

Policy
**Requirements for Laboratories Performing Testing for DAIDS-Supported and/or
Sponsored Clinical Trials**

Effective Date: 09/10/19

Document No.: **POL-A-OD-002.01**

1.0 PURPOSE

1.1 The National Institute of Allergy and Infectious Diseases (NIAID), Division of Acquired Immunodeficiency Syndrome (DAIDS), has established specific requirements for laboratories processing and testing biologic samples from participants enrolled in clinical trials supported and/or -sponsored by the NIAID (DAIDS). These requirements relate to general laboratory operations, quality assurance and control procedures, management of specimens, and management of laboratory data. The purpose of this policy is to ensure the reliability and validity of all laboratory measurements made to determine eligibility, identify and manage adverse events, and assess outcomes during the course of the clinical trial and to safeguard participants enrolled in clinical trials and individuals who perform laboratory testing. This policy aligns with the DAIDS framework for conducting oversight and monitoring of laboratories participating in DAIDS-supported and/or -sponsored clinical trials and clinical research projects that require laboratory oversight.

2.0 SCOPE

2.1 This document applies to laboratories performing testing for clinical trials where: 1) the clinical trial is conducted by a DAIDS-funded clinical trials network; or, 2) the clinical trial is conducted by a DAIDS-funded Principal Investigator and DAIDS is the IND holder. In some cases, for clinical trials that are funded, in part or in whole, by DAIDS, but where DAIDS does not hold the IND, these requirements may also apply.

3.0 BACKGROUND

3.1 This policy identifies requirements regarding laboratory operations in order to ensure compliance of laboratories with the Code of Federal Regulations (CFR) and the DAIDS Guidelines for Good Clinical Laboratory Practice (GCLP) Standards. The DAIDS GCLP concept possesses a unique quality, as it embraces both the research/pre-clinical and clinical aspects of Good Laboratory Practice (GLP). GCLP standards encompass applicable portions of 21 CFR part 58 or GLP, and 42 CFR part 493, or Clinical Laboratory Improvement Amendments (CLIA), and they are enhanced by standards from accrediting bodies such as the College of American Pathologists (CAP), South African National Accreditation System (SANAS) and International

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Organization for Standardization (ISO). The purpose of these regulations and standards are to promote good laboratory practices and to ensure reliable and reproducible laboratory results and documentation/records, and to ensure that laboratory data and results will be acceptable to regulatory agencies (e.g. Food and Drug Administration (FDA) and European Medicines Agency (EMA)).

4.0 DEFINITIONS

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

5.0 RESPONSIBILITIES

5.1 This policy, and the associated specific requirements for U.S. and non-U.S. laboratories (Appendices I and II), have been created by DAIDS Clinical Laboratory Oversight Team (DCLOT) whose responsibility is to oversee the laboratory component of NIAID (DAIDS) sponsored clinical trials. DCLOT will be responsible for updating this policy and supporting appendices in response to changes in federal and international regulations and based on continued experience in the conduct of clinical trials. DCLOT will be responsible for working in partnership with the clinical trial network and non-network grantees and contractors - to determine if laboratories have acceptable performance.

5.2 The Principal Investigator of a NIAID supported grant and/or Investigator of Record (IoR) is responsible for ensuring that laboratories processing and testing biologic samples from participants enrolled in clinical trials adhere to the laboratory requirements identified in this policy, as well as follow specific guidance described in individual clinical trial protocols. DCLOT will be responsive to queries by investigators who need assistance with understanding this policy and with implementing the specific requirements for U.S. and non-U.S. laboratories. Please email: [DCLOT \(NIAIDDCLOT@niaid.nih.gov\)](mailto:DCLOT@niaid.nih.gov) for enquiries about the laboratory policy.

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6.0 POLICY

- 6.1 NIAID (DAIDS) sponsored clinical trials involving human subjects must be performed in compliance with federal regulations, including procedures to protect the safety of all participants. These studies must be conducted in a manner to assure the sponsor, and regulatory agencies, that all data submitted are a true reflection of the results obtained during a study, and that this data can be relied upon when making risk, safety, or advancement assessments of study products. DAIDS has determined that GCLP standards are the minimal requirements that clinical research laboratories should follow (see [DAIDS Guidelines for Good Clinical Laboratory Practice Standards \(https://www.niaid.nih.gov/sites/default/files/gclp.pdf\)](https://www.niaid.nih.gov/sites/default/files/gclp.pdf)).
- 6.2 In addition to maintaining operations in compliance with GCLP standards, DAIDS has established, and maintains, specific requirements for laboratory performance in five areas.
- 6.2.1 Laboratory Safety, Diagnosis and Eligibility and Other Tests Used for Participant Management
Tests that are used for diagnosis, determining eligibility, monitoring the safety of the intervention, and making participant management decisions, should be performed in laboratories that conduct operations in accordance with GCLP standards. These tests should be quality assured by External Quality Assurance (EQA) surveys. When commercial or standard EQA is not available, alternative EQA plans should be devised and proposed to DAIDS for approval. U.S. laboratories must be CLIA-certified or waived as appropriate for certain testing.
- 6.2.2 Endpoint Tests not approved by FDA
Primary endpoint tests should be documented as fit-for-purpose. If the purpose is to submit to a regulatory agency for decision making, then full validation is required according to FDA Guidance on Biomedical Method Validation. If the purpose is exploratory and the data would not be submitted for decision-making, then optimized or qualified assays demonstrating the desired results (i.e. it is fit-for-purpose) may be sufficient. See Appendix III DCLOT Algorithm for Determining Level of Validation Required for Endpoints Assays. EQA should be applied to

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primary study endpoint tests. If existing EQA surveys are not available, a suitable form of alternative EQA should be devised and proposed to DAIDS for approval.

6.2.3 Specimen Management

Procedures for the management of trial specimens must be documented and followed to ensure the integrity of specimens and their timely testing. Procedures must address specimen acquisition, receipt, processing, testing, storage and shipping according to regulations (e.g. International Air Transport Association (IATA)) and under conditions that preserve specimen integrity (e.g. maintaining the cold chain) and tracking as applicable.

6.2.4 Laboratory Data Management

Procedures for the management of laboratory data must be documented and followed to ensure data integrity and timely reporting of results and are required to include appropriate procedures for data quality assurance (QA) and corrective actions. Procedures should address data acquisition, recording/entry, data modification, signatures, export, archiving and security, as well as integration of the laboratory data with the main study database.

Computerized laboratory systems should be validated and compliant with 21 CFR Part 11.

6.2.5 Laboratory Quality Management Plan

Laboratories must have a documented Quality Management Plan (QMP) that describes the overall quality management program of the laboratory. For additional information please refer to the

[DAIDS Guidelines for GCLP Standards](#)

(<https://www.niaid.nih.gov/sites/default/files/gclp.pdf>). DAIDS

recommends laboratories designate a senior staff member to be responsible for executing the laboratory QMP.

6.3 Laboratory Oversight

DAIDS Laboratory Oversight framework involves four key components, namely: QA oversight, GCLP Audit, GCLP Training, and Lab Quality Improvement. The oversight framework is guided by the GCLP Standards, and other applicable regulatory guidelines and requirements.

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QA oversight

The DCLOT representatives work closely with DAIDS external laboratory partners to oversee quality assurance performance in compliance with GCLP guidelines.

GCLP Audit

Laboratories participating in NIAID (DAIDS)-supported and/or -sponsored clinical trials may be subject to DAIDS GCLP audits in accordance with the GCLP guidelines. The audit activities involve three phases, namely: pre-audit, audit and post-audit. The pre-audit phase involves activities related to the planning and scheduling of GCLP audits. The audit phase involves on-site activities and assessment of GCLP compliance of the laboratories. The post-audit phase involves activities related to the review and resolution of GCLP audit reports.

GCLP Training

DAIDS GCLP Training component involves the online and face-to-face formats. The DAIDS GCLP online training is offered through GCLP eLearning modules available on the DAIDS Learning Management System (LMS). DAIDS Face-to-Face GCLP training is offered on an as needed basis, with DCLOT approval, based on lab quality performance and improvement outcomes. Clinical laboratory staff, who process and test specimens for DAIDS-supported and/or -sponsored clinical trials, should take GCLP training.

Lab Quality Improvement

DAIDS Laboratory Quality Improvement component involves activities to assess the overall quality improvement of laboratories participating in DAIDS-supported and/or sponsored clinical trials and clinical research projects. DCLOT conducts periodic surveys to assess laboratory staff satisfaction with DAIDS oversight resources. DCLOT team members participate in a small number of GCLP audits to assess the overall conduct of the audit. DCLOT, with support from DAIDS laboratory partners, conducts trend analysis of the laboratory GCLP audit observations/findings to monitor lab performance over time.

These laboratory requirements may be reviewed periodically and updated

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as necessary to remain current with accepted practices and technological innovation. For the convenience of current and potential investigators and collaborating laboratories, separate documents with specific requirements are provided for U.S. based laboratories (Appendix I) and non-U.S. laboratories (Appendix II). Differences in these documents pertain largely to laboratory accreditation bodies and procedures within and outside of the United States.

7.0 REFERENCES

- 7.1 [U.S. Code of Federal Regulations, Title 21, Parts 11 and 58](#)
- 7.2 [U.S. Code of Federal Regulations, Title 42 CFR Part 493](#)
- 7.3 [CLIA Program – Clinical Laboratory Improvement Amendments](#)
- 7.4 [International Air Transport Association \(IATA\) Dangerous Goods Shipping Regulations](#)
- 7.5 [U.S. Food and Drug Administration, Guidance for industry: bioanalytical method validation, 2018](#)
- 7.6 [DAIDS Guidelines for Good Clinical Laboratory Practice Standards](#)

8.0 APPENDICIES

- 8.1 Appendix I - DAIDS Requirements for U.S. Laboratories
- 8.2 Appendix II - DAIDS Requirements for non-U.S. Laboratories
- 8.3 Appendix III - DCLOT Algorithm for Determining Level of Validation Required for Endpoints Assays

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9.0 REVISION HISTORY

- 9.1 POL-A-OD-002.00 is the initial version of Requirements for DAIDS Supported and/or Sponsored Laboratories in Clinical Trials Policy submitted to the DAIDS QMS. There were four previous versions of this policy published on the DAIDS Clinical Research Policies webpage prior to the implementation of the DAIDS QMS in 2018. Changes from the previous version includes addition of language on level of validation required for Endpoints Assays not approved by the FDA in Section 6.2.2. and addition of 6.3. Laboratory Oversight Section.
- 9.2 POL-A-OD-002.01 was revised on 06/27/19 to include the following changes: The following language was added to the Revision History to clarify changes made to the initial version of Requirements for DAIDS Supported and/or Sponsored Laboratories in Clinical Trials Policy submitted to the DAIDS QMS: Main changes from the previous version includes addition of language on level of validation required for Endpoints Assays not approved by the FDA in Section 6.2.2. and addition of 6.3. Laboratory Oversight Section.