

DAIDS  
Bethesda, MD USA

POLICY  
Requirements for On-Site Monitoring

Approval Date: 10 JUL 2015  
Effective Date: 07 AUG 2015

No.: DWD-POL-SM-01.03

**CHANGE SUMMARY NOTE:** This policy has been reviewed for accuracy and updated to meet 508 compliance guidelines. Modifications include the change to a risk-based approach which is applied to the frequency, duration and intensity of monitoring activities. This version supersedes version 2.0 dated 05 FEB 2007.

### 1.0 PURPOSE

This policy defines the minimum requirements for on-site and electronic data monitoring of Division of Acquired Immunodeficiency Syndrome (DAIDS) - supported and/or sponsored clinical trials to ensure adequate protection of the rights and safety of human subjects, compliance with all requirements, and the quality and integrity of the resulting data.

### 2.0 SCOPE

This policy applies to all sites conducting DAIDS-supported and/or sponsored clinical trials within DAIDS HIV/AIDS Clinical Trials Networks and collaborations with other entities, including investigator-initiated clinical trials and external groups.

### 3.0 BACKGROUND

The monitoring of clinical research sites is one element of a larger program of clinical trials oversight developed by DAIDS to fulfill its responsibilities to:

1. Ensure the safety and welfare of participants
2. Maximize adherence in the conduct of clinical trials with applicable regulations, policies, standard procedures, required guidelines and study protocols
3. Verify data accuracy, completeness and quality

The overall monitoring program involves careful review of proposed clinical trials; a requirement for meaningful quality control/quality assurance programs, site performance evaluation systems, structured interim reviews of trial data (DSMB, SMC), and appropriate site monitoring.

In addition to Food and Drug Administration (FDA) regulated Investigational New Drug Application (IND) studies, DAIDS supports clinical research, that may involve approved study agents used in new indications or treatment strategies or other interventions that may involve substantial risks to participants. DAIDS uses a risk-based approach that is applied to the frequency, duration and intensity of

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monitoring activities. This relative risk, as well as the scope and complexity of the research protocol will influence the type and extent of monitoring required.

The DAIDS assigns each new protocol a risk level (Level 1-3). Each risk level corresponds to a percentage range of Patient Identification numbers (PIDs) to be monitored at each site for informed consent, eligibility verification, and on-going record review (protocol visits) through an identified target or off-study visit. At each participating site most protocols will have the first two enrolled PIDs monitored at each visit that the protocol is designated for review, through the target or off-study visit. The DAIDS may also direct the monitors to review additional items specifically, to address areas of potential risk within a given protocol. Such direction is documented in a Protocol-Specific monitoring plan (PSMP) or special assignment.

DAIDS delegates its monitoring function to a Contract Research Organization (CRO) to oversee these aspect of its supported and/or sponsored clinical trials.

#### 4.0 DEFINITIONS

For definitions, see [DAIDS glossary](#).

#### 5.0 RESPONSIBILITIES

*Clinical site monitors* will conduct on-site and/or electronic review of source documents, participant records, regulatory files, facilities, laboratories and pharmacies. Detailed reports will be provided to the Principal Investigator (PI)/ Clinical Trials Unit (CTU) PI, CTU Coordinator, (CRS) Leader, CRS Coordinator, Pharmacist of Record (PoR) (if applicable), as well as DAIDS staff.

*The PI/CTU PI* is ultimately responsible for the correction of deficiencies identified during a monitoring visit.

*DAIDS Program staff* is responsible for reviewing monitoring reports and ensuring that the PI has a plan of action for correction of deficiencies and follows through on actions items.

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**6.0 POLICY**

- 6.1 Monitoring for all DAIDS-supported and/or sponsored clinical trials
  1. All clinical trials requiring monitoring for which DAIDS is the IND-holder must be monitored by a DAIDS monitoring contractor (DAIDS monitors). The extent of monitoring will be based on the assigned risk level as it relates to the size (N=) or magnitude of the protocol, participant risk and complexity of the trial. Monitoring may change depending upon the status of the trial, the needs of DAIDS and the performance of the site. For some trials, non-DAIDS monitoring may also be performed.
  2. Clinical trials for which DAIDS does not hold an IND will be monitored by a DAIDS monitor and/or by a non-DAIDS monitor.  
Use of external non-DAIDS monitoring and internal non-DAIDS monitoring must be specifically approved in writing by DAIDS. If approved, the monitors must be identified and a detailed monitoring plan approved by DAIDS prior to enrollment. If internal non-DAIDS monitoring is approved, DAIDS may also conduct site monitoring or auditing through the use of DAIDS monitors or other contractors. The monitoring frequency and intensity level will be determined by DAIDS staff.
- 6.2 Minimum standards for site monitoring of clinical trials
  1. Selection and Qualifications of the Clinical Site Monitor
    - a. CROs must use monitors who meet the qualifications set forth in their respective contracts with DAIDS, unless exceptions are specifically granted by DAIDS.
    - b. If site monitors are provided or contracted by an entity other than DAIDS, DAIDS may request the SOPs and description of planned reporting procedures to ensure the procedures meet DAIDS requirements.
    - c. Monitors should be qualified by experience and training and will have at a minimum a Bachelor's/University degree or equivalent

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in nursing, pharmacy, biology, or other biomedical sciences.

- d. Monitors should have experience in clinical research, and preferably have experience in monitoring clinical trials, implementing HIV/AIDS studies, working with community and/or hospital clinic or laboratory staff, teaching clinical staff, and/or performing quality assurance audits.

Note: Exceptions to these qualifications will require review and approval from DAIDS staff.

2. Frequency of monitoring visits

- a. DAIDS staff will determine the frequency of monitoring visits taking into consideration the assigned risk level of protocols being conducted at a site, the size of the protocols, number of participants enrolled and past site performance.
- b. The degree and frequency of monitoring will be re-assessed periodically.

6.3 Review of Clinical Research Participant Records at Each Visit

1. Based on the risk level of a protocol, a corresponding percentage of PIDs (monitoring goals) are reviewed for informed consent, eligibility and data verification. This review continues at every site monitoring visit until the monitoring goals are met.
2. The documented informed consent process will be reviewed for compliance with 21 CFR Part 50 and 56, Good Clinical Practice (GCP) and the DAIDS Policy Requirements for Source Documentation in DAIDS -supported and/or sponsored Clinical Trials.
3. Original source documentation will be reviewed to verify documentation of all inclusion/exclusion criteria, including pertinent negatives, and compliance with protocol requirements and DAIDS policies.
4. Individual participant's original source and other supporting documents will be reviewed and compared to the protocol requirements and the completed case report forms.

6.4 Review of Site Regulatory Files

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1. At a minimum, the regulatory file must be reviewed once per year. Please refer to DAIDS policy *Requirements for Essential Documents at Clinical Research Sites Conducting DAIDS-supported and/or sponsored Clinical Trials* for more details.
- 6.5 Facility and Operations Assessment
1. Biennial, facility assessment will be conducted to ensure that the facilities used for the clinical investigation continue to be acceptable. Site operations assessments may also be requested when a major change has occurred at the site, such as a move to a new location.
- 6.6 Clinical Site Monitoring Visit Reports
1. Written reports of the reviews of research records, regulatory files, and site and pharmacy operations must be submitted to DAIDS by the monitoring contractor within the DAIDS contract timelines. The report must include date of the visit, name of the monitor, name and address of investigator site visited and a statement of findings and conclusions.
  2. Prior to its distribution, information that could lead to unblinding will be removed from the report. Information that is removed from a report due to potential for unblinding, such as, but not limited to, physical inventories, is to be submitted in a separate document to DAIDS PAB.
  3. Distribution of visit reports will include (but not be limited to): appropriate DAIDS staff, the Principal Investigator, and other site staff as appropriate.
- 6.7 Issues or Findings Requiring Expedited Reporting
1. Reporting of "Critical Events" will be expedited according to standard operating procedures. In general, these issues/events should be reported to DAIDS as soon as possible, per DAIDS Critical Events Policy.
  2. Suspected instances of scientific misconduct will be immediately reported directly to the Director, Office of Clinical Site Oversight (OCSO), the DAIDS Monitoring Contract COR (Contracting Officer Representative) (if applicable), and Program Officer(s) responsible

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for the site and study at DAIDS.

## 7.0 REFERENCES

[U.S. Code of Federal Regulations, Title 21, Part 312.56: Review of Ongoing Investigations](#)

[Oversight of Clinical Investigations — A Risk-Based Approach to Monitoring](#)

[DAIDS Policy Requirements for Source Documentation in DAIDS Funded and/or Sponsored Clinical Trials](#)

[DAIDS Policy Requirements for Essential Documents at Clinical Research Sites Conducting DAIDS funded and/or Sponsored Clinical Trials](#)

[DAIDS Critical Events Policy](#)

## 8.0 INQUIRIES

Questions and comments regarding this SOP may be directed to the [OPCRO Policy Group](#).

## 9.0 AVAILABILITY

This policy is available electronically on the [Division of AIDS \(DAIDS\) Clinical Research Policies and Standard Procedures Documents](#) webpage.

## 10.0 APPENDICIES

None

## 11.0 APPROVAL

Carol J. Worrell, M.D.

Director, Office for Policy in Clinical Research Operations (OPCRO)