delavirdine (Rescriptor)	20 Tipranavir	



AIN005 Triple-X (078)

SRA-6 (035)

Participant ID

XXX -

Screening Assessment

DRUG AND MEDICATION USE

25. In the last 3 years, how many times have you used a needle to inject illicit drugs, including steroids, under your skin or into a vein?.....

→ If 000, go to item 27.

In the last 6 months...

26. after how many people did you use needles or syringes?.....

→ If 000, go to item 27.

26a. How many of these people were known to be HIV-infected?.....

27. how many times have you used poppers or inhaled nitrates including ampules?

28. how many times have you swallowed, snorted, or smoked amphetamines such as speed, crystal, or crank?

29. how many times have you used Ecstasy?.....

30. have you used anti-HIV medications before or after a risky exposure to try to prevent HIV infection?

yes no

→ If no, go to item 31.

30a. What medications did you use? Refer to the code list on the back of the form. A dose is any number of pills taken at one time. A dose is considered missed after 24 hours.

	Drug Code	# Days Taken	# Doses Missed
30a1. Medication	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>
30a2. Medication	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>
30a3. Medication	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>

**Screening Assessment
Form Instructions**

Page 7

- If a data item is not available, draw a line through the response boxes.



AIN005 Triple-X (078)

SRA-7 (036)

Participant ID

XXX - [][][][]

Screening Assessment

OTHER

31. Have you ever had or been vaccinated against Hepatitis A? yes no [] [] -> If no, go to item 32.

31a. When did you receive your last shot? [][] [][][] [][] OR [] still expecting additional shot dd MMM yy

32. Have you ever had or been vaccinated against Hepatitis B? yes no [] [] -> If no, go to item 33.

32a. When did you receive your last shot? [][] [][][] [][] OR [] still expecting additional shot dd MMM yy

33. In the last 6 months, have you received any vaccinations other than Hepatitis A or Hepatitis B? yes no [] [] -> If no, go to item 34.

33a. Specify other vaccinations: _____

34. Have you ever been told you were positive for Hepatitis C? yes no don't know [] [] []

35. Have you ever been told you were positive for Cytomegalovirus? yes no don't know [] [] []

In the last 6 months...

36. outside of sexual activity, have you gotten blood or bloody fluid on a mucous membrane such as the mouth or eyes or had a needle stick with a blood-contaminated object? yes no don't know [] [] []
37. have you had unprotected sex with anyone who used injection drugs? [] [] []
38. have you had unprotected sex with a hemophiliac? [] [] []
39. have you had unprotected sex in exchange for money or other favors such as drugs? [] [] []
40. have you had transfusions of blood or blood products? [] [] []

[] [] [x] [] 25-JUL-01

Staff Initials / Date

**Screening Assessment
Form Instructions**

Page 8

- If the exact number of times or date of most recent time is not known, ask the participant to give his/her best guess.
- If a data item is not available, draw a line through the response boxes.



AIN005 Triple-X (078)

SRA-8 (037)

Participant ID

XXX -

Screening Assessment

SEXUALLY TRANSMITTED DISEASES

41. In the last 6 months, has a medical provider diagnosed or treated you for any sexually transmitted diseases? *yes* *no* **→ If no, go to item 42.**

Instructions: For each sexually transmitted disease experienced, complete the number of times, most recent date, and if participant was treated by a medical provider.

Mark all that apply	How many times?	When was the most recent time?			Were you treated?	
		<i>dd</i>	<i>MMM</i>	<i>yy</i>	<i>yes</i>	<i>no</i>
<input type="checkbox"/> 41a. chlamydia or non-specific urethritis (NSU, NGU)	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> 41b. urethral gonorrhea or "clap"	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> 41c. rectal gonorrhea or "clap"	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> 41d. pharyngeal gonorrhea or "clap"	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> 41e. syphilis	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> 41f. genital or rectal herpes	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> 41g. genital or rectal warts	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> 41h. acute hepatitis B (serum hepatitis)	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> 41i. trichomoniasis or "trich"	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> 41j. pelvic inflammatory disease (PID)	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="checkbox"/>	<input type="checkbox"/>

42. In the last 6 months, has a medical provider diagnosed or treated you for either of the following?

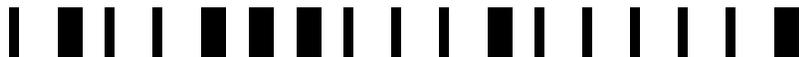
Mark all that apply	How many times?	When was the most recent time?			Were you treated?	
		<i>dd</i>	<i>MMM</i>	<i>yy</i>	<i>yes</i>	<i>no</i>
<input type="checkbox"/> 42a. atypical pap smear	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> 42b. cervical cancer	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="checkbox"/>	<input type="checkbox"/>

22-AUG-01

Staff Initials / Date

Enrollment Assessment Form Instructions

- The Enrollment Assessment form is completed for all screened participants, regardless of eligibility status.



AIN005 Triple-X (078)

EA (065)

Participant ID

XXX -

Enrollment Assessment

1. Does the participant meet all eligibility criteria? *yes* *no* → *If no, end of form.*

2. Was the participant previously enrolled in the Triple X study (i.e., an "old participant")? *yes* *no* → *If yes, go to item 4.*

3. *Complete for new participants only:*
Is the participant enrolling in the Triple X study? *yes* *no* → *If no, go to item 5.*

4. Date of enrollment: → *End of form.*
dd *MMM* *yy*

5. Reason(s) participant will not enroll. *Mark all that apply.*

- Participant is planning to leave area.
- Participant has insufficient knowledge of study.
- Participant is unable/unwilling to provide adequate blood specimens.
- Participant is unable/unwilling to commit time required for the study.
- Advice of primary medical provider or others.
- Other clinical judgment, please specify: _____

- Other reason, please specify: _____

6. *Complete only for previously enrolled participants:*
What is the visit code for the next expected visit? .
Visit #

If the participant is not enrolling in the Triple X study, no further forms are required.

11-JUN-01

Staff Initials / Date

**Follow-up Assessment
Form Instructions**

Page 1

- If a complete date is unavailable, draw a line through the day or month boxes as needed.
- If a data item is not available, draw a line through the response boxes.
- If the last visit occurred more than 6 months ago, ask questions in the context of, “In the last 3 months,” rather than “since your last visit.”



AIN005 Triple-X (078)

FRA-1 (130)

Visit Code

Participant ID

XXX -

Follow-up Assessment

Form Completion Date

dd MMM yy

QUESTIONS ABOUT SEXUAL BEHAVIOR

We define SEX to include encounters in which either partner's genitals contact the other partner's mouth, tongue, anus, or genitals. We define UNPROTECTED sex as sex without a latex condom or sex during which the condom broke. We define PROTECTED sex as sex using a latex condom which was put on before "penetration" and did not break.

- Since your last visit, did you have one regular sex partner? *A regular partner is the one person you consider your primary sexual partner.*

yes no
 → If no, go to item 18.
- Is your regular sex partner male or female?

male female
- Is this a new partner since your last visit?

yes no
- What is his/her HIV status?

HIV-positive
 HIV-negative and no reason to doubt it → If HIV-negative or unknown, go to item 5.
 unknown
- When did your regular partner first test HIV-positive?

dd MMM yy OR unknown
- Is your regular partner currently taking any anti-retroviral drugs?

yes no don't know
- If your regular partner is male, has he been circumcised?

yes no N/A
- Since your last visit, how often have you had sex with your regular partner?

never less than 1 day a week 1-2 days a week 3-6 days a week daily

→ If never, go to item 18.
- When did you most recently have sex with your regular partner?

today within the last month
 within the last 3 days more than 1 month ago
 within the last 2 weeks

25-JUL-01

Staff Initials / Date

**Follow-up Assessment
Form Instructions**

Page 2

Sexual Behavior with Your Regular Partner

- To the left of items 9–17 are the initials M or M/F, indicating whether the item applies to male participants only (M) or either male or female participants (M/F). There are no female-only items.
- For items 9–17, a response or marking the N/A box is required.
- Mark the N/A box next to each item that does not apply to the participant. For example, if the participant is female, the N/A box should be marked for items 11 and 12.
- If an exact number is not known, ask for the participant's best guess.
- If a data item is not available, draw a line through the response boxes.
- If the last visit occurred more than 6 months ago, ask questions in the context of, "In the last 3 months," rather than "since your last visit."



AIN005 Triple-X (078)

FRA-2 (131)

Visit Code

Participant ID

XXX -

Follow-up Assessment

8. The last time you had sex with your regular partner, which of the following sexual activities did you have? Mark all that apply.

- active oral sex (your mouth/tongue on your partner's genitals)
receptive oral sex (your partner's mouth/tongue on your genitals)
receptive fisting/insertive rimming
receptive vaginal/anal sex with a condom, as the "bottom"
receptive vaginal/anal sex without a condom, as the "bottom"
insertive vaginal/anal sex with a condom, as the "top" (men only)
insertive vaginal/anal sex without a condom, as the "top" (men only)

SEXUAL BEHAVIOR WITH YOUR REGULAR PARTNER

I am now going to ask you some detailed questions about sex with your regular partner.

Since your last visit...

- 9. how many times did you have unprotected receptive vaginal/anal sex (your partner's penis in your vagina/anus) with your regular partner (male partner only)?
10. how many times did you have protected receptive vaginal/anal sex (your partner's penis in your vagina/anus) with your regular partner (male partner only)?
11. how many times did you have unprotected insertive vaginal/anal sex (your penis in your partner's vagina/anus) with your regular partner?
12. how many times did you have protected insertive vaginal/anal sex (your penis in your partner's vagina/anus) with your regular partner?
13. how many times did you engage in receptive fisting or insertive rimming with your regular partner?
14. how many times did you have active oral sex (your mouth on your partner's genitals) with your regular partner where your partner ejaculated or "came" in your mouth without a condom (does not include pre-cum) (male partner only)?
15. how many times did you have active oral sex (your mouth on your partner's genitals) with your regular partner where you were exposed to his pre-cum (male partner only)?
16. how many times did you have active oral sex (your mouth on your partner's genitals) with your regular partner where a condom was used OR your partner did NOT ejaculate or "pre-cum" into your mouth (male partner only)?
17. how many times did you have receptive oral sex (your partner's mouth on your genitals) with your regular partner?

25-JUL-01

Staff Initials / Date

**Follow-up Assessment
Form Instructions**

Page 3

- If an exact number is not known, ask for the participant's best guess.
- For vaginal or anal sex, "unprotected" refers to sex without a latex condom or where the condom broke. "Protected" refers to sex using a latex condom which was put on before penetration and did not break.
- If a data item is not available, draw a line through the response boxes.
- If the last visit occurred more than 6 months ago, ask questions in the context of, "In the last 3 months," rather than "since your last visit."



AIN005 Triple-X (078)

FRA-3 (132)

Visit Code

Participant ID

XXX -

Follow-up Assessment

SEXUAL BEHAVIOR WITH HIV-POSITIVE NON-REGULAR SEX PARTNERS

The following section refers to sex partners other than your regular partner.

18. Since your last visit, how many sex partners have you had, other than your regular partner, who were known to be HIV-positive?

→ If 000, go to item 21.

18a. How many of these partners are new since your last visit?

Instructions: For items 18b–18g, complete the “yes/no” section first, then obtain the approximate number of times and partners.

ACTIVITY

UNPROTECTED/UNSAFE SEX

PROTECTED/POSSIBLY SAFE SEX

			UNPROTECTED/UNSAFE SEX			PROTECTED/POSSIBLY SAFE SEX			
	yes	no	# of times	# of male partners	# of female partners	# of times	# of male partners	# of female partners	
18b. penile-vaginal sex	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/>						
18c. anal receptive sex	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	NOT ASKED	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	NOT ASKED	
18d. anal insertive sex (male ppt. only)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/>						
18e. receptive fisting/insertive rimming	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	NOT ASKED	NOT ASKED	NOT ASKED	
18f. active oral sex	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/>						
18g. receptive oral sex	<input type="checkbox"/>	<input type="checkbox"/>	NOT ASKED	NOT ASKED	NOT ASKED	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	
18h. Total # of unprotected/unsafe times			<input type="text"/> <input type="text"/> <input type="text"/>			18i. Total # of protected/possibly safe times	<input type="text"/> <input type="text"/> <input type="text"/>		

19. For activities listed under Unprotected/Unsafe Sex above, since your last visit, what is the total number of different partners involved in all of these activities combined?

20. For activities listed under Protected/Possibly Safe Sex above, since your last visit, what is the total number of different partners involved in all of these activities combined?

25-JUL-01

Staff Initials / Date

**Follow-up Assessment
Form Instructions**

Page 4

- If an exact number is not known, ask for the participant's best guess.
- For vaginal or anal sex, "unprotected" refers to sex without a latex condom or where the condom broke. "Protected" refers to sex using a latex condom which was put on before penetration and did not break.
- If a data item is not available, draw a line through the response boxes.
- If the last visit occurred more than 6 months ago, ask questions in the context of, "In the last 3 months," rather than "since your last visit."



AIN005 Triple-X (078)

FRA-4 (133)

Visit Code

Participant ID

XXX -

Follow-up Assessment

SEXUAL BEHAVIOR WITH HIV-NEGATIVE NON-REGULAR SEX PARTNERS

The following section refers to sex partners other than your regular partner.

21. Since your last visit, how many sex partners have you had, other than your regular partner, who said they were HIV-negative and you had no reason to doubt it?

→ If 000, go to item 24.

21a. How many of these partners are new since your last visit?

Instructions: For items 21b–21g, complete the “yes/no” section first, then obtain the approximate number of times and partners.

ACTIVITY

UNPROTECTED/UNSAFE SEX

PROTECTED/POSSIBLY SAFE SEX

			UNPROTECTED/UNSAFE SEX			PROTECTED/POSSIBLY SAFE SEX		
	yes	no	# of times	# of male partners	# of female partners	# of times	# of male partners	# of female partners
21b. penile-vaginal sex	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/>					
21c. anal receptive sex	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	NOT ASKED	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	NOT ASKED
21d. anal insertive sex (male ppt. only)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/>					
21e. receptive fisting/insertive rimming	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	NOT ASKED	NOT ASKED	NOT ASKED
21f. active oral sex	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/>					
21g. receptive oral sex	<input type="checkbox"/>	<input type="checkbox"/>	NOT ASKED	NOT ASKED	NOT ASKED	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>
21h. Total # of unprotected/unsafe times			<input type="text"/> <input type="text"/> <input type="text"/>					
21i. Total # of protected/possibly safe times						<input type="text"/> <input type="text"/> <input type="text"/>		

22. For activities listed under Unprotected/Unsafe Sex above, since your last visit, what is the total number of different partners involved in all of these activities combined?

of different partners

23. For activities listed under Protected/Possibly Safe Sex above, since your last visit, what is the total number of different partners involved in all of these activities combined?

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**Follow-up Assessment
Form Instructions**

Page 5

- If an exact number is not known, ask for the participant's best guess.
- For vaginal or anal sex, "unprotected" refers to sex without a latex condom or where the condom broke. "Protected" refers to sex using a latex condom which was put on before penetration and did not break.
- If a data item is not available, draw a line through the response boxes.
- If the last visit occurred more than 6 months ago, ask questions in the context of, "In the last 3 months," rather than "since your last visit."



AIN005 Triple-X (078)

FRA-5 (134)

Visit Code

Participant ID

XXX -

Follow-up Assessment

SEXUAL BEHAVIOR WITH HIV-STATUS UNKNOWN NON-REGULAR SEX PARTNERS

The following section refers to sex partners other than your regular partner.

24. **Since your last visit**, how many sex partners have you had, other than your regular partner, who never told you their HIV status or told you they were negative but you had reason to doubt it?

→ **If 000, go to item 27.**

24a. How many of these partners are new **since your last visit**?

Instructions: For items 24b–24g, complete the “yes/no” section first, then obtain the approximate number of times and partners.

ACTIVITY

UNPROTECTED/UNSAFE SEX

PROTECTED/POSSIBLY SAFE SEX

			UNPROTECTED/UNSAFE SEX			PROTECTED/POSSIBLY SAFE SEX		
	yes	no	# of times	# of male partners	# of female partners	# of times	# of male partners	# of female partners
24b. penile-vaginal sex	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/>					
24c. anal receptive sex	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	NOT ASKED	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	NOT ASKED
24d. anal insertive sex (male ppt. only)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/>					
24e. receptive fisting/insertive rimming	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	NOT ASKED	NOT ASKED	NOT ASKED
24f. active oral sex	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/>					
24g. receptive oral sex	<input type="checkbox"/>	<input type="checkbox"/>	NOT ASKED	NOT ASKED	NOT ASKED	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>
24h. Total # of unprotected/unsafe times			<input type="text"/> <input type="text"/> <input type="text"/>					
24i. Total # of protected/possibly safe times						<input type="text"/> <input type="text"/> <input type="text"/>		

25. For activities listed under Unprotected/Unsafe Sex above, **since your last visit**, what is the total number of different partners involved in all of these activities combined?

of different partners

26. For activities listed under Protected/Possibly Safe Sex above, **since your last visit**, what is the total number of different partners involved in all of these activities combined?

25-JUL-01

Staff Initials / Date

**Follow-up Assessment
Form Instructions**

Page 6

- If a data item is not available, draw a line through the response boxes.
- If the last visit occurred more than 6 months ago, ask questions in the context of, “In the last 3 months,” rather than “since your last visit.”

Medication Code List

01 AZT (zidovudine; Retrovir)	11 Efavirenz (Sustiva)	21 Lopinavir (ABT-378)/Ritonavir (Kaletra)
02 3TC (Lamivudine; Epivir)	12 Indinavir (Crixivan)	22 ABT-378
03 Combivir (AZT + 3TC)	13 Saquinavir (Invirase; Fortovase)	23 Drug study (unknown or placebo)
04 ddl (didanosine; Videx)	14 Nelfinavir (Viracept)	24 Remune
05 ddC (zalcitabine; HIVID)	15 Ritonavir (Norvir)	25 Trizivir (AZT + 3TC + Abacavir)
06 d4T (Stavudine; Zerit)	16 Amprenavir (Agenerase)	26 Tenofovir
07 Abacavir (Ziagen)	17 Hydroxyurea (Hydrea)	27 T-20
08 Adefovir (Preveon)	18 IL2	99 Other (specify)
09 Nevirapine (Viramune)	19 <i>no longer used</i>	
10 Delavirdine (Rescriptor)	20 Tipranavir	



AIN005 Triple-X (078)

FRA-6 (135)

Visit Code [][] . []

Participant ID

XXX - [][][][]

Follow-up Assessment

DRUG AND MEDICATION USE

Since your last visit...

27. how many times have you used a needle to inject illicit drugs, including steroids, under your skin or into a vein?

[][][]

If 000, go to item 29.

28. after how many people did you use needles or syringes?

[][][]

If 000, go to item 29.

28a. How many of these people were known to be HIV-infected?

[][][]

29. how many times have you used poppers or inhaled nitrates including ampules?

[][][]

30. how many times have you swallowed, snorted, or smoked amphetamines such as speed, crystal, or crank?

[][][]

31. how many times have you used Ecstasy?

[][][]

32. have you used anti-HIV medications before or after a risky exposure to try to prevent HIV infection? yes no [] []

If no, go to item 33.

32a. What medications did you use? Refer to the code list on the back of the form. A dose is any number of pills taken at one time. A dose is considered missed after 24 hours.

Table with 4 columns: Medication, Drug Code, # Days Taken, # Doses Missed. Rows 32a1, 32a2, 32a3.

OTHER

Since your last visit...

33. have you received any vaccinations? yes no [] []

If no, go to item 34.

33a. Specify vaccinations: _____

34. outside of sexual activity, have you gotten blood or bloody fluid on a mucous membrane such as the mouth or eyes or had a needle stick with a blood-contaminated object?

yes no don't know [] [] []

35. have you had unprotected sex with anyone who used injection drugs?

[] [] []

36. have you had unprotected sex with a hemophiliac?

[] [] []

37. have you had unprotected sex in exchange for money or other favors such as drugs?

[] [] []

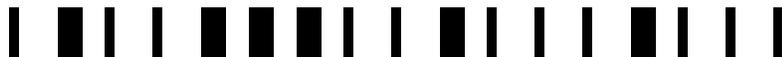
38. have you had transfusions of blood or blood products?

[] [] []

**Follow-up Assessment
Form Instructions**

Page 7

- If the exact number of times or date of most recent time is not known, ask the participant to give his/her best guess.
- If a data item is not available, draw a line through the response boxes.
- If the last visit occurred more than 6 months ago, ask questions in the context of, “In the last 3 months,” rather than “since your last visit.”



AIN005 Triple-X (078)

FRA-7 (136)

Visit Code

Page 7 of 9

Participant ID

XXX -

Follow-up Assessment

SEXUALLY TRANSMITTED DISEASES

39. Since your last visit, has a medical provider diagnosed or treated you for any sexually transmitted diseases? *yes* *no* **→ If no, go to item 40.**

Instructions: For each sexually transmitted disease experienced, complete the number of times, most recent date, and if participant was treated by a medical provider.

Mark all that apply	How many times?	When was the most recent time?			Were you treated?	
		dd	MMM	yy	yes	no
<input type="checkbox"/> 39a. chlamydia or non-specific urethritis (NSU, NGU)	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> 39b. urethral gonorrhea or "clap"	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> 39c. rectal gonorrhea or "clap"	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> 39d. pharyngeal gonorrhea or "clap"	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> 39e. syphilis	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> 39f. genital or rectal herpes	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> 39g. genital or rectal warts	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> 39h. acute hepatitis B (serum hepatitis)	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> 39i. trichomoniasis or "trich"	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> 39j. pelvic inflammatory disease (PID)	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="checkbox"/>	<input type="checkbox"/>

40. Since your last visit, has a medical provider diagnosed or treated you for either of the following?

Mark all that apply	How many times?	When was the most recent time?			Were you treated?	
		dd	MMM	yy	yes	no
<input type="checkbox"/> 40a. atypical pap smear	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/> 40b. cervical cancer	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="checkbox"/>	<input type="checkbox"/>

Continue to Seroconversion Symptoms on page 8.

25-JUL-01

Staff Initials / Date

**Follow-up Assessment
Form Instructions**

Page 8

- If a data item is not available, draw a line through the response boxes.

- **SYMPTOMS:**
 - Use your best clinical judgment to determine if a participant's symptoms are associated with seroconversion.
For example, if a participant reports experiencing a skin rash 8 months prior to his/her first HIV-positive test, this symptom is clearly not associated with seroconversion and should not be recorded on this form.
 - Mark the box next to each seroconversion symptom the participant reports experiencing.
 - If the participant experienced a symptom that does not appear on the list, mark the "Other" box and specify the symptom.
 - If the participant experienced more than one symptom that doesn't appear on the list, record information about the most severe symptom.
 - If exact information is not known, ask the participant for his/her best guess.
 - If no symptoms, mark the "No Symptoms Reported" box.



AIN005 Triple-X (078)

FRA-8 (137)

Visit Code

Participant ID

XXX -

Follow-up Assessment

SEROCONVERSION SYMPTOMS

41. Since the last visit, have you experienced any of the following symptoms associated with seroconversion?

	How many different times did you have this symptom?	When was the first time this symptom began?		How long did this symptom last?	When was the second time this symptom began?		How long did this symptom last?
	# of episodes	MMM	yy	# of days	MMM	yy	# of days
<input type="checkbox"/> 41a. fever; highest temp: <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> . <input type="text"/> °F	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>
<input type="checkbox"/> 41b. drenching sweats that left your bedclothes soaked at night	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>
<input type="checkbox"/> 41c. headache, not from a hangover	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>
<input type="checkbox"/> 41d. stiff neck, not from exercise or injury	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>
<input type="checkbox"/> 41e. sore muscles or joints, not from exercise, arthritis, or injury	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>
<input type="checkbox"/> 41f. new body rash	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>
<input type="checkbox"/> 41g. nausea or sick to your stomach	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>
<input type="checkbox"/> 41h. diarrhea	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>

Continue to 41i on page 9.

25-JUL-01

Staff Initials / Date

**Follow-up Assessment
Form Instructions**

Page 9

- If a data item is not available, draw a line through the response boxes.
- **SYMPTOMS:**
 - Use your best clinical judgment to determine if a participant's symptoms are associated with seroconversion.
For example, if a participant reports experiencing a skin rash 8 months prior to his/her first HIV-positive test, this symptom is clearly not associated with seroconversion and should not be recorded on this form.
 - Mark the box next to each seroconversion symptom the participant reports experiencing.
 - If the participant experienced a symptom that does not appear on the list, mark the "Other" box and specify the symptom.
 - If the participant experienced more than one symptom that doesn't appear on the list, record information about the most severe symptom.
 - If exact information is not known, ask the participant for his/her best guess.
 - If no symptoms, mark the "No Symptoms Reported" box.



AIN005 Triple-X (078)

FRA-9 (138)

Visit Code

Page 9 of 9

Participant ID

XXX -

Follow-up Assessment

SEROCONVERSION SYMPTOMS, continued

	How many different times did you have this symptom?	When was the first time this symptom began?		How long did this symptom last?	When was the second time this symptom began?		How long did this symptom last?
	<i>Mark all that apply.</i> # of episodes	MMM	yy	# of days	MMM	yy	# of days
<input type="checkbox"/> 41i. vomiting	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>
<input type="checkbox"/> 41j. fatigue	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>
<input type="checkbox"/> 41k. light hurting your eyes	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>
<input type="checkbox"/> 41l. swollen or painful glands or lymph nodes	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>
<input type="checkbox"/> 41m. sore throat	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>
<input type="checkbox"/> 41n. sores in your mouth/thrush	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>
<input type="checkbox"/> 41o. pain behind your eyes	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>
<input type="checkbox"/> 41p. other, please specify:	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>

41q. NO SYMPTOMS REPORTED

25-JUL-01

Staff Initials / Date

**Specimen/Test Order
Form Instructions**

- The Specimen/Test Order form is used for all types of shipped specimens collected for any follow-up visit.
 - ***Note:** For tests ordered or specimens collected for a screening visit, record the visit code as 02.0. For those collected at the Enrollment visit, record the visit code as 03.0.*
- Record the specimen collection date, and mark each type of test ordered or specimen collected on that date.
- If specimens for a visit are collected on additional dates due to shipping errors, re-draws, etc., update the form to include additional collection information and refax the form to SCHARP DataFax.



AIN005 Triple-X (078)

ST (140)

Visit Code

Participant ID

XXX -

Specimen/Test Order

1. Specimen Collection Date

Mark all that apply.

dd MMM yy

- ELISA/Western Blot
- PBMC DNA PCR
- VE-8
- EBV
- Plasma RNA PCR
- STD tests, specify:

- Plasma bDNA PCR
- Qualitative Culture
- Quantitative Culture
- Specimens for storage
- Semen
- Cervical Cytobrush

- Saliva
- Rectal Wick
- Rectal Biopsy
- Leukapheresis
- Lymph Node Biopsy
- Other, specify:

2. Specimen Collection Date

Mark all that apply.

dd MMM yy

- ELISA/Western Blot
- PBMC DNA PCR
- VE-8
- EBV
- Plasma RNA PCR
- STD tests, specify:

- Plasma bDNA PCR
- Qualitative Culture
- Quantitative Culture
- Specimens for storage
- Semen
- Cervical Cytobrush

- Saliva
- Rectal Wick
- Rectal Biopsy
- Leukapheresis
- Lymph Node Biopsy
- Other, specify:

3. Specimen Collection Date

Mark all that apply.

dd MMM yy

- ELISA/Western Blot
- PBMC DNA PCR
- VE-8
- EBV
- Plasma RNA PCR
- STD tests, specify:

- Plasma bDNA PCR
- Qualitative Culture
- Quantitative Culture
- Specimens for storage
- Semen
- Cervical Cytobrush

- Saliva
- Rectal Wick
- Rectal Biopsy
- Leukapheresis
- Lymph Node Biopsy
- Other, specify:

Comments: _____

04-MAY-01

Staff Initials / Date

**Termination
Form Instructions**

- If a data item is not available, draw a line through the response boxes.



AIN005 Triple-X (078)

TM (499)

Participant ID

XXX -

Termination

Form Completion Date

dd *MMM* *yy*

Instructions: Complete this form whenever a participant terminates from the study.

1. Date of last visit:
dd *MMM* *yy*

2. Reason for termination: *Mark only one.*

- 2a. Exit visit/End of study.
- 2b. Participant refused further participation.
- 2c. Unable to adhere to visit schedule.
- 2d. Relocated.
- 2e. Investigator decision.
- 2f. Unable to contact participant.
- 2g. Participant seroconverted during the study.

If participant enrolls into the PIC study, please provide the participant's new PIC Participant ID:

PIC ID Number

- 2h. Death (*please indicate date and cause if known*).

Cause of death _____ **OR** Cause unknown

Date of death **OR** Date unknown
dd *MMM* *yy*

- 2i. Other reason for termination; please specify: _____

APPENDIX II INFORMED CONSENT

EVALUATION OF HIV-SPECIFIC IMMUNOLOGICAL AND VIROLOGICAL RESPONSES OF HIV-1 MULTIPLY-EXPOSED SERONEGATIVE INDIVIDUALS

Version 1

INTRODUCTION

We are asking you to be in a research study. The purpose of this consent form is to give you the information you will need to help you decide whether to be in the study or not. This study will be discussed with you by the study nurses. You may ask questions about the purpose of the research, what we would ask you to do, the possible risks and benefits, your rights as a volunteer, and anything else about the research or this form that is not clear. You should not agree to take part unless you are completely happy with the study, and you feel that you understand the information that has been given to you. Once you understand the study and agree to take part, you will be asked to sign the informed consent sheet, or make a mark in front of a witness. You will be given a copy to keep. Participation in this study is completely voluntary. Over the period of two years we hope to enrol approximately 130 participants. You will be asked to take part for as long as you are willing and able, preferably for a period of 2 years.

PURPOSE AND BENEFITS

This study will look at several important elements of the HIV pandemic in South Africa. HIV is the virus that causes AIDS. HIV-1 infection is spread mainly by sex. It can lead to progressive loss of the body's immune function (ability to fight infection) which eventually leads to severe medical problems, potentially fatal infections and cancers.

It has been estimated that over 80 - 90% of HIV-1 infections occur during sexual activity. During unprotected sexual activity HIV-1 can infect cells in the mucosal linings of the body (such as vagina or rectum, or less often, the mouth). The purpose of this study is to examine cells from the vagina, mouth, and blood of individuals who have been exposed to HIV but are not infected with HIV. These cells are part of the immune system. We will test whether these cells have the ability to recognize and fight HIV, which is called an HIV-specific immune response. Another purpose is to look for genetic changes which may help some individuals resist HIV infection more than others.

PROCEDURES

If you decide to take part in the study, you will be called in to the clinic where you will be given a medical examination by one of the hospital doctors. As your HIV status is very important for this study, you will be screened for HIV. The duration of this study is a minimum of twenty four months (2 years). Visits will be approximately every 3 months. At each clinic visit you will be asked questions about your sexual behaviour, general health as well as other questions related to your lifestyle. If you are a woman who can fall pregnant, you will be given a urine pregnancy test. A specimen of urine will be collected for this. A brief physical exam will be done including blood pressure, pulse, temperature, and feeling for lymph nodes in the neck and under the arms. You will be asked to give tubes of blood. Each tube is between 5 and 10 mls of blood (1 to 2 teaspoons) and you will be asked to give around 10 to 16 tubes of blood.

Counseling about exposure to HIV and the meaning of HIV testing will be done at each visit. Some of the blood drawn each visit will be used for more in-depth tests for HIV infection. If test results should indicate at any time that you are infected with HIV, the study clinician will promptly notify you and refer you to appropriate medical and/or health care providers. It is your responsibility to notify your partner(s) who may have been exposed to the virus and to encourage them to be tested. The study clinicians will counsel you and your sexual partner(s) regarding the meaning of the test results and about how to prevent the spread of the virus. In addition, you will be asked to continue to be followed in the study for another 2 years. Visits after you become infected would initially be more frequent and then involve visits

every 3-6 months. Samples collected will be the same as before. If you agree to participate in the study, you have the right to decline further participation or withdraw at any time.

We will be performing several experimental blood tests including tests on your genes. There are many different strains of HIV and the virus is always changing. Some HIV strains may be able to readily infect people who have certain gene types. New strains may also arise in the future with this capability.

There are a number of genetic variations which may play a role in an individual's ability to become infected with HIV or speed of progression to AIDS in those already infected. You may be tested for these other variations as well. However, because little is known about the significance of these variations, you will **not** be told the results of these tests. Again, the results will be kept private. As far as is known, the results will not affect your health, medical care, or employment.

As previously discussed, this study is designed to evaluate the immune response at mucosal surfaces. Therefore, at each visit several samples from different mucosal surfaces will be collected and some of these will be stored. If you do not agree to have these samples collected and stored then you will not be able to participate in the study. We will collect the samples described below.

Saliva: A small plastic container will be placed between your cheek and gum for a few minutes.

Cervical (the opening to the uterus) (female volunteers): You will be asked not to have sexual intercourse for at least three days before your visit and for the remainder of the day of the visit. To collect cervical samples a speculum will be placed in the vagina. A special piece of absorbent paper will be placed in the opening of the cervix, called the os, for a few minutes to absorb some of the fluid. A small brush will also be used to collect some cells from the cervix. This involves inserting the small brush into the os and rotating it gently. The entire procedure will take approximately ten minutes.

Semen (male volunteers only): To donate semen you will be asked to abstain from sexual activity for forty-eight hours prior to the day of collection. To collect the semen you will be asked to masturbate and collect semen either at home or in a private room at the clinic. The clinic staff will explain how to collect the semen samples and will offer you an instruction sheet.

You may be asked to come in for additional visits between scheduled visits. At the time you are called, you will be informed of what samples are needed for the additional visit. Samples may include blood, semen or cervical cytobrush, and/or saliva. These additional visits are strictly optional and you may decline any additional visits.

A long term study is important for understanding how the immune system responds to exposure to HIV. Therefore, it is important that you be available for a minimum of 2 years.

At the end of 2 years, you will be given the option of continuing indefinitely as part of a long-term natural history study. This would involve visits every 3 months with samples collected as before. Even if you choose to continue in long-term follow-up, you may still decline further participation at any time.

BENEFITS

There are no direct benefits. You will be made aware of your HIV status, and you will receive HIV/STI prevention education. This will help you protect yourself and others from sexually transmitted illnesses. If you contract a treatable STI during the course of this study, you will receive treatment for these infections at no cost to you.

If you are HIV positive, you will be referred to a health facility where you can get further care and treatment. We hope that the study will help our understanding of how a person's immune system responds to exposure to HIV.

RISKS, STRESSES OR DISCOMFORTS

The risks and discomforts of this study are related to collection of blood and mucosal samples. Blood drawing may cause pain, bleeding, and bruising, and rarely, infection at the place where the needle entered the skin. Sometimes, drawing blood causes people to feel lightheaded or even faint. The procedures to collect saliva and cervical samples may cause temporary discomfort. The rotation of the cervical brush may make this procedure more uncomfortable than a regular gynecological exam. Being asked to collect a semen sample can be stressful and embarrassing. Being asked personal questions about sexual practices and drug use, and answering those questions, can be stressful and embarrassing. You may refuse to answer any question you do not feel comfortable answering.

PARTICIPANT RESPONSIBILITY

By signing this informed consent form, you are undertaking to make yourself available to attend the scheduled clinics. You are not, however, giving up your right to freely withdraw from this study at any time.

COMPENSATION

You will be compensated for your costs, including transport costs and time, when you come in to the scheduled clinics. Since clinic visits can sometimes take a few hours, and you will be provided with food and refreshments for the time that you are at the clinic.

COSTS OF THE STUDY

There is no cost to you for the physical exam or laboratory tests that you will receive during the course of this study. You will receive treatment for all sexually transmitted infections that are detected while you take part in this study.

CONFIDENTIALITY

In order to protect your right to confidentiality, you will be assigned a code number. This will be used to identify you, rather than your name. Your personal information will not be released without your permission. No publications based on this research will contain your name. Only the project and clinic co-ordinators will know both your name and your identification number. This is necessary so that the co-ordinators can ensure that you will receive the correct tests and that you are called in to the correct clinics. The co-ordinators will not release your number and name to anyone else on the research team.

RESEARCH RELATED INJURIES

In the case of a research related injury, you will be referred to the King Edward hospital for treatment. The cost of this treatment will be free.

PERSONS TO CONTACT FOR PROBLEMS OR QUESTIONS

If you have any questions about your involvement in this study, or would like to know more about the study, please call either of the following:

Project Co-ordinator: Mr Francois van Loggerenberg 031-260 4564
Principal Investigator: Professor SS Abdool Karim 031-260 4550

You are not giving up your legal rights by signing the informed consent document. 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

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 screening tests, please sign your name or make your mark after reading the statements below:

- I hereby consent to the procedures as outlined in the Informed Consent document being conducted on myself.
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- I acknowledge that I have been informed by the clinic staff concerning the possible advantages and possible adverse effects which may result from my involvement in the abovementioned study
- I acknowledge that I understand and accept that this study involves research and that a copy of this form has been offered to me to keep.
- I agree that the study will be conducted under the supervision of Dr K. Mlisana and Professor SS Abdool Karim.
- I acknowledge that I understand the contents of this form, including all the information regarding the procedures and purpose of the study.
- I am aware that I may withdraw my consent at any time without prejudice to further care.

Signed: _____ Date:
Subject

Signed: _____ Date:
Researcher

For illiterate or Zulu speaking only subjects:

Mark with an 'X' (or sign): _____ Date:

Independent Witness: _____ Date:

Title and Name: _____

Telephone Number: _____

Appendix III
Informed consent for storage

**EVALUATION OF HIV-SPECIFIC IMMUNOLOGICAL AND VIROLOGICAL RESPONSES OF HIV-1
MULTIPLY-EXPOSED SERONEGATIVE INDIVIDUALS**

Sponsored by: The National Institute of Allergy and Infectious Diseases
Division of AIDS (DAIDS), 6700B Rockledge Drive,
Bethesda, Maryland 20852, United States

Principal Investigator: Professor Salim Abdool Karim, MBChB, PhD

INTRODUCTION

If you decide to participate in this study, blood and other biological samples will be taken from you for testing. Some of these samples may be kept for future research relating to the study of HIV. This consent form gives you information about this storage and use of samples. You are being asked to consent to the storage of your blood and other samples. The study staff will discuss this with you. Please ask if you have any questions. If you agree to the storage of your blood and other samples, you will be asked to sign this consent form. You will be given a copy of this form to keep.

BLOOD AND BIOLOGICAL SAMPLES

At each of your clinic visits, blood and other biological samples (sputum, urine, cervical swabs, semen) will be taken from you. Some of the blood and biological samples obtained during the study will be stored. As with your other samples, only a number, not your name, will be used to identify these samples. These samples may provide valuable information in the future when different immune system and HIV tests become available.

USE OF STORED SAMPLES

The stored samples may be used for future research, to confirm test results, or to do additional testing and may be shared with international laboratories. Your samples will not be sold or used in products that make money for the researchers. Any studies that use your samples will be reviewed by the Nelson R Mandela School of Medicine Biomedical Research Ethics Committee.

The researchers do not plan to contact you or your regular doctor with any results that are done on the stored samples after the study has been completed. This is because research tests are often done with experimental procedures so the results from one 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 will notify the study doctor who will try to contact you or your regular doctor. If you wish to be notified of this type of test result, you need to make sure that you contact the study nurse or doctor with any changes to your phone number or address. If you want your regular doctor to be told about this kind of test result, you need to provide the study team with the contact details of your regular doctor.

STORAGE OF SAMPLES

Your samples will be stored at laboratories that are specially designed to keep stored samples safely. Only approved researchers working on this project and related projects will be able to access your samples. The people who work at these laboratories will have access to your samples when they store them and keep track of them, but they will not know who you are as your samples will be stored by number. There is no time limit on how long your samples may be stored.

BENEFITS

There is no direct benefit to you through having your samples stored and tested later. Information learned from stored samples may help others who have HIV/AIDS.

RISKS

There is very little risk to you when you have your samples stored. There is a small risk that others may find out information about your HIV status from stored samples. This risk is reduced as your sample is stored under a study number, and not your name. You are entitled to the same protections of confidentiality and privacy for stored samples as you are for the samples that are drawn and used during the study. It is possible that tests that have yet to be developed may tell us things about your health we cannot currently test for. Results from these tests may cause distress to you.

CONFIDENTIALITY

The results of future tests of your samples will not go into your medical record. Although every effort is made to make sure that your samples are stored confidentially (by number and not name), we cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law. Your records may also be reviewed by regulatory authorities, such as the Ethics Committees, the U. S. National Institutes of Health (NIH), study staff and study monitors.

PARTICIPANT RIGHTS

The decision to allow your samples to be stored is completely voluntary. If you do not allow your samples to be stored, you will be able to participate in the main study. You may decide not to allow your samples to be stored after the tests that are needed for this study have been done or you decide to stop participating in the study. If you do decide to allow your samples to be stored, you can change your mind at any time and still participate in the main study. You must contact the study doctor or nurse and let them know that you do not want your samples to be stored any more. If you decide to do this, your samples will no longer be stored. You will then be asked if you want all stored samples to be destroyed. In this case, any samples that have been stored will be destroyed. You will then be asked to sign this form again under the section, "Withdrawal of Consent" so that there is a record of your decision. At the end of the study you will also be given the opportunity to review your consent for the storage of your samples.

WHAT DO I DO IF I HAVE QUESTIONS OR PROBLEMS?

If you have any questions about your involvement in this study, or would like to know more about the study, please call either of the following:

Project Co-ordinator: Mr Francois van Loggerenberg 031-260 4564
Principal Investigator: Professor SS Abdool Karim 031-260 4550

You are not giving up your legal rights by signing the informed consent document. 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

SPECIMEN STORAGE CONSENT FORM SIGNATURES PAGE

Please read the statement below and think about your choice. No matter what you decide, it will not affect your care.

I agree to allow some of my biological samples to be stored and used for testing and future research in HIV studies (please tick only one).

_____ Yes

_____ No

I am aware that I may withdraw my consent at any time without prejudice to further care.

Signed: _____ Date: _____
Participant/Guardian

Signed: _____ Date: _____
Witness

Signed: _____ Date: _____
Researcher

For illiterate participants:

Mark or thumbprint: _____ Date: _____

Independent Witness: _____ Date: _____

Title and Name: _____

Telephone Number: _____

Withdrawal of Consent

I hereby withdraw my consent for the storage of my biological samples. It is my wish that (please tick only one):

_____ Samples that have already been stored may continue to be stored and used.

_____ All samples that have already been stored must be destroyed.

Signed: _____ Date: _____
Participant/Parent/Guardian

Signed: _____ Date: _____
Witness

Signed: _____ Date: _____
Researcher

For illiterate participants:

Mark or thumbprint': _____ Date: _____

Independent Witness: _____ Date: _____

Title and Name: _____

Telephone Number: _____