1.0 PURPOSE

1.1 The purpose of the policy is to describe the minimum requirements for the development, implementation, and evaluation of a CQMP at National Institute of Allergy and Infectious Disease (NIAID) Division of AIDS (DAIDS) supported and/or sponsored CRSs to ensure that the rights and safety of participants are protected, that data collected are Attributable, Legible, Contemporaneous, Original, Accurate and Complete (ALCOA-C) and that clinical trials are conducted in compliance with applicable regulations.

2.0 SCOPE

2.1 This applies to all CRSs conducting or participating in NIAID (DAIDS) supported and/or sponsored clinical research which includes all clinical and regulatory activities at the CRS.

2.2 This policy applies to all DAIDS Program Officers who provide oversight of the CRSs. To ensure consistency of operations, the Clinical Trial Unit (CTU) will fulfill the requirement of the CQMP policy by developing a Standard Operating Procedure (SOP) that clearly describes how its CRS components plan to implement the CQMP.

2.3 The requirement for the CQMP policy at a Non-Network site should be discussed with the assigned DAIDS Program Officer.

3.0 BACKGROUND

3.1 Quality Management (QM) is part of a system of oversight required for the conduct of NIAID (DAIDS) supported and/or sponsored clinical research. A QM system includes defined quality requirements comprised of site procedures, forms and templates, quality control (QC), quality assurance (QA), corrective and preventative action (CAPA) processes and continuous quality improvement activities that support process standardization, data accuracy, completeness and data integrity.

3.2 QC encompasses the routine site operations, techniques and activities undertaken within the QM system to verify the trial requirements are executed correctly, at the time the work is being performed.

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3.3 QA is a retrospective, objective, systematic, and periodic review of trial-related activities to ensure that the trial has been/is conducted, and the data have been/are generated, documented and reported in compliance with Good Clinical Practice (GCP), Sponsor and any other applicable regulatory requirements.

3.4 QM activities will allow planning for effective protocol implementation, assure compliance with sponsor and applicable regulatory requirements, identify areas in need of corrective action, verify data accuracy, and assure a constant state of readiness for an external audit or monitoring visit.

3.5 The Clinical Quality Management Plan (CQMP) is a "living document" that will incorporate tools, checklists and reports of QM activities to drive and determine the effectiveness of the CQMP. The CQMP will be updated as site procedures are streamlined and new areas of focus are identified.

3.6 To fulfill Sponsor responsibilities, DAIDS has instituted a requirement for each CRS to develop, implement and evaluate a CQMP.

4.0 DEFINITIONS

4.1 For additional definitions, see DAIDS glossary.

5.0 RESPONSIBILITIES

5.1 The Principal Investigator (PI) is ultimately responsible for the development, implementation, and evaluation of a CQMP at the CRS. The PI may delegate QM activities to the CRS Leader and other clinical research personnel qualified by documented training and experience. These delegated activities should be clearly described in the CQMP.

5.2 DAIDS Program Officers are responsible for the review of the CQMP at their CRS, providing feedback as necessary and for ensuring biannual site submission of the CRS QA Summary Report to DAIDS.

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5.3 DAIDS will periodically review QM activities at CRSs to determine their effectiveness and relevancy.

6.0 POLICY

All DAIDS supported and/or sponsored sites conducting clinical research will develop, implement, and evaluate a CQMP.

6.1 DAIDS requires that the CQMP include the following:

6.1.1 Description of roles and responsibilities of key personnel involved in the development, implementation, and evaluation of the CQMP.

6.1.2 At a minimum, inclusion of the following key indicators (as applicable) for QA/QC review:

1. Informed Consent Form (ICF) and Process
2. Assessment of Understanding of ICF as applicable
3. Eligibility Criteria and Process
4. Protocol Required Tests and Procedures
5. Visits/Missed Visits
6. Concomitant/Prohibited Medications
7. Study Product Administration/Dosing
8. Adverse Events (AE), Serious Adverse Events (SAE) and DAIDS Expedited Adverse Events (EAE) identification and reporting
9. Protocol Defined Endpoint Identification and reporting as applicable
10. Source Documents, Signatures, Initials, Dates (See Appendix I DAIDS CQMP Participant Chart Review Tool)
11. Investigator File Review Deficiencies (See Appendix II: DAIDS CQMP Protocol Regulatory File Review Tool)

6.1.3 Description of Quality Management (QM) Activities

6.1.3.1 Quality Control (QC)

QC activities function to support and ensure that the staff performing the work are doing so correctly per the designated instructions and requirements, while the work is being performed. QC activities also support GCP compliance, human subject protection (HSP), adherence to protocol requirements and site procedures.

Examples include:

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1. Re-review eligibility checklists before any protocol procedures are performed.
2. At the end of a participant visit, double check and verify that all required tests and procedures on the Study Visit Checklist have been completed prior to the participant departure from the clinic.
3. Re-review Informed Consent documents to ensure that all required dates, entries and signatures are recorded prior to participant departure from the clinic.

6.1.3.2 Quality Assurance (QA)

QA audit activities are conducted periodically in a systematic and independent manner for a defined period of time, on a defined subset of the sites' clinical trial related activities and documents. Example: number of participant charts QA reviewed in a defined period of time. The QA audits are conducted after the work has been completed and function as an independent examination for adherence to GCP, HSP, protocol and all other Sponsor and regulatory requirements.

Examples include:

1. Periodic evaluations to determine agreement between key elements of source documentation when compared to completed Case Report Forms (CRFs). (See Appendix I DAIDS CQMP Participant Chart Review Tool).
2. Periodic assessment of regulatory file documents to ensure that contents are current and complete (See Appendix II: DAIDS CQMP Protocol Regulatory File Review Tool).

6.1.3.2.1 Description of tools to be used in the QA and QC processes

Examples may include but are not limited to the following: visit reminder checklists, data entry, query reports from the Data Management Center,

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Clinical Site Monitoring Reports, Chart and Protocol Regulatory Review Tools.

6.1.4 QA Audit Sample Size

6.1.4.1 QA Audit sample size determination

1. Designation of a minimum percent of participant charts for QA audit. Sample size should be adequate to represent a valid assessment based on, but not limited to: higher risk protocols, higher accruing protocols, initial enrollments in new protocols, and protocol visits conducted by new or less experienced staff members.
2. DAIDS may set a minimum required percent of participant records for QA audit for a particular trial or for a CRS at DAIDS discretion.

6.1.5 Description of QA activities to be performed in order to ensure that the contents of the protocol regulatory files are complete and current. Example: list tool used with frequency of review.

6.1.6 Documentation of QM activities to include the following:

1. Name and role of reviewer
2. Date of the review
3. Participant identification (PID) numbers reviewed
4. Specific indicators that were reviewed
5. Protocol regulatory documents reviewed
6. Time period covered by the review
7. Findings/results of review
8. Corrective actions
9. Preventative actions

6.1.7 Description of the CQMP Evaluation Process

6.1.7.1 The CQMP will describe how the findings from QC and periodic QA activities will be analyzed and evaluated.

6.1.7.2 The CQMP will describe the process for communication of findings to appropriate staff.

6.1.7.3 The CQMP will describe the process for corrective and preventative action and continuous improvement that may require changes to site practices and the CQMP.

6.2 Quality Assurance Reporting Requirements

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6.2.1 QA findings will be reported to DAIDS bi-annually using the CRS QA Summary Report template. (See Appendix III, DAIDS CQMP CRS QA Summary Report.) At DAIDS discretion, QA reporting may be required more frequently based on site performance, higher enrollment etc. The CRS will evaluate the CQMP after each QA review.

6.2.2 The CRS QA Summary Report will include identification of problems, identification of possible causes, and any corrective and preventative actions taken.

6.2.3 If an unreported SAE is identified during the QM activities, the event must be reported per protocol, DAIDS EAE policy and institutional requirements.

6.3 DAIDS review of the CQMP and CRS QA Summary Report

6.3.1 DAIDS will review the CQMP prior to its implementation. DAIDS will make recommendations as needed.

6.3.2 The CRS will submit any subsequent non-administrative changes of the CQMP to DAIDS.

6.3.3 DAIDS will review the CRS QA Summary Report using a DAIDS defined process and communicate any recommendations and/or requests for additional information to the CRS.

6.4 Retention of QM documents

6.4.1 The CQMP will be signed and dated by the PI and/or the CRS Leader and kept on file.

6.4.2 Completed CRS QA Summary Reports, Chart Review Tools and Protocol Regulatory File Review Tools will be kept on file and accessible upon DAIDS request.

7.0 REFERENCES

7.1 Integrated Addendum to ICH E6R1: Guideline for Good Clinical Practice E6R2

7.2 E6(R2) Good Clinical Practice: Integrated Addendum to ICH E6(R1) FDA Guidance for Industry

8.0 APPENDICES

8.1 Appendix I- Clinical Quality Management Plan (CQMP): Participant CHART Review Tool APP-A28-OCS-001

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8.2 Appendix II- Clinical Quality Management Plan (CQMP): Protocol Regulatory File Review Tool APP-A28-OCS-002

8.3 Appendix III- Clinical Research Site (CRS) Quality Assurance (QA) Summary Report APP-A28-OCS-003

9.0 REVISION HISTORY

9.1 POL-A28-OCS-001.00 is the initial version of Requirements for Clinical Quality Management Plans (CQMP) 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. This version has been revised to include the following changes:

9.1.1 Additional background on Quality Management (QM) to reflect the expansion of the QM described in the International Conference on Harmonisation (ICH) Guideline for Good Clinical Practice Integrated Addendum E6(R2).

9.1.2 Role of the Division of Acquired Immunodeficiency Syndrome (DAIDS) in the review of the Clinical Research Site (CRS) Quality Assurance (QA) Summary Report is outlined.

9.1.3 A new DAIDS key indicator for QA/QC review has been added.

9.1.4 The Clinical Quality Management Plan (CQMP) Clinical Research Site (CRS) QA Summary Report has been revised.

*Note: This policy has been reissued on 10/22/19 to correct the document numbering in section 8.0.

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