MATRIX-001 Study-Specific Procedures (SSP) Manual
Section 10 – Counseling Considerations

TABLE OF CONTENTS

10 Introduction

This section contains guidance on the following types of counseling provided in MATRIX-001:

- HIV Pre- and Post-Test Counseling
- HIV and STI Risk Reduction Counseling
- Contraceptive Counseling
- Study Product Counseling
- Protocol Adherence Counseling
- Genital Procedures Counseling

All counseling should be provided in a non-judgmental client-centered manner that responds to current participant needs for information, education, support, motivation, skills-building, and/or referrals as needed. Because of this, specific content to cover, or skills to emphasize, are not standardized. Rather, the process for these discussions is to allow for appropriate tailoring and targeting to an individual participant's needs at a given point in time. To support continuity in the ongoing client-centered counseling over time, documentation of each counseling session should include sufficient information and detail to inform subsequent counseling sessions. Sites are encouraged to use flags or alert notes in participant study charts to highlight issues requiring follow-up at subsequent visits.

All counseling and referrals should be documented in participant study records per site SOPs. Proper documentation may be achieved through use of counseling worksheets, and/or chart notes.
Sample counseling worksheets are available on the MATRIX-001 webpage.

10.1 HIV Pre- and Post-Test Counseling

HIV testing is required at Screening, Enrollment, Randomization, Visits 7 and 8. HIV pre-test and post-test counseling is required at each visit at which HIV testing is performed. The sample Protocol Counseling Guide and Worksheet available on the MATRIX website under Study Documents provides a guide to the minimum requirements for HIV and risk reduction counseling sessions; this worksheet may be tailored for use at all study sites.

All HIV counseling should be provided in accordance with local counseling standards. Study staff who provide HIV counseling should be trained to do so per local practice standards. Study staff should also be trained on study-specific HIV testing methods and interpretation of test results per the testing algorithm in Protocol Appendix II.

Information on interpretation of screening, enrollment, and follow-up test results is provided in Table 1 which can be referenced as needed when providing pre-test and post-test counseling.

Participant-centered approaches should be used to assess participant knowledge of relevant information, dispel any misconceptions, ensure participant readiness for HIV testing, and ensure participant understanding of test results. Study staff should provide and explain test results in a private setting per site SOPs. Study staff should assess participant understanding of results and provide clarification and further information as necessary. Regardless of status, continued risk-reduction should be emphasized.

Table 1: Interpretation of HIV Test Results per Protocol Appendix II Algorithm

Test	Test Result	Interpretation
HIV Immunoassay	negative	HIV-uninfected; test results indicate that you are not infected with HIV.
	positive or indeterminate	HIV status not clear; test results indicate that you may be infected with HIV but additional testing is needed to confirm your status.
Sample 1 Confirmatory Test	positive	*If Screening or Enrollment Visit:* HIV-infected; test results indicate that you are infected with HIV. You are not eligible for enrollment in this study, but additional counseling and referrals for care are available per site SOPs. *If Follow-up Visit:* HIV-infected; test results indicate that you are infected with HIV, however additional testing is needed for study purposes.
	negative or indeterminate	HIV status not clear; additional testing is needed to determine your status.
Sample 2 Confirmatory Test	positive	HIV-infected; test results have confirmed that you are HIV infected. You will be exited from the study at this time, but additional counseling and referrals for care or direct referral for treatment is possible per site SOPs.

	negative or indeterminate (the participant may have already been given positive clinical lab results)	HIV status not clear; test results indicate that you may be infected with HIV but additional testing is needed to confirm your status.

10.2 HIV and STI Risk Reduction Counseling

Risk reduction counseling is required per protocol at Screening, Enrollment, Randomization, Visits 7, 8 and any other visit as needed. Sites are required to develop and follow SOP(s) for HIV pre- and post-test counseling as well as HIV risk reduction counseling. Participant-centered approaches should be used when assessing participant risk for HIV and STI infection and providing risk reduction counseling. The study staff should ask open-ended questions, actively listen to participant responses, probe as needed for further information, and guide the participant in identifying their risk factors and barriers to risk reduction, as well as strategies and action plans to try to address these.

Supported and facilitated by the study staff, the risk reduction plans identified by the participant should reflect and respond to their current low risk assessment and should be practical yet encourage the participant toward further risk reduction. For participants whose risk reduction barriers change over time (e.g., due to a partner change), risk reduction plans may need to change over time. Importantly, all risk reduction plans should be agreed upon by the participant and should be documented in the participant's study records, with a copy made available to the participant if she wishes.

The sample Protocol Counseling Guide and Worksheet posted on the MATRIX-001 website (http://www.matrix4prevention.org) incorporates a structure that study staff may find helpful for documenting current risk factors and barriers, experiences with risk reduction since the last session, and risk reduction plans until the next session.

Referrals are expected components of risk reduction plans when indicated based on participant needs and should be fully documented as part of their counseling.

10.3 Contraceptive Counseling

Contraceptive counseling for participants is required at all study visits from Screening through Visit 8, as needed. At the Screening, Enrollment and Randomization visits, contraceptive counseling should be provided in the context of assessing study eligibility criteria. Per MATRIX-001 inclusion criteria, a potential participant must be using an effective method of contraception at enrollment and agree to use an effective method of contraception throughout the duration of study participation. Counseling provided at these visits should explain which methods are acceptable for study purposes and emphasize that if the participant cannot commit to using one of these methods during study follow-up, the participant should not enroll in the study. Study site staff must have documented confirmation of the specified reliable form of contraception from local agencies or other documents as outlined in site specific SOP.

Effective methods include:

- minimum of 3 months of use of a combined hormonal contraceptive method (except vaginal rings)
- minimum of 6 months of use of a progestin only contraceptive method or copper IUD

- Sterilization of participant or partner
- Correct and consistent condom use (for US site only)
- Abstinence from penile-vaginal intercourse (for US site only)

During follow-up visits, client-centered counseling should continue, but may be abbreviated. Issues discussed at the previous counseling session should be reviewed and discussed with the participant as needed and the study staff should determine whether the participant has any current issues, questions, problems, or concerns with the current contraceptive method being used.

Some participants may wish to discontinue use of a contraceptive method during follow-up. In these cases, study staff should explore the participant's reasons for this and determine if other options would be acceptable to her. If no other options are acceptable, the participant may not remain in the study and should discontinue using study product per Protocol Section 5.2 inclusion criteria for contraceptive use.

Study staff who provide contraceptive counseling should be trained to do so per local practice standards and should also be trained on MATRIX-001 protocol specifications related to contraception. Contraception may be provided on-site, however sites may opt to refer participants to non-study providers for contraception. All sites are strongly encouraged to obtain credible medical records as part of their verification procedures for participant reported contraceptive methods. Starting at enrollment, staff should monitor when a new contraceptive prescription i.e. new pill prescription, Depo injection, IUD, is needed and should actively review this information at every follow-up visit to ensure that adequate contraceptive coverage is available for the duration of study participation. Expiration/replacement of a currently prescribed contraceptive can be documented on the counseling worksheet, in chart notes, or other site-specific form.

All contraceptive counseling sessions should be fully documented in participant study records. For each session, sufficient information and detail should be recorded to support review and appropriate follow-up at each subsequent visit. Staff members providing the contraceptive counseling can document details of each session on the Protocol Counseling Guide and Worksheet, a site-specific counseling worksheet, or in chart notes.

10.4 Product Use Counseling

Administration of the vaginal inserts will be done in-clinic and at home by the participants. Clinician may verify the placement of the insert at in-clinic insertions, as needed. This can be done with visual inspection using a speculum. Participants will be provided verbally with an explanation of product use/administration, using the MATRIX-001 Vaginal Insert Guide, which provides an overview of the study product administration procedures to follow while in the clinic and at home. Participants should be reminded to keep the inserts in a secure location, away from children and pets.

An Adherence Tool, found on the website, can also be provided to the participant to assist with home insertion tracking and questions. Site staff should explain each step. Staff should take as much time as needed to ensure the participant is comfortable and that all questions or concerns have been addressed prior to and after insertion. Site staff should encourage participants to use this tool as timing of product application is critical for certain study procedures and collections. Site staff should inform the participants that the study product should fully dissolve within four hours after insertion in the vagina. This discussion

should be done in conjunction with each study product dose on-site administration (Visits 3, 5 and 6) and documented on the Protocol Counseling Guide and Worksheet or in chart notes. Participants should be counselled to insert at approximately the same time on assigned days or if late, as soon as possible. However, two inserts should not be used on the same day. Any missed doses should be reported.

10.5 Protocol Adherence Counseling

Protocol adherence counseling is required at Screening, Enrollment, Randomization and Visits 4-7. As safety is of the utmost importance, site staff will counsel participants to refrain from using prohibited medications and engaging in certain practices during study participation. Please refer to Protocol Section 6.7 and SSP Section 7 (Clinical Considerations) for the complete list of prohibited medications and activities.

Participants should be counseled that engaging in these practices or using any prohibited products while in the study may make the insert work differently. These products and practices could irritate the rectum or vagina and increase the risk of side effects.

Each counseling session should be fully documented in chart notes and/or using the Protocol Counseling Guide and Worksheet.

10.6 Genital Procedures Counseling

Participants will be counseled for all cervicovaginal and rectal procedures performed at each visit. Study staff will explain the cervicovaginal and rectal collection procedures that will be collected at each visit.

10.6.1 Cervicovaginal Fluid Collection Procedural Counseling

Participants will undergo collection of vaginal swabs and aspirates for fluid collection for PK, PD and biomarker analysis. At Visits 2-8 at which the samples will be collected, study staff will explain what procedures will be performed at the visit and what to expect.

Participants will be counseled that vaginal fluid collection is a procedure using cotton-tipped swabs to collect fluids from the vagina for analysis. A speculum is placed into the vagina to aid in collection of these samples. Using either one swab at a time or multiple swabs at once, fluid is collected by placing swab(s) against the vaginal side wall. In addition to swabs, a vaginal lavage will be performed which involves placing neutral saline solution into the vagina and collecting it for additional study specific analyses of secreted soluble markers.

Participants should be counseled that they may experience slight discomfort and pressure during these cervicovaginal collections. Pain and spotting are possible but rare.

10.6.2 Biopsy Procedural Counseling

Participants will undergo collection of vaginal biopsies for PK, PD, and biomarker analysis. At Visits 2, 4 and 7 in which samples are collected, study staff will explain what procedures will be performed at the visit and what to expect.

Participants will be counseled that a vaginal or cervical (EVMS site only) biopsy is a procedure to remove a small piece of tissue (about the size of a grain of rice) for examination. Approximately 2-4 biopsies will be collected at any given time point. A speculum is placed into the vagina. Participants will be instructed to cough at the time of biopsy collection. Participants can be given acetaminophen / paracetamol prior to the procedure for pain relief. If adequate pain control is not achieved, injection of local anesthetics may be administered by the clinician, as appropriate. Of important note, tissue to be used to assess HIV (BXC-HIV1/2) and IHC (BXV-IHC) should not be treated with benzocaine or any other anesthetic prior to biopsy. Only the EVMS site will be collecting BXC for HIV analysis.

Participants should be counseled that they may experience some cramping, discomfort or pain during the procedure and for a few hours afterwards. Participants will be counseled to refrain from NSAIDs or aspirin use 3 days before and after PK sample collection. Participants should be counseled to contact the site if they experience excessive bleeding (defined as bleeding heavier than a menstrual period or should not soak a pad in less than an hour) following the biopsy collection. In addition, participants should be counseled to refrain from intercourse for at least 10 days post biopsy visits to allow for healing of biopsy site. Per Protocol section 6.7.2, participants should be counseled to refrain from any vaginal or anal activity starting 48hrs prior to enrollment sampling at Visit 2 until 10 days post last dose Visit 7.

10.6.3 Rectal Fluid Collection Procedural Counseling

During the informed consent process, participants will be asked to agree to have rectal fluid collected for PK analysis. Participants will be counseled that they may choose to not participate or withdraw their rectal fluid collection consent at any time during the study and still remain in the study.

Participants will be counseled that a rectal fluid collection is a procedure using cotton-tipped swabs to collect fluids from the rectum for analysis for Visits 3-8. There is the risk of mild discomfort in addition to a slight risk of bleeding with the insertion of rectal swabs. Per Protocol section 6.7.2, participants should be counseled to refrain from prohibited anal activity during the study.