Division of AIDS (DAIDS) Site Clinical Operations and Research Essentials (SCORE) Manual: Clinical Research Site Personnel Qualifications, Training and Responsibilities

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Clinical Research Site Personnel Qualifications, Training and Responsibilities

To conduct a clinical trial safely and properly, the Principal Investigator (PI)/Investigator of Record (IoR) must comply with applicable laws/regulations and institutional policies governing the conduct of sponsored research. In addition, the PI/IoR is responsible and accountable for selecting an adequate number of qualified, trained Clinical Research Site (CRS) staff and must review their qualifications before delegating any study-related duties/tasks.

CRS Personnel Education and Experience

When selecting individuals to support clinical trial implementation and perform study-specific duties, the PI/IoR must consider the following factors:

- Adequacy of training, qualifications, and/or degree(s) for the role
- Prior experience in clinical trials as well as in the specific role
- Ability to devote sufficient time and effort per the role's complexity
- Current credentials/license/certification, as applicable

In selecting staff, the PI/IoR may reference on-site job descriptions defining the requisite experience, qualifications, licenses, etc., providing clear guidance on the main duties and responsibilities for each role.

DAIDS requires CRSs to use a standard operating procedure (SOP) for staff qualifications, one that also advises on curricula vitae (CV) content requirements and keeping such professional documents up to date. The PI/IoR must retain signed/dated CV and related records (e.g., training records) documenting an individual's qualifications to perform delegated duties and tasks, following the *FDA Guidance for Industry: Investigators Responsibilities* and other applicable regulatory requirements. Furthermore, DAIDS' Protocol Registration Manual requires CVs to be updated at least every two years for IoRs, or whenever there is a major change in contact information, education, new training, publications and/or others. In addition, as part of the site activation process, the Office of Clinical Site Oversight (OCSO) Program Officers (POs) collect CVs from within the last three years for the Clinical Trial Unit (CTU) PI, CTU Coordinator, CRS leader, CRS Coordinator, and Pharmacist of Record (PoR).

As applicable, CVs for delegated staff must show a current CRS affiliation, and the PI/IoR, sub-investigators, and other delegated staff must, for the study's duration, maintain evidence in the CRS files of any valid credentials/licenses/certification additionally required per role.

CRS Personnel Training

The PI/IoR is responsible for ensuring that CRS staff are adequately trained before delegating any study-specific duties/tasks to them and that an established SOP for such training is in place. Training should include:

- International Council for Harmonisation (ICH) Good Clinical Practice (GCP) guidelines (ICH E6)
- Human Subjects Protection (HSP)
- Protocol and related documents and study product(s) requirements
- DAIDS required training
- Any training specific to their delegated duties and functions

Human Subjects Protection and Good Clinical Practice Training

DAIDS requires that individuals engaged in the conduct of clinical trials complete HSP and GCP trainings. The Office for Human Research Protections (OHRP) says that this requirement applies to anyone in roles that:

- *"*Interact with living individuals by performing invasive or noninvasive procedures for research purposes (e.g., drawing blood, collecting other biological samples, dispensing drugs, administering other treatments, employing medical technologies, utilizing physical sensors, utilizing other measurement procedures).*"* or
- *"*Obtain individually identifiable private information that is considered to be engaged in research*."*

The personnel to whom this applies include:

- Physicians/clinicians/nurses on staff (full or part time) or on fellowship, who interact with study participants (or their individually identifiable, private information) for research purposes
- Pharmacists, pharmacy technicians, data managers, laboratory personnel, and counselors

The HSP and GCP trainings must be completed before delegating staff to any clinical trial-specific duties, and every three years thereafter. Acceptable HSP training includes the United States (U.S.) Code of Federal Regulations (CFR) 45 Part 46 Protection of Human Subjects, which is required for all National Institute of Health (NIH)-funded clinical research, and which covers:

- Subpart A – Basic U.S. Department of Health and Human Services (HHS) Policy for Protection of Human Research Subjects ("Common Rule")

- Subpart B – Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research
- Subpart C – Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects
- Subpart D – Additional Protections for Children Involved as Subjects in Research
- The Belmont Report
- Declaration of Helsinki (strongly encouraged)
- The Nuremberg Code (strongly encouraged)

All CRS staff must receive GCP training covering:

- Investigator roles and responsibilities (ICH E6, Section 4)
- Relevant topics in sponsor responsibilities (ICH E6, Section 5), such as Investigator Selection, Confirmation of Review by IRB/EC, Trial Management, Data Handling and Recordkeeping, Quality Assurance (QA), and Quality Control (QC), etc.
- Essential Documents (ICH E6, Section 8)
- Source Documents (ICH E6, Sections 4 and 8)

The PI/IoR ensures that:

- CRS staff receive the appropriate trainings for HSP and GCP.
- New staff (added since a protocol's initiation) receive these trainings during orientation (if not having completed them within the past three years) and are adequately supervised until completion.

The level of training may vary for individuals in supporting roles, such as couriers, drivers, receptionists, and administrative personnel, at the discretion of the PI/IoR. Minimally, these individuals should receive training on protection of participant privacy and confidentiality.

The GCP and HSP training modules are available on the DAIDS Learning Portal (DLP). Other trainings, such as those provided by an institution, may be acceptable if they meet all the required elements as described above.

Certificates and dates for completed HSP and GCP trainings are to be uploaded into the Site Hub within the National Institute of Allergy and Infectious Diseases (NIAID) Clinical Research Management System (CRMS).

Regulatory Authority Training

The PI/IoR is responsible for identifying any local laws/regulations applicable to clinical trials being conducted at the CRS, including but not limited to U.S. CFR requirements, and ensuring that CRS staff are trained before performing any study-related activities.

Protocol-Specific Training

The PI/IoR must conduct studies according to the protocol (refer to ICH E6 4.5.1, 21 CFR Part 312.60, Form FDA 1572, 21 CFR Parts 812.43 and 812.100, and local regulations) and must ensure that the CRS keeps on file documentation that personnel were trained on all study procedures before being delegated and/or performing any of those duties/tasks and remained trained throughout the study.

The CRS personnel should have access to and be trained on protocol and related documents, such as study-specific procedures, Letters of Amendments, Clarification Memos, Manuals of Operations/Procedures, study product specifics, Study Specific Procedures, any specific laboratory procedures, Case Report Form completion guidelines, and any other applicable documentation required to conduct their duties.

The PI/IoR informs CRS staff of any pertinent changes during the study conduct and documents further training as appropriate.

DAIDS-Required Trainings

In addition to GCP and HSP training, DAIDS requires CRS staff to complete role-specific training to facilitate their understanding of DAIDS policies, systems, and general requirements.

CRS staff can access the DLP DAIDS-required training webpage to complete all required training sessions, such as Investigator Responsibilities, Source Documents. Optional trainings are also available in the DLP. Refer to the Introduction to DAIDS Systems section for information on how to access the DLP.

Training Delivery Methods

CRSs may deliver training using the following training delivery methods. Other training delivery methods should be discussed with DAIDS.

- DAIDS-sponsored HSP/GCP/Food and Drug Administration (FDA) training sessions
- Annual and regional HIV Network Meeting trainings
- Commercial training programs

- Online training programs (e.g., National Cancer Institute online training for HSP or university based online modules may meet HSP/GCP/FDA requirements)
- Self-training/reading
- Face-to-face training
- Internal meetings
- CRS-offered trainings

Note: Several types of training may be needed to meet requirements.

Study initiation visits, program webinars, and CRS meetings are examples of training methods. The level of training may also be at the discretion of the PI/IoR, depending on an individual's level of study involvement.

Documenting Training

The PI/IoR must maintain current and complete training records and make them available to DAIDS, DAIDS representatives, and inspectors, as requested or during site visits.

A training completion record, such as a training certificate, is usually provided to the trainee after the completion of training. However, when the documentation is not provided from the training vendor/provider in the form of a certificate, the training must be documented by the site and should include the following details:

• Date of training

• Name of trainer and affiliation (if applicable)

• Title of course or training topic

- If the title of the course does not provide enough details on the content covered during the training (e.g., site initiation training covering several different topics), include primary contents/topics covered in the training

- For document review (e.g., protocol and/or manual of procedures), include the document title, version number, and date)

• Trainee name and role

- Trainee signature and date (alternatives for documenting wet signatures and dates may be used in certain situations (e.g., staff working remotely). These alternatives should be described in the site's Personnel Training and Certification Documentation SOP or other process document. For use of electronic signatures please refer to the Electronic Systems Section.

- Training Log Template (Training Topic Specific) - to record a single training topic conducted by one or more staff members.
- Training Log Template (Trainee specific) - to record multiple types of training (such as onboard sessions or re-education on study-specific procedures, where a deficiency or trend has been identified).

Sites may use the template logs, or use their own template, but should ensure that the minimum information described above is present.

Delegation of Duties

The ICH E6 lists the following PIs/IoRs responsibilities when delegating study-related tasks:

- Maintain a list of personnel assigned significant, study-related duties.
- Supervise individuals performing these duties.
- Ensure that individuals performing these duties are qualified and trained.

The PI/IoR must maintain a study-specific, version-controlled DoD. CRSs may use the DAIDS DoD template, which is provided as an appendix to this manual. If a site chooses to develop their own DoD log, they MUST include all of the fields present in the DAIDS DoD Log template. Note that the DoD log is also commonly called the Delegation of Authority (DoA) log.

The PIs/IoRs must record duties/tasks they are delegating to the individuals, under his direct or indirect supervision, only after completion of all protocol-specific training. Each individual must personally sign (i.e., handwritten signature), initial, and date the DoD log in the corresponding columns for the delegated duties/tasks at the time the delegation is made. CRS staff may sign the DoD with an electronic signature (eSignature), but to do so, the CRS must have an established procedure in place for using eSignatures according to local laws and regulations, as well as 21 CFR Part 11 for clinical trials under the FDA Investigational New Drug (IND) application. Refer to the DAIDS Electronic Information Systems (EIS) policy and Electronic Systems section of this manual for more information on the use of eSignatures.

The PI/IoR ensures that the DoD log is updated in real time as new staff are added or removed and/or study-related roles and responsibilities change. The PI/IoR must initial and date the applicable row(s) for each entry.

If there is a change of PI/IoR, the new individual in the role should review the DoD log, initial, and date next to all previous PI's/IoR's initials as an agreement with each delegated duty/task. Any changes should be specified in a new line. In addition, the new

PI/IoR should write a note in the comments section that they reviewed the log and agree with tasks delegated by the previous PI/IoR or clarify any changes in the delegated tasks fields. The new PI/IoR must sign and date this note. Alternatively, the new PI/IoR may complete a new DoD log, in which case, the outgoing PI/IoR must close out the DoD by:

- Completing end dates for all site staff, and initial/date the DoD log in the respective field
- Completing the end date on the investigator statement page and signing/dating the date entry
- Writing in the comments section the PI/IoR change as “effective on” and that a new version of the DoD has been created

Note: When a new version of the DoD log is created, the end date of the old DoD log version must be used as the start date for current staff delegated duties. All DoD log versions must be kept in the CRS files.

The PI/IoR must adequately supervise staff who are performing delegated duties/tasks, because the PI/IoR retains overall responsibility for the conduct of the clinical trial (including all such delegated duties/tasks). Therefore, the PI/IoR is accountable for any non-compliance with the protocol and applicable requirements that occur during the conduct of the clinical trial, even if a duty/task has been delegated to another person. At the end of the clinical trial, the PI/IoR should review the DoD log entries, update, and sign/date the log in the End of Study Declaration section, attesting to the accuracy and completion of the log.

Similar to participant research records and other essential documents, PIs/IoRs must retain all previous and current versions of the DoD, so DAIDS, DAIDS representatives and inspectors can access, inspect, and (as necessary) reproduce those documents as needed. For additional information on the completion and maintenance of the DoD log, please refer to the appendix Guidance on Completion of Delegation of Duties Log. The Delegation of Duties Frequently Asked Questions are also available on the NIAID website.

Identification of DAIDS CTU/CRS Grant-specific Key Personnel

Key personnel for all DAIDS clinical trials CRSs are identified on the CTU Notice of Award (NOA).

For the purpose of this section, DAIDS key personnel definitions are as follows:

- CTU PI: Individual responsible for all CTU activities and performance. This includes responsibility for affiliated CRSs, including communications, site performance, and financial management. The PI also provides CTU scientific and administrative representation to the Network(s).

- CTU Coordinator: Individual responsible for coordination and facilitation of activities across the CTU that may include administration, financial management, training, personnel supervision, evaluation, and logistics.

- CRS Leader: Onsite senior research scientist responsible for the administrative and scientific components of the CRS. The CRS leader is responsible for overall site activities, including day-to-day operations, performance, and compliance at the site level.

- CRS Coordinator: Individual at each CRS assisting in the oversight of all day-to-day activities.

- Licensed/Registered PoR: Individual performing the day-to-day pharmacy activities and study product management, including but not limited to, procurement, storage, preparation, dispensing, and final disposition of study products for the DAIDS clinical trials.

Changes in CTU/CRS Grant-specific Key Personnel

CRSs must notify the OCSO PO if key personnel (except for the PoR) change during the clinical trial. Change requests are to be sent through the authorized Business Official at the grantee institution by email or formal letter on official letterhead and must include the reason for the change, the CV or bio sketch, documentation of GCP and HSP training (or a plan to complete these trainings within 90 days of assignment to the grant), and other supporting and level-of-effort documentation for the proposed new key personnel.

For a change in the PoR role, the departing PoR or Associate Pharmacist (AP) must directly send this request to the Pharmaceutical Affairs Branch in accordance with the *Pharmacy Guidelines and Instructions for DAIDS Clinical Trials Networks*.

Note: Changes in key personnel at a protocol-specific site not affiliated with a CTU (CRS funded directly through one of the DAIDS Clinical Trials Networks) should be requested through the CRS Leader or CRS Coordinator.

DAIDS personnel will provide approval/rejection of any change requested via an email notification. Changes to CTU PI or CRS Leader for a CTU-affiliated CRS will also be reflected in a revised NOA. Additionally, once approved, a CTU must update the

Essential Contacts form on the Site Hub in the NIAID CRMS with the new key personnel name, title, and contact information. Sites must also update any study-related documents (i.e., FDA 1572, DAIDS IoR Form) if a change in Key Personnel affects any of those documents.

Appendices

1. Training Log Template (Training Topic Specific)
2. Training Log Template (Trainee specific)
3. Division of AIDS (DAIDS) Delegation of Duties Log Template
4. Guidance on Completion of Delegation of Duties Log

References

1. U.S. Code of Federal Regulations, Title 21, Parts 11, 50, 54, 56, 312 and 812
2. U.S. Code of Federal Regulations, Title 45, Part 46 and Subparts
3. International Council for Harmonisation Good Clinical Practice (ICH E6)
4. FDA Guidance: Investigator Responsibilities - Protecting the Rights, Safety, and Welfare of Study Subjects [Oct 2009]
5. DAIDS Learning Portal: DAIDS-required Training Webpage
6. TransCelerate Information and Guidance Sheet for the Completion of the Site Signature and Delegation of Responsibilities Log
7. The Belmont Report
8. NIH Required Education in the Protection of Human Research Participants Policy
9. Office for Human Research Protections
10. The Declaration of Helsinki
11. The Nuremberg Code
12. Protocol Registration Manual
13. Delegation of Duties Policy and Related Document Frequently Asked Questions
14. General Considerations for Clinical Studies E8(R1)

Version History

V1.0	1/19/2021	Original Version
V2.0	10/22/2021	• Clarification of information to be documented when a Certificate of Training is not provided • Removal of requirement for documenting: Role of the trainer, Signature of trainer, Training delivery method • Addition of language regarding alternatives to use of wet signatures. • Updates to optional Training template logs to remove the following fields: o Training delivery method (Training-specific log only) o Principal Investigator / Investigator of Record Name o Protocol Number o Trainer Signature and Date