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## 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 quality 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 NIAID 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 non-network 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 DEFINITIONS

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


## 4.0 RESPONSIBILITIES

- 4.1 DAIDS Clinical Laboratory Oversight Team (DCLOT)

This policy, and the associated policies with specific requirements for U.S. and non-U.S. laboratories, 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 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.


- 4.2 Principal Investigator of a NIAID supported grant and/or Investigator of Record (IoR)

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(NIAIDDCLOT@niaid.nih.gov)) for enquiries about the laboratory policy.

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## 5.0 POLICY

- 5.1 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 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))
- 5.2 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/gclpstandards.pdf) (<https://www.niaid.nih.gov/sites/default/files/gclpstandards.pdf>)).
- 5.3 In addition to maintaining operations in compliance with GCLP standards, DAIDS has established, and maintains, specific requirements for laboratory performance in five areas.
- 5.3.1 **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 Clinical Laboratory Improvement Amendments (CLIA) -certified or waived as appropriate for certain testing.
- 5.3.2 **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 may be 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

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sufficient. See Appendix I DCLOT Algorithm for Determining Level of Validation Required for Endpoints Assays. EQA should be applied to 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.

#### 5.3.3 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.

#### 5.3.4 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.

#### 5.3.5 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/gclpstandards.pdf)

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

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


### 5.4 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.

Laboratories performing testing for clinical trials should maintain satisfactory performance in all applicable aspects of the lab oversight framework activities.

#### 5.4.1 QA oversight

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

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#### 5.4.2 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 or remote 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.

#### 5.4.3 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 Portal \(https://daidslearningportal.niaid.nih.gov/\)](https://daidslearningportal.niaid.nih.gov/). DAIDS face-to-face GCLP training is offered on an as needed basis, with DCLOT approval, based on lab quality performance and improvement outcomes.


CLIA requirements overlap to a large extent with GCLP, therefore the DAIDS GCLP training is not required for clinical laboratory personnel in laboratories in the United States that are CLIA certified. For U.S. specimen processing laboratories and endpoints laboratories, GCLP training is highly recommended. For non-U.S. laboratories that are not covered under CLIA, all clinical laboratory personnel involved in specimen processing and testing must take GCLP training, available on the [DAIDS learning portal \(https://daidslearningportal.niaid.nih.gov/\)](https://daidslearningportal.niaid.nih.gov/). GCLP training of study nurses and any other non-lab personnel performing specimen processing and/or testing in the clinic or clinical laboratory is under the purview of laboratory management. Laboratory management should ensure that training frequency is sufficient to ensure that personnel remain familiar with the GCLP requirements applicable to them.

#### 5.4.4 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, with support from DAIDS laboratory partners and in alignment with GCLP guidelines, monitor lab performance throughout the life cycle of the clinical trial.

## 6.0 REFERENCES

- 6.1 [U.S. Code of Federal Regulations, Title 21, Parts 11 and 58](#)
- 6.2 [U.S. Code of Federal Regulations, Title 42 CFR Part 493](#)
- 6.3 [CLIA Program – Clinical Laboratory Improvement Amendments](#)
- 6.4 [International Air Transport Association \(IATA\) Dangerous Goods Shipping Regulations](#)

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6.5 [U.S. Food and Drug Administration, Guidance for industry: bioanalytical method validation, 2018](#)

6.6 [DAIDS Guidelines for Good Clinical Laboratory Practice Standards](#)

## 7.0 APPENDICES

### 7.1 Appendix I

#### 7.1.1 SCOPE

Applies to any laboratory developed test (LDT) used for endpoint determination that may be submitted to the FDA in support of licensure or used to advance a product to subsequent clinical trial phases.

#### 7.1.2 Notes on the use of this algorithm:

7.1.2.1. This algorithm is separate from CLIA certification [7.3] or GCLP compliance of a laboratory [7.6]. If CLIA or GCLP is required for testing, the laboratories would also need to be in compliance with those requirements in addition to the requirements described in the algorithm.

7.1.2.2 In the “fit-for-purpose” concept, the required performance characteristics of the assay are first determined for the study [7.1]. Will the assay need to be qualitative or quantitative? Are positivity criteria developed for a qualitative assay? If quantitative, what range is needed? What level of precision is needed for the study? Is there a “gold standard” assay that measures the same analyte for assessing accuracy? What level of sensitivity and specificity? After the required performance characteristics are determined and pass/fail criteria set, the assay is performed with controls to confirm whether the assay meets pre-specified criteria. If one or more of the assay parameters do not meet the acceptance criteria, the assay cannot be accepted as fit-for-purpose and cannot be used for testing clinical trial samples. Additional assay optimization work is required so the assay meets all acceptance criteria before being used to test clinical trial samples.

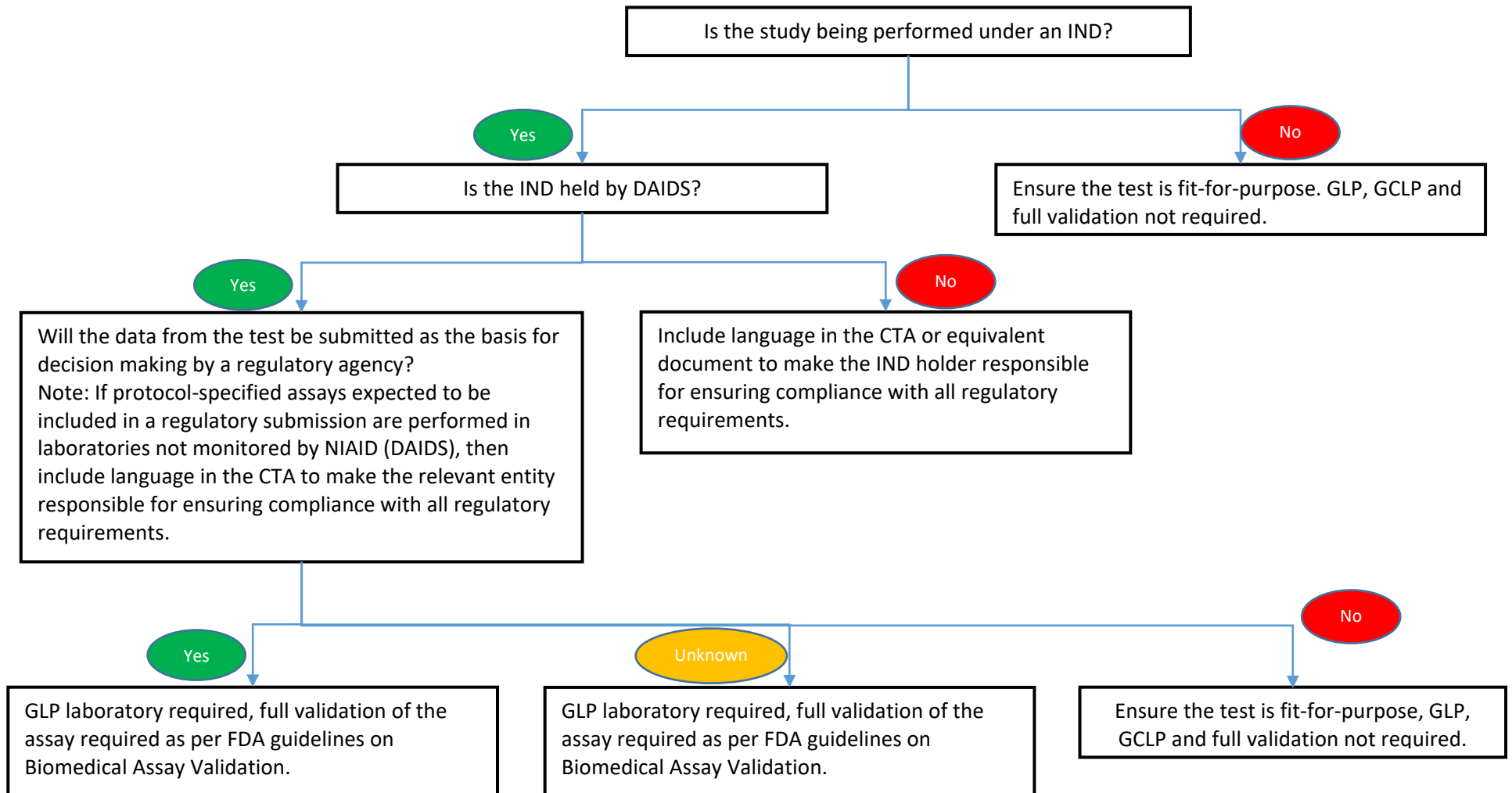
7.1.2.3. The algorithm employs the “fit-for-purpose” concept which means:

- The level of validation should be appropriate for the intended purpose of the study.
- If data from the assay in question will be submitted to a regulatory agency for decision making for approval, safety or labeling, then full validation is required according to the FDA Guidance on Biomedical Method Validation.



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- If the endpoint is considered exploratory and the data would not be submitted for decision-making, then less stringent approaches (standardization or qualification) demonstrating that the assay can provide the desired results (i.e., it is fit-for-purpose) may be sufficient.
- For exploratory research, the methods should be documented to be fit-for purpose, since the LDT are being used to evaluate responses to interventions given to research participants, which may expose the participants to some level of risk.
- The final report should include data on the sensitivity and specificity of qualitative methods, and data on the accuracy, precision, linear range, sensitivity and specificity of quantitative methods. The report must be signed by the lab director and kept at the lab and provided to the trial sponsor if requested.







## 8.0 REVISION SUMMARY

- 8.1 POL-A-OD-002.01 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.
- 8.2 DAIDS-OD-POL-00002 rev 01 is the first revision of this procedure within the electronic Quality Management System. The document format and document numbering have been updated to reflect current requirements. The web links have been updated as well as the inclusion of Appendix 1 as this was previously a separate document.