

DAIDS Bethesda, MD USA	POLICY	No.: DWD-POL-LB-01.00
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	Approval Date: 20 DEC 06 Effective Date: 05 FEB 07	Replaces: V 1.0

1.0 PURPOSE

The Division of Acquired Immunodeficiency Syndrome (DAIDS), National Institute of Allergy and Infectious Diseases (NIAID) has established specific requirements for laboratories processing and testing biologic samples from participants enrolled in clinical trials funded and/or sponsored by 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 safeguard participants enrolled in clinical trials and to ensure the reliability and validity of all laboratory measurements taken to determine eligibility, identify and manage adverse events, and assess outcomes during the course of the clinical trial.

2.0 SCOPE

This policy applies to all laboratory procedures in support of a therapeutic, vaccine, or prevention clinical trial funded and/or sponsored by DAIDS outside of networks.

3.0 BACKGROUND

This policy identifies requirements regarding laboratory operations in order to ensure compliance of U.S. laboratories with the federal Clinical Laboratory Improvement Amendments (CLIA) rules (42 CFR Part 493), and the Code of Federal Regulation for Good Laboratory Practice (21 CFR Part 58). The purpose of these regulations is to promote good laboratory practices and to assure reliable laboratory results and documentation/records. Regulations under these guidelines define requirements for personnel, procedures, and policies. DAIDS strives to achieve an equivalent level of quality in the operations of its non-U.S. laboratories that support DAIDS international trials.

4.0 DEFINITIONS

See DAIDS glossary.

5.0 RESPONSIBILITIES

This policy, and the associated specific requirements for U.S. and non-U.S. laboratories has been created by DAIDS staff whose responsibility is to oversee the laboratory component of DAIDS clinical trials. DAIDS staff will be responsible for updating this standard in response to changes in federal regulations and based on continued experience in the conduct of clinical trials. DAIDS staff 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.

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The Principal Investigator 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. The lab manager is responsible for the day-to-day operations of the laboratory and for ensuring that the requirements of this policy are met.

6.0 POLICY

6.1. DAIDS has established and maintains specific requirements for laboratory performance in six areas:

6.1.1. Diagnosis, Safety Tests, CD4 and Virological Tests

Tests that are used for diagnosis, determining eligibility, endpoints, monitoring the safety of the intervention and making patient management decisions must be performed in laboratories that conduct operations in a Good Clinical Laboratory Practice (GCLP) manner and tests must be quality assured by external proficiency testing surveys. When not available, external quality assurance measures should be devised. U.S. laboratories must be CLIA-certified and non-U.S. laboratories are encouraged to become accredited by CLIA or an equivalent organization.

6.1.2. Research Use Only (RUO) Tests (research tests not yet validated and approved by an International Conference on Harmonisation (ICH) regulatory body such as the U.S. Food and Drug Administration (FDA).

RUO endpoint tests are required to be performed in laboratories that conduct operations in a GCLP manner. External proficiency testing (PT) should be applied. It is recommended that GCLP and external PT be applied also to non-endpoint RUOs.

6.1.3. Study 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, 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.

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6.1.4. Study 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 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, taking into account the elements of 21 CFR Part 11 compliance.

6.1.5. Laboratory Quality Assurance

Laboratories that are not accredited by CLIA or equivalent organization must have a laboratory quality assurance (QA) plan to regularly review all components of laboratory activities, including intervention and corrective action plan, and plans for backup testing facilities. All labs must designate a QA manager to be responsible for executing the lab Quality Management Plan (QMP).

6.1.6. Laboratory Audits Provided by DAIDS

DAIDS and/or its contractors will conduct laboratory-specific audit visits to determine laboratory readiness to participate in trials, and, as indicated, during the conduct of a trial.

6.2. These laboratory requirements are reviewed periodically and updated as necessary to maintain currency 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 1) and non-U.S. laboratories (Appendix 2). Differences in these documents pertain largely to laboratory accreditation bodies and procedures within and outside of the United States.

6.3. Comprehensive Laboratory Plan: Applications in response to PAR-05-113 'NIAID Clinical Trial Implementation (U01) Cooperative Agreement' must include a Comprehensive Laboratory Plan in the Appendix that identifies all proposed laboratories and plans to ensure they meet DAIDS requirements. The required

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content and suggested formats for components of the Comprehensive Laboratory Plan are detailed in the above referenced documents.

7.0 REFERENCES

U.S. Code of Federal Regulations, Title 21, Parts 11 and 58

<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm>

U.S. Code of Federal Regulations, Title 42 CFR Part 493

<http://www.phppo.cdc.gov/clia/pdf/CMS-2226-F.pdf>

CLIA Program – Clinical Laboratory Improvement Amendments

<http://www.cms.hhs.gov/clia/>

Department of Health and Human Services (DHHS)/Centers for Disease Control and Prevention (CDC) Presentation

<http://www.phppo.cdc.gov/dls/ila/cd/botswana/Presentations/QS%20-%20Overview.ppt>

Morbidity and Mortality Weekly Report (MMWR) 1997; 46 No. RR-2 Dual-platform technology <http://www.cdc.gov/mmwr/preview/mmwrhtml/00045580.htm>

MMWR 2003; 52(RR-02) Single-platform technology

<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5202a1.htm>

International Air Transport Association (IATA) Dangerous Goods Shipping Regulations

<http://www.iata.org/ps/publications/9065.htm>

8.0 INQUIRIES

Questions and comments regarding this policy may be directed to the OPCRO Policy Group at: NIAIDOPCROPOLICYGROUP@mail.nih.gov

9.0 AVAILABILITY

This policy is available electronically at the following URL:

<http://www3.niaid.nih.gov/research/resources/DAIDSclinRsrch/Default.htm>

The signed original is maintained in the OPCRO policy office.

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10.0 CHANGE SUMMARY

Version #	Date	Replaces	Date of Revision	Rationale for Revision/Retirement
2.0	20 DEC 06	V 1.0	20 DEC 06	DAIDS Final Review
1.0	14 JUL 06	N/A	N/A	N/A

11.0 APPENDICES

Appendix 1 - DAIDS Requirements for U.S. Laboratories

Appendix 2 - DAIDS Requirements for non-U.S. Laboratories

12.0 APPROVAL

Signature	Program/Branch	Date
Authorized By: <u><i>Richard Hafner</i></u> Richard Hafner, MD Director	Office for Policy in Clinical Research Operations (OPCRO)	<u>December 20, 2006</u>