MATRIX-002 Study-Specific Procedures (SSP) Manual
Section 6 – Study Product Considerations for Non-Pharmacy Staff

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6 Introduction

This section provides information and instructions for study staff related to the ordering, transport, delivery and provision of MATRIX-002 study product (vaginal film) to study participants. Associated instructions for pharmacy staff are provided in the MATRIX-002 Pharmacy Manual, which will be made available to each site Pharmacist of Record (PoR) by the CTH Consultant Pharmacist/Product Developer.

6.1 Study Product Regimen

Participants will use two (of the same assigned) vaginal films during their study participation; vaginal films will be inserted approximately 28 days apart.

- First vaginal film is inserted at V2: Enrollment
- Second vaginal film is inserted at V6: 4 Week Visit

6.1.1 Randomization Assignment

The CTH Data Management and Statistical Support team will generate and maintain the study randomization scheme.

Study randomization will occur as described in detail in SSP Section 12 (Data Collection). At V2 (Enrollment Visit), only after a participant has been confirmed as eligible, a clinic staff will randomize the participant by assigning and opening the next sequential sealed MATRIX-002 Randomization Envelope. The assigned film (Film A or Film B) will be printed on the MATRIX-002 Randomization Sheet inside the envelope. The MATRIX-002 Randomization Sheet should be completed as described in SSP Section 12, signed and dated by clinic staff and a certified copy made. The copy will be taken to the pharmacy with the original prescription (described below).

Once the participant is randomized to a film assignment, the participant is considered enrolled in the study.

6.2 Study Product(s)

MATRIX-002 will use two placebo vaginal films (Film A or Film B). Participants will be randomly assigned to Film A or Film B. The participant will insert the assigned film at both V2 and V6. IRB/IEC approved insertion instructions will be reviewed with/by the participant prior to attempting to insert the film. The vaginal film will be provided to the participant for self-insertion as described in SSP Section 5 Study Procedures. The participant will have two attempts to insert the film (at each time point, V2 and V6) using two separate films. If after two attempts the participant is unsuccessful, a clinician will insert a new film using a speculum as described in SSP Section 5 Study Procedures.

Three (of the assigned) films will be dispensed from the pharmacy at V2 and at V6 using the provided MATRIX-002 Prescription. A separate prescription should be used at each visit. Three films will be dispensed for convenience of clinic staff and the participant, however based on the participant's success at self-insertion, one to three films per visit (V2 and V6) may be used. For example,

- If the first self-insertion attempt is successful, one film is used;
- If the second self-insertion is successful, two films are used;
- If the clinician needs to insert the film, three films are used

Any film that is not used during the visit should be returned to the pharmacy and placed in quarantine.

6.3 Prescriptions and Dispensing Study Product

6.3.1 Clinic Procedures

MATRIX-002 prescriptions are available to print from the MATRIX-002 webpage under Study Documents (https://www.matrix4prevention.org/activity-hubs/clinical-trials/matrix-002/matrix-002-study-documents). A prescription will be required for each film administration visit (V2 and V6). In addition, sites may also use their own prescription/study medication order form as required by their institution or local requirements.

Clinic staff will complete a study prescription and send the original to the designated site pharmacy staff, as described below, to notify the site pharmacist that the participant has been randomized and needs to

be dispensed the assigned film. A separate prescription is completed at V2: Enrollment and at V6: 4 Week Visit to request the assigned vaginal films. The completed prescription includes PTID, verification of signed inform consent, and indication of the quantity to be dispensed. Three films should be dispensed initially at each visit (V2 and V6). If an additional film is needed (i.e., a film that is needed is dropped on floor), a new prescription is completed to get an additional film.

The middle section of the prescription includes the printed name and signature of the authorized prescriber, hand signed signature and date. This section must be completed by a study staff member designated in the site's Delegation of Duties (DoD) Log as an authorized prescriber of study product. This person should also be listed as an investigator (either the Investigator of Record or a Sub-Investigator) on the current Investigator of Record Form.

A certified copy of the MATRIX-002 Randomization Sheet, described above, should accompany the original prescription to the pharmacy to indicate the randomization number and assignment for the pharmacist. The original MATRIX-002 Randomization Sheet should be filed in the participant's research record along with a certified copy of the prescription.

6.3.2 Pharmacy Procedures

The Prescription (original) and the Randomization Sheet (certified copy) should be delivered to the pharmacy by clinic staff or a runner, or faxed and then followed by delivery of the actual documents. Upon receiving the completed MATRIX-002 Prescription and Randomization Sheet, the pharmacist will review the documents for completion and accuracy. If pharmacy staff identifies possible errors on the original Prescription prior to making a copy, they will request clarification or correction from clinic staff. Correction to original study prescriptions should only be made by an authorized prescriber and fully documented in the participant's chart notes. The same holds true for any corrections to the Randomization Sheet. If any corrections are needed on the Randomization Sheet, the original must be retrieved and corrected and a new certified copy provided to the pharmacist.

The PoR will verify the randomization assignment by reviewing the accompanying copy of the MATRIX-002 Randomization Sheet. The PoR verification should be documented on the appropriate section of the Prescription. The PoR will print their name, sign and date the prescription. The PoR will prepare the requested product as documented on the prescription.

Once the entire MATRIX-002 Prescription is completed, the PoR double-checks the accuracy of all entries and then makes a certified copy of the prescription. The original Prescription stays with pharmacy, the copy is certified and filed in the participant study notebook.

If corrections are needed to the Prescription or Randomization Sheet after a copy is made, the same corrections must be made separately on both the original and the copy. A signed and dated note explaining the correction also should be recorded on both sheets. Identical corrections and notes should be recorded on both the original and copy, on the same date, by the same person.

6.4 Chain of Custody

6.4.1 Dispensing from the Pharmacy to Clinic Staff

Each participant is assigned to placebo Film A or placebo Film B as detailed in SSP Section 12 Data Collection.

Each vaginal film will be dispensed from the pharmacy in its original sealed foil pouch. The vaginal film(s) will be dispensed from the pharmacy to an authorized clinic staff member who will then deliver the film(s) to the participant. The pharmacist will not dispense the placebo film until the completed prescription is received. **Each site must develop an SOP on product dispensation and include information on Chain of Custody (dispensing/provision) for study product**. The SOP should be developed with input from both pharmacy and clinic staff.

The MATRIX-002 Record of Receipt Log must be completed to document dispensing of study product to clinic staff for a given participant. For each log, pharmacy staff will complete the top section (site name, site ID number) and the first five columns of the log. When receiving study product from the pharmacy for a participant, clinic staff should confirm the entries made by the pharmacist (including PTID, quantity, and the assigned film is correct). The clinic staff should then complete the remaining four columns of the log.

Comments may be recorded in the designated column and, if additional space is needed, on the back of the record. All MATRIX-002 Study Product Dispensing Logs will be retained at the site pharmacy.

Clinic staff are responsible for the study products once in their custody and for ensuring that the products are provided to the participant for whom they were intended. Clinic staff must document provision of the study products to a participant in the participant's study chart (i.e., visit checklists, chart notes or on other source documents used for this purpose). In the event study products dispensed for a participant are not provided to/used by the participant, clinic staff will document this in the participant's study chart and return the study products to the pharmacy as soon as the participant's visit is completed, or as soon as clinic staff learn that the participant will not be completing her study visit on the scheduled date.

6.5 Study Product Return

If a vaginal film is dispensed from the pharmacy and not administered, it should be returned to the pharmacy for quarantine the same day. If the study product cannot be returned the same day, it must be kept in a secure, locked location and returned the following day. Upon the clinic staff returning the unused study product to the pharmacy, both the clinic staff member and the pharmacist will together complete the designated MATRIX-002 Study Product Return Log.

Each time the clinic staff member returns unused study product to the pharmacy, they will complete the first five columns on the Study Product Return Log including the date/time, PTID, the quantity returned, lot number, and clinic staff initials. When receiving the returned unused study product, the pharmacist will verify the information and complete the remaining columns on the Study Product Return Log (date/time

returned to the pharmacy and pharmacist initials). Comments may be recorded in the designated space, and if additional space is needed, on the back of the record. All Study Product Return Logs will be retained in the site pharmacy.

MATRIX-002 Record of Receipt Log and Study Product Return Log are available to print from the MATRIX-002 webpage under Study Documents (https://www.matrix4prevention.org/activity-hubs/clinical-trials/matrix-002/matrix-002-study-documents).