Title:	Terminology Criteria and Responsibilities for Reporting DAIDS GCLP Laboratory Audits or Initial Assessments v2.0		
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Revision History	For a complete revision history, see Appendix A

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Contents

1. Introduction

This document was prepared by the Cross-Network Laboratory Focus Group (LFG) and Division of AIDS Clinical Laboratory Oversight Team (DCLOT) and represents a consensus from the Laboratory Centers of the HIV Vaccine Trials Network (HVTN), HIV Prevention Trials Network (HPTN), the Advancing Clinical Therapeutics Globally (ACTG), and the International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) Group, and DCLOT.

2. Terminology Criteria, Consequences and Responsibilities

Review of DAIDS requested laboratory audits or initial assessments will result in the completion of an action plan detailing site queries and suggested corrective or preventative actions. Each specific action will initially be labeled with one of five designations indicating the level of action to be undertaken by the reviewed laboratory. Specifically, in order of corrective need and study related priority, they are: Critical, Major, Minor, Recommendations and Not Applicable.

2.1. Critical

2.1.1. Definition of Critical

Necessary for the success, progress, or continuation of overall laboratory operation and function.

A. Where evidence exists that significant and unjustified departure(s) from applicable requirements has occurred with evidence that:
   - The safety, well-being or confidentiality of trial subjects either have been or have significant potential to be jeopardized, and/or
   - The clinical trial data, trial specimens, safety of associated lab staff and/or trial-specific equipment are at risk, and/or
   - There are a number of Major audit findings across areas of responsibility, indicating a systematic quality assurance failure

B. Where inappropriate, insufficient or untimely corrective action has taken place regarding previously reported Major audit findings

2.1.2. Reasons for Critical finding

May include, but not limited to:

- Scientific misconduct
- Irresponsible or incompetent administration
- Financial improprieties
- Fraud (including intentional EQA procedure performance and resulting)
- Continued failure to provide standard of medical care
- Progressive deterioration of clinical site's required standards (such as supplies, personnel (e.g. untrained or non-competent staffing), physical facilities, organization, etc.)
- Severely negative "political environment" at the site/lab or geographical region
- Failure to provide a safe working environment

Note: Any individual involved with or overseeing the laboratory supporting the DAIDS sponsored/funded clinical trial (including but not limited to DAIDS networks, Trial Principal Investigators (PI), support staff, laboratorians, DAIDS employees and contractors, internal/external "whistle-blowers") can notify DAIDS of a suspected critical situation requiring immediate action. DAIDS, in consultation with other partners, will facilitate the investigation and assign the Critical label.

2.1.3. Potential consequences of Critical finding

May include, but not limited to:

- Full site closure on a temporary or permanent basis
- Temporary or permanent closure to participant enrollment
- All or specific testing moved to a backup laboratory
- Cessation of funding
- Referral to local legal authorities or other official actions
- Rejection of data
- Withdrawal of manuscripts or publications
- Study activation delay

2.2. Major

2.2.1. Definition of Major

A. A non-critical finding where evidence exists that a significant and unjustified departure from applicable requirements has occurred that may not have arisen to the level of a critical issue, but may have the potential to do so unless addressed, and/or

B. Where evidence exists that several departures from applicable requirements and/or established DAIDS GCLP guidelines have occurred within a single area of responsibility, indicating a systematic quality assurance failure, and/or

C. Where inappropriate, insufficient or untimely corrective action has taken place regarding previously reported Minor findings

2.2.2. Reasons for Major finding

May include, but not limited to:

- Severe shortage or major turnover in laboratory staffing
- Improperly trained or incompetent technical staff
- Severe constrains on equipment
- Reagent shortages and use of expired reagents
- Chronic equipment breakdowns
- Severe EQA performance failure
- Unintentional EQA procedure performance and resulting
- Continued failure to implement prior corrective actions and/or preventative actions
- Failure to adequately document the specimen "chain-of-custody"
- Failure to follow SOPs

2.2.3. Potential consequences of Major finding

May include, but not limited to:

- Study activation delay
- All or specific testing moved to a backup laboratory
- Written and approved corrective actions are required and implemented without delay
- Additional audits or site visits

2.3. Minor

2.3.1. Definition of Minor

Where evidence exists that a departure from applicable requirements and/or established DAIDS GCLP guidelines and/or procedural requirement has occurred, but it is neither Critical nor Major.

2.3.2. Reasons for Minor finding

Any findings discovered or identified during routine annual audits where DAIDS GCLP guidelines are not or were not being followed.

2.3.3. Potential consequences of Minor finding

- Corrective actions and/or preventative actions must be addressed
- Study activation delay

2.4. Recommendations

2.4.1. Definition of Recommendations

DAIDS GCLPs are being adhered to in the strict sense of the guidelines, but improvement with the procedures to adhere to the intent or spirit of the guidelines can be made. Recommendations can also be made if the guidelines are currently being adhered to but potential for deterioration is observed or otherwise detected.

2.4.2. Potential consequences of Recommendations finding

No consequences are warranted and no further follow up is needed.

2.5. Not Applicable

2.5.1. Definition of Not Applicable

Items not in violation of GCLP guidelines or not specific to a network or ongoing study.

3. Discrepant Labeling of Action Plan Items

3.1. Critical

If two or more networks disagree on designating an action plan item as Critical, then the process for resolution is as follows:

3.1.1. DCLOT will notify and hold a mandatory conference call with at least one representative from the respective networks within 3 working days.

- The network(s) applying the Critical designation is required to provide:

- Rationale for the item being labeled as Critical.
- Recommended consequences and corrective actions for the lab in question.

3.1.2. DCLOT and representative(s) from the networks involved will come to an agreement on whether the Critical label is applied, and if so, the resulting consequence(s) for the lab in question.

3.2. Non-Critical

If two or more networks label the same action plan item with a different non-Critical designation (i.e. Major, Minor, or Recommendations), then the more severe designation will apply by default (e.g. Major over Minor).

4. Network Responsibilities for Enforcing Consequences for Major Findings

A. Recommend consequence(s) and corrective actions for the lab in question

B. Notify the lab in question of any consequence(s) and corrective actions. Include other involved networks and DCLOT (NIAIDDCLOTNetworkPOCs@niaid.nih.gov)

Appendix A: Revision History

Version Effective Date (dd/mm/yy)	Section(s)	Revision
2.0 21Mar2025	All	Updated numbering system and improved document formatting
	Approvals	Removed MTN authorization
	Approvals	Updated HVTN authorization contact from Michael Stirewalt to Kathryn Dougherty
	Approvals	Updated IMPAACT authorization contact from Carolyn Yanovich to Grace Aldrovandi
	1	Removed reference to MTN to reflect current DAIDS networks
	1	Updated ACTG name from "AIDS Clinical Trials Group" to "Advancing Clinical Therapeutics Globally"
	2	Added "Consequences" to the title of Section 2
	2	Added "Study activation delay" to Section 2.1.3
	2	Added "Failure to follow SOPs" to Section 2.2.2
	2	Added "Study activation delay" to Section 2.3.3
	2	Added new section titled "Not Applicable" as Section 2.5
	2	Added "no further follow-up is needed" to Section 2.4.2
	Appendix A	Relocated the Revision History section from page 1 to page 7 as new Appendix A