Section 9. Study Product Considerations for Non-Pharmacy Staff

Attention: This section provides information and instructions for non-pharmacy staff related to the ordering, transport, and delivery of MTN 004 study products for study participants. Record keeping requirements for non-pharmacy staff also are provided. Please also refer to related information in Sections 4 and 6 of this manual.

9.1 Responsibilities and Obligations with Regard to Blinding

MTN 004 Investigators of Record (IoRs), and by delegation all MTN 004 study staff, are responsible for maintaining the integrity of the study's blinded design. All Protocol Team members and study participants, without exception, will not be provided information on the identity of the specific study gel (VivaGel®, VivaGel® placebo or HEC placebo gel) to which participants have been assigned. The Pharmacist of Record (PoR) at all sites will be blinded to all treatment assignments. Access to study pharmacy facilities, and all study gel supplies and documentation stored in these facilities, is limited to study pharmacy staff only. The IoR or designee must ensure the security of study pharmacy facilities by empowering the MTN 004 PoR to control access to these facilities and all study gel supplies and documentation stored therein.

Blinding will be maintained throughout the study and until all study endpoint data have been verified and are ready for final analysis. There are no circumstances under which it is expected that unblinding will be necessary to protect the safety of study participants. In the event that study staff becomes concerned that a participant may be put at undue risk by continuing use of her assigned study gel, the IoR or designee may discontinue study gel use by the participant. Knowledge of the specific study gel to which the participant was assigned should not be necessary to guide further follow-up and/or treatment. If an IoR or designee feels that study gel-specific information is necessary to protect participant safety, he/she should notify the MTN 004 Protocol Safety Review Team (PSRT).

Additional operational requirements to preserve blinding are as follows:

- Clinic staff should respond to participant questions about how to store gel supplies and use gel applicators. Sample gel cartons and applicators (provided by the MTN CORE) should be stocked at all clinic locations for educational/training/counseling purposes. Actual study products may not be used for educational/training/ counseling purposes.
- Clinic staff may observe the participant remove the first dose from the carton and observe the participant administer the gel.
- Clinic staff may observe or handle individual wrapped gel applicators for purposes of counting the number of returned unused applicators (to document on the CRF).
- All study locations should be stocked with suitable biohazard containers, provided by the Nework Lab, in which to store unused applicators that participants may bring with them to the Two-Week Clinic Visit. (see Section 9.6. for further information related to unused applicators).
- After administration of the first dose at the site, under no circumstances should clinic staff dispense gel from any applicators. These restrictions also apply to pharmacy staff, unless specific instructions to inspect or examine applicators are received from the MTN Pharmacist.
- In the event that a participant reports damage to her gel supplies, difficulty using her applicators, or other issues or problems with her applicators or gel — other than signs, symptoms, or other adverse events associated with gel use — clinic staff should refer the participant to the PoR to further discuss and evaluate her report or concern.

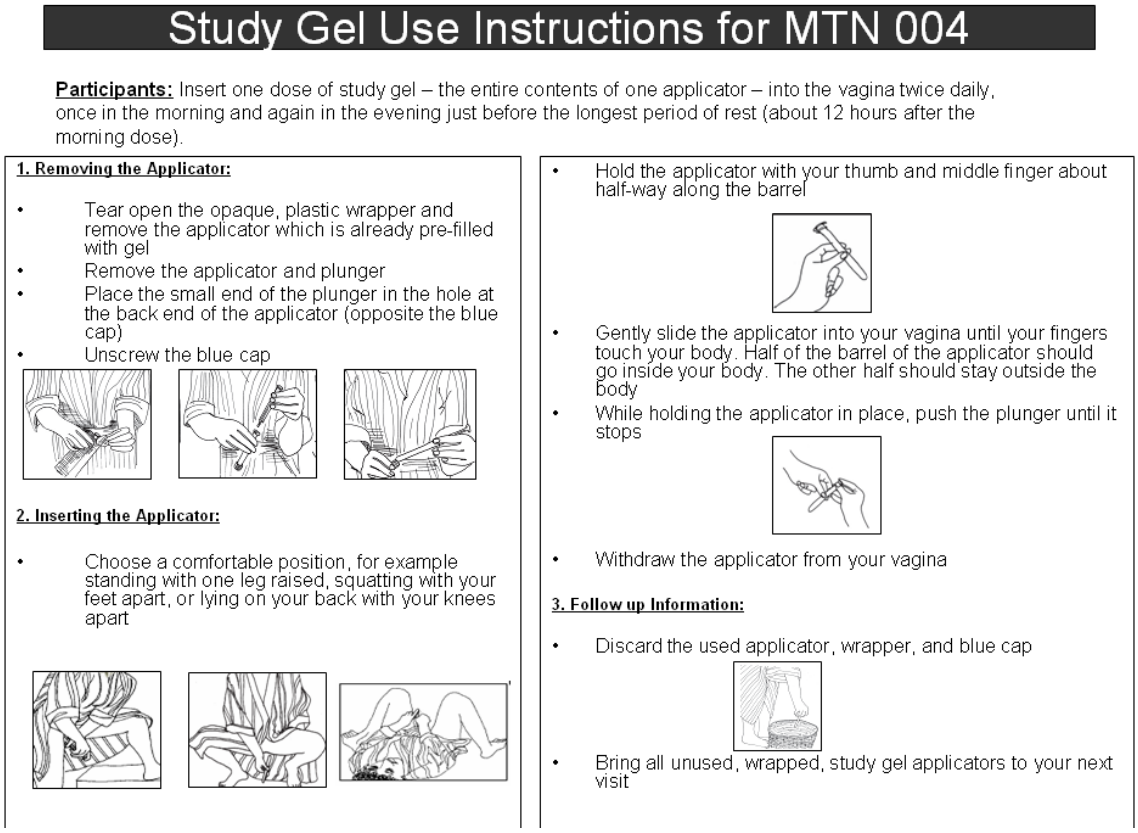
- If the participant's applicators have been damaged, the PoR will collect the damaged supplies from the participant (if she has brought them with her) and dispense replacement supplies for her as ordered by site clinic staff.
- If the PoR determines that the participant requires additional instruction on how to use the applicators, he/she will refer the participant back to clinic staff for refresher instruction.
- If the PoR identifies problems with the participant's applicators or gel, the PoR will immediately inform the MTN Pharmacist of the problem and take action per instructions received from the MTN Pharmacist. The MTN Pharmacist will inform the Pharmaceutical Co-Sponsors, MTN CORE (FHI), DPT and Brecon Pharmaceuticals Ltd.

The PoR will document his/her interactions with participants, and subsequent action taken, in signed and dated notes that are retained in participant-specific pharmacy files. The PoR will forward photocopies of his/her notes — and/or other forms of documentation — to clinic staff to ensure timely clinic staff awareness of the resolution of participant reports. If circumstances require the PoR to dispense replacement gel supplies to a participant, the PoR will need to obtain an MTN 004 Replacement Prescription from site clinic staff.

9.2 Gel Use Instructions

Participants will be instructed to insert one applicatorful of study gel – the entire contents of one applicator – into the vagina twice daily, in the morning and in the evening. The evening dose should be administered at bedtime or longest period of rest. Detailed instructions for insertion of study gel are listed in Figure 9-1 below. These instructions will be translated into Spanish at the Puerto Rico site, and will be illustrated to optimize participants' understanding of them. A listing of frequently asked study gel use questions, and answers to these questions, is provided in Section Appendix 9-1.

Figure 9-1



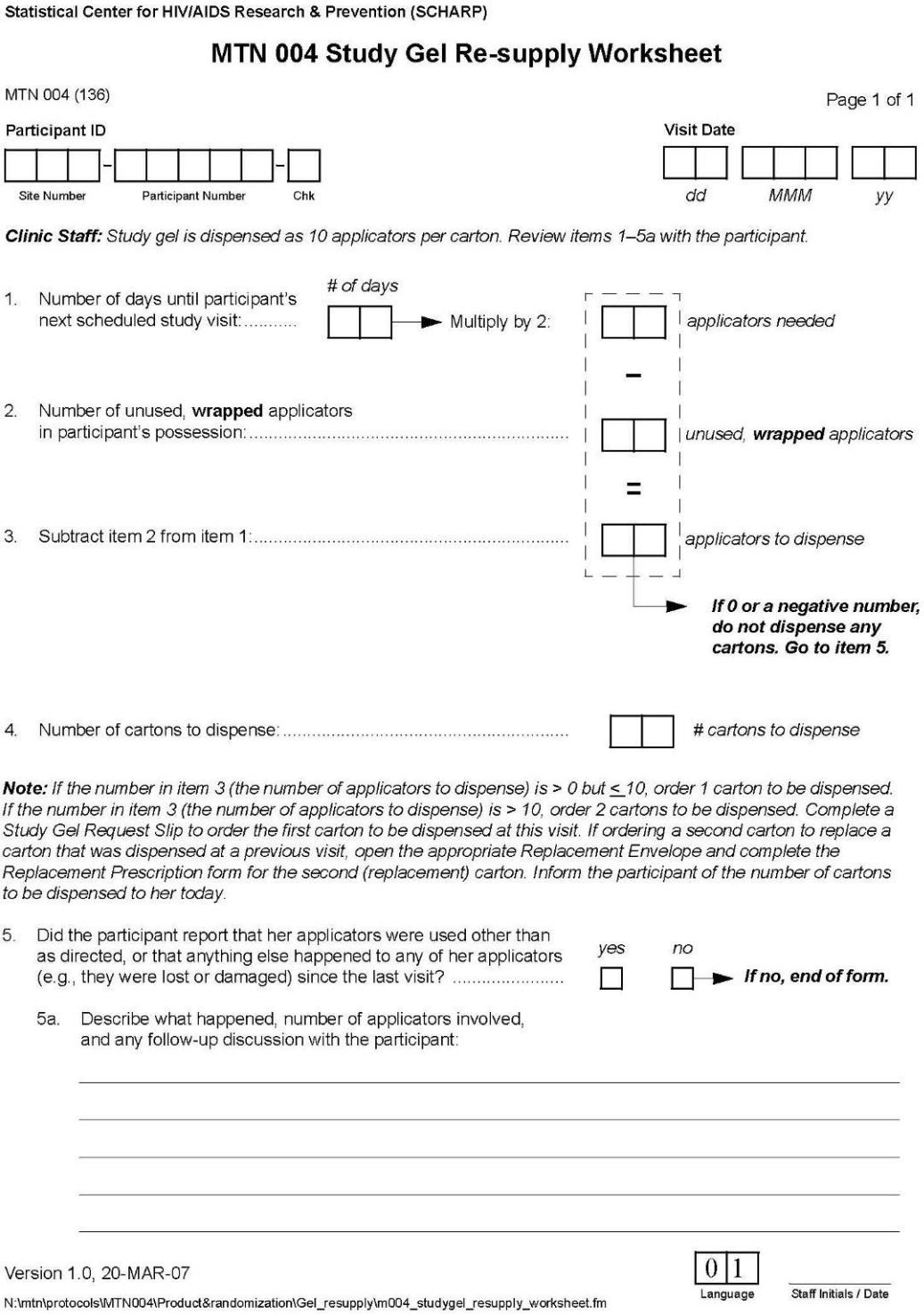
Note: Study Staff should inform participants that they may experience some minor gel leakage from the vagina, when inserting the filled applicator into the vagina.

9.3 MTN 004 Study Gel Re-Supply Worksheet

The MTN 004 Study Gel Re-Supply Worksheet (Figure 9-2) is an operational tool and source document designed to assist clinic staff in calculating the quantity of study gel to be ordered (and dispensed by study pharmacy staff) at a given study follow-up visit for participants.

At the Enrollment Visit, clinic staff will instruct participants to bring all unused study gel applicators to the site clinic at their One-Week Clinic Visit, when new study gel supplies will be dispensed (unless study gel is held or permanently discontinued). At the One-Week Clinic Visit, clinic staff will instruct participants to continue to use any unused, wrapped (unopened) study gel applicators in their possession (from study gel cartons dispensed at enrollment), and to use applicators from the new study gel supplies (dispensed at the One-Week Clinic Visit), until they come in for the Two-Week Visit. Clinic staff will instruct participants to return all unused study gel applicators in her possession to the Two-Week Clinic Visit. If a participant does not return the study gel applicators in her possession at the Two-Week Clinic Visit, clinic staff will make every effort to collect the study gel applicators at the participant's Three-Week Clinic Visit, or as soon as possible thereafter.

Figure 9-2



Statistical Center for HIV/AIDS Research & Prevention (SCHARP)

MTN 004 Study Gel Re-supply Worksheet

MTN 004 (136)

Page 1 of 1

Participant ID ☐☐☐-☐☐☐☐☐-☐ (Site Number – Participant Number – Chk)

Visit Date ☐☐ *dd* ☐☐☐ *MMM* ☐☐ *yy*

Clinic Staff: *Study gel is dispensed as 10 applicators per carton. Review items 1–5a with the participant.*

1. Number of days until participant's next scheduled study visit: ..... *# of days* ☐☐ → Multiply by 2: ☐☐ *applicators needed*

−

2. Number of unused, **wrapped** applicators in participant's possession: ..... ☐☐ *unused, **wrapped** applicators*

=

3. Subtract item 2 from item 1: ..... ☐☐ *applicators to dispense*

→ ***If 0 or a negative number, do not dispense any cartons. Go to item 5.***

4. Number of cartons to dispense: ..... ☐☐ *# cartons to dispense*

Note: *If the number in item 3 (the number of applicators to dispense) is > 0 but ≤ 10, order 1 carton to be dispensed. If the number in item 3 (the number of applicators to dispense) is > 10, order 2 cartons to be dispensed. Complete a Study Gel Request Slip to order the first carton to be dispensed at this visit. If ordering a second carton to replace a carton that was dispensed at a previous visit, open the appropriate Replacement Envelope and complete the Replacement Prescription form for the second (replacement) carton. Inform the participant of the number of cartons to be dispensed to her today.*

5. Did the participant report that her applicators were used other than as directed, or that anything else happened to any of her applicators (e.g., they were lost or damaged) since the last visit? ..... *yes* ☐ *no* ☐ → ***If no, end of form.***

   5a. Describe what happened, number of applicators involved, and any follow-up discussion with the participant:

_____

_____

_____

_____

_____

Version 1.0, 20-MAR-07

N:\mtn\protocols\MTN004\Product&randomization\Gel_resupply\m004_studygel_resupply_worksheet.fm

0 1 Language

_____ Staff Initials / Date

9.4 MTN 004 Study Gel Request Slip

The MTN 004 Study Gel Request Slip (Figure 9-3) should be used by clinic staff to communicate to pharmacy staff:

- The number of cartons to be re-supplied to each participant at each visit. At the One-Week Clinic Visit participants should usually require one carton of study product. If more than one carton is needed, the first carton would be requested with Study Gel Request Slip. To request an additional carton(s) (e.g., to replace a previously dispensed carton) a Replacement Envelope must be opened and the replacement Prescription form completed. . **Note: the MTN 004 Study Gel Request Slip should not be completed to order replacement cartons (e.g., for previously dispensed cartons that are lost or damaged).**
- Clinic staff decisions to hold study gel use for a participant, to resume study gel use after a prior hold, or to permanently discontinue study gel use
- The cartons being ordered are for a replacement participant.

The MTN 004 Study Gel Request Slip is a two-part no carbon required (NCR) document that is available in pads of 50 and provided by the SDMC. In the event that clinic staff requires additional pads, they should contact the Protocol Pharmacist and SDMC Project Manager for a resupply. Complete the Study Gel Request Slip as follows:

- Record the clinic name at the top of the slip. The name recorded must be identical to the clinic name listed on the site's randomization envelopes and prescriptions, unless an alternative clinic name or abbreviation is designated in the site SOP for study gel re-supply during follow-up.

- Record the PTID and the number of the Clinic Randomization Envelope (or Replacement Randomization Envelope, for replacement participants) assigned to the participant in the boxes provided.

- Mark the box for either "RE-SUPPLY," "HOLD," "PERMANENT DISCONTINUATION" or "RESUME" to indicate the action to be taken in the study pharmacy. When marking "RE-SUPPLY" or "RESUME," record the number of cartons of study gel to be dispensed to the participant.

    - When "RE-SUPPLY" is marked, study gel will be dispensed for the participant in the quantity entered on the slip.

    - When "HOLD" is marked, study gel will not be dispensed for the participant unless/until another slip marked RESUME is subsequently completed and received in the pharmacy.

    - When "PERMANENT DISCONTINUATION" is marked, no study gel will be dispensed to the study participant starting from the point the Study Gel Request Slip is received in the pharmacy.

    - When "RESUME" is marked, a previous hold will end, and study gel will be dispensed for the participant in the quantity entered on the slip. A signed, dated photocopy of the chart note documenting the original purpose for HOLD should be attached to the Study Gel Request Slip marked "RESUME."

- The clinic staff name, signature, and signature date must be completed on the same day as the participant's visit by a clinic staff member authorized to order study gel supplies for participants during follow-up. DAIDS does not require that an authorized prescriber sign and date the Study Gel Request Slips; however site-specific pharmacy regulations may be more stringent than DAIDS requirements. All sites must comply with local requirements.

Double-check the accuracy of all entries and then separate the two parts of the completed Study Gel Request Slip. Retain the yellow copy (labeled "Clinic") in the participant study notebook. Deliver the white original (labeled "Pharmacy") to the study pharmacy in the same manner that original prescriptions are delivered to the pharmacy. Both the original and clinic copy of the slip may be hole-punched.

Figure 9-3

MTN 004 Study Gel Request Slip

Clinic Name: | **Randomization Envelope #** ☐☐☐

Participant ID ☐☐☐-☐☐☐☐☐-☐ **First Randomization Code** ☐☐☐ **Second Randomization Code** ☐☐☐ **OR** *N/A* ☐

Clinic Staff Instruction: *Mark whether this is a study gel re-supply, hold, resume, or permanent discontinuation request. Record the number of study gel cartons to be dispensed (if applicable), and sign and date. Deliver the original white copy (labeled "Pharmacy") to the pharmacy. File the yellow copy (labeled "Clinic") in the participant study notebook.*

☐ **RE-SUPPLY** → **Pharmacy:** Dispense ☐ cartons of study gel (10 applicators per carton).

☐ **HOLD** → **Pharmacy:** Do not dispense study gel to participant unless another MTN 004 Study Gel Request Slip marked "Resume" is received.

☐ **RESUME** → **Pharmacy:** Dispense ☐ cartons of study gel (10 applicators per carton) as authorized by the Investigator of Record and/or designated clinic staff.

☐ **PERMANENT DISCONTINUATION** → **Pharmacy:** Do not dispense any further study gel to participant.

Clinic Staff Name (please print): _____

Clinic Staff Signature: _____

Date: ☐☐ ☐☐☐ ☐☐
dd *MMM* *yy*

Pharmacy

9.5 Dispensing Study Gel During On-Site Visits

Refer to Section 4 of this manual for further information on procedures for participant randomization, initial ordering and dispensation of study gel for enrolled study participants. Detailed instructions for completing MTN 004 Prescriptions, and MTN 004 Replacement Prescriptions are provided in Section 4

Upon receipt of a completed and signed MTN 004 Prescription at the Enrollment Visit (or MTN 004 Replacement Prescription for replacement participants), pharmacy staff will dispense study gel supplies.

Gel supplies will be dispensed in cartons containing ten (10) identically-packaged, individually-wrapped, pre-filled applicators each. Two cartons, containing (20 applicators), will be dispensed at the Enrollment Visit. At the One-Week Visit (or at interim visit(s), for participants who need replacement gel, site clinic staff will complete the Study Gel Re-supply Worksheet and order study gel supplies in quantities expected to be sufficient until the participant's next follow-up visit. It is anticipated that most participants will receive one additional carton (10 applicators) of study gel.at the One-Week Clinic Visit. Cartons will be sealed with tamper-evident tape and labeled by the PoR in accordance with US and local requirements. In all cases, carton labeling will include a randomization code.

Participant-specific study gel cartons may be dispensed to participants in one of three ways:

- From the pharmacy directly to the participant
- From the pharmacy to authorized clinic staff who will then deliver the cartons to the participant
- From the pharmacy to authorized transport staff (or "runners") who will transfer the cartons to authorized clinic staff who will then deliver the cartons to the participant
- Each study site must designate its dispensing method in the MTN 004 standard operating procedures (SOPs) for participant randomization and gel re-supply during follow-up. These SOPs should be developed with input from both pharmacy and clinic staff. They must be approved by the MTN Pharmacist prior to study activation and may only be modified after consultation with the MTN Pharmacist. Further information related to each method is provided in Sections 9.5.1-9.5.3 below.

9.5.1 Dispensing from the Pharmacy Directly to Participants

At sites choosing to dispense study gel cartons directly from the pharmacy to participants, prescriptions and Study Gel Request Slips are expected to be delivered to the pharmacy by the participants themselves, although this may be done by clinic staff or a runner. Upon receipt of a completed and signed prescription or Study Gel Request Slip, the PoR will prepare the number of participant-specific study gel cartons entered on the prescription or request slip. Cartons may be prepared based on either original documents or faxed copies, but cartons will not be released to participants until the original prescription or original Study Gel Request Slip is received by the site pharmacy.

9.5.2 Dispensing from the Pharmacy to Clinic Staff

At sites choosing to dispense gel cartons to clinic staff who will then deliver the cartons to participants, prescriptions and Study Gel Request Slips are expected to be delivered to the pharmacy by clinic staff or a runner. Upon receipt of a completed and signed prescription or Study Gel Request Slip, the PoR will prepare the number of participant-specific study gel cartons entered on the prescription or slip. Cartons may be prepared based on either original documents or faxed copies, but cartons will not be released to clinic staff until the original prescription or request slip is received by the site pharmacy.

The MTN 004 Record of Receipt of Participant-Specific Gel Cartons (see Section Appendix 9-2) must be used to document dispensing of participant-specific study gel cartons to clinic staff. Pharmacy staff will complete the top section (site name, clinic name) and the first four columns on the Record of Receipt. When receiving study gel cartons from the pharmacy, clinic staff will verify the PTIDs, confirm the number of cartons received for each PTID, and complete the remaining three columns on the Record of Receipt for

each PTID. Comments may be recorded in the designated column and, if additional space is needed, on the back of the record. All Records of Receipt will be retained in the pharmacy.

Clinic staff are responsible for controlling access to the gel cartons dispensed into their custody and ensuring that the cartons are delivered to the participants for whom they were dispensed. Clinic staff also must document delivery of the cartons to designated participants in the participants' study charts. Delivery may be documented in chart notes, on visit checklists, or on other source documents designated for this purpose by clinic staff. In the event that all gel cartons dispensed for a participant are not delivered to the participant, clinic staff will document this in the participant's study chart and return the remaining cartons to the pharmacy as soon as the participant's visit is completed.

9.5.3 Dispensing from the Pharmacy to Runners for Further Transfer to Clinic Staff

At sites choosing to dispense gel cartons to runners who will transfer the cartons to clinic staff for subsequent delivery to participants, prescriptions and Study Gel Request Slips are expected to be delivered to the pharmacy by a runner. Upon receipt of a completed and signed prescription or Study Gel Request Slip, the PoR will prepare the number of participant-specific study gel cartons entered on the prescription or slip. Cartons may be prepared based on either original documents or faxed copies, but cartons will not be released to a runner until the original prescription or request slip is received by the site pharmacy.

The MTN 004 Record of Receipt of Participant-Specific Gel Cartons (see Section Appendix 9-2) must be used to document dispensing of participant-specific study gel cartons to runners. MTN 004 Daily Runner Logs (see Section Appendix 9-3) must be used to document transfer of participant-specific study gel cartons from runners to clinic staff.

Pharmacy staff will complete the top section (site name, clinic name) and the first four columns on the Record of Receipt. When receiving study gel cartons from the pharmacy, runners will verify the PTIDs, confirm the number of cartons received for each PTID, and complete the remaining three columns on the Record of Receipt for each PTID. Comments may be recorded in the designated column and, if additional space is needed, on the back of the record. All Records of Receipt will be retained in the pharmacy.

At the beginning of each work day, runners will complete the top section (site name, clinic name, date) of their Daily Runner Logs. When receiving study gel cartons from the pharmacy, in addition to completing the Record of Receipt for each PTID, runners will complete the first three columns on the Daily Runner Log for each PTID.

Runners are expected to deliver participant-specific gel cartons to authorized clinic staff directly after collecting the cartons from the pharmacy. Runners must control access to the cartons dispensed into their custody and deliver the cartons only to authorized clinic staff. Runners also must retain and control access to their Daily Runner Logs until the logs are returned to the pharmacy, at which time pharmacy staff assume responsibility for the logs. If completed logs are not returned to the pharmacy by the end of each work day, the PoR will notify appropriate clinic or pharmacy supervisory staff (per site SOPs) to ensure timely recovery of the logs. If completed logs are not recovered and delivered to the pharmacy within five calendar days, the PoR will notify the MTN Pharmacist via email.

When receiving study gel cartons from runners, clinic staff will verify the PTIDs, confirm the number of cartons received for each PTID, and complete the remaining two columns on the Daily Runner Log for each PTID. Comments may be recorded in the designated column and, if additional space is needed, on the back of the log.

Clinic staff is responsible for controlling access to the study gel cartons transferred into their custody, ensuring that the cartons are stored appropriately while in their custody, and ensuring that the cartons are delivered to the participants for whom they were dispensed. Clinic staff also must document delivery of gel cartons to designated participants in the participants' study charts. Delivery may be documented in chart notes, on visit checklists, or on other source documents designated for this purpose by clinic staff. In the event that all gel cartons dispensed for a participant are not delivered to the participant, clinic staff will document this in the participant's study chart and return the remaining cartons to the pharmacy as soon as possible after the participant's visit is completed.

9.6 Return of Study Gel Supplies

Study participants will routinely return unused study gel supplies to the study site. The number of unused applicators returned at each study visit should be recorded on the Follow-up Visit form, or for interim visits, the Interim Visit form.

Participants will receive 2 cartons (20 pre-filled applicators) at the Enrollment Visit and one carton (10 applicators) at the One-Week Visit. If a participant loses or misplaces study gel after leaving the site, she will be instructed to return to the site to have new study supplies dispensed. Participants will also be given a bag containing condoms and panty liners at these visits.

ENROLLMENT VISIT

At the Enrollment Visit, site staff will instruct participants to bring all unused **wrapped** applicators, and all unused **unwrapped**, applicators that were not inserted into the vagina for any reason (i.e., fell on the floor, dropped in the toilet, etc.) to the clinic at the One-week Visit. Participants should be encouraged to keep the unused (wrapped) applicators in the carton and bring the carton with them to the clinic at the One-Week Visit Participants are asked to return only **unused** (wrapped or unwrapped) applicators to the study clinic, Participants will be instructed to dispose of used applicators at home if possible.

ONE-WEEK VISIT

When a participant returns for the One-Week Clinic Visit, the study staff will count the unused (wrapped and unwrapped) applicators. The number of unused applicators returned should be counted and recorded on the Follow-up Visit form. The participant will keep the unused (wrapped only) applicators and bring them home after the visit for use during their second week of study participation. At the One-Week Clinic Visit, clinic staff will instruct participants to continue to use the unused, wrapped (unopened) study gel applicators in their possession first (from study gel cartons dispensed at enrollment), and then to use applicators from the new study gel supplies (dispensed at the One-Week Clinic Visit), until they come in for the Two-Week Visit. Participants will be instructed to return to the clinic for the Two-Week Clinic Visit bringing all remaining unused applicators (wrapped and unwrapped).

TWO-WEEK VISIT

When the participant returns for the Two-Week Visit, the study staff will collect all unused (wrapped and unwrapped) study product. The number of unused applicators returned should be counted and recorded on the Follow-up Visit form

All unused applicators (wrapped and unwrapped) should be stored in a biohazard container in accordance with the guidelines of the institution. The container should be a biohazard container specifically provided by the MTN for unused applicators. When the study is completed or the container is full, the biohazard container should be destroyed by autoclave in accordance with the policy of the institution.

OTHER UNUSED STUDY PRODUCT

If a participant becomes pregnant or experiences an adverse event that requires permanent discontinuation of gel use (per protocol Section 4), any unused applicators (wrapped and unwrapped) remaining in her possession should be collected from her as soon as possible and returned to the clinic on the day of collection.

It is not necessary to collect remaining applicators from participants for whom gel use is temporarily held. However, applicators may be collected from such participants, to protect their safety, if it is suspected that the participant may not comply with clinic staff instructions to refrain from gel use for the duration of the temporary hold. For all product holds requiring collection of unused applicators, if the applicators are not collected within five working days of initiating the product hold, the MTN004 PSRT must be informed, using the PSRT Query Form. When informing the PSRT, please describe the reason for the product hold, actions taken to try to collect the unused applicators, and plans and timelines for further action to collect the applicators.

If an issue or problem is identified that would necessitate collection of unused applicators from all participants, detailed instructions for collection and handling of the applicators, and documentation thereof, will be provided by the MTN Pharmacist. Other associated operational and/or data collection instructions also may be provided by the MTN CORE (FHI) and/or MTN SDMC. Clinic and pharmacy staff will follow all such instructions.

Any unused applicators remaining in a participant's possession at the time of study exit must be collected from the participant and returned to the clinic study staff on the day of collection. When planning and scheduling study exit visits, clinic staff should instruct participants to bring all remaining unused applicators to their exit visits. For participants who do not bring their remaining applicators to their exit visits, arrangements should be made to collect the applicators at the final participant contact described in protocol Section 5. For participants who do not bring their applicators to their exit visits or their final contacts, clinic staff should make all reasonable efforts to collect the remaining applicators in as timely a manner as possible, and document all such efforts in the participants' study charts. For participants for whom all reasonable efforts fail, guidance should be sought from the MTN004 PSRT.

Unused applicators collected from participants for any reason on the day of collection, should be returned to the clinic staff, clinic staff should place them in the MTN provided biohazard container. The contents of the biohazard container should be destroyed by autoclave as per site policy.

9.7 Product-Related Scenarios

For illustrative purposes, a number of product-related scenarios are provided in Section 4 of this manual (see Section Appendix 4-2b).

Section Appendix 9-1

Frequently Asked Gel Use Questions

Q1: What is the best position to insert the gel?

A: Any position that is comfortable can be used to insert the gel. The positions that are recommended are shown in the leaflet and include sitting, standing, and lying down.

Q2: What should I do if it hurts when I use the applicator to insert the gel?

A: Inserting the gel should not be painful. If you have pain when inserting the gel, try another position (sitting, standing, or lying down). If you still have pain in the new position, perhaps you need to change the angle of the applicator. The applicator should be angled slightly upward, towards your back, when you insert it. If you try to change the angle, and you still feel pain on insertion, please contact the study clinic.

Q3: Where does the gel go to after I put it inside?

A: The gel stays in the vagina until you have sex. Some gel will likely come out of the vagina during sex. The rest of the gel will come out of the vagina (through the same opening where it was inserted) over the next day after having sex. Sometimes when the gel comes out it looks clear. Sometimes it has a white color, and sometimes it has white clumps. This has been seen in other studies of the gels and it is normal. It is not normal to see a yellow or green discharge from the vagina, or a discharge with a bad odor, or with pain or itching. If this happens, it could mean you have an infection, in which case you should contact the study clinic.

Q4: Can the applicator get lost inside me?

A: No, the applicator cannot get lost inside you. When you use the applicator, hold it with your fingers about half-way along the barrel, and insert it until your fingers touch your body. Half of the barrel of the applicator should go inside your body. The other half should stay outside the body.

Q5: What should I do if I have trouble applying the gel with the applicator?

A: The applicators should be easy to use. If you have difficulty using the applicators, please contact the study clinic, as the clinic staff may be able to show you different ways that you can insert the gel, which might make it easier.

Q6: What should I do if I think there is something wrong with an applicator or its gel?

A: If an applicator does not seem to be working properly (for example, you find it difficult to push the gel out of the applicator, or if gel has leaked out, or you think there is some other problem), do not use the applicator. Use another applicator instead. Keep the applicator that had something wrong and place it in the UNUSED APPLICATOR BAG and bring it to the study staff at your next study visit. If you think that something is wrong with all of your applicators, contact the study staff as soon as possible (i.e., do not wait until your next visit) so the staff can make sure you have enough working applicators.

Q7: What happens if I press the plunger too early and most of the gel comes out on my outside?

A: If most of the gel comes out on your outside, discard that applicator and use a new applicator to insert another dose of gel.

Q8: What if I have bleeding between periods?

A: Please contact the study clinic.

Q9: How do I store the gel?

A: Store the gel in a cool, dry place.

Q10: What happens if the applicators get wet before I use them?

A: If only the wrapper gets wet, the applicator can still be used. Dry the wrapper off before taking out the applicator. If the applicator itself gets wet, it should not be used, but this might only happen if the wrapper is already open.

Q11: What should I do if the wrapper is already open when I want to use the gel?

A: You should only use applicators with sealed wrappers, so you should always open the wrapper right before inserting the gel. If you notice an applicator with a wrapper that is not sealed, do not use that applicator. Use a different applicator with a sealed wrapper instead. Keep the applicator with the open wrapper and place it in the UNUSED APPLICATOR bag and bring it to the study staff at your next study visit.

Q12: What should I do if I forget to use the gel ?

A: You should insert the gel when you remember the missed dose. If there is less than 2 hours until you will insert the next dose, that dose will be missed. Resume the schedule with the next dose. Inform the study staff of any missed doses at the next visit.

Q13: Is the gel contraceptive?

A: We don't know if the study gels will prevent pregnancy during sex acts when the gels are used. It is possible that the gels could prevent pregnancy. It also is possible they could have no effect on pregnancy (especially the placebo gel). There is no reason to think the gels will prevent pregnancy during sex acts when they are not used. If you wish to avoid pregnancy, you should use known reliable method of contraception (such as pills, injections, and condoms) while you are in this study.

Q14: Will the gel affect my partner's ability to father children?

A: No. The ingredients in the gels are not known to have any effect on male fertility. The ingredients also are not known to have any effect on female fertility.

Q15: What should I do if my partner has a reaction to the gel?

A: Contact the study clinic and ask their advice. They might ask your partner to go to the clinic to be assessed and receive treatment if needed. However, previous studies have shown this is unlikely to happen.

Q16: What should I do if I have a reaction to the gel (e.g., unusual itching, stinging)?

A: Contact the study clinic.

Q17: What should I do if I think I am pregnant?

A: Contact the study clinic immediately. The clinic staff will give you a pregnancy test to find out if you are pregnant or not.

Q18: If I use the gel, and then have oral sex, will there be a problem if my partner takes some of the gel on or in his mouth?

A: Although the safety of the study gels taken by mouth has not been studied directly, the gels are not expected to pose a safety risk if taken into the mouth or swallowed during oral sex. If at any time your

partner has a reaction to the gel, contact the study clinic and ask their advice. They might ask your partner to go to the clinic to be assessed and receive treatment if needed .

Q19: What should I do if my partner touches me in the vaginal area after the gel has been inserted? Should I re-apply the gel?

A: It is not necessary to re-apply the gel in this situation, unless you think that most of the gel has been removed. In that case, you should use another applicator to insert another dose of gel.

Q20: Does it matter what brand of condoms we use?

A: Ideally, you should use the condoms given to you by the study clinic staff. However, if you do not have one of those condoms, and you have a different condom, use that condom. Condoms are the only known way to protect against HIV and other sexually transmitted diseases (STDs), so it is always better to use any condom (even if it was not given to you by the study) than to use no condom.

Q21: Do we have to use condoms or can we rely on another form of birth control?

A: You should try to use condoms each time you have sex because condoms also protect against HIV and other sexually transmitted diseases (STDs). We do not know if the microbicide gels tested in this study protect against HIV and other STDs. Also, not all women in the study will get the microbicide gels. Some will get the placebo gel and some will get no gel. If you do not use a condom, you increase your risk of getting pregnant as well as getting HIV and other STDs. You can use another method of birth control (such as pills or injections) while in the study to give more protection against pregnancy, but you should also use condoms to protect against HIV and other STDs.

Q22: What should I do if the gel leaks out?

A: It is likely that some gel will leak out. This is normal and you don't need to do anything about it. You should always apply the full amount in the applicator. It may be helpful to wipe yourself on the outside with a dry cloth/tissue if you have been standing for a minute or two after you applied the gel, if you find that a small amount leaks out.

Q23: Can I use herbs or other substances for tight or dry sex while I am using the gel?

A: Herbs or other substances could damage the inside of the vagina. These substances also could interfere with the study gels. Therefore we recommend that you do not use herbs or other substances in the vagina.

Q24: Can my partner insert the gel for me?

A: It is preferable that you insert the gel yourself, but if you are happy that your partner knows how to do it in a way that won't cause you discomfort, then this is acceptable. It is better for your partner to insert the gel for you than to not use the gel at all.

Q25: Will I have access to the gel if it is shown to be effective?

A: If the gel is shown to be safe and effective, it will take some time for the gel to be allowed to be sold in the shops, but we will try to make sure this happens as quickly as possible.

Q26: My sister and I are both in the study and we live in the same house. What should we do if we mix up our gel?

A: First, try not to mix up your gel. If possible, keep the applicators in the cartons, and check for your study number on the carton to help make sure you each use the gel that you received. We also can give you some

colored stickers (or other identifiers if applicable) to put on your cartons and applicators to help keep track of whose gel is whose.

If you do mix up your applicators, the most important thing for you to do is inform the study staff, so we can have the pharmacist help you sort out whose gel is whose. It is okay to report mix-ups to us. We know that mix-ups can happen, and you will not be penalized if you mix up your applicators. You can still be in the study, and keep using gel, so long as you are willing to try to avoid more mix-ups. Please tell us as soon as possible if any mix-ups occur.

Section Appendix 9-2

MTN 004 Record of Receipt of Participant-Specific Gel Cartons

Site Name:
Site Number:

Clinic Name:

PHARMACY STAFF				CLINIC STAFF			
Date Dispensed by Pharmacy dd-MMM-yy	*PTID	No. of Study gel cartons Dispensed by Pharmacy	Pharmacist Initials	PTID *(Verify PTID transcribed from box matches PTID recorded by Pharmacist in Pharmacy Staff Section)*	Date and Time Received in Clinic (dd MMM yy, 00:00 AM/PM)	Clinic Staff Initials	COMMENTS

Instructions: Complete one row each time participant-specific study gel cartons are dispensed to non-pharmacy staff for delivery to a study participant. All entries must be made in dark ink. Corrections may be made by drawing a single line through incorrect entries, entering correct information, and initialing and dating the correction.

*** Form must be returned to the pharmacy at the end of every business day**

Section Appendix 9-3

MTN 004 Daily Runner Log

Site Name:
Site Number:

Clinic Name:

PHARMACY STAFF				RUNNER			
Date Dispensed by Pharmacy dd-MMM-yy	*PTID	No. of Study gel cartons Dispensed by Pharmacy	Pharmacist Initials	PTID *(Verify PTID transcribed from box matches PTID recorded by Pharmacist in Pharmacy Staff Section)	Date and Time Received by Clinic Staff (dd mmm yy, 00:00 AM/PM)	Runner Initials	COMMENTS

Instructions: Complete one row each time participant-specific study gel cartons are dispensed to non-pharmacy staff for delivery to a study participant. All entries must be made in dark ink. Corrections may be made by drawing a single line through incorrect entries, entering correct information, and initialing and dating the correction.

*** Form must be returned to the pharmacy at the end of every business day**