Pharmacy Guidelines and Instructions Manual for MTN Clinical Trials

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A. Background, Purpose and Contacts

1. Background and Purpose

In conducting clinical trials, the Microbicide Trials Network (MTN) must comply with U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA) regulations governing the receipt, use and disposition of all MTN study product. The MTN must assure that all investigators establish and maintain adequate records of study product receipt, use and disposition and that the records comply with FDA/EMA regulations and the standards of research involving the use of study products.

The Pharmacist of Record (PoR) at each clinical site/center participating in an MTN trial is the primary individual who is expected to develop and maintain a site pharmacy, investigational agent management system, which includes the technical procedures for study product ordering, storage, dispensing and accountability, and return/destruction. The pharmacist must be licensed and/or registered to practice pharmacy in the jurisdiction in which he/she is working. The PoR may be expected to participate in: preparation of blinded study products; preparation of special dosage forms and packaging; monitoring of study participant adherence to study product administration regimens; preparation of study product information/data sheets for pharmacy, nursing and other personnel; and data collection and documentation. In addition, the PoR must establish internal pharmacy policies and procedures for the safe and proper use of investigational agents.

This document is written for the PoR and other pharmacy staff involved in dispensing for the study and includes general information, responsibilities of the pharmacist and guidelines for study product management. Study products used in MTN-sponsored trials will be managed and controlled by the PoR.
Pharmacists should have knowledge regarding local and national regulations governing the practice of pharmacy. The guidelines in this manual are designed to assist pharmacists in meeting the requirements of the Food and Drug Administration and the European Medicines Agency and are to be used as a reference for the conduct of MTN- trials. Pharmacists are expected to follow these guidelines.

2. Contacts

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B. Responsibilities of Pharmacists

The PoR is responsible for demonstrating that internal policies and procedures are in place to assure the safe and proper storage and use of study products at their site and that study products will be dispensed only to eligible study participants. The PoR is also responsible for maintaining records of ordering and receipt of all protocol-related study products, and disposition of study products received for the MTN trial. If study products are received directly from sources other than the MTN, maintaining records of ordering, receipt and disposition are similarly required. Maintaining accountability records showing dispensing to participants including quantity and dates must also be kept.

The MTN Pharmaceutical Product Manager expects the site PoR to meet the following standards and requirements:

1. Devote the necessary and appropriate amount of time to meet the pharmacy needs and requirements of MTN clinical trials. Some protocols may require that a pharmacist manage the preparation as well as the dispensing of blinded products. Some study products may require either special storage conditions or special preparation methods.

   All issues related to study product supply are the responsibility of the PoR. The PoR is expected to handle the ordering, receipt, control, dispensing, accountability and unused return/destruction for the protocol-provided study product(s) for the Investigator of Record (IoR).

2. Provide adequate space, equipment, and supplies for the storage, preparation, packaging, and dispensing of study products that require special handling.

3. Provide the proper storage conditions for protocol-provided study products, including segregation, security, temperature, and temperature monitoring, light, moisture, ventilation and sanitation. The pharmacy temperature monitoring devices manufacturer, location and serial number or other identifier must be documented for each MTN trial on the pharmacy temperature logs.

4. Study products must be stored in a limited access area; i.e., an area that is locked when not in use. The study products should be accessible only to authorized personnel, such as the PoR and his/her pharmacist designee. The study products are shipped on a site-specific, investigator-specific, protocol-specific basis and should be stored with separate supplies for each clinical site and affiliated site.

   If upon arrival to the site pharmacy, the study product supplies appear to be damaged or the storage conditions have not been maintained (refrigerated items are not refrigerated upon receipt), the PoR should contact the MTN Pharmaceutical Product Manager immediately by phone or e-mail. The PoR should not dispense the protocol-provided study products until he/she has been notified in writing (e.g., electronically by the MTN Pharmaceutical Product Manager that the protocol-provided study products may be safely used. The PoR should maintain a hardcopy document of the notification from the MTN Pharmaceutical Product Manager in their study files.

5. Maintain all records of the receipt and disposition of the protocol-specific study products including dates, quantities, lot numbers of product(s) used by participants, unused/returned quarantined and unused/returned destroyed product. Each shipment of study product for a protocol should contain a record of the contents shipped. This will usually be an invoice identifying the shipment, including the lot number and the quantity of the product shipped. The pharmacist must verify that the quantity received matches the shipping documentation or invoice. If there are discrepancies, the MTN Pharmaceutical Product Manager should be notified and this notification should be documented on the invoice, signed and hand-dated.

   There should be an established method to account for all study protocol products. The MTN Study Product Accountability Record (see page 25), Study Product Accountability Record, equivalent computerized record or other document providing the same information must be used to document the receipt and disposition of all study products received for MTN clinical trials. If using a record other than the one provided here, documentation must include at least the drug name and dosage form, strength, lot number and protocol. Records should be study-specific. Physical inventories must be conducted to reconcile the quantity on hand with the inventory balances on the accountability record. It is recommended that these inventories be performed every 28-31 days. These periodic inventories should be documented with a date and signature on the accountability record itself by entering this information on the first available line of the record. (See Section D, Study Product Accountability for more detailed information). A procedure should always be developed and documented to ensure that sufficient supplies of the study product(s) are always available in the institution for the duration of the study.

6. Verify in writing on the accountability records, either before or at study completion, when protocol-provided study product supplies are returned to the supplier, the MTN Pharmaceutical Product Manager or shipped for destruction, No study supplies are to remain with the study site once the study has deregistered with DAIDS. If there are discrepancies between the accountability records and the physical supplies, the pharmacist must attempt to reconcile them. If the attempt to reconcile the differences is unsuccessful, the actions to reconcile must be documented on the accountability records and in a signed and dated, written report to the MTN Pharmaceutical Product Manager.

   Instructions specified in a protocol-specific document regarding returns and/or destruction supersedes the above instructions. If sites are instructed to send remaining study product for destruction, the original destruction certificate and the identity, quantity and lot number(s) of the materials sent for destruction must remain on file and a copy sent to the MTN Pharmaceutical Product Manager.

   There will usually be a specific document provided for each trial in the study-specific Pharmacy Study Product Management Procedures Manual provided by the MTN.

7. Retain all records for protocol-provided study product (order forms, receipts for transfers and returns, packing slips, inventory and accountability records, etc.). International sites

should also retain a copy of all shipping documents, packing slips, commercial invoices, import permits, etc. that may have been received. These records and any other unique pharmacy records should be retained for at least two years following the date that a United States New Drug Application (NDA) is approved for the drug for the indication which it is being investigated or, if the application is not approved for such indication, until two years after the investigation of the study product is discontinued and the United States FDA notified. If the application is not approved for such indication, all study product records should be retained for two years after the Investigational New Drug (IND) application is withdrawn or study of the investigational product is discontinued, and the FDA is notified. If an NDA is not be filed, or the protocol-supplied product was not being studied under an IND, then the accountability records must be kept for at least three years and until the site is notified that the protocol associated Case Report Forms may be destroyed. If local policies are stricter than these policies, then follow the local policies. (See MTN Manual of Operational Procedures, Sections 18.2.2 and 18.3; *Long-Term Storage of Study Records* and *Study Record Destruction*, respectively.)

Participant-specific pharmacy accountability and dispensing records and any other unique pharmacy information should be archived with clinic case report forms after the protocol database is closed and the study is unblinded, if applicable. When archiving, participant specific pharmacy records should be placed in a folder or envelope and clearly marked as pharmacy records. The pharmacy records should then be placed at the front of the case report forms. Never mix the pharmacy records in the middle of the case report forms. All other pharmacy study-specific documents such as order forms, receipts for transfers and returns, packing slips and the study product accountability records should be archived in the pharmacy. (See MTN Manual of Operational Procedures, Sections 18.2.2 and 18.3; *Long-Term Storage of Study Records* and *Study Record Destruction*, respectively.)

8. Study product accountability records need to be available for inspection and copying by an authorized employee or representative of the MTN, FDA, EMA or other international regulatory body as applicable, upon request.

9. A mechanism needs to be established to ensure that study products are dispensed only after the written order of the IoR or upon the order of a licensed clinician directly responsible to the IoR as stated on the Form FDA 1572. If the Form FDA 1572 is not required for protocol registration, then an Authorized Prescribers List may replace the Form FDA 1572. The criteria for being on the authorized prescribers list should be the same as being on the Form FDA 1572. Such lists should be updated whenever authorized prescribers are added or deleted, but at a minimum of once yearly. Prescribers must be clinicians authorized to prescribe in the site's jurisdiction.

10. Maintain the confidentiality of the participant, the participant's pharmacy file, and the study product accountability record. Maintain the blinding of the participant's study product assignment to investigators, study nurses, clinical staff and the participant.

11. Establish a communication system with other site staff to assure the protocol has been approved by the appropriate medical ethics committee(s) such as the Institutional Review Board (IRB) etc.

12. A system needs to be established to ensure that the participant has provided written informed consent before dispensing protocol-provided study products. Either a copy of the informed consent document or a log which designates who has provided verbal assurance that the informed consent has been signed or a notation on the prescription will suffice.

13. The PoR should have on file a copy of the most current version of the protocol, and any additional versions of the protocol if there are participants being followed on that version. The pharmacist must establish a system to ensure that when dispensing the protocol-specific products that the most current version is being followed. The PoR must also receive and retain a copy of all bulletins, emails, clarifications, or letters of amendment (LoA) for each protocol. These documents may be obtained from the study coordinator.

14. The pharmacy needs to establish a central system for maintaining essential information on study agents. An Investigator's Brochure or most current Product Package Insert, which contains current information about the investigational agent as supplied by the manufacturer, is distributed to the clinical sites with the first final version of a particular protocol. The study coordinator is responsible for distribution of the Investigator's Brochure/Product Package Insert to the PoR at the main site and to any affiliated sites. The information in the Investigator's Brochure is confidential and should not be reproduced or distributed to individuals outside of the research team. The investigational product information is to be used only by the pharmacist, investigators, and other health professionals on the research team. Investigator's Brochures no longer required (i.e., associated trial is complete) to be on file should be destroyed by shredding.

15. The MTN Pharmaceutical Product Manager must be notified in writing of any incidents or matters that could affect the outcome of the study, such as a study product preparation and /or administration problem, study product dispensing error, product complaint and participant complaints and/or suggestions. In addition to informing the IoR in writing of situations that could affect the outcome of the study or the safety of study participants, the pharmacist must complete a Protocol Deviation Form and submit this to SCHARP. THE REPORT MUST NOT UNBLIND THE INVESTIGATOR OR OTHER STUDY PERSONNEL.

    The following are examples of incidents that are reportable:

    - A participant was dispensed an incorrect study product.
    - A participant was assigned an incorrect participant identification number, incorrect randomization number, or was enrolled in the incorrect clinical trial.
    - Any un-blinding activity by the site pharmacist.
    - Participants exchanged or shared study medications.
    - Improper storage of study products.
    - Accountability discrepancies that were not able to be reconciled.

- Study products were dispensed or administered to individuals not participating in the protocol.
- Any product issue (packaging, labeling or actual product abnormality)

The PoR's report to the MTN of an incident must include:

- All participant identification numbers such as PTIDs, randomization number and product code (if applicable).
- Clinical site name and number and site PI name.
- A description of the incident or problem.
- The reason(s) for the incident.
- Resolution and/or follow-up of the incident.
- A description of the steps that have been taken to ensure that similar incidents do not happen again.
- A statement whether the incident resulted in a reportable adverse experience report.
- Send this report to the MTN Pharmaceutical Product Manager listed in section A.2.

16. The quality and appropriateness of the investigational pharmacy service should be internally reviewed and evaluated. A systematic process for quality assurance monitoring should be established and in place. Actions taken when a problem is identified must be appropriately documented and reported. Internal quality assurance monitoring should be performed at specific periodic intervals.

17. Pharmacy records must be available to clinical site monitors. The frequency with which pharmacies are visited will depend on the specific protocol. If problems are found the frequency of visits may be increased. The focus of monitoring visits could be either on the site operations of the pharmacy or on the conduct of a specific protocol or both. Site-operations audits are requested when there is a new site established, a new location, a new facility, or a new PoR. Reports of these site operations audits and protocol conduct audits will be provided to the PoR, MTN Pharmaceutical Product Manager, and the site and protocol Principal Investigator.

18. Expiration dates must be monitored on all product labels or other product documentation. Expired product must be removed from active stock and placed separate from active stock until returned to the MTN (quarantined). Expired product should be returned to the MTN as soon as possible, if requested by the MTN Pharmaceutical Product Manager

19. Obtain and maintain a prescriber sample signature list.

20. A pharmacy plan must be created by the PoR for each clinical research site participating in MTN studies, addressing the control and use of Investigational Products. The pharmacy plan must be submitted to the DAIDS PAB for approval prior to the receipt and distribution of study product. The PoR is encouraged to work with other staff members on the formulation of this plan. If a DAIDS PAB plan has not been submitted/approved, an MTN Pharmacy Plan must be submitted to the MTN Pharmaceutical Product Manager.

Complete an MTN Pharmacy Establishment Plan whenever:

- **A DAIDS PAB plan is not in place or is not acceptable to MTN Pharmaceutical Product Manager**
- A new site is being established
- A pharmacy that is affiliated with a site in one network is now being established in a second or other additional network.
- Amended changes whenever the location of the pharmacy changes
- Whenever there is a substantial change in procedures outlined in the previous pharmacy plan
- Upon MTN request, if a situation has deemed necessary to require a new pharmacy plan.

20. If the PoR will be responsible for dispensing activities at more than one clinical site, a separate pharmacy plan for each clinical site is required. In the event that a Site Pharmacist is responsible for the dispensing of investigational products to participants enrolled in other protocols at other sites, a letter describing the dispensing procedures must be co-signed by the IRB chairman and Director of Pharmacy at the second site. This letter serves to document the concurrence of these individuals with the proposed plan for dispensing of investigational products to participants at that site. This letter also serves to notify the MTN that all parties have been properly notified of these procedures.

21. Submit a Notification of Change in Pharmacist Form whenever there is a change in pharmacy personnel or contact information. If a DAIDS PAB PEP is in place, PAB must be notified on their form of the change. The MTN Pharmaceutical Product Manager should receive a copy of this notification. If the PEP in place is an MTN Pharmacy Plan, the Notification of Change in Pharmacist Form is located at the end of the MTN Pharmacy Establishment Plan. A curriculum vitae for a new PoR or primary back-up pharmacist should be forwarded with this form to the MTN.

22. Submit a Notification of Change in Pharmacy Address or Information Form to PAB (if applicable) and the MTN Pharmaceutical Product Manager whenever there is a change in the mailing address, shipping address, courier address, phone or fax number, or internet address.

MTN PHARMACY ESTABLISHMENT PLAN

A. Background

1. Name, Address, and site number of the clinical research site this pharmacy plan is for.

   Site Number:

2. Name, degree, title or position, site mailing address, email address, telephone, and fax numbers of the PoR who is responsible for this pharmacy plan?

3. Provide shipping address where study products are to be shipped.

4. Name, degree, title or position of the Associate Pharmacist(s) who will assume these responsibilities when the PoR is not available.

5. Does the pharmacy have written policies and procedures for handling Investigational products? If yes, attach.

6. Describe the system for organizing protocol information, (for example, the current IRB approved version of the protocol (and amendments if applicable), participant treatment assignment lists, order forms, packing slips, accountability records, written prescriptions, return records, letters and memos from MTN, Investigator's Brochures, etc.), the process for keeping this information up to date, where it will be located and who will have access.

7. How will the PoR be informed of the IRB approval of a protocol? How will the PoR verify that s/he is working with the current IRB-approved version of a protocol?

8. How will authorized prescribers be identified for a protocol so as to prevent the unauthorized prescribing of investigational products?

9. What procedures will be followed by the PoR to maintain confidentiality of a participant's pharmacy file and the investigational product accountability records?

10. Does the pharmacy utilize a computerized investigational drug system (e.g. accountability/inventory, study information and/or medication order entry)? If so, describe.

11. Is the access to the pharmacy limited to only pharmacy personnel? If no please explain.

12. Is access to study products limited to only pharmacy personnel? If no please explain.

13. What are the security measures in place limiting study product access to only authorized pharmacy personnel?

B. Investigational Product Control

Each of the following questions must be answered.

1. Room Temperature Storage

a) Where will investigational products be stored?

b) Who will have access to investigational products?

c) How will access to investigational products be limited to only those listed in b) above?

d) If prescriptions are prepared prior to a participant's visit, where will they be stored?

e) Is the access limited in the storage area listed in d) above?

f) At what temperature range is the storage area(s) maintained?

g) How often is the storage area(s) monitored for temperature control?

h) Is there documentation of the temperature monitoring of the storage area(s)?

i.) Do the temperature monitoring logs include the location, manufacturer and serial number (or other identifier) of the device?

2. Refrigerated Storage in the Pharmacy

   a) Is refrigeration available? Yes? No?

   b) Where is the refrigerator located?

   c) How large is the refrigerator? Indicate whether cubic feet or cubic meters.

   d) Who will have access to the refrigerator?

   e) How will access to the refrigerator be limited?

   f) At what temperature (°C/°F) is the refrigerator maintained?

   g) Is there documentation of the temperature monitoring of the refrigerator?

   h) How often is the refrigerator monitored for temperature control?

3. Refrigerated Storage in the Clinic

   a) If study products that require refrigeration are prepared in advance for a participant's collection (pick up) at the clinic, will refrigeration be available in the clinic? Yes ? No ?

   b) How is access to the refrigerator in this area limited?

4. Freezer Storage in the Pharmacy (-20°C to -10°C)

   a) Is a -20°C to -10°C (-4°F to 14°F) freezer available? Yes ? No ?

   b) If yes, where is the freezer located?

   c) How large is the freezer? Indicate whether cubic feet or cubic meters.

   d) Who will have access to the freezer?

   e) How will access to the freezer be limited?

   f) At what temperature is the freezer maintained?

   g) Is there documentation of the temperature monitoring of the freezer?

   h) How often is the freezer monitored for temperature control?

5. Freezer Storage in the Pharmacy (-70°C)

   a) Is -70°C (-94°F) freezer storage space available? Yes ? No?

   b) If yes, where is this -70°C freezer storage space located?

   c) How many cubic feet or cubic meters are available?

   d) Who will have access to the -70°C freezer storage space?

   e) How will access to the -70°C freezer storage space be limited?

   f) Is there documentation of the temperature monitoring of the -70°C freezer?

   g) How often is the -70°C freezer monitored for temperature control?

6. The PoR is required to keep complete written records (accountability records) of all investigational products/study drugs that are received from the Sponsor or Distributor and of all investigational products/study drugs that are dispensed to participants. The count or quantity of investigational products/study drugs that you have at your site must match the quantity on the accountability records at all times. How often will the investigational products/study drugs on the shelves and in the refrigerator/freezer be counted and compared with the accountability record?

C. Investigational Product Dispensing

1. An authorized prescriber listed on the FDA form 1572 (or equivalent document) must sign a written prescription at the time that a participant is registered/randomized to the protocol, or when there is a change in treatment, in order for the pharmacist to dispense study product. How will the PoR receive this written prescription? (If electronic prescriptions are used describe this process.)

2. Describe how an initial study product order will be prepared and dispensed at this institution. Will study product be prepared in the in-patient or outpatient pharmacy? (If both, describe both procedures.)

3. How will it be documented that the informed consent was signed prior to dispensing the investigational product(s)?

4. How will the PoR be informed that subsequent prescriptions/refills need to be prepared? How will study products be delivered to the participant for follow-up visits?

5. Written prescriptions must be used to notify the PoR when a study drug dose is changed. How will the PoR receive the written prescription that notifies that a dose has been changed?

6. Is a biological safety cabinet or an isolator available for preparing study products?

7. How will the PoR dispense study products? (Check all that apply)

___ Directly to participants.
___ Deliver study products to other healthcare providers who will distribute it to participants.
___ Through other procedures (describe).

8. How will the PoR receive study drugs returned by the participant? (Check all that apply)

___ Directly from participants.
___ From other healthcare providers.
___ Through other procedures (describe).

PoR Signature_____

Date: _____

NOTE: Pharmacy plans will not be approved without the PoR's dated signature and an attached copy of the PoRs *curriculum vitae*. A copy of this completed Pharmacy Establishment Plan must be kept on file in the pharmacy.

TEMPORARY/PERMANENT NOTIFICATION OF CHANGE IN PoR OR BACK-UP PHARMACIST

Site Name: _____ Site Number (s): _____

Permanent: ☐ Y ☐ N Date from: ____/____/____ Date to: ____/____/____

Temporary: ☐ Y ☐ N Date from: ____/____/____ Date to: ____/____/____

Name of **PREVIOUS** PoR or Back-up Pharmacist: _____
(print)

Name of **NEW** PoR or Back-up Pharmacist: _____
(print)

Degree, Title, Position: _____

Mailing Address: _____

_____

Telephone Number: _____

Email Address: _____

Please complete the following:

_____ I, the new PoR or Back-up Pharmacist (circle one) have attached a copy of my CV.
(initial here)

_____ I agree to comply with all of the information contained in the previous or revised MTN Pharmacy Establishment Plan. If the Pharmacy Plan was revised, please attach.
(initial here)

Sign and Date:

_____
Signature of NEW PoR or Back-up Pharmacist Date

Return this form to:

Cindy Jacobson, PharmD
Microbicide Trials Network
Pharmaceutical Product Manager
204 Craft Avenue
Pittsburgh, PA 15213
(412) 657-5538
cjacobson@upmc.edu

NOTIFICATION OF CHANGE IN PHARMACY ADDRESS OR INFORMATION

Site Name: _____ Site Number (s): _____

Name of PoR: _____
(print)

Telephone Number: _____

Check all that apply:

Change of address: _____Change of phone/fax: _____ Change of email address: _____

New Address:

Please check all that apply: Mailing: _____ Shipping: ____ Courier: _____

_____

_____

_____

Additional Address (if needed):

Please check all that apply: Mailing: _____ Shipping: ____ Courier: _____

_____

_____

_____

NEW Phone Number: _____

NEW Email Address: _____

_____ _____
Signature of PoR Date

Return this form to:
Cindy Jacobson, PharmD
Manager Pharmaceutical Product Manager
Director, Pharmacy Affairs
204 Craft Avenue
Pittsburgh, PA 15213
(412) 657-5538
cjacobson@upmc.edu

C. Study Product Ordering

Once the site is approved to order study product it should be ordered for the specific protocol for which it will be used. The study product order should be placed by the PoR or another pharmacist at the site who the PoR identified in writing to the MTN Pharmaceutical Product Manager. The order must include the name and identification number of the Investigator of Record (IoR) for the protocol. A separate supply of study product must be ordered for each site number, even if the same pharmacist is handling the supplies for the same protocol for different clinical site/center and affiliated sites.

Sites should refer to the protocol document and/or the study specific "Pharmacy Study Product Management Procedures Manual" regarding the quantities and manner in which the study products will be obtained. To order supplies of study products, please use the MTN Study Product Order Form and send it to the supplier via scan/email or FAX.

Instructions for completing the Study Product Order Form appear below. This is a standard form for all MTN sponsored studies. This form may be photocopied.

a. Please type or clearly print all of the information requested on the form.
b. Complete site information by entering the following:
    i. Protocol number
    ii. Principal Investigator's name (IoR)
    iii. Site name
    iv. Site number
    v. Pharmacist requesting supplies (PoR or designee)
    vi. Telephone number of the requesting pharmacist.
c. c. Complete the order request including the number of units for each product requested. Be sure to include (if not preprinted) a detailed description of the product requested. Example: 32 applicators of tenofovir rectal gel 1% gel.
d. The shipping information on the form must include:
    i. Pharmacy shipping address
    ii. Signature of PoR
    iii. Date the request was submitted
    iv. Requested date by which supplies must be received
    v. Check if Saturday delivery is required

e. The MTN/Study Product Distributor will complete the bottom box with:
    i. Date order is received
    ii. Order number
    iii. Lot #
    iv. Authorized by
    v. Initials of the person(s) who pulled check and packed the order.
    vi. Date shipped

f. Scan/email using the information that appears on the bottom left corner of the order form. Since the MTN may have different suppliers depending on the study, this address will change.

g. When this order form is scanned/emailed or faxed, keep the original in the protocol-specific pharmacy binder/folder.

STUDY PRODUCT ORDER FORM

Protocol #: _____ Investigator Name: _____

Site Name: _____ Site #: _____

Pharmacist (Requestor): _____ Phone #: _____

INSTRUCTIONS: Type or print clearly except signature. Complete all sections except for box labeled **MTN/Distributor**. Sign and date order. Enter requested receipt date. Use this order form for initial and subsequent order(s) of study product.

THIS ORDER IS TO REQUEST THAT:

BE FORWARDED TO OUR SITE PHARMACY FOR DISPENSING TO MTN-XX PARTICIPANTS

Pharmacy Shipping Address:	Pharmacist Signature: Date Completed: Requested Receipt Date: Saturday delivery requested ☐ YES

Return to: Attn: Address: Phone: Fax: Email:	MTN/Distributor to complete: Date Received: _____ Order #: _____Lot#_____ Authorized by: _____ Pulled by: _____ Checked by: _____ Packed by: _____ Date shipped: _____

D. Study Product Accountability

The MTN Study Product Accountability Record must be used to document the receipt and disposition of ALL study product for an MTN study. However, an equivalent computerized record or other document may be used only if the same information is provided and is approved by the MTN Pharmaceutical Product Manager. The accountability record is to be used for recording data on the accountability (receipt from source, dispensing, inventory audits, and returning to source) of the protocol- and lot-specific study products.

Information to be recorded on the Accountability Record includes:

a. Study site information (protocol number, investigator name, site name and number)
b. Study product name/strength/dosage form, manufacturer and lot number, storage temperature and expiration date (if necessary).
c. Participant identification number or study kit identification number
d. Quantity dispensed or received or returned to the MTN or other source
e. Current balance
f. Pharmacist's initials
g. Date
h. Comments

An example of a Study Product Accountability Record is included at the end of this section. This is a standard form that may be photocopied and used as the study product accountability record for all MTN studies. This form may also be revised and will be provided in the Pharmacy Study Product Management Procedures Manual to accommodate documentation for a specific protocol. This form utilizes a single study product lot per page. The lot number is recorded on the top section of the form. In instances where more than one lot is on inventory, it will be necessary to have separate accountability records for each lot of that product. Each product for a protocol should have a separate accountability record form. If other accountability records are used in place of the MTN provided accountability record, these records, at a minimum, must contain the same information as the MTN form.

Each time study product is dispensed to a participant, received from the designated source, and/or returned to the designated source, it should be documented on this form or its equivalent. The inventory balance documented on this form should match the actual study product inventory on hand at all times. Every time that a physical inventory is conducted and reconciled with the accountability records, an entry should be made with the date and pharmacist's initials. When the recorded balance and the actual inventory are not the same, the discrepancy and the reason for the discrepancy should be documented on the study product accountability record and reported to the MTN Pharmaceutical Product Manager. A written report describing the discrepancy and resolution should be emailed or faxed to the MTN Pharmaceutical Product Manager. After documentation of the discrepancy and authorization from the MTN Pharmaceutical Product Manager, the balance may be adjusted to match the actual inventory count.

All entries on the study accountability record must be made in dark ink, not in pencil. If corrections are needed, draw a single line through the incorrect information. Initial, date, state reason for the change (if necessary), and insert the correction. Explanations of corrections or other relevant

comments may be written on the back of the form by writing "see back" in the comment space for that line, then writing the line number and explanation on the back. Never use "white-out" or obliterate entries that require correction. Never destroy original documents even if they require error correction.

It is required that the prescription for the corresponding entry in the Study Product Accountability Record be maintained and easily retrievable for review by authorized representatives of the MTN, FDA and other international regulatory authorities as applicable.

Identification of the dispensing pharmacist is always necessary when there is an audit or review of the study product accountability records and prescriptions. A list of pharmacists' signatures and initials to identify each dispensing pharmacist must be available. Upon request, the list of pharmacists' signatures and initials must be made available to authorized representatives of the MTN, DAIDS, FDA and other international regulatory authorities as applicable.

Study Product Accountability Records, shipment invoices and return receipts should be maintained in the pharmacy until the study is completed. When the database for the study has been closed, the records should be stored, either in the pharmacy or with other study records from the clinic; do not send originals or copies of accountability records to the MTN unless requested. By United States Law, accountability records for completed studies must be retained for two years following the date that a United States New Drug Application (NDA) is approved for the drug for the indication which it was being investigated or, if an NDA is not be filed or if the application is not approved for such an indication, until two years after the study of the study product is discontinued and the United States FDA notified. If an NDA is not being filed, or the protocol-supplied product was not being studied under an IND, then the accountability records must be kept until the site is notified that the protocol assisted Case Report Forms may be destroyed. Furthermore, these records shall be made available, upon request, for inspection and copying by a properly authorized employee, representative, or monitor of the MTN, FDA, EMA or other international regulatory body as applicable, upon request.

STUDY PRODUCT ACCOUNTABILITY RECORD TEMPLATE

Protocol Number:	Site Name and Number:	Investigator of Record:

Manufacturer:	Lot Number* and Exp:	Study Product Name/Strength/Dosage Form:

*Please use only **one** lot number per page.

	PTID	Quantity dispensed (-) Or received (+)	Balance Forward	RPh initials	Date	Comments
1						
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
13						
14						
15						
16						
17						
18						
19						
20						

E. Participant Randomization

Prior to site activation, SCHARP will configure the randomization within the Medidata Balance system and upload into this system a permuted block randomization schedule. This schedule will be of adequate size to enroll the expected number of participants per site plus additional randomization slots in case some sites enroll more than the expected number of participants and to allow for the potential randomization of additional participants in consultation with the Study Monitoring Committee (SMC) and/or DSMB if loss to follow-up is higher than expected.

For most MTN trials, the first step in study randomization is for CRS clinic staff to complete the Eligibility Criteria electronic CRF (eCRF) with all responses indicating that the participant is eligible to participate in the study. Upon completion, site staff will navigate to the Randomization eCRF in the Enrollment folder to randomize a study participant and will mark the response box (shown in image below) for the question "Is the participant ready to be randomized?". Once this response is saved, the database (via the Medidata Balance module) will assign the participant to a product sequence and the Randomization Date and Time will appear automatically on the Randomization eCRF. Note: If a CRS clinic staff attempts to randomize a participant via the Randomization CRF without having indicated that the participant is eligible on the Eligibility Criteria CRF, Medidata Rave will not allow the participant to be randomized, and an error message will appear.

1. Un-blinding Procedures

<u>The pharmacist should never be involved in the decision to unblind the study product assignment.</u> While a trial is ongoing, permissions to participant-specific treatment assignments are limited to those statisticians that comprise the study unblinded statistical team and are designated as such per SCHARP Work Instruction 0016 Implementation of Efficacy Trial Dual Statistical Team. Typically, members of a study's independent Data and Safety Monitoring Board (DSMB) have limited access to unblinded treatment assignments via closed session DSMB reports produced by the SDMC.

Except in the case of a medical emergency, unblinding of study participants and study site staff to individual participant treatment assignments occurs only after the Protocol Chair(s), NIAID, study co-sponsor(s) and the SDMC have approved the decision to unblind the study. As a rule, unless otherwise requested by the DSMB, a study is not unblinded until after the study database has been locked.

F. Study Product Dispensing

1. Prescriber Responsibility

The PoR must ensure that study products are dispensed only upon written order from the Investigator of Record (IoR) or upon the order of a licensed clinician directly responsible under IoR as stated on the Form FDA 1572 (IND studies) or the authorized prescribers list (non-IND studies). It is not permitted for an individual who is not an authorized prescriber to sign a prescription with an authorized prescriber's name and then add his/hers name to it to make it legal. For example, a nurse may not sign a doctor's name to a prescription and then add his/her name to it if he/she is not an authorized prescriber.

By signing the Form FDA 1572, the IoR has certified that the investigational agent will be administered only to subjects under his/her personal supervision or under the supervision of sub-investigators responsible to him/her.

2. General Prescription Requirements

The prescription issued for each study subject shall be written in dark ink, typewriter, or computer generated and shall be signed by the clinician. Prescriptions are to be manually/hand completed. Signature stamps are not permitted. The use of electronic signature is acceptable in institutions that have adopted a validated electronic medical record system. If the institution has deemed that practice acceptable, then the MTN will accept this practice. Signing blank prescriptions and/or post-dated prescriptions are not permitted. An agent for the IoR or sub-investigator may prepare prescriptions in advanced for the signature of an IoR or sub-investigator.

A copy of the prescription must be kept in the patient's study chart. Prescriptions or medication orders must include all of the following:

a. Date
b. Study number
c. PTID or other participant identifier
d. Randomization number (if applicable)
e. Weight and BSA or height (if applicable)
f. Medication or study product prescribed
g. Quantity or instructions to indicate amount to be dispensed
h. Directions for participant
i. Any special instructions regarding dose reduction, dose escalation, etc.
j. Prescriber's printed name and signature and date

3. Pharmacist's Responsibilities

The PoR must establish a method to verify that a valid consent form was signed by the participant prior to dispensing the supply of protocol specific study product. The study product must be dispensed in accordance with the current IRB/EC-approved protocol. A copy of the signed IC document for each participant and a copy of IRB approval letters for all amendments and protocol

versions should be in the files unless verification is provided on the prescription and is acceptable in accordance with government and institutional guidelines.

It is the site pharmacists' responsibility to know the labeling requirements for their jurisdiction. Prescription labels should be prepared so that the format complies with all applicable requirements and maintains participant confidentiality. Supplemental or axillary labels may be added by the site pharmacist in order to comply with local or institutional requirements. Prescription labels for study products should be distinguishable from other labels by an appropriate legend, "Investigational Product" or "For Investigational Use Only".

MTN study product labels at minimum will include the following:

a. Study sponsor information
b. Participant ID
c. Dispensing date
d. Directions
e. Study number
f. Number of dosing units dispensed
g. Name of investigational product or protocol-provided product if unblinded study and confidentiality is not an issue.

Disposition of the study products must be documented on the MTN Study Specific Investigational Accountability Record or an MTN Pharmaceutical Product Manager-approved computerized form or other accountability form providing equivalent information that is study product- and protocol-specific.

The PoR must maintain the confidentiality of the participant, the participant's pharmacy file, and the investigational study product accountability record, and for the blinded studies, maintain blinding of the participant's study product assignment to the clinical site staff and participant. The pharmacist should inform the Principal Investigator (IoR) of any study product administration errors, without un-blinding him or her or other research staff members to the participant's treatment assignment.

G. Study Product Transfers

Intra-institutional Study Product Transfer

Under NO conditions should study products be transferred from one protocol to another protocol without **prior authorization** from the MTN Pharmaceutical Product Manager. Study product transfer, as outlined below, refers to **intra-institutional** transfer of study products that were shipped for a specific MTN protocol and, after authorization by the MTN Pharmaceutical Product Manager, are transferred to another MTN protocol at the same site.

Study product transfers may occur if ALL of the following conditions are met:

2. A transfer request has been approved by the MTN Pharmaceutical Product Manager.
3. Study product is being transferred within the same site number.
4. Study product is being transferred from a completed or discontinued protocol to an actively accruing protocol within the same network/program.
5. Study products for both protocols are provided by the same supplier.

Study product transfers will NOT be approved when:

1. Study product that is being transferred has not been supplied by the MTN or an MTN supplier.
2. Both protocols are active at the site.
3. Study product has expired.

To request study product transfer, the Study Product Transfer Request form must be completed and sent to the MTN Pharmaceutical Product Manager via scan/email, or FAX. A copy of the form appears at the end of this section. The MTN Pharmaceutical Product Manager will determine if it is appropriate to transfer the study product and will notify the PoR via email or FAX. A copy of the approval notice should be retained at the clinical center/site pharmacy for documentation.

The transfer MUST BE RECORDED on the corresponding STUDY PRODUCT ACCOUNTABILITY RECORDS.

STUDY PRODUCT TRANSFER FORM – INTRA-INSTITUTIONAL

Study Number: _____ Site Name: _____

Investigator Name: _____ Investigator Number: _____
(Investigator transferring drug)

Protocol Number	Transfer to Protocol Number	Product Name	Strength/Dose	Quantity & Dosage Form (tablet, vial, applicator)	Mfg.	Lot #

*This form is to be used to obtain approval for the transfer of products for MTN studies. **This form is for intra-institutional transfers only.**

Instructions:

1. One lot number per line
2. Type or print in ink, sign and date form
3. Return to: Cindy Jacobson, PharmD
   Pharmaceutical Product Manager
   204 Craft Avenue
   Pittsburgh, PA 15213
   cjacobson@upmc.edu

Pharmacist Signature: _____ Telephone Number: _____

Complete Address: _____

_____

_____

MTN/Drug Transfer Use Only:

MTN Pharmaceutical Product Manager Signature: _____

Approved: _____ Disapproved: _____

Inter-institutional Study Product Transfer

1. Prior to the initiation of a MTN protocol-specific study product transfer between two sites, the PoRs at both sites must confirm with the MTN LOC Pharmacy that a study product transfer is allowable based upon local regulations.
    a. If allowable, each site PoR will need to inform the MTN LOC Pharmacy of the necessary documentation that is needed from the MTN LOC Pharmacy and from the other site participating in the transfer.
2. In order for a study product transfer to be initiated, the MTN LOC Pharmacist will send an email to the MTN CRS Pharmacists (PoR and Back-up Pharmacists) at both MTN CRS pharmacies that will be involved in the protocol-specific study product transfer.
    a. This email from the MTN LOC Pharmacist will include a statement requesting a study product transfer between the two sites. Attached to the email, the MTN LOC Pharmacist will provide a blank MTN Protocol-Specific Study Product Form document.
3. The transferring/sending CRS Pharmacist will complete the MTN Protocol-Specific Study Product Request document. (S)he will scan/email the completed form to the MTN LOC Pharmacist and cc the receiving CRS Pharmacist (PoR and Back-up Pharmacists).
4. The MTN LOC Pharmacist will review the completed request form. If approved, the MTN LOC Pharmacist will print/sign name and date the bottom of the document. The MTN LOC Pharmacist will scan/email the document to the transferring/sending pharmacy and cc the receiving pharmacy, as notification of study product transfer approval.
5. Pharmacy staff at both sites must keep a hard copy of this email communication and completed/approved study product transfer request document in their MTN protocol-specific pharmacy file. Following email confirmation, the transferring pharmacy can begin the study product transferring process, which includes proper documentation, storage, and shipment procedures.
    a. In addition to documentation required based on local guidelines, documentation to be included in the shipment: The transferring MTN CRS pharmacy must include a hard copy of the storage temperature log that clearly indicates that the study product that is to be transferred was stored at the appropriate temperature/humidity environment during its entire time at this pharmacy. The transferring pharmacy should also include a hard copy of the original shipping documents. The temperature log and original shipping documents should be marked "COPY." A study product CofA and packing slip should also be included in this shipment. The packing slip should be the original, not a copy. Refer to Appendix II.
        i. The transferring MTN CRS pharmacy should keep a hard copy of the packing slip for their MTN protocol-specific file.
    b. The transferring MTN CRS PoR or Back-up Pharmacist must document the quantity of study product removed from stock on the appropriate MTN protocol-specific study product accountability log/record.
    c. Shipment: The study product shipment must be temperature controlled and temperature monitored, preferably with a TempTale®4 USB monitor. Study product will be shipped via World Courier. If another carrier is preferred by either

site, the MTN LOC Pharmacy must provide approval. The MTN LOC Pharmacy will provide a World Courier account number so that all costs associated with the study product shipment will be covered by the MTN LOC.

6. Upon shipment, the transferring MTN CRS pharmacy should notify via email the receiving MTN CRS pharmacy and MTN LOC Pharmacist that study product shipment has occurred. This email should include all related shipment tracking information.
7. Upon shipment receipt, the receiving MTN CRS pharmacy should immediately remove the temperature monitor(s) from the shipping container(s). The receiving MTN CRS PoR or Back-up Pharmacist should immediately download the temperature files. These files should be sent to the MTN LOC Pharmacist to confirm that no temperature excursion occurred.
    a. If a temperature excursion did occur, the receiving MTN CRS pharmacy should place the study product in quarantine. The MTN LOC Pharmacist will provide guidance on how to proceed at this point.
    b. If no temperature excursion occurred, the study product can be dispensed from the pharmacy for the specified MTN protocol.
8. The receiving MTN CRS pharmacy should also confirm that the following documents were included with the shipment (at minimum): Copy of storage temperature log from originating MTN CRS pharmacy and packing slip.
9. The receiving MTN CRS pharmacy should store the storage temperature log from originating MTN CRS pharmacy, packing slip, shipment temperature record, and any other shipping documents in their MTN protocol-specific file.
10. The receiving MTN CRS PoR or Back-up Pharmacist must document the quantity of study product received on the appropriate MTN protocol-specific study product accountability log/record.

MTN PROTOCOL-SPECIFIC STUDY PRODUCT TRANSFER FORM

A MTN protocol-specific study product transfer is being requested for the following MTN protocol:

Protocol Name	
MTN Study #	

This study product transfer is to occur between the following two MTN clinical research site pharmacies:

SENDING Pharmacy	
CRS Name	
CRS ID	
IoR Name	
PoR Name	
PoR Email Address	
CRS Pharmacy Address	
CRS Pharmacy Telephone	

RECEIVING Pharmacy	
CRS Name	
CRS ID	
IoR Name	
PoR Name	
PoR Email Address	
CRS Pharmacy Address	
CRS Pharmacy Telephone	

The study product requested to be transferred:

Study Product Name/Dosage Form	
LOT # (if known)	
Expiration Date (if known)	
Quantity to be Transferred	

This study product must be shipped by: _____ (dd-MMM-yy)

APPROVAL OF STUDY PRODUCT TRANSFER

_____
MTN Pharmaceutical Product Manager (Print Name)

_____ _____
MTN Pharmaceutical Product Manager (Sign Name) **Date (dd-MMM-yy)**

PACKING SLIP

TO (RECEIVING Pharmacy):	
CRS Name	
CRS ID	
IoR Name	
PoR Name	
PoR Email Address	
CRS Pharmacy Address	
CRS Pharmacy Telephone	

FROM (SENDING Pharmacy):	
CRS Name	
CRS ID	
IoR Name	
PoR Name	
PoR Email Address	
CRS Pharmacy Address	
CRS Pharmacy Telephone	

Study Product Information	
Protocol Name	
MTN Study #	
Study Product Name/Dosage Form	
LOT # (if known)	
Expiration Date (if known)	
Quantity Transferred	

Transferring Pharmacist (Print Name)

Transferring Pharmacist (Sign Name) **Date (dd-MMM-yy)**

H. Study Product Disposal and Return

The PoR must conduct periodic (every 28-31 days) inventory of study product through the review of records relating to study product shipping, dispensing and return to source or destruction. Disposition of the returned or destroyed study product must be documented on the Study Product Accountability Record. The PoR must also conduct a periodic inventory of expired or recalled study products and dispose of them as directed by the MTN Pharmaceutical Product Manager. Expired, recalled, and study products that have been stored improperly must be separated from the active stock (quarantined).

At the request of the MTN Pharmaceutical Product Manager, study products should be returned to the protocol study product supplier (distributor or MTN Pharmaceutical Product Manager) or sent for destruction for the following reasons:

a. The protocol is completed, terminated, or the protocol has been de-registered at the site, and undispensed study products remain at the site that may not be transferred to another MTN protocol at the same site (see Study Product Transfers).
b. The study product has been dispensed to the participant and unused product was returned to the site/center or affiliated site.
c. The study product has expired. Expired product must be removed from active stock and placed in quarantine until returned to the supplier.
d. The study product has been improperly stored and can no longer be safely used.
e. The MTN Pharmaceutical Product Manager has requested return of the study product.
f. The study product is requested to be returned due to a product recall letter:
    1.) When the study is terminated, or
    2.) When the investigational label does not contain an expiration date and the manufacturer has notified the MTN that the product is expired. The pharmacist must respond immediately to recall notices and study product returns as indicated on the recall notice. Recall notices are not issued for investigational or commercial research products that are labeled with an expiration date.
g. If a site wishes to prematurely discontinue study participation.

Instructions for returning study products from MTN trials appear below. A copy of the MTN Study Product Return/Destruction Form appears at the end of this section. This is a standard form that may be photocopied and used for returning study products for all MTN studies.

1. Use the MTN Study Product Return/Destruction Form only for all MTN clinical trials. Note: This form may be modified by the MTN Pharmaceutical Product Manager for a specific clinical trial.
2. Complete the entire form in dark ink, print or type.
3. Use a separate form for each investigator and site.
4. Specify the specific quantity of study product returned. For undispensed study products, enter the total number of dosage units returned. For example, if returning 1 bottle of 100 tablets, document this as 1 x 100. If you are returning a carton (box) of 14 applicators,

document this as 1 x 14. If you are returning a partial bottle of box, indicate the number of tablets, capsules, or applicators.

For participant returns, list each line item by lot number. It is NOT necessary to list each participant's returned dispensing container as a separate line item. Simply list the total number of capsules, tablets or applicators being returned for each lot. If unable to determine the lot number of a product because, for example, a participant combined the contents of several vials, then list this item separately and enter "various lots" in the lot number column.

5. To ensure confidentiality, all participant names or identifiers must be removed or obliterated.
6. The PoR must sign and date the form.
7. The PoR must either complete the Study Product Return or Study Product Destruction section.
8. DO NOT enclose any dirty needles, syringes, IV bottles, opened or broken ampoules, or used applicators. (Unless otherwise directed to do so).
9. If Study Product Return:
    a. Enclose only those items that were provided by the MTN or supplier.
    b. Enclose the completed MTN Study Product Return Form with the package.
    c. Pack the materials so that they will not leak or break during transit.
    d. The return address for the form will be provided on an individual study basis.
10. If Study Product Destruction:
    a. Scan/Email a copy of the completed form to the MTN Pharmaceutical Product Manager.
    b. Destroy study products as indicated on the form.
11. Keep the original completed Study Product Destruction/Return Form in the protocol-specific pharmacy file.

STUDY PRODUCT RETURN/DESTRUCTION FORM

DAIDS Site ID:	CRS Name:
Product Lot:	

Participant ID (PTID) (if applicable)	# Unused Returned Study Product	Lot #	Date Dispensed (if applicable)	Date Returned (if applicable)	Comments

Study Product Return:

1. Pack material well to prevent leakage and/or breakage. RPh Name:_____
2. Enclose completed form with products RPh Signature: _____
3. Return to: Cindy Jacobson, PharmD Date: _____
   Microbicides Trials Network Telephone Number:_____
   204 Craft Avenue #507 Email address:_____
   Pittsburgh, PA 15213 Complete Address:_____
   _____
   _____

Study Product Destruction:

1. Did study product destruction occur for all product on this form? ___YES ___NO. If no, please circle the product and reason for no destruction.
   _____
2. Were study product destroyed on site? ___YES ___NO
   a. If no, please indicate facility where they were destroyed.
      _____
   b. Will the destruction company provide documentation for destruction? ___YES (attached) ___NO

The PoR attests that this information is accurate and in accordance with the site pharmacy's destruction SOP for destruction of study products.

RPh Name: _____ RPh Signature: _____

Date: _____

I. Study Protocol Close-Out

Upon completion of an MTN study protocol, whether early or scheduled, each site pharmacy should perform the following tasks:

- **Review of essential documents:**
  - Complete an internal review of all essential document files, focusing on completion and organization of records.
  - Review and assemble for long term storage all required study documents.
  - Prepare a written inventory of all MTN protocol-specific pharmacy documentation and storage locations. Note: MTN protocol-specific pharmacy documents should be stored with MTN protocol-specific clinic documents. Submit a copy of this inventory to the MTN CORE Pharmacy.
  - Resolve any outstanding MTN protocol-specific pharmacy-related monitoring finding and/or actions items and confirm with the appropriate monitor(s) that all have been resolved/completed.
  - If a pharmacy-related monitoring finding or action item need to be resolved/completed at study protocol close-out, please also inform the MTN CORE Pharmacist.

- **Study product documents:**
  - Pharmacy source documents (e.g. accountability records or any other record that captures dispensing data) must be kept in the pharmacy until the study has reached the DAIDS Enterprise System status of Concluded. Once this occurs, participant specific dispensing records and other participant specific pharmacy documents should be archived in a folder or envelope marked as "pharmacy records" and stored together in the front of the case report forms. These pharmacy documents must be placed in a folder or envelope marked "pharmacy records".
  - Pharmacy documents including order forms, receipts for transfers and returns (if applicable), communications, packing slips and destruction documentation MUST BE RETAINED IN THE PHARMACYA checklist is provided at the end of this section.

- **Study product notes and queries:**
  - Resolve any outstanding study product-related QC notes and queries. Confirm with MTN CORE Pharmacy that there are no outstanding study product-related QC notes or queries for the site pharmacy to address.
  - Return or shred/destroy all unused MTN protocol-specific pharmacy documents (prescriptions, request slips, etc.). Inquire with MTN Pharmacy as to which specific action is required.

- **Study product final disposition:**
    - Perform a final count of study product. Indicate this final count on the study product accountability record.
    - Return or Destruction of study product:
        - The MTN CORE Pharmacist will inform each site pharmacy whether it is to proceed with study product destruction or to proceed with return of study product to MTN CORE Pharmacy.
        - If the site pharmacy is to send the study product for destruction, indicate 'sent for destruction' on the study product accountability record. Prepare and file the necessary additional documentation for study product destruction and send the study product for destruction. Inform/email the MTN CORE Pharmacist of destruction.
        - If the site pharmacy is to send the study product to the MTN CORE Pharmacy, indicate 'return to MTN CORE Pharmacy' on the study product accountability record. Prepare and file any additional documentation for study product return and send the study product to the MTN CORE Pharmacy or other designated location. Inform/email the MTN CORE Pharmacist of the study product return.

Pharmacy[1]				
	Regulatory Reference	Completed/ Available	Incomplete/ Unavailable	Comments or check N/A if not applicable
Study Team				
CV of pharmacist(s) Signed CV for pharmacist: _____	ICH GCP 8.2.10 Industry standard	☐	☐	☐N/A
CVs of key pharmacy personnel	ICH GCP 8.2.10 Industry standard	☐	☐	☐N/A
Licenses of pharmacy personnel	ICH GCP 8.2.10	☐	☐	☐N/A
Label(s)				
Sample of label(s) attached to investigational product container(s)	21 CFR 312.6 ICH GCP 8.2.13	☐	☐	☐N/A
Logs/Records				
Signature list and/or Delegation log	ICH GCP 8.3.24	☐	☐	☐N/A
Investigational agent accountability logs	21 CFR 312.62(a) ICH GCP 8.4.1	☐	☐	☐N/A
Current IRB approved version of the protocol	ICH GCP 8.2.2.	☐	☐	☐N/A
Records of study product dispensation to appropriate staff member	ICH GCP 8.3.23	☐	☐	☐N/A
Shipping receipts and records for investigational product(s) and trial related materials	ICH GCP 8.2.15	☐	☐	☐N/A
Documentation of study drug transfers, returns, and destruction	21 CFR 312.62(a) ICH GCP 8.4.2	☐	☐	☐N/A
Temperature logs for applicable equipment (refrigerators, freezers, storage cabinets, etc.)	21 CFR 58.63	☐	☐	☐N/A
Calibration and maintenance records for all equipment (if applicable)	21 CFR 58.63	☐	☐	☐N/A
Investigators Brochure				
Most recent version of Investigator's Brochure(s) or Package Insert(s)	21CFR 312.55; ICH GCP 8.2.1	☐	☐	☐N/A
Certificates of Analysis				
Certificates of analysis of investigational product shipped	ICH GCP 8.2.16	☐	☐	☐N/A
Certificates of analysis for new batches of investigational products	ICH GCP 8.3.9	☐	☐	☐N/A

J. Miscellaneous

Attempting to prepare for all of the MTN protocol-specific pharmacy/study product related challenges in advance is critical to the success of study product management for a clinical trial. Each site pharmacy should keep in mind the following points prior to, at the start of, and during a trial:

- Maintain adequate study product accountability records showing the disposition of all study product. Proper study product accountability procedures and scheduled counts/audits can prevent errors/findings such as the following:
    - Study product dispensing records are incomplete/inaccurate
    - Physical study product inventory does not match the recorded quantity on the accountability record
        - Note: The PoR should be able to perform a study product reconciliation within 20 minutes.
    - Dispensing/accountability records reflect more study product dispensed than received on the shipping invoices. Note: The amount of study product remaining, returned, or destroyed, plus the amount of study product dispensed/administered should equal the amount of study product originally received.
    - Study product dispensing records are not available
    - Study product is missing or unaccounted for
    - Source documents (such as prescriptions, request slips) are inadequate or inaccurate
- The site Investigator of Record (IoR) must ultimately ensure proper security and storage of the investigational study product (21 CFR 312.60 and 312.61)
    - IoR must be able to confirm that the storage of study product is sanitary, secure, and temperature/humidity controlled.
    - IoR must be able to confirm that the study product has not been dispensed to a non-study participant.
    - IoR must be able to confirm that the study product was stored and dispensed as per the MTN specified protocol.
    - At any time during the clinical trial, the IoR, PoR, specified monitor, and the sponsor should know the storage location of the study product(s) for a specified MTN trial.
- In order to achieve successful study product management for each MTN trial, the site pharmacy should have in place a Quality Management Plan.
    - This Quality Management Plan should include quality control and quality assurance processes specific to study product management within the site pharmacy.
    - This Quality Management Plan must be submitted to the MTN CORE Pharmacy for review and approval.

This Manual has been adopted from the NIAID *Pharmacy Guidelines and Instructions for DAIDS Clinical Trials Networks.*

VERSION REVISION HISTORY

Version	Supersedes	Effective Date	Change(s)
3.0	2.0	20JUN2018	See attached list
4.0	3.0	15JAN2023	See attached list

APPROVAL

Author

DocuSigned by:
Cindy Jacobson
Signer Name: Cindy Jacobson
Signing Reason: I am the author of this document
Signing Time: 18-Jan-2023 | 13:48 EST
D2E8D331F02D43ECAD026E3D8C6D874A

18-Jan-2023 | 13:48 EST

Cindy Jacobson, PharmD | Signature | Date

Approver

DocuSigned by:
Sharon Hillier
Signer Name: Sharon Hillier
Signing Reason: I approve this document
Signing Time: 18-Jan-2023 | 13:34 EST
437BF8C12B1541729992EA42A322B571

18-Jan-2023 | 13:35 EST

Sharon Hillier, PhD | Signature | Date

DOCUMENT CHANGES 3.0

MTN not described as sponsor
Chris Rullo deleted, and Lindsay Kramzer added
Temperature log information requirements revised and expanded
Records to be available for representative of the MTN, FDA, EMA or other international regulatory body as applicable, upon request
Back-up changed to Associate Pharmacist
MTN Pharmacy Establishment Plan expanded
Principal Investigator clarified as IoR
Participant Randomization revised to include Mediata
Unblinding procedures revised
Dispensing to another institution not in network was deleted
Version history added

DOCUMENT CHANGES 4.0

Lindsay Kramzer deleted
Updated title to MTN Pharmaceutical Product Manager
Updated contact information
Deleted inclusion of FAX number
Added expiration date to the accountability log
Updated version number and date

DocuSign

Certificate Of Completion

Envelope Id: 176B8133F5FD4D7BA43D0AF525EDF1FE
Status: Completed
Subject: Complete with DocuSign: MTN_Pharmacy Guidelines Instructions_V4.0_01.15.23.docx
CF02:
Project Code/Charge Code: 100124.003.017.021.001
Source Envelope:
Document Pages: 43
Signatures: 2
Certificate Pages: 5
Initials: 0
AutoNav: Enabled
EnvelopeId Stamping: Enabled
Time Zone: (UTC-05:00) Eastern Time (US & Canada)

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IP Address: 66.190.197.195

Record Tracking

Status: Original
1/18/2023 1:22:00 PM
Holder: Nicole Macagna
NMacagna@fhi360.org
Location: DocuSign

Signer Events	Signature	Timestamp
Cindy Jacobson cjacobson@fhi360.org Security Level: Email, Account Authentication (Required)	Cindy Jacobson Signature Adoption: Pre-selected Style Signature ID: D2E8D331-F02D-43EC-AD02-6E3D8C6D874A Using IP Address: 174.51.244.55 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I am the author of this document	Sent: 1/18/2023 1:28:47 PM Viewed: 1/18/2023 1:46:41 PM Signed: 1/18/2023 1:48:24 PM
Electronic Record and Signature Disclosure: Accepted: 7/8/2022 11:43:21 AM ID: 3b0fb5da-ab4e-4592-9343-2eae73bdfa88		
Sharon Hillier hillsl@mwri.magee.edu Security Level: Email, Account Authentication (Required)	Sharon Hillier Signature Adoption: Pre-selected Style Signature ID: 437BF8C1-2B15-4172-9992-EA42A322B571 Using IP Address: 128.147.28.1 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	Sent: 1/18/2023 1:28:46 PM Viewed: 1/18/2023 1:34:32 PM Signed: 1/18/2023 1:35:00 PM
Electronic Record and Signature Disclosure: Accepted: 1/10/2020 5:59:38 PM ID: 9e1eb861-e38f-45ed-96a7-907d88be496a		

In Person Signer Events	Signature	Timestamp

Editor Delivery Events	Status	Timestamp

Agent Delivery Events	Status	Timestamp

Intermediary Delivery Events	Status	Timestamp

Certified Delivery Events	Status	Timestamp

Carbon Copy Events	Status	Timestamp

Witness Events	Signature	Timestamp

Notary Events	Signature	Timestamp

Envelope Summary Events	Status	Timestamps
Envelope Sent	Hashed/Encrypted	1/18/2023 1:28:47 PM
Certified Delivered	Security Checked	1/18/2023 1:34:32 PM
Signing Complete	Security Checked	1/18/2023 1:35:00 PM
Completed	Security Checked	1/18/2023 1:48:24 PM

Payment Events	Status	Timestamps

Electronic Record and Signature Disclosure

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