1. PURPOSE

1.1 All Division of Microbiology and Infectious Diseases (DMID)-funded clinical sites are required to ensure that there are quality assurance and quality control processes established to ensure the integrity of the data collected. This document describes the process for DMID review and acceptance of clinical site Clinical Quality Management Plans (CQMPs).

2. SCOPE

2.1 This procedure applies to CQMPs for clinical protocols where DMID is the Investigational New Drug (IND)/Investigational Device Exemption (IDE) sponsor or equivalent, and high-resource clinical trials funded by contract or cooperative agreement.

3. DEFINITIONS

3.1 **Quality Assurance (QA)**: All planned and systematic actions established to ensure that the trial is performed, and the data are generated, documented (recorded), and reported in compliance with Good Clinical Practice (GCP) and the applicable regulatory requirements.

3.2 **Quality Control (QC)**: The operational techniques and activities undertaken within the quality assurance system to verify that the requirements for the quality of the trial-related activities have been fulfilled.

3.3 **Clinical Quality Management Plan (QMP)**: A written description of the quality control (QC) and quality assurance (QA) procedures, roles and responsibilities, scope, sample size, and frequency of these activities to ensure a level of quality in clinical research activities. Synonymous terms found in funding agreements may include 'quality assurance and quality control procedures' or 'quality management plan'.

3.3.1 **Protocol specific**: A single protocol-specific CQMP centrally developed and disseminated to all sites for consistent implementation across multiple sites.

3.3.2 **Single site**: A site-specific CQMP developed by a site and its subcontractor(s) (as applicable) conducting a single protocol or multiple protocols

For additional definitions, see DMID glossary.

4. RESPONSIBILITIES

4.1 The Clinical Project Manager (CPM): facilitates requests for DMID-Clinical Research Operations and Management Support (CROMS) Clinical Quality Management (CQM) service, as applicable. The CPM communicates the DMID CQMP requirement, training, and tools to the Principal Investigator (PI) and their respective site investigators or site management organizations.

4.2 The DMID program official (Contracting Officer's Representative [COR]/ Program Officer [PO]): Responsible for award management of the clinical site, or their delegate, and works with DMID representatives to determine which type of CQMP is necessary for a site or protocol.

4.3 DMID-CROMS Clinical Quality Management (CQM) Team: Includes members with expertise in quality systems who provide operational support and sample CQMP guidance to the sites, review and acceptance of site or protocol-specific CQMPs, review of findings from clinical site quality management activities as applicable and ensure accepted CQMPs are in the DMID files.

4.4 OCRA Nurse Consultants for Clinical Quality Management (NC CQM): DMID point of contact for clinical research site quality management and member of the DMID-CROMS CQM Team. The NC CQMs provide oversight to the CROMS CQM Team and CROMS on-site consultative support and provide guidance for site CQM staff as necessary. The NC CQM ensures the review and acceptance of CQMPs according to DMID policies.

4.5 Program Officer (PO): Oversees a scientific program and research grants portfolio and ensures that grantees establish a plan for clinical site quality management.

5. PROCEDURE

5.1 Establishing the need for a CQMP

5.1.1 For contracts and cooperative agreements, DMID requires sites/PIs to proactively submit CQMPs for review and acceptance as described in the DMID policy.

5.1.2 For grants, the PO may request a copy of a CQMP for review or may request an alternate method of site quality management (e.g., Quality Assurance Surveillance Plan, laboratory quality documentation, or quality management checklist) to meet the grant requirements.

- If the CQMP is not required, comparable documentation of the QC/QA plan or activities of a site would be maintained by the Branch/Office according to grant requirements.

5.2 Initiation of a CQMP or alternative agreement for quality management

5.2.1 The appropriate DMID representative, CPM or COR/PO assigned, will notify the PI of the requirement for CQMP development, implementation, and evaluation as necessary.

5.2.2 The CPM or COR/PO or site staff will notify the OCRA NC CQM via email to CQMP@dmidcroms.com regarding when a CQMP is requested to be reviewed and accepted by DMID.

5.2.3 When the OCRA NC CQM receives a CQMP for review without prior CPM or COR/PO notification, the OCRA NC CQM will assess, in consultation with CPM and COR/PO, the need for a review of the plan.

5.3 CQMP Basic Requirements

5.3.1 The CQMP must include at a minimum the planned QC and QA activities that will be performed, the frequency, the information that will be reviewed, and the responsible parties.

5.3.2 The CQMP will describe an overall process for identifying deviations, summarizing and reporting trends or issues, the corrective and preventive actions taken, and evaluating the effectiveness of actions.

5.3.3 Formalized tools should be utilized to document the reviews and summaries.

5.3.4 It is recommended that the DMID CQMP templates and tools be utilized; however, alternative equivalent documentation may be acceptable as determined by the appropriate DMID representative.

5.4 Initial CQMP Submission

5.4.1 If a CQMP is required, the CPM or COR/PO or site will submit the CQMP with any associated documents (e.g., QA/QC tools or checklists) as Word Documents. The applicable version of the protocol is needed (protocol-specific CQMPs only) for review/acceptance via email to the OCRA NC CQM and the CQMP team, at CQMP@dmidcroms.com as a Word document.

5.4.2 The DMID-CROMS CQMP Team will generate a confirmation of receipt email within 2 business days.

5.4.3 The DMID-CROMS CQMP Team will review the submitted plan with any associated documents (e.g., QA/QC tools or checklists) including the applicable version of the protocol (protocol-specific CQMPs only) and provide any feedback to the DMID NC CQM within 7 business days of receipt.

5.4.4 The OCRA NC CQM will review the DMID-CROMS CQMP Team comments along with the submitted CQMP and associated documents within 10 business days of receipt.

5.5 Review and Acceptance

5.5.1 Once the CQMP review has been completed, the OCRA NC CQM will submit any review comments or recommendations to the CPM, COR/PO, or requestor.

5.5.2 Once all agreed-upon modifications have been made, the OCRA NC CQM will email acceptance of the CQMP (version and date) and any associated documents (i.e., QMP QA tools) to the CPM, COR/PO, and site representative(s)/requestor.

5.6 Tracking and Posting the CQMP

5.6.1 For CQMPs reviewed by DMID-CROMS:

- Once accepted, the Branch CPM or site will submit the signed CQMP with any associated documents (e.g., QA/QC tools, checklists) in PDF format via email to CQMP@dmidcroms.com.
- The signed CQMP will be posted electronically in the DMID-CROMS CQMP Team Document Library and tracked by version and date according to DMID-CROMS Clinical Quality Management (CQM) Team processes.

5.6.2 For CQMPs or alternate documentation of quality management activities (e.g. QA/QC checklists) not reviewed by DMID-CROMS CQMP Team:

- The final documentation of quality activities at a site (e.g., Quality Assurance Surveillance Plan, laboratory quality documentation, or quality management checklist) in PDF format will be sent to CQMP@dmidcroms.com (DMID-CROMS CQMP Team) by the site.
- The date of the plan or agreement will be tracked for studies that are monitored on behalf of DMID for verification by a monitor.
- The final document will be uploaded to the DMID-CROMS Document Library by protocol number, and where applicable, by site and document category (e.g., Quality Management).

5.7 Revisions to the CQMP

5.7.1 Clinical site staff must review the CQMP at a minimum annually to ensure CQM processes are adequate, and the review is internally documented. Revisions to the plan should be made if issues have been identified in the previous calendar year.

5.7.2 For revisions to the CQMP that would impact the effectiveness of the quality management processes (e.g., frequency of reviews or changes to the information reviewed), a review of these changes by the DMID-CROMS CQMP Team will occur.

- Sites should submit the modified CQMP via email as a Word document in Track Changes mode.
- The email message should request a review for revisions that are more than administrative.

5.7.3 For administrative changes only to a CQMP, a formal review by the DMID-CROMS Clinical Quality Management (CQM) Team will not be conducted.

- Sites should send the revised CQMP via email as a signed PDF.
- The email message should state the changes were administrative and list the administrative changes made.
- The administrative change acceptance will be acknowledged via email by the DMID-CROMS Clinical Quality Management (CQM) Team.

5.7.4 Once accepted, the COR/PO, CPM, or site will submit the signed CQMP with any associated documents (e.g., QA/QC tools, checklists) in PDF format via email to CQMP@dmidcroms.com.

5.7.5 The signed CQMP will be posted electronically in the DMID-CROMS Document Library and tracked by version and date according to DMID-CROMS Clinical Quality Management (CQM) Team processes.

6. REFERENCES

6.1 DMID-SM-POL-00005 Clinical Quality Management in Clinical Research

6.2 United States Food and Drug Administration (FDA) Code of Federal Regulations (CFR) Title 21

6.2.1 21 CFR Part 50: Protection of Human Subjects

6.2.2 21 CFR Part 56: Institutional Review Boards

6.2.3 21 CFR Part 312: Investigational New Drug Application

6.2.4 21 CFR Part 812: Investigational Device Exemptions

6.3 European Medicine Agency (EMA) Guidelines

6.3.1 ICH E6(R2): Good Clinical Practice

6.3.2 ICH E8: General Considerations for Clinical Trials

6.3.3 EMA/INS/GCP/856758/2018: Guideline on GCP Compliance

6.3.4 EMA/CHMP/ICH/135/1995: Guideline on the Responsibilities of the Sponsor

6.4 National Institute of Health (NIH) Grants Policy Statement (NIHGPS)

6.4.1 Part II: Terms and Conditions of NIH Grant Awards

6.4.2 Part III: Financial and Administrative Requirements

6.4.3 Part IV: Public Policy Requirements and Objectives

6.5 FDA Guidance Documents

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

6.5.2 FDA Guidance for Industry: Oversight of Clinical Investigations — A Risk-Based Approach to Monitoring

6.5.3 FDA Compliance Program Guidance Manual: Inspection of Clinical Investigators

6.6 The International Council for Harmonisation ICH E6(R2) Good Clinical Practice

6.6.1 Section 2: Principles of ICH GCP

6.6.2 Section 4: Investigator Responsibilities

6.6.3 Section 5: Sponsor Responsibilities

7. APPENDICES

7.1 N/A

8. REVISION HISTORY

8.1 DMID-SM-SOP-00009 is the original version of this procedure within the eQMS.

9. ADDITIONAL INFORMATION

9.1 Document Lead: Office of Clinical and Regulatory Affairs (OCRA)

9.2 Posting externally: Yes