## 12. TRAINING

The Microbicide Trials Network (MTN) is committed to developing qualified, trained staff to conduct MTN studies. This section describes the training requirements and procedures that are applicable to MTN studies.

Training for Clinical Trials Unit (CTU) and Clinical Research Site (CRS) staff adheres to the standards listed below:

- All key CTU and CRS staff must complete Human Subjects Protection (HSP) training (Section 12.2) as well as Good Clinical Practice (GCP) training (Section 12.3) before screening and enrollment of the first study subject, prior to functioning without direct supervision and every three years thereafter. The Principal Investigator (PI) of the CTU grant is responsible for ensuring that the Investigator of Record (IoR) maintains training records onsite and makes these records available to the Clinical Site Monitor, the Program Officer and/or other designated U.S. National Institute of Allergy and Infectious Diseases (NIAID) Division of AIDS (DAIDS) staff upon request. The DAIDS Policy: *Requirements for Human Subjects Protections (HSP) and Good Clinical Practice (GCP) Training for Clinical Research Site Personnel* gives further detail.
- All key personnel involved in clinical trials subject to U.S. Food and Drug Administration (FDA) regulations must receive training prior to study initiation, or prior to assuming responsibility for an ongoing study, and every three years thereafter. This training must include relevant aspects from the following U.S Code of Federal Regulations (CFR):
    - Electronic Records and Signature (21 CFR Part 11)
    - Investigational New Drug Application (21 CFR Part 312)
    - Protection of Human Subjects (21 CFR Part 50)
    - Financial Disclosure by Clinical Investigators (21 CFR Part 54)
    - Institutional Review Boards (21 CFR Part 56).

- Laboratory related training is required as specified in Section 12.4 and Section 14 of this manual
- The MTN, in accordance with the U.S. CFR., requires study-specific site training prior to study initiation (Section 12.6)
- Training regarding IoR responsibilities must be completed prior to study initiation or prior to assuming responsibility for an ongoing study; this training remains current for a period of three years and must be undertaken again after that period for any IoRs responsible for active studies
- CTUs/CRSs are expected also to provide training for new staff and continuing training for current staff (Section 12.7)

## 12.1 DAIDS Training Resources

The Office of HIV/AIDS Network Coordination (HANC) serves as a resource for information about training programs available to site staff working with MTN and other clinical trials networks that are funded by NIAID/DAIDS.

The HANC website provides a calendar that lists DAIDS-sponsored training sessions and locations (http://www.hanc.info/training/Pages/default.aspx). Information can be searched by topic or date. The website also includes a link to the Collaborative Institutional Training Initiative (CITI), which offers online training in HSP, GCP and responsible conduct of research to DAIDS-sponsored CRSs. CITI training also can be accessed directly at the following website: https://www.citiprogram.org/. Interested individuals should follow the instructions on the HANC website to make sure they obtain access to appropriate training.

In addition to the HANC website, the DAIDS Learning Portal (https://www.daidslearningportal.com/) provides access to DAIDS training materials and resources, a social learning community to share training resources and new information, a training navigator to ask questions about DAIDS trainings and a direct link to the DAIDS Learning Management System (LMS). The LMS allows site staff and network members to access online training on a variety of topics related to clinical research, including policies, laboratory and pharmacy. LMS offers sites the capability to assign required training, track and monitor its progress and run reports on its completion. Site staff and network members accessing the DAIDS Learning Portal and LMS can use the same username and password.

## 12.2 Human Subjects Protection Training

MTN study sites must comply with the HSP training requirements specified in the DAIDS policy on *Requirements for Human Subjects Protection and Good Clinical Practice Training for Clinical Research Site Personnel*, which can be accessed at this site: https://www.niaid.nih.gov/sites/default/files/gcp_hsp_sitetrain_policy.pdf.

All key personnel must have completed the required training within three years prior to participating in any MTN study. Key personnel must repeat their training every three years to maintain their qualified status throughout their involvement in MTN studies. For new key personnel, documentation of required training must be completed within 90 days of assignment to an MTN study and prior to functioning without direct supervision. The DAIDS policy defines key personnel as individuals who are involved in the design and conduct of human subjects clinical research funded by the National Institutes of Health (NIH). This includes any site

personnel who are more than minimally involved with the conduct of the research (such as performing study evaluations, participating in procedures or providing intervention) or who have more than minimal contact with study participants or confidential study data, records or specimens related to study conduct. All other personnel who have minimal involvement in the conduct of the research or minimal study-related contact with participants should receive training that emphasizes the protection of participant privacy and confidentiality. Drivers, couriers, clerical staff and administrative staff are considered minimally involved personnel.

Documentation of HSP training must be maintained on site and made available upon request to DAIDS study monitors or sponsor representatives, such as the FDA, Office of Human Research Protections (OHRP) and local site regulatory authorities, the MTN Leadership and Operations Center (LOC), the Statistical and Data Management Center (SDMC), the Laboratory Center (LC) and other designated MTN site visitors. Training documentation should consist of the trainee's name, the date, title and main content of the training; and the trainer's name and affiliation.

The DAIDS policy describes a number of acceptable training resources and methods, including the CITI HSP training (mentioned in Section 12.1) and the NIH online training module, *Protecting Human Research Participants,* which is accessible at the following website (login required): http://phrp.nihtraining.com/users/login.php.

In addition to these resources, the *Research Ethics Training Curriculum* (developed by FHI 360) is recommended for use at MTN study sites. This curriculum is accessible at the following website: http://www.fhi360.org/sites/all/libraries/webpages/fhi-retc2/.

### 12.3 Good Clinical Practice Training

MTN study sites must comply with GCP training requirements specified in the DAIDS policy on *Requirements for Human Subjects Protection and Good Clinical Practice Training for Clinical Research Site Personnel* (see website above). All key personnel must complete the required training within three years prior to participating in MTN research and every three years thereafter. For new key personnel (staff hired after study activation), documentation of the required training must be completed within 90 days of assignment to an MTN study and prior to their functioning without direct supervision. For key personnel involved in studies that are subject to FDA regulations, this training must include relevant aspects of 21 CFR parts 11, 50, 54, 56, and 312. The CFR can be accessed at the following website: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm.

Documentation of GCP training must be maintained on site and made available upon request to the following: DAIDS study monitors or sponsor representatives (such as FDA, OHRP and local site regulatory authorities); the LOC, SDMC and LC; and other designated MTN site visitors. Training documentation should consist of the trainee's name; the date, title and main content of the training; and the trainer's name and affiliation.

The DAIDS policy referenced above describes acceptable training resources and methods. Online training and additional resources are available on the HANC and DAIDS Learning Portal websites as stated in Section 12.1.

## 12.4 Laboratory-Related Training

The HSP and GCP training requirements described in Sections 12.2 and 12.3 apply to MTN CRS laboratory staff who are considered key personnel. In addition, key laboratory personnel should complete Good Clinical Laboratory Practice (GCLP) training prior to involvement in an MTN study. At a minimum, the site Laboratory Director, Laboratory Manager/Supervisor or Laboratory Quality Assurance/Quality Control (QA/QC) Technologist(s) must complete GCLP training prior to conducting MTN research. GCLP training of all key MTN laboratory staff is facilitated through online HANC training, accessible via the DAIDS LMS (website listed above).

Site laboratory staff involved in MTN studies must have the appropriate education and experience for the positions they hold. Before performing any laboratory tests or other laboratory-related activities for MTN studies, these staff must receive proper training. A staff member's training and competency in performing laboratory tests and other laboratory-related activities must be demonstrated and documented before he or she begins performing any test or activity (after 6 months, after 12 months and annually thereafter). If there is any question of competency, re-training should occur and competency should be re-assessed, confirmed and documented. Other laboratory-related training requirements, such as training in laboratory safety, specimen transportation and the use of the laboratory data management system (LDMS), are cross-referenced in Section 14 of this manual.

## 12.5 Standard Operating Procedures

The DAIDS policy on *Requirements for Manual of Operational Procedures*, which can be accessed at the website below, specifies a core set of Standard Operating Procedures (SOPs) that must be in place at each site prior to the initiation of any DAIDS-funded or DAIDS-sponsored studies: https://www.niaid.nih.gov/sites/default/files/mop_policy.pdf

Prior to the initiation of any MTN study, all personnel assigned to the study must complete training on the core SOPs that are relevant to their study roles and responsibilities, as determined by the IoR or designee. Study staff who have previously been trained on the required SOPs must repeat the training if it was not completed within the past 12 months or when a new version is released. (For more information about site-specific study activation requirements see Section 11 of this manual.)

In addition to the core set of DAIDS SOPs, the MTN Director of Pharmacy Affairs and staff from the SDMC, LOC (FHI 360), and/or LC may require site- or study-specific SOPs to be in place prior to the initiation of an MTN study. Prior to the initiation of any MTN study, all personnel assigned to the study must complete training on the study-specific SOPs that are relevant to their study roles and responsibilities, as determined by the IoR or designee. Study personnel must be re-trained when SOPs are updated during the course of the study.

All SOP training must be documented. Documentation must be maintained on site and must be made available upon request to DAIDS study monitors; the MTN Director of Pharmacy Affairs; and staff from the LOC (FHI 360), SDMC, LC and other designated MTN site visitors.

## 12.6 Study-Specific Training

Each site's IoR is responsible for ensuring that all study staff are adequately trained to serve their designated site- and study-specific functions for a protocol. The MTN Director of Pharmacy Affairs, staff from the LOC (FHI 360), SDMC, LC, the BRWG, and other LOC (Pitt) and DAIDS personnel collaborate with the IoR to fulfill this responsibility by conducting study-specific training. Study-specific training may be provided in various formats and for various durations depending on the training needs of the site and the study. The MTN staff mentioned above work closely with the Protocol Chair(s) and site IoRs to determine the optimal format and length of each study-site training.

The objectives of study-specific training are to:

- Ensure that study-staff members are informed of how the study should be conducted on a day-to-day basis, in accordance with the protocol, study-specific procedures (SSP) manual and GCP guidelines
- Ensure standardization of study implementation across sites, so that data can be combined for analysis

During study-specific training, site staff and the MTN training team examine and discuss in detail the study protocol, regulatory requirements, procedural requirements and data-collection specifications. Broad responsibilities for planning and conducting study-specific training are shown in Table 12.1. Documentation of all study-specific training must be maintained in each site's Essential Document files.

**Table 12.1 Responsibilities for Study-Specific Training**

| Task | Responsible Persons |
|---|---|
| Schedule training | LOC (FHI 360) Clinical Research Manager (CRM), with input from study training team, key site staff and Protocol Chair(s), as applicable |
| Arrange training logistics | LOC (FHI 360) CRM, designated site staff |
| Develop training agenda and training materials, conduct training | LOC (FHI 360) CRM, with input from study training team and study-site staff |
| Translate training materials (if applicable) | Study-site staff |
| Arrange for specialized procedural training (if applicable) | LOC (FHI 360) CRM, study-site staff |
| Evaluate training | Study-site staff training participants |
| Document training participation and maintain this documentation | LOC (FHI 360) CRM, study-site staff |

### 12.6.1 Scheduling Study-Specific Training

The LOC (FHI 360) CRM develops the study-specific training agenda and schedules training for each site in coordination with the MTN Director of Pharmacy Affairs, a BRWG representative (if applicable), the SDMC Clinical Data Manager (CDM), the LC designee, other LOC (Pitt) and DAIDS personnel and key site staff. Protocol Chair(s) are also informed and involved as needed in developing the training agenda and schedule.

The MTN makes every effort to conduct site training as close as possible to the initiation of the anticipated study to maximize its effectiveness in preparing site staff. To achieve this goal, each site must complete certain study-activation requirements before it can reserve training dates. The remaining activation requirements must be met prior to the actual conduct of study-specific

site training (see Table 12.2). In cases where the reserved training dates are approaching and a site has not met all of the requirements needed to proceed with the training, a revised set of training dates may be reserved. Any deviation from this process requires approval from the MTN Principal Investigator (PI) and co-PI.

**Table 12.2 Guidelines for Scheduling MTN Study-Specific Training**

| | |
|---|---|
| **To be completed prior to reserving (assigning) dates for study-specific training:** | |
| 1 | Current Federal Wide Assurance(s) should be in place for the study-site institution(s). |
| 2 | The FDA 30-day review period/Safe to Proceed Notice (if applicable) should be completed. |
| 3 | Review dates should be set for all required, local regulatory authority reviews (such as the Institutional Review Board (IRB), Independent Ethics Committee (IEC), medical control boards, etc.). All applicable drug import, specimen export and other applicable approvals should be in process. |
| 4 | Hiring of adequate staff should be completed or in-process and expected to be completed by time of training. |
| 5 | Ideally the Clinical Trial Agreement between DAIDS and the drug company and/or study sponsor should be finalized and signed. |
| **To be completed prior to the training dates (Day 1 of study-specific training). If not, new (later) training dates may be reserved for the site.** | |
| 6 | HSP training for all key personnel should be completed. |
| 7 | Completion of GCP training by all key personnel (For studies subject to FDA regulations, this training must include relevant aspects of 21 CFR parts 11, 50, 54, 56 and 312). |
| 8 | Pharmacy requirements (if applicable) should be approved, based on:<br>• The approval of a DAIDS Pharmacy Establishment Plan (PEP) by DAIDS Pharmaceutical Affairs Branch or an MTN PEP by the MTN Director of Pharmacy Affairs<br>• Draft SOPs for managing, dispensing and accounting for study products (if applicable) (final versions required before activation)<br>• Import and export approvals for study products (if applicable) should be obtained |
| 9 | The SDMC requirement for successful installation of required internet-enabled equipment, for study data collection and management, should be completed. |
| 10 | The LC approval of local laboratory requirements has been obtained, including approval or confirmation of the following:<br>• GCLP training completed by at least one key on-site laboratory staff member with responsibility for laboratory QA<br>• Established local laboratory back-up arrangements<br>• CLIA certification (as appropriate)<br>• Completed validation of study-specific testing-methods (if applicable)<br>• Proficiency in performing all protocol-required tests<br>• Documented validation of reference ranges for all protocol-required tests, and process for annual review<br>• Draft SOPs for performing all protocol-required tests (final versions required before activation)<br>• Draft SOPs for specimen management and chain of custody (final versions required before activation)<br>• Well-developed QA/QC procedures (final versions required before activation)<br>• Well-established Internet connectivity to Frontier Science and Technology Research Foundation, Inc. (FSTRF) for LDMS<br>• International Air Transport Association (IATA) specimen-shipping certification within the last 24 months for all laboratory staff members who transport, ship or receive infectious substances and diagnostic specimens<br>• Laboratory safety training within the last 12 months for all laboratory staff members |
| 11 | If required, the site-initiation visit by the DAIDS Clinical Site Monitoring Group has been made. |

| | |
|---|---|
| 12 | Well-developed drafts of required site or study-specific SOPs as defined in the study activation checklist have been completed. (See Section 11 of this manual for more information on site-specific study activation requirements). |
| 13 | The study-staff roster, signature sheet and delegation of duties log should be reasonably complete. |
| 14 | If IRB/IEC approval has been obtained, a submitted DAIDS Protocol Registration package is expected, including:<br>• U.S. and in-country IRB/IEC approvals of protocol and approved informed consent forms (ICF) (local language and back-translation, where applicable)<br>• Signed FDA Form 1572 or DAIDS IoR Agreement<br>• Curriculum vitae of the IoR<br>Protocol registration approval is not required prior to scheduling training; but if IRB/IEC approval has been obtained, the DAIDS Protocol Registration package must be submitted or the training will be postponed. |
| 15 | A training version of the SSP Manual should be available on site. |

### 12.6.2 Site Preparation for Training

In addition to completing requirements for scheduling and conducting study-specific training, site staff must conduct other activities in preparation for study-specific training and conducting the study. Under the supervision of the IoR and other designated staff member(s), site staff will:

- Work with the LOC (FHI 360) CRM to schedule the training, finalize the training agenda and identify and meet needs for translations and interpreters
- Arrange access to training facilities and any required training equipment
- Hire staff (if needed)
- Designate staff members' study-specific roles and responsibilities
- Assess local training needs
- Provide orientation and background training as needed, including:
  - Local staffing and organizational plan (including roles and responsibilities)
  - Local site operations and SOPs
  - Local role-specific training/certification
  - Other local requirements
- Review and become thoroughly familiar with the study protocol, ICFs, case report forms, training materials and other materials for study implementation
- Discuss and develop study-specific SOPs and other study-implementation plans and materials
- Complete mock visits using materials for study implementation, ideally in the facilities that will be used for the study (may also be scheduled after the training)
- Identify issues and questions that require input from the training team
- Prepare site-specific training modules, presentations and materials per the training agenda
- Ensure availability of relevant staff to attend training sessions

### 12.6.3 Conduct of Study-Specific Training

The MTN Director of Pharmacy Affairs, the study representative from the BRWG (if applicable), the SDMC CDM, the LOC (FHI 360) CRM and the LC designee are responsible for providing the training and training materials. Additional MTN members, such as MTN Safety Physician(s), DAIDS representatives, and Protocol Chair(s), may also provide components of the training, as needed.

All site staff members who have been delegated duties or responsibilities for an MTN study will take part in study-specific training. This includes the IoR, study coordinator, clinical staff (such as physicians, clinicians and nurses), counseling staff, pharmacy staff, laboratory staff, data management staff, QA/QC staff, participant recruitment and retention (outreach) staff, community education staff and administrative staff.

It is especially important that site staff members make every effort to attend all of the sessions or modules that are most relevant to their responsibilities. Failure to attend required relevant training sessions in their entirety will result in a delay of site-specific study activation, and additional training will be required before study activation can be approved. If it is not possible for study staff to attend all sessions or modules of study-specific training, it is the responsibility of the IoR to ensure that training is provided to those staff who could not attend, using materials provided at the training.

During training, site-training staff are expected to:

- Present training sessions or modules as outlined in the training agenda
- Present local study-implementation plans, SOPs and other such materials
- Fully engage in the training: ask questions; identify issues requiring additional clarification; and identify best site-specific study-implementation plans, materials and tools
- Complete a training evaluation

The LOC (FHI 360) CRM will provide a study-specific training report to the site following the training. This documentation as well as a copy of the agenda, training materials and staff attendance list, must be maintained in the on-site Essential Document files. Documentation of training for key staff who did not attend study-specific training, but were trained by the IoR, must also be maintained in on-site Essential Document files.

### 12.7 Continuing Study-Specific Training

It is the IoR's responsibility to ensure that study staff members are adequately trained and prepared to serve in their designated study roles. The study training team does not routinely conduct on-site training for site staff who are hired after the initial study-specific training has taken place. The training team will, however, ensure that study-specific training materials are provided for the purpose of training future staff and will make every effort to answer questions for and provide technical assistance to new study staff members. The study training team also will participate in one or more additional training sessions via teleconference, if requested by the site. If a new study coordinator or lead clinician joins a site after the initial study-specific training, the LOC (FHI 360) CRM will consider visiting the site to assess study implementation and possibly provide targeted training soon after the new staff member begins work on a study.

Once a study is under way, the MTN Director of Pharmacy Affairs, the SDMC, LOC and LC staff issue study-related communications, answers to frequently asked questions, data communiqués and other similar documents to clarify and guide study implementation at each site. The IoR or designee — typically, the study coordinator — must inform study staff when such documents are issued, provide training on them (as needed) and incorporate their content into day-to-day study operations. Designated site staff also should file such documents with other study training and implementation materials for future reference.

When considered useful and timely, the MTN Director of Pharmacy Affairs, the SDMC, LOC (FHI 360) and/or LC staff provide study-specific refresher training to site staff in the context of routine site visits and other MTN meetings (such as annual and regional meetings). Other methods, such as videos of previous training sessions, teleconferences and web-based training, also may be used for continuing training.

### 12.8 Research Ethics Training for Community Representatives

The purpose of the FHI 360 *Research Ethics Training Curriculum for Community Representatives* is to educate community representatives about their roles and responsibilities as well as the roles and responsibilities of a research team and IRBs/IECs about the principles of research ethics. The curriculum includes easy-to-use materials, such as slides, case studies, activities, facilitator notes and a training certificate. Community-education staff, community advisors and partners are encouraged to complete this training. The curriculum can be accessed at the following website: http://www.fhi360.org/sites/default/files/webpages/RETC-CR/en/RH/Training/trainmat/ethicscurr/RETCCREn/index.html.

Additional education/training materials for community representatives are available at the following website:

- Community Clinical Research Training: http://mtnstopshiv.org/node/1425