

Quality Control and Quality Assurance

DMID/ICSSC

10-07-08

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Quality Control and Quality Assurance

Quality Control (QC)

- ◆ Daily, ongoing, “real time” review of site’s work processes to ensure that procedures are being followed

Example:

- ◆ QC is performed on 100% of CRFs prior to entry into the database

Quality Control and Quality Assurance

Quality Assurance (QA)

- ◆ A periodic, planned, objective review of research related activities to ensure compliance with GCP and other regulatory requirements

Example:

A monthly review of source documents and CRFs to ensure agreement

Quality Control and Quality Assurance

◆ Quality Management (QM)

- The overall process for assessing quality and encompasses both **quality control** and **quality assurance**

$$QM = QC + QA$$

Quality Control and Quality Assurance

ICH E6 5.1

Sponsor is responsible for quality

- ◆ Sponsor must implement and maintain QC and QA systems with written SOPs

So what systems has the sponsor got in place?

Quality Control and Quality Assurance

- ◆ Clinical Quality Management Plan Policy
- ◆ Clinical Quality Management Plan template
- ◆ Chart audit tool
- ◆ Regulatory file review tool
- ◆ Quality Management summary report tool
- ◆ Annual Clinical Quality Management Plan evaluation tool

Quality Control and Quality Assurance

Clinical Quality Management Plan

- A written document
- Details frequency and sample size of QA and QC activities; lists who is responsible

Clinical Quality Management Plan
Site Name, Location
Version #, Date

1. **RESPONSIBILITY AND DELEGATION**
2. **PROTOCOL IDENTIFICATION**
3. **DESCRIPTION OF QUALITY MANAGEMENT PROCESSES**
 - Quality Assurance (QA) – describe ongoing review activities that will be conducted as part of the QA process
 - Quality Control (QC) Activities - describe ongoing day-to-day activities that will be conducted as part of the QC process
4. **RECORD SELECTION** – describe method of record selection for QA review (minimum percentage and frequency of review)
5. **KEY QUALITY INDICATORS** – list key quality indicators that will be reviewed in each subject record selected, for example:
 - Informed Consent Form and Process
 - Eligibility Criteria
 - Protocol-specific Procedures
6. **REGULATORY FILE REVIEW** – activities that will be completed to ensure regulatory binder complete and up-to-date
7. **STAFF TRAINING AND COMPETENCY** – list specific training; documentation of which staff members attended each training
8. **QUALITY MANAGEMENT SUMMARY REPORTS** – describes how review findings will be summarized, analyzed and communicated to staff
9. **ANNUAL EVALUATION OF THE QUALITY MANAGEMENT PLAN**- process for completing annual review of CQMP for effectiveness

Signature of CQMP Developer Date: _____

Principal Investigator Signature Date: _____

Quality Control and Quality Assurance

Subject chart audit

Indicator	Criteria	Yes / No	Comments
Consent	Current, approved version of consent signed and dated?		
	Consent form signed and dated in ink by subject/ legally authorized representative prior to study procedures being performed?		
Missed visits	Has subject missed any visits? If yes, documented?		
AE/SAE reporting	AEs and SAEs recorded and reported properly?		
Documentation Standards	Source documentation complete and accurate?		
	Does CRF data and source documentation data match?		
	Are handwritten chart notes legible, signed & dated by clinician?		
	Errors corrected: single line, initialed, dated, reason?		

Quality Control and Quality Assurance

Regulatory file review

Document	Criteria	Yes / No	Comments
IRB/EC approval	Initial IRB/EC approval letter present?		
Protocol	Current IRB-approved version of protocol on file?		
ICF	Current IRB-approved ICF on file?		
Sample CRF	Sample copy of CRF on file?		
CVs	Are CVs on file for investigators?		
Laboratory	Are normal ranges for protocol-required tests on file?		

Quality Control and Quality Assurance

Summary Reports

- ◆ Summarize findings of QC and QA reviews
- ◆ Share reports with PI and other site staff – share areas for improvements, trends, etc

Annual evaluation of CQMP

- ◆ By PI and other site staff
- ◆ CQMP modified to increase effectiveness

National Institute of Allergy and Infectious Diseases / Division of Microbiology and Infectious Diseases	Policy Clinical Quality Management Plan	No.: DMID.OP.QMP001
	Approved: March 23, 2009 Effective Date: April 1, 2009	Version: 3.0

1.0 **Purpose**

The purpose of this policy is to describe the requirements for the development, implementation and evaluation of a Clinical Quality Management Plan (CQMP) for sites conducting Division of Microbiology and Infectious Diseases (DMID)-supported clinical research.

This policy lists *basic requirements* necessary for sites to comply with applicable federal and state regulations including protections of human subjects, [International Conference on Harmonization \(ICH\) E6 Good Clinical Practice](#) (GCP) guidance, the National Institute of Allergies and Infectious Diseases (NIAID) [Clinical Research Standards](#), and [NIAID Clinical Terms of Award](#).

2.0 **Scope**

This policy and applicable procedures apply to clinical research sites conducting DMID-supported clinical research.

DMID may request a copy of a site or protocol-specific CQMP for review and acceptance. For many sites, written agreements with DMID require sites / principal investigators to proactively submit clinical quality management plans for review and acceptance by DMID. For other sites, DMID may request a copy of a site or protocol-specific CQMP for review and acceptance, as DMID deems appropriate.

DMID reserves the right to review site CQMP findings.

3.0 **Background**

The CQMP policy describes elements to assist sites, conducting DMID-supported clinical research, with developing, implementing and evaluating such a plan. The CQMP should be easy to implement and serve as an on-site management tool to *internally* evaluate and document site performance of the protocol procedures, enable site staff to ensure that the rights and safety of human subjects are protected, and verify the data collected are accurate and complete throughout the implementation of the protocol. DMID makes available through the NIAID public website adaptable sample quality management plan templates and tools to meet the specific site/protocol needs. (<http://www3.niaid.nih.gov/research/resources/DMIDClinRsrch/quality.htm>)

Quality Management (QM) is an overall system of oversight to document and track site performance of DMID-supported clinical research. The QM activities facilitate planning for effective protocol implementation, ensure compliance with DMID requirements, identify areas in need of corrective action, verify the accuracy of data, and promote a constant state of readiness for an external audit or clinical monitoring visit.

The QM system includes Quality Control (QC) and Quality Assurance (QA). The focus is to provide site staff with the means to proactively identify and resolve problems with protocol implementation and regulatory compliance, *in the early stages*.

4.0 **Definitions**

- **Clinical Research**: Per the [NIAID definition](#), patient-oriented research, including epidemiologic and behavioral studies, outcomes research, and health services research; research on mechanisms of human disease, therapeutic interventions, clinical trials, and development of new technologies, not including in-vitro studies using human tissues not linked to a living individual.

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- **Clinical Quality Management Plan (CQMP):** A clinical quality management plan is a written document that encompasses both quality assurance and quality control procedures and details the responsibility, scope, and frequency of these activities. A CQMP is designed to assess the site performance of clinical research.
- **Corrective Action Plan (CAP):** A corrective action plan is a written document that details the implementation of actions taken to detect and eliminate the cause of an area of non-compliance, and prevents reoccurrence of non-compliance.
- **Key Quality Indicator (KQI):** Key quality indicators are selected performance areas and activities that are vital to compliance with accepted standards of performance. For example, verify for eligibility and proper implementation of the informed consent process.
- **Quality Assurance (QA):** Quality assurance is the periodic, systematic, objective and comprehensive examination of the total work effort to determine the level of compliance with accepted Good Clinical Practice standards. For example, a monthly review of source documents compared to case report form (CRF) pages determine adherence to protocol requirements.
- **Quality Audit:** An evaluative process for determining the compliance and/or effectiveness of a process or system. A quality audit is a positive and constructive process intended to identify the activities apt to create problems.
- **Quality Control (QC):** Quality control is the real time (“day-to-day”) observation and documentation of the site’s work processes to ensure that accepted procedures are followed. For example, review of demographic information for accuracy on each case report form (CRF) prior to entry into a database.
- **Quality Management (QM):** Quality management is the overall system that includes all activities involved in Quality Assurance and Quality Control, including the assignment of roles and responsibilities, the reporting of results, and the resolution of issues identified during the review.
- **Root Cause Analysis:** The process for identifying the most basic or causal factor(s) of a problem, inadequate performance, or an obstacle to improvement exists.
- **Sample Size:** Sample size is the quantitative selection of items or units (records) from a total population for review.

5.0 Responsibilities

Role	Responsibility
Division of Microbiology and Infectious Diseases (DMID)	<ul style="list-style-type: none"> • Notifies Principal Investigators of their responsibility for CQMP development, implementation and evaluation. • Reviews <i>findings</i> from CQMP activities, as applicable.
Clinical Research Site Principal Investigator (PI), or designee Clinical Research staff	<ul style="list-style-type: none"> • Develops, implements and evaluates the CQMP. • Conducts internal quality management activities, including corrective and preventive actions. • Provides a written CQMP to DMID, upon request. • Reviews CQMP, annually. • Submits revisions to DMID for review and acceptance as appropriate or requested.
Office of Clinical Research Affairs (OCRA)	<ul style="list-style-type: none"> • Reviews and accepts site/protocol-specific CQMP for

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	protocols with an assigned Medical Monitor.
DMID Clinical Trials Management contractor	<ul style="list-style-type: none"> Assists DMID with review of and recommendations for CQMP plans submitted by DMID-supported clinical research sites.

6.0 **Policy Implementation**

DMID requires clinical research sites to develop, implement, and evaluate a CQMP.

6.1 **Clinical Quality Management Plan Basic Requirements**

6.1.1 **Plan Type: Site or Protocol Identification**

6.1.1.1 Include Site name

6.1.1.2 Include protocol title and number (if protocol-specific plan)

6.1.1.2.1 [Version control](#): include version number and/or date to correspond with a specific CQMP and associated tools.

6.1.2 **Responsibility**

6.1.2.1 Name the person(s) responsible for the development, implementation, and evaluation of the CQMP.

6.1.3 **Quality Management Process Description** – The CQMP describes the quality assurance and quality control activities conducted at the site or per the protocol. [Sample quality management tools](#) are provided by DMID and available for use.

6.1.3.1 **Quality Assurance (QA)** – The quality assurance process determines the type and accuracy of the data reviewed by assessment of the key quality indicators (Section 6.1.4).

6.1.3.2 **Quality Control (QC)** – The quality control activity is an ongoing day-to-day review of 100% of all data collection forms for completeness, accuracy and logic.

6.1.3.3 **Record Selection** – The clinical research site determines when reviews occur and the minimum percentage of records to be reviewed based on, but not limited to new protocols, initial enrollment, protocols involving study product and/or a procedure, and new clinical research staff. Records include, but are not limited to, case report forms (paper and electronic CRFs), clinical laboratory reports, specimen logs, clinic notes, subject charts, and other source documents.

6.1.4 **Key Quality Indicators** – The following key quality indicators, as applicable, could be audited in each subject record selected for review. A [Sample Chart Audit Tool](#) is provided by DMID and available for use.

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- 6.1.4.1 Informed consent form and process
- 6.1.4.2 Eligibility criteria
- 6.1.4.3 Study product preparation, administration, and accountability. The CQMP describes the periodic QM activities that are performed in accordance with the ICH Guidelines for Good Clinical Practice; E6, Section 4.6 Investigational Product(s), and applicable regulatory requirements, addressing study product accountability, management and protection of human subjects. Blind for study product must be maintained during internal review of these documents and systems. Study product review activities may include, as applicable, but are not limited to the following:
 - 6.1.4.3.1 Review and comparison of the study product accountability logs, shipping records, and the study product inventory
 - 6.1.4.3.2 Randomization code list and decoding procedures
 - 6.1.4.3.3 Study product storage, handling, and labeling procedures
 - 6.1.4.3.4 Vaccine or other study product preparation procedures
 - 6.1.4.3.5 Study product administration processes
- 6.1.4.4 AE/SAE identification and reporting
- 6.1.4.5 Protocol Visits
- 6.1.4.6 Protocol-specific procedures
- 6.1.4.7 Intervention/study discontinuation
- 6.1.4.8 Reactogenicity
- 6.1.4.9 Specimens (processing, storage, documentation)
- 6.1.4.10 Other protocol-specific indicators, as determined by the site staff.

6.1.5 **Regulatory File Review** – Regulatory file review is performed, once during the active study period, or annually. A sample [Regulatory File Review Tool](#) is provided by DMID and available for use.

6.1.6 **Tools, Checklists, and Reminders** – The CQMP describes the types of tools, checklists, and reminders used during the QM process. Examples may include, but are not limited to, the following:

- 6.1.6.1 Internal (site) sources:
 - 6.1.6.1.1 Visit reminder checklists, chart audit worksheets/tools ([Sample Chart Audit Tool](#))
 - 6.1.6.1.2 Regulatory File Review Tool ([Sample Regulatory File Review Tool](#))
 - 6.1.6.1.3 Summary Reports from Internal QA/QC Findings ([Sample Quality Management Summary Report Tool](#))
- 6.1.6.2 External sources:
 - 6.1.6.2.1 Data Entry, query/error, or transmission Reports from the Data Management Center

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6.1.6.2.2 Clinical Site Monitoring Reports

6.1.6.3 Other QA/QC Forms

6.1.7 **Staff Training/Qualifications** – The CQMP describes the processes for ensuring and documenting qualified personnel. Examples may include, but are not limited to the following:

- 6.1.7.1 Institution-Specific Training (i.e., Human Subjects Protection, Phlebotomy, Dangerous Goods Regulations, research staff training, applicable site policies/procedures)
- 6.1.7.2 Protocol-Specific Training (i.e., specimen handling/processing, study product, data management)
- 6.1.7.3 DMID-Specific Training
 - 6.1.7.3.1 Human Subjects Protection Training (Required)
 - 6.1.7.3.2 Good Clinical Practice Training (Recommended)
 - 6.1.7.3.3 DMID Regulatory File Document Guidelines
 - 6.1.7.3.4 DMID Source Documentation Guidelines

6.1.8 **Quality Management Summary Reports** – The CQMP describes how findings are summarized, analyzed, and communicated to the staff. A sample [Quality Management Summary Report](#) tool is available for use. The basic elements of the Summary Report include, but are not limited to, the following:

- 6.1.8.1 Staff participation in audits
- 6.1.8.2 Identification of problem areas
- 6.1.8.3 Trend analysis
- 6.1.8.4 Corrective action plan(s)
- 6.1.8.5 Possible need for revision to CQMP

6.2 CQMP Submission, Review, and Acceptance – Overview

6.2.1 Submission:

- 6.2.1.1 DMID or its designee may request the PI or their designee to submit a protocol-specific or site CQMP. The CQMP must address the applicable DMID basic requirements as described above. (See Scope, Section 2.0)
- 6.2.1.2 DMID will query organizations, which provide structure to multiple sites, to submit their CQMP.

6.2.2 Review:

- 6.2.2.1 CQMPs requested by DMID are reviewed against the DMID basic requirements outlined in this policy. This responsibility may be delegated to the DMID Clinical Trials Management (CTM) contractor.
- 6.2.2.2 DMID will communicate review findings and recommendations to the PI/designee via email within fourteen (14) calendar days.

6.2.3 Acceptance:

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6.2.3.1 As applicable (see *Review 6.2.2.1*), following resolution of the CQMP review, DMID will provide to the PI/designee a written notification accepting the CQMP.

6.3 Site Evaluation of the Clinical Quality Management Plan

6.3.1 DMID recommends the PI/designee document, in the CQMP, plans for evaluating the effectiveness of the CQMP annually, at a minimum. If the CQMP is modified to increase the effectiveness, the submission process is reactivated (See Scope, section 2.0).

7.0 References

7.1 [International Conference on Harmonization \(official website\)](#)

7.1.1 [Guidelines for Good Clinical Practice \(GCP\) E6 \(R1\)](#)

7.2 Office for Human Research Protections

7.2.1 [Code of Federal Regulations 45 Public Welfare, Department of Health and Human Services Part 46 Protection of Human Subjects](#)

7.2.2 [Code of Federal Regulations, Title 21 \(applicable parts 11, 50, 54, 56, 312, 812\)](#)

7.3 Division of Microbiology and Infectious Disease

7.3.1 [Regulatory File Guidelines](#)

7.3.2 [Source Documentation Standards](#)

7.3.3 [Quality Management Policy, Tools and Guidance](#)

8.0 Inquiries

Questions or comments regarding this policy may be directed to:

Claudia Baxter, RN, BSN

Nurse Consultant

NIH / NIAID

Division of Microbiology and Infectious Diseases (DMID)

Office of Clinical Research Affairs (OCRA)

Bethesda, MD 20892

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9.0 Availability

This policy, guidance and sample tools are available electronically:

NIAID Internet/DMID/Policies and Procedures

<http://www3.niaid.nih.gov/research/resources/DMIDClinRsrch/quality.htm>

DMID Clinical Trials Management contractor (PPD)

<http://www.dmidctm.com/partners/SectionQualityManagement/PageSOPs/SOPs.htm>

An original signed approval is located within the OCRA Clinical Trials Management Section (CTMS)

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office.

10. Change Summary

Version Number:	Date of Revision: DD/MMM/YYYY	Replaces:	Effective Date: DD/MMM/YYYY	Description of Revision/Retirement:	Revision Initiated by:
1.0	N/A	N/A	14-Jan-2008	N/A	N/A
2.0	18/AUG/2008	1.0	1-Sept-2008	Update links, clarify purpose, workflow, administrative corrections	DMID Policy Development Team
3.0	23/FEB/2009	2.0	1-Apr-2009	Add KQI, clarifying language; sample tools revised	DMID Policy Development Team

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Template: \\niaid-fas2.niaid.nih.gov\citrix-folders\mbooth\Application
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DMID CLINICAL QUALITY MANAGEMENT PLAN FACT SHEET

Objective

Sites conducting DMID-supported clinical research must have a written Clinical Quality Management Plan (CQMP) which complies with the current [DMID Clinical Quality Management Plan Policy](http://www3.niaid.nih.gov/research/resources/DMIDClinRsrch/quality.htm), available on the NIAID public website, www3.niaid.nih.gov/research/resources/DMIDClinRsrch/quality.htm

Instructions for submission, review and acceptance, are provided, below. *Note: If your current CQMP is dated prior to January 15, 2008, confirm with the DMID Clinical Project Manager (CPM) or Program/Project Officer that the CQMP is both consistent with the research study being conducted and meets the DMID policy requirements.*

Definitions

Quality Management (QM):	The overall system that includes all activities involved in quality assurance and quality control, including the assignment of roles and responsibilities, the reporting of results, and the resolution of issues identified during the review.
Quality Assurance (QA):	The periodic, systematic, objective, and comprehensive examination of the total work effort to determine the level of compliance with Good Clinical Practice (GCP) standards.
Quality Control (QC):	The real time ("day-to-day") observation and documentation of the sites work processes to ensure that accepted procedures are followed.
Clinical Quality Management Plan (CQMP):	A written document that encompasses both Quality Assurance and Quality Control procedures and details the responsibility, scope, and frequency of these activities.

Clinical Quality Management Plan Policy Training Module

The DMID CQMP Policy training module, located on the DMID-CTM Partners site, (select the Quality Management menu option and then the Training option) has been designed to provide:

- Policy Review
- Comprehensive instruction in CQMP development for sites conducting DMID-supported clinical research
- On-demand access to clinical research resources referenced throughout the training

www.dmidgetm.com/partners/SectionTrainingResources/PageSelfGuidedTraining/QM_Captivate/home.htm

Clinical Quality Management Plan – Development

The DMID Clinical Quality Management Plan Policy, Sample Tools, and guidance listed below are available on the NIAID public website, www3.niaid.nih.gov/research/resources/DMIDClinRsrch/quality.htm

- DMID Clinical Quality Management Plan Policy
- DMID Clinical Quality Management Plan Fact Sheet
- Sample Chart Review Tool
- Sample Regulatory File Review Tool
- Sample Quality Management Summary Report
- Sample Clinical Quality Management Plan (Instructional Template)

The following are the basic components of a CQMP that are required by the [DMID CQMP Policy](#):

- Plan Type: Site and Protocol Identification
- Responsibility
- Quality Management Process Descriptions (QA/QC and Record Selection)
- Key Quality Indicators
- Regulatory File Review Tools, Checklists, and Reminders
- Staff Training and Competency
- Quality Management Summary Reports
- Annual Evaluation of CQMP

Clinical Quality Management Plan - Submission, Review, and Acceptance

- **Submission:** For many sites, written agreements with DMID require sites / principal investigators to proactively submit clinical quality management plans for review and acceptance by DMID. For other sites, DMID may request a copy of a site or protocol-specific CQMP for review and acceptance, as DMID deems appropriate. Submit the site or protocol-specific CQMP electronically to DMID_QMP_Reviewers@lists.ppd.com.
- **Review:** CQMPs requested by DMID are reviewed against the DMID basic requirements outlined in this policy. This responsibility may be delegated to the DMID Clinical Trials Management (CTM) contractor.
- **Acceptance:** Following resolution of the CQMP review, DMID will provide a written notification of acceptance to the PI/designee.

Questions?

Regarding your specific CQMP, or questions about access to the DMID-CTM website, contact the DMID Clinical Project Manager, Project/Program Officer assigned to your protocol.

For questions about the policy, tools and guidance, contact Claudia Baxter, baxterc@niaid.nih.gov

DMID SAMPLE CLINICAL QUALITY MANAGEMENT PLAN INSTRUCTIONAL TEMPLATE INSTRUCTIONS

This sample Clinical Quality Management Plan (CQMP) Instructional Template has been developed in Microsoft Word as a sample that may be adapted, as needed, to develop a CQMP. This sample CQMP Instructional Template reflects the basic requirements outlined in the current DMID CQMP Policy.

1. Begin using this tool by completing the header information (name of site, version number and date).
2. Address each of the ten sections of the CQMP instructional template, modifying as necessary. The following tools are available to complement the CQMP development:
 - [DMID Sample Chart Audit Tool](#)
 - [DMID Sample Regulatory File Review Tool](#)
 - [DMID Sample Quality Management Summary Report Tool](#)
3. Submit the completed draft CQMP via email to the DMID Reviewers at DMID_QMP_Reviewers@lists.ppd.com for review against the basic requirements outlined in the current DMID CQMP Policy and other written agreements as applicable. In this correspondence also include appropriate DMID personnel.

**DMID SAMPLE CLINICAL QUALITY MANAGEMENT PLAN
(INSTRUCTIONAL TEMPLATE)**

<Replace DMID SAMPLE with Institution/Site Name>

<Insert Version # and Date of CQMP>

1.0 PROTOCOL IDENTIFICATION

1.1 Protocol Title and Number: *<Insert protocol title and number if a protocol-specific CQMP>*

2.0 RESPONSIBILITY

<Insert Title of Quality Assurance Designee> <Name> has been designated by principal investigator *<insert PI name>* to develop, implement, and oversee all functions of this quality management plan.
<Insert any other functional roles of site staff associated with the Quality Management Process>

3.0 QUALITY MANAGEMENT PROCESS DESCRIPTION

3.1 Quality Assurance (QA) Activities: *<Describe the ongoing review of activities that will be conducted at the site as part of the QA process>*

3.2 Quality Control (QC) Activities: *<Describe the ongoing, day-to-day activities that will be conducted at the site as part of the QC process>*

4.0 RECORD SELECTION

<Describe the methods of record selection for QA review including, but not limited to, the following minimum priorities: >

4.1 New Protocols: *<Insert minimum percentage and frequency of review for new protocols if a site-specific CQMP>*

4.2 Initial Enrollment: *<Insert minimum percentage and frequency of review>*

4.3 Protocols involving study product and/or a procedure: *<Insert minimum percentage and frequency of review>*

4.4 New Clinical Research Staff: *<Insert minimum percentage and frequency of review>*

4.5 *<Add any additional methods of record selection>*

5.0 KEY QUALITY INDICATORS

<List the Key Quality Indicators that will be audited in each subject record selected for internal QA review>

5.1 Informed Consent Form and Process

5.2 Eligibility Criteria

5.3 Study Product Preparation, Administration, and Accountability (if applicable) *<Describe the following applicable components: >*

5.3.1 Review and comparison of the study product accountability logs, shipping records, and the study product inventory

5.3.2 Randomization code list and decoding procedures

5.3.3 Study product storage, handling, and labeling procedures

5.3.4 Vaccine or other study product preparation procedures

5.3.5 Study product administration processes

5.4 AE/SAE Identification and Reporting

5.5 Protocol Visits *<evaluate for missed visits, out of window visits, lost to follow-up, etc.>*

5.6 Protocol-specific Procedures (all inclusive)

5.7 Intervention/Study Discontinuation

5.8 Reactogenicity (if applicable)

5.9 Specimens *<Describe the following components: >*

5.9.1 Processing

- 5.9.2 Storage
- 5.9.3 Documentation
- 5.10 <Add any additional protocol-specific indicators>

6.0 REGULATORY FILE REVIEW

<Describe the QM activities that will be completed on the Regulatory File, ensuring the file is complete and up to date>

- 6.1 Frequency of Review: *<Insert how often the Regulatory File will be reviewed>*
- 6.2 Regulatory File Review Tool: *<Insert name and location of tool to be used for regulatory review>*
- 6.3 <Add any additional regulatory QA activities>

7.0 TOOLS, CHECKLISTS, AND REMINDERS

<Describe the tools, checklists, and reminders that will be used in the QM process. Examples include, but are not limited to the following: >

- 7.1 Internal (site) Sources: *<Visit Reminder Checklists, Chart Audit Worksheets, Regulatory File Review Tool, Summary Reports from Internal QA/QC Findings>*
- 7.2 External Sources: *<Data Entry, Query/Error, or Transmission Reports from the Data Management Center, Clinical Site Monitoring Reports>*
- 7.3 <Add any additional tools/forms>

8.0 STAFF TRAINING / QUALIFICATIONS

<Describe the site processes for ensuring and documenting qualified staff and competency>

- 8.1 Institution-specific Training: *<List specific trainings, i.e., Human Subjects Protection, Phlebotomy, Dangerous Goods Regulations, research staff training, applicable site policies/procedures, etc.>*
- 8.2 Protocol-specific Training: *<List specific trainings, i.e., specimen handling/processing, study product, data management, etc.>*
- 8.3 DMID-specific Training: *<List specific trainings, i.e., Human Subjects Protection, Good Clinical Practice, DMID Regulatory File Document Guidelines, DMID Source Documentation Guidelines>*
- 8.4 <Add any additional training>

9.0 QUALITY MANAGEMENT SUMMARY REPORTS

<Describe how the results of the internal assessments will be summarized, analyzed, and communicated to the staff. Include the following information within the summary reports: >

- 9.1 Staff Participation in Audits
- 9.2 Identification of Problem Areas
- 9.3 Trend Analysis
- 9.4 Corrective Action Plan(s)
- 9.5 Possible Need for Revision to CQMP

10.0 SITE EVALUATION OF THE CLINICAL QUALITY MANAGEMENT PLAN

<Describe the process for completing the annual internal review of the CQMP for effectiveness>

- 10.1 CQMP Review: *<Insert time frame for CQMP review; the minimum is annually depending on the length of study>*

Signature of CQMP Developer

Date

Signature of Principal Investigator

Date

DMID SAMPLE REGULATORY FILE REVIEW TOOL INSTRUCTIONS

This sample Regulatory File Review Tool is derived from the DMID Regulatory File Guidelines and the International Conference on Harmonisation Guidelines for Good Clinical Practice (ICH GCP). This tool has been developed in Microsoft Word as a sample that may be adapted, as needed, to reflect protocol and regulatory requirements. This tool is recommended for the internal review of the regulatory files for each individual protocol conducted at the site. The review of the regulatory file should be completed at a minimum of *once* during the active study period *or annually* if the study is long term.

For each protocol reviewed:

1. Begin using this tool by completing the header information (name of site, name of reviewer, date of review, and the protocol number) for the protocol being reviewed. For each section reviewed, check the appropriate boxes ('N/A', 'Yes', or 'No'). If the 'No' box is checked for any question, provide a description for each 'No' response in the area provided within that section.
2. At the conclusion of the review, summarize findings in the Summary of Findings section.
3. The Quality Assurance reviewer signs and dates the Regulatory File Review Tool and files it within the sites Quality Management binder.
4. Follow your site/protocol-specific Clinical Quality Management Plan regarding communication and resolution of findings from internal reviews.

References:

OHRP Code of Federal Regulations Title 45 Part 46:
www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm

ICH Guideline for Good Clinical Practice E6 (Section 8):
www.ich.org/LOB/media/MEDIA482.pdf

U.S. Food and Drug Administration, Title 21 Part 312, Investigational New Drug:
www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcr/CFRSearch.cfm?CFRPart=312

U.S. Food and Drug Administration, Title 21 Part 812, Investigational Device Exemptions:
www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcr/CFRSearch.cfm?CFRPart=812

DMID Clinical Research Resources - Regulatory File Document Guidelines:
www3.niaid.nih.gov/research/resources/DMIDClinRsrch/PDF/regulatoryfiledocumentguidelines.pdf

DMID Clinical Quality Management Plan Policy:
www.dmidctm.com/partners/SectionQualityManagement/PageSOPs/SOPs.htm

DMID SAMPLE REGULATORY FILE REVIEW TOOL

<Replace DMID SAMPLE with Institution/Site Name>

Reviewer: *<Name of person reviewing chart>*

Review Date: *<Date of chart review>*

Protocol Number: *<DMID Protocol Number>*

Form FDA 1572 / Investigator of Record (IOR) Agreement			
1.	Is a Form FDA 1572 (for IND studies) or an IOR (for non-IND studies) on file?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2.	Is the agreement current and accurate?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3.	Does the agreement include a hand written signature and date by the Principal Investigator?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
For each no response, provide a description:			

Study Personnel Signature / Responsibility List			
1.	Does the Study Personnel Signature / Responsibility List contain all study personnel, including those who are making entries or corrections on the case report forms, as well as all ancillary study personnel?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2.	Does the Study Personnel Signature / Responsibility List contain the name, title, signature, initials, delegated tasks, phone number, e-mail address, start date, and end date for each study staff member listed?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
For each no response, provide a description:			

Protocol			
1.	Is a current and valid copy of the IRB-approved protocol on file? Version #: _____ Date: _____	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2.	Are all previous versions of the protocol on file?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3.	For protocols with a Protocol Signature Page, is it complete, signed, and dated by the Principal Investigator?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
4.	For multi-center studies, is the Protocol Signature Page from the site Principal Investigator on file?	<input type="checkbox"/> N/A	<input type="checkbox"/> Yes <input type="checkbox"/> No
For each no response, provide a description:			

Informed Consent Form(s) (ICFs)			
1.	Is a current and valid copy of the Informed Consent Form on file? Version #: _____ Date: _____	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2.	Are all previous versions of the Informed Consent Form on file?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3.	If applicable, are other consent forms (current and previous versions) on file? For example: assent forms, short forms, screening consents, or future use consents.	<input type="checkbox"/> Yes	<input type="checkbox"/> No
For each no response, provide a description:			

IRB/IEC Approvals and Final Reports				
1.	Does the file contain an up to date Regulatory Review History Form or IRB equivalent form? Note: Review site regulatory history against IRB regulatory history.	<input type="checkbox"/> N/A	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2.	Is the initial IRB/IEC approval for the protocol and the ICF present? Date: _____ Are all IRB/IEC approvals on file for advertisements, recruitment/telephone scripts, and participant information materials?		<input type="checkbox"/> Yes	<input type="checkbox"/> No
4.	If applicable, are subsequent approvals present? Include Continuing / Annual Reviews, and amendments.	<input type="checkbox"/> N/A	<input type="checkbox"/> Yes	<input type="checkbox"/> No
5.	Do the IRB/IEC approval letters include the full protocol title and list all study documents (identified with version number/date) that were reviewed?		<input type="checkbox"/> Yes	<input type="checkbox"/> No
6.	Does the IRB/IEC documentation include the date of approvals and/or duration of approval? Expiration date: _____		<input type="checkbox"/> Yes	<input type="checkbox"/> No
7.	If a lapse in IRB/IEC approval has occurred, is it documented properly? Note: A lapse in IRB/IEC approval requires IRB/IEC and DMID notification.	<input type="checkbox"/> N/A	<input type="checkbox"/> Yes	<input type="checkbox"/> No
8.	Are periodic reports to the IRB/IEC present? If not, where are they located?	<input type="checkbox"/> N/A	<input type="checkbox"/> Yes	<input type="checkbox"/> No
9.	If applicable, is the Final Report to the IRB/IEC present?	<input type="checkbox"/> N/A	<input type="checkbox"/> Yes	<input type="checkbox"/> No
10.	If applicable, is the Final Report to the sponsor present?	<input type="checkbox"/> N/A	<input type="checkbox"/> Yes	<input type="checkbox"/> No
For each no response, provide a description:				

IRB/IEC Composition			
1.	Is a current IRB/IEC Roster or Membership composition on file? If the IRB/IEC does not provide a roster, is a letter on file stating the names are not released and the IRB/IEC is in compliance with 45 CFR 46 regulations?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2.	If any site personnel are members of the IRB/IEC; is there documentation that the member absented from voting on this protocol?	<input type="checkbox"/> N/A	<input type="checkbox"/> Yes <input type="checkbox"/> No
For each no response, provide a description:			

Study-specific Procedures / Manual of Procedures			
1.	Does the file contain the current study-specific procedures or the Manual of Procedures (MOP) with version and date?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
For each no response, provide a description:			

Screening / Enrollment Log			
1.	Is the Screening/Enrollment Log present and current?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2.	For all ineligible subjects, is the reason for ineligibility documented on the Screening/Enrollment Log?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
For each no response, provide a description:			

ID Code List			
1.	Is the ID Code List present and up to date for all enrolled subjects?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2.	Is the ID Code List stored in a secure location separate from where source documents and personal identifiers are maintained? Include the location of the ID Code List in the regulatory file.	<input type="checkbox"/> Yes	<input type="checkbox"/> No
For each no response, provide a description:			

Study Product (Should be performed ONLY by unblinded personnel if study is blinded) <input type="checkbox"/> Not applicable			
1.	Is a sample study product label on file?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2.	Are the study product accountability records accurate, current, and on file? Do they agree with the actual inventory on hand?	<input type="checkbox"/> Yes	<input type="checkbox"/> No

3.	Are instructions (protocol-specific MOP) for the storage, mixing, and handling of study product easily accessible and on file?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
4.	Are shipping records for study product documenting the receipt date, quantity, and lot numbers of all study products on file?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
5.	Is the randomization list and decoding procedures for blinded study product on file?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
6.	Is disposition of used and unused study products captured on the accountability logs?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
7.	Are study product temperature logs on file? (includes receipt and storage)	<input type="checkbox"/> Yes	<input type="checkbox"/> No
For each no response, provide a description:			

Specimen Retention		<input type="checkbox"/> Not applicable	
1.	Are specimen retention records on file?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2.	Are research specimen temperature logs on file?		
2.	Are shipping documents accurate and complete? Note: Global Trace, EMMES Missing Specimens Report, Shipping Logs, Shipping Receipts, etc.	<input type="checkbox"/> Yes	<input type="checkbox"/> No
If no, provide a description of the issue(s):			

Serious Adverse Events (SAEs) / IND Safety Reports				
1.	Are all SAEs reported to the DMID and IRB/IEC present in the file?	<input type="checkbox"/> Yes	<input type="checkbox"/> No	
2.	Are IND Safety Reports/Memos for this protocol on file?	<input type="checkbox"/> N/A	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3.	Have these IND Safety Reports been submitted to the IRB/IEC?	<input type="checkbox"/> N/A	<input type="checkbox"/> Yes	<input type="checkbox"/> No
For each no response, provide a description:				

Protocol Deviations			
1.	Are all protocol deviations on file?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2.	Have all protocol deviations been submitted to DMID and IRB/IEC per their guidelines? Note: Protocol Deviation submission may be required by other organizations such as EMMES, PPD, etc.	<input type="checkbox"/> Yes	<input type="checkbox"/> No
For each no response, provide a description:			

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Investigator Brochures (IB) / Package Inserts		<input type="checkbox"/> Not applicable	
1.	Are IBs for investigational products present, current, and available? All versions should be present.	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2.	If applicable, are package inserts present, current, and available for approved drugs?	<input type="checkbox"/> N/A	<input type="checkbox"/> Yes <input type="checkbox"/> No
3.	Was the IB and/or package inserts submitted to the IRB?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
For each no response, provide a description:			

Laboratory Normals and Accreditations		<input type="checkbox"/> Not applicable	
1.	Are laboratory certifications and accreditations present for U.S. labs? (CAP and CLIA Accreditation, JCAHO, CLIA Compliance, CLIA exempt, etc.)	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2.	If not a U.S. lab, are other certificates of qualification for the lab on file? If no certification or qualification provided, is a statement included explaining the reason, and a description of the standard being used?	<input type="checkbox"/> N/A	<input type="checkbox"/> Yes <input type="checkbox"/> No
3.	Are Normal Ranges for all protocol-required tests on file? This must include all clinical laboratory tests required by the protocol, the unit of measure, the laboratory name, and the date of the document.	<input type="checkbox"/> N/A	<input type="checkbox"/> Yes <input type="checkbox"/> No
4.	Are approvals from collaborating Research Laboratories on file? Note: After initial IRB approval, should specimens be sent to collaborating laboratories, documentation of IRB approval needs to be on file.	<input type="checkbox"/> N/A	<input type="checkbox"/> Yes <input type="checkbox"/> No
For each no response, provide a description:			

Sample Case Report Forms			
1.	Are final (actually used) versions of the sample CRFs (including eCRFs, if applicable), subject diaries, or other forms used for entering data, on file?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
For each no response, provide a description:			

Curricula Vitae (CVs) and Medical Licenses			
1.	Are CVs present for the Principal Investigator and sub-investigators listed on the Form FDA 1572 / Investigator of Record (IOR)?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2.	Are the CVs current (within 5 years of the current date)?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3.	Are the medical licenses present and current for the Principal Investigator and sub-investigators listed on the Form FDA 1572 / IOR?	<input type="checkbox"/> Yes	<input type="checkbox"/> No

For each no response, provide a description:

Financial Disclosure (applicable for DMID IND studies only) Not applicable

1.	Are financial disclosure forms for all personnel listed in Section 1 and Section 6 of the Form FDA 1572 present on-site? Note: These forms should not be filed in the site's regulatory file, but in a separate location.	<input type="checkbox"/> Yes	<input type="checkbox"/> No
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For each no response, provide a description:

Federal Wide Assurances (FWA)

1.	Is the current FWA document from Office of Human Research Protections (OHRP) present? Is the expiration date present? Expiration Date: _____	<input type="checkbox"/> Yes	<input type="checkbox"/> No
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2.	Is the IRB/IEC approving this protocol registered with OHRP and linked with this FWA?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
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For each no response, provide a description:

Local and Foreign Regulatory Approvals

1.	Are all local, state, and/or special authorizations related to the protocol maintained and up to date? (related to Study Product, Special Populations, legally authorized representatives consenting)	<input type="checkbox"/> Yes	<input type="checkbox"/> No
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2.	If this is a non-U.S. site, is documentation of foreign regulatory body approval or clearance on file?	<input type="checkbox"/> N/A	<input type="checkbox"/> Yes	<input type="checkbox"/> No
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For each no response, provide a description:

Site Monitoring Log and Reports

1.	Are copies of Site Monitoring Logs and Site Monitoring Reports on file? (Assessment, Initiation, Interim Monitoring, Close-out)	<input type="checkbox"/> Yes	<input type="checkbox"/> No
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For each no response, provide a description:

Sponsor Correspondence

1.	Does the file contain all up-to-date correspondence between the site and sponsor?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
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DMID SAMPLE CHART AUDIT TOOL INSTRUCTIONS

This protocol-specific Chart Audit Tool is derived from the DMID Source Documentation Standards, the International Conference on Harmonisation Guidelines for Good Clinical Practice (ICH GCP), and the Code of Federal Regulations Title 45 Public Welfare Part 46 Protection of Human Subjects. This tool is used to document the review of Case Report Forms (CRF)/Electronic Case Report Forms (eCRF) for accuracy when compared to the source documents and protocol for agreement. Source documents are original documents/data/records (i.e. clinic charts/notes, checklists, lab reports, diagnostic reports, etc.) for each subject chart reviewed.

For each subject reviewed:

1. Begin using this tool by completing the header information (name of site, name of reviewer, date of review, subject number, protocol number, and review period). For each section reviewed, check the appropriate boxes ('N/A', 'Yes', 'No'). If the 'No' box is checked for any question, provide a description for each 'No' response in the area provided within that section.
2. At the conclusion of the review, summarize findings in the Summary of Findings section. These summaries are a useful reference when completing the Quality Management Summary Report. (See [DMID Sample Quality Management Summary Report Tool](#))
3. The Quality Assurance reviewer signs and dates the Chart Audit Tool and files it within the sites Quality Management binder.
4. Follow your site/protocol-specific Clinical Quality Management Plan regarding communication and resolution of findings from internal reviews.

Note: Other indicators or criteria may be added as determined by study documentation and site staff.

References:

OHRP Code of Federal Regulations Title 45 Part 46:
www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm

ICH Guideline for Good Clinical Practice E6 (Section 8):
www.ich.org/LOB/media/MEDIA482.pdf

DMID Clinical Research Resources – Source Documentation Standards:
www3.niaid.nih.gov/research/resources/DMIDClinRsrch/PDF/sourcedocumentationstandards.pdf

DMID Clinical Quality Management Plan Policy:
www.dmidctm.com/partners/SectionQualityManagement/PageSOPs/SOPs.htm

DMID SAMPLE CHART AUDIT TOOL
 <Replace DMID SAMPLE with Institution/Site Name>

Reviewer: <Name of person reviewing chart>

Review Date: <Date of chart review>

Subject Number: <Patient Identification Number>

Protocol Number: <DMID protocol number>

Reviewed Period: From Date <dd-mmm-yyyy> Through Date <dd-mmm-yyyy>

Informed Consent / Assent Form(s) and Process (See Code of Federal Regulations: 45 CFR 46 , Sections 46.116 and 46.117)			
1.	Enrollment: Was the IRB/IEC-approved version used to consent/assent the subject, valid at the time of signature? Version #: _____ Date: _____ Note: Review the regulatory file for IRB/IEC subsequent revisions/amendments to the consent forms.	<input type="checkbox"/>	<input type="checkbox"/>
		Yes	No
2.	Was the Informed Consent/Assent Form signed and dated in ink by the subject, parent/guardian and/or legally authorized representative prior to implementation of screening/protocol-specific procedures?	<input type="checkbox"/>	<input type="checkbox"/>
		Yes	No
3.	Amendments to consent: If applicable, are amended versions of the ICF signed and dated in ink by the subject, parent/guardian and/or legally authorized representative on file? Version #: _____ Date: _____	<input type="checkbox"/>	<input type="checkbox"/>
		N/A	Yes
			No
4.	Are all applicable Informed Consent/Assent Forms present in their entirety?	<input type="checkbox"/>	<input type="checkbox"/>
		Yes	No
4a.	Is documentation present describing the Informed Consent process with the subject, parent/guardian and/or legally authorized representative, including: 1. an explanation of the study, subject confidentiality ? 2. in a language they understands? 3. ample opportunity provided for questions? 4. copy of the ICF/Assent form provided to subject, parent/guardian and/or legally authorized representative,	<input type="checkbox"/>	<input type="checkbox"/>
		Yes	No
5.	IF APPLICABLE: Illiterate subject(s): Was the Informed Consent or short form written consent been provided orally to the subject, parent/guardian and/or legally authorized representative?	<input type="checkbox"/>	<input type="checkbox"/>
		N/A	Yes
			No
5a.	Was a witness present for the oral presentation?	<input type="checkbox"/>	<input type="checkbox"/>
		N/A	Yes
			No
5b.	Has this process been documented in the source documents?	<input type="checkbox"/>	<input type="checkbox"/>
		N/A	Yes
			No
6.	If applicable, are Informed Consent deviations documented?	<input type="checkbox"/>	<input type="checkbox"/>
		N/A	Yes
			No
6a.	Was the DMID Protocol Deviation Form completed, submitted to DMID and the IRB/IEC per reporting guidelines, and filed in the regulatory file?	<input type="checkbox"/>	<input type="checkbox"/>
		N/A	Yes
			No
For each no response, provide a description:			

Eligibility Criteria – Inclusion/Exclusion Criteria			
1.	Is documentation of eligibility criteria (inclusion/exclusion) in the source documents? Note: Eligibility checklists may be used as long as the criteria correspond with the protocol and each criterion is addressed. A blanket statement regarding all inclusion and/or exclusion criterion is not considered accurate.	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2.	Are the Concomitant Medications documented accurately? Note: Check spelling, coding, and consistency between medical history and adverse events.	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3.	Was the eligibility documentation signed, credentialed, and dated by the clinician responsible for enrolling the subject?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3a.	Is this individual listed on the Study Personnel Signature/Responsibility List?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
4.	If applicable, were enrollment deviation documented?	<input type="checkbox"/> N/A	<input type="checkbox"/> Yes <input type="checkbox"/> No
4a.	Was the DMID Protocol Deviation Form completed, submitted to DMID and the IRB/IEC per reporting guidelines, and filed in the regulatory file?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
For each no response, provide a description:			

Study Product – Administration and Documentation			<input type="checkbox"/> NOT APPLICABLE
Note: Unblinded personnel must not perform chart reviews.			
1.	Was the study product dispensed upon written order of the investigator (or designee) as listed on the FDA Form 1572?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
1a.	Is this study product administrator listed on the Study Personnel Signature/Responsibility List?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2.	Is documentation present describing the study product administration (according to the current version of the protocol and MOP)? Version # ____ Date: _____	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3.	Are dosing, vaccination, administration or blinding deviations identified? Note: This includes a review of labeling, cold and custody chain, licensed personnel, and blinded/unblinding handling and administration.	<input type="checkbox"/> N/A	<input type="checkbox"/> Yes <input type="checkbox"/> No
3a.	Are deviations documented in the source documents and the DMID Protocol Deviation Form completed and submitted to DMID and the IRB/IEC per reporting guidelines?	<input type="checkbox"/> N/A	<input type="checkbox"/> Yes <input type="checkbox"/> No
For each no response, provide a description:			

Adverse Event (AE) and Serious Adverse Event (SAE) Identification and Reporting			
1.	Are all adverse events and/or laboratory abnormalities found in the subject chart identified?	<input type="checkbox"/> N/A	<input type="checkbox"/> Yes <input type="checkbox"/> No
1a.	Are all adverse events assessed for clinical significance and/or severity, and relationship to the study product and documented in the source documents?	<input type="checkbox"/> N/A	<input type="checkbox"/> Yes <input type="checkbox"/> No
2.	Were all adverse events identified in the protocol as critical to safety evaluations reported according to the protocol and/or MOP within the specific time periods?	<input type="checkbox"/> N/A	<input type="checkbox"/> Yes <input type="checkbox"/> No

3.	Were all solicited adverse events (i.e. reactogenicity) recorded at protocol-specified timeframes with appropriate follow-up?	<input type="checkbox"/> N/A	<input type="checkbox"/> Yes	<input type="checkbox"/> No
4.	Were all adverse events meeting the serious adverse event criteria (see DMID SAE Recording and Reporting Guidelines) reported within the DMID specified timelines of site awareness or as specified by the protocol?	<input type="checkbox"/> N/A	<input type="checkbox"/> Yes	<input type="checkbox"/> No
5.	Was the Serious Adverse Event(s) Report completed accurately? Note: See DMID SAE Recording and Reporting Guidelines.	<input type="checkbox"/> N/A	<input type="checkbox"/> Yes	<input type="checkbox"/> No
6.	Were all serious adverse events been reported to the local IRB/IEC, as required?	<input type="checkbox"/> N/A	<input type="checkbox"/> Yes	<input type="checkbox"/> No

For each no response, provide a description:

Deviations from Protocol – Missed Tests/procedures and Missed Visits				
1.	Were all protocol-specific tests and/or procedures completed?		<input type="checkbox"/> Yes	<input type="checkbox"/> No
1a.	If no, was the DMID Protocol Deviation Form completed and submitted appropriately?	<input type="checkbox"/> N/A	<input type="checkbox"/> Yes	<input type="checkbox"/> No
1b.	Was the deviation(s) documented in the source documents?	<input type="checkbox"/> N/A	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2.	Were all missed visits and/or out of window visits identified?		<input type="checkbox"/> Yes	<input type="checkbox"/> No
2a.	If yes or no, was the DMID Protocol Deviation Form completed and submitted appropriately?	<input type="checkbox"/> N/A	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2b.	Was the deviation documented in the source documents?	<input type="checkbox"/> N/A	<input type="checkbox"/> Yes	<input type="checkbox"/> No

For each no response, provide a description:

Endpoints				
1.	Were applicable study-defined clinical and/or laboratory assessments/endpoints documented in the subject's source documents and/or an endpoint-specific CRF/eCRF as required by the protocol?		<input type="checkbox"/> Yes	<input type="checkbox"/> No

For each no response, provide a description:

Intervention/Study Discontinuation				
1.	If the subject discontinued study intervention; were protocol-required steps followed?		<input type="checkbox"/> Yes	<input type="checkbox"/> No
2.	If the subject discontinued from the study; were protocol-required steps followed?		<input type="checkbox"/> Yes	<input type="checkbox"/> No

For each no response, provide a description:

Documentation Standards

1.	Were source documents complete and accurate?	<input type="checkbox"/>	<input type="checkbox"/>
		Yes	No
2.	Does the CRF/eCRF data and source documentation data match?	<input type="checkbox"/>	<input type="checkbox"/>
		Yes	No
1.	Addenda: Are all addenda signed or initialed and dated in present time by the person making the entry i.e. ? Note: Do not alter past-dated addenda, chart notes, progress notes, etc.	<input type="checkbox"/>	<input type="checkbox"/>
		Yes	No
2.	Chart Note(s): Are all handwritten notes legible and signed and dated by the responsible credentialed clinician?	<input type="checkbox"/>	<input type="checkbox"/>
		Yes	No
3.	Case Report Forms (CRF/eCRF): Prior to commencement of the study, were CRFs/eCRFs used as source documents as identified in the protocol, MOP, or source document agreement/statement?	<input type="checkbox"/>	<input type="checkbox"/>
		N/A	Yes
			No
3a.	Are the CRFs/eCRFs used as source documents signed and dated?	<input type="checkbox"/>	<input type="checkbox"/>
		N/A	Yes
			No
4.	Error Correction(s): Are all error corrections clear with a single line drawn through the incorrect information, initialed, dated, and a reason for change (if necessary)? Note: Never obliterate entries or destroy original documents that require correction. Never use whiteout or pencils.	<input type="checkbox"/>	<input type="checkbox"/>
		Yes	No
5.	Patient Identification Numbers: Are all source documents labeled with appropriate patient identification numbers (PID)?	<input type="checkbox"/>	<input type="checkbox"/>
		Yes	No
6.	Death: If a subject death was identified; has the incident been documented in the source documents by one of the following: 1. Obituary 2. Autopsy Report 3. Death Certificate 4. Verbal Communication Contact Report Note: See DMID SAE Recording and Reporting Guidelines.	<input type="checkbox"/>	<input type="checkbox"/>
		N/A	Yes
			No
7.	Certified Copies and Verification: Are all documents received from outside facilities to be used as original source documents verified, as indicated by signature and date, as an exact copy having all the same attributes and information as the original? Note: Documents received via fax are not considered to be original, and must be certified.	<input type="checkbox"/>	<input type="checkbox"/>
		N/A	Yes
			No
8.	Flow-sheets used as Source Documents: Are all entries onto flow-sheets initialed and dated by the responsible clinician?	<input type="checkbox"/>	<input type="checkbox"/>
		N/A	Yes
			No
9.	Chronology of Source Documents: Are source documents maintained chronologically?	<input type="checkbox"/>	<input type="checkbox"/>
		Yes	No

For each no response, provide a description:

Case Report Form and electronic Case Report Form Submission

1.	Are all scheduled CRFs present?	<input type="checkbox"/>	<input type="checkbox"/>
		Yes	No

DMID SAMPLE QUALITY MANAGEMENT SUMMARY REPORT TOOL INSTRUCTIONS

This sample Quality Management Summary Report Tool has been developed in Microsoft Word as a sample that may be adapted, as needed, to adequately capture how findings are summarized, analyzed, and communicated to site staff. This report includes the aggregated information from completed chart review tools, regulatory file review tools, and any other site-developed internal quality management tools. This report and any other internal quality management report tools should be filed in a separate quality management binder, separate from the site regulatory documents.

1. Begin using this tool by completing the header information (name of site, reporting period, and audit participants).
2. Complete Section 2. Identification of Problem Areas per protocol. This form may be modified as necessary.
3. To ensure the content of reporting adequately addresses site performance, please include applicable key quality indicators, as listed in your Clinical Quality Management Plan (i.e. informed consent, eligibility, specimen collection, etc.), as well as broader processes (i.e. quality control, quality assurance, etc).

Note: When preparing a summary report consider data collection/reporting sources (i.e. local/regional/centralized databases) supporting protocol activity and ongoing reporting requirements.

References:

OHRP Code of Federal Regulations Title 45 Part 46:

www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm

ICH Guideline for Good Clinical Practice E6 (Section 8):

www.ich.org/LOB/media/MEDIA482.pdf

U.S. Food and Drug Administration, Title 21 Part 312, Investigational New Drug:

www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcr/CFRSearch.cfm?CFRPart=312

U.S. Food and Drug Administration, Title 21 Part 812, Investigational Device Exemptions:

www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcr/CFRSearch.cfm?CFRPart=812

DMID Clinical Research Resources - Regulatory File Document Guidelines:

www3.niaid.nih.gov/research/resources/DMIDClinRsrch/PDF/regulatoryfiledocumentguidelines.pdf

DMID Clinical Quality Management Plan Policy:

www.dmidctm.com/partners/SectionQualityManagement/PageSOPs/SOPs.htm

DMID SAMPLE QUALITY MANAGEMENT SUMMARY REPORT TOOL

<Replace DMID SAMPLE with Institution/Site Name>

Date of Report: *<enter date report was written>*

Reporting Period: From *<dd-mmm-yyyy>* Through *<ddd-mmm-yyyy>*

1. **Staff Participation in Audits:** *<List the name, title, and role of each staff member involved in the internal review processes>*

- <Name, Title, and Role>*
- <Name, Title, and Role>*

2. **Identification of Problem Areas**

- 2.1. Quality Control Activities – Quality Control is the real time, day-to-day, observation and documentation of the sites work processes to ensure that accepted procedures are being followed. For example, review of demographic information for accuracy on each Case Report Form (CRF) prior to entry into a database.

Quality Control Reviews: *<insert the protocol number, CRF number/name and a summary of the findings>*

Protocol Number	CRF Number/Name	Summary of Finding(s)
<i><Insert or delete rows as needed></i>		

Trend Analysis: *<describe any trends found during the review of findings>*

Corrective and Preventive Actions: *<describe any corrective and preventive actions, including training>*

Evaluation/Re-Evaluation: *<describe the any follow-up actions verifying resolution>*

Resolution Date: *<provide the date the findings are confirmed to be resolved >*

- 2.2. Quality Assurance Activities - Quality Assurance is the periodic, systematic, objective, and comprehensive examination of the total work effort to determine the level of compliance with accepted Good Clinical Practice Standards. For example, a monthly review of source documents compared to Case Report Form pages to determine adherence to protocol requirements.

Subject Record Review: *<insert the Protocol Number and a summary of the findings found during subject record review>*

Protocol Number	Summary of Finding(s)
<i><Insert or delete rows as needed></i>	

Trend Analysis: *<describe any trends found during the review of findings>*

Corrective and Preventive Actions: *<describe any corrective and preventive actions, including training>*

Evaluation/Re-Evaluation: *<describe the any follow-up actions verifying resolution>*

Resolution Date: *<provide the date the findings are confirmed to be resolved >*

Regulatory Files Reviewed: *<Insert the protocol number and a summary of the findings found during regulatory file review>*

Protocol Number	Summary of Finding(s)
<i><Insert or delete rows as needed></i>	

Trend Analysis: *<describe any trends found during the review of findings>*

Corrective and Preventive Actions: *<describe any corrective and preventive actions, including training>*

Evaluation/Re-Evaluation: *<describe the any follow-up actions verifying resolution>*

Resolution Date: *<provide the date the findings are confirmed to be resolved >*

Study Product Review: *<insert the protocol number and a summary of the findings found during study product review>*

Protocol Number	Summary of Finding(s)
<i><Insert or delete rows as needed></i>	

Trend Analysis: *<describe any trends found during the review of findings>*

Corrective and Preventive Actions: *<describe any corrective and preventive actions, including training>*

Evaluation/Re-Evaluation: *<describe the any follow-up actions verifying resolution>*

Resolution Date: *<provide the date the findings are confirmed to be resolved >*

Other Areas of Review: *<insert the protocol number and a summary of the finding from other areas reviewed>*

Protocol Number	Summary of Finding(s)
<i><Insert or delete rows as needed></i>	

Trend Analysis: *<describe any trends found during the review of findings>*

Corrective and Preventive Actions: *<describe any corrective and preventive actions, including training>*

Evaluation/Re-Evaluation: *<describe the any follow-up actions verifying resolution>*

Resolution Date: *<provide the date the findings are confirmed to be resolved >*

DMID SAMPLE ANNUAL CLINICAL QUALITY MANAGEMENT PLAN EVALUATION TOOL

Name(s) of Evaluator(s):

Site Name:

Date of Evaluation: ____-____-_____
 dd mmm yyyy

Sites conducting DMID-supported clinical research are required to evaluate the effectiveness of their Clinical Quality Management Plan (CQMP) on an annual basis, at a minimum. Please refer to DMID CQMP Policy section 6.3 Site Evaluation of the Clinical Quality Management Plan, and submit the revised CQMP to DMID_QMP_Reviewers@lists.ppd.com, if applicable.

Bolded items below may indicate a change in the effectiveness of the CQMP.

1. Is the site and/or protocol identification information within the CQMP correct?
2. Does the CQMP require updates to the roles and responsibilities of staff responsible for the development, implementation, and evaluation of the CQMP?
3. **Does the CQMP describe the Quality Assurance processes accurately and completely?**
4. **Does the CQMP describe the Quality Control processes accurately and completely?**
5. **Does the CQMP describe percentages and frequencies of record reviews accurately? Are the percentages and frequencies adequate to evaluate the conduct of the protocol?**
6. **Are Key Quality Indicators (KQI) adequate and accurate?**
 - a. **Should additional KQIs be added to increase quality management effectiveness?**
 - b. **Does the Chart Audit Tool need to be updated?**
7. **Is the frequency of regulatory file reviews adequate?**
 - a. **Does the Regulatory File Review Tool need to be updated?**
8. **Are all tools, checklists, and reminders accurately described and listed in the CQMP?**
 - a. **Have any tools been updated during the year?**
 - b. **Do any of the tools need to be updated?**
9. **Are the processes for ensuring and documented qualified staff accurate?**
10. **Does the CQMP accurately describe how findings from internal review are summarized, analyzed, and communicated to the staff?**
 - a. **Does the Summary Report Tool need to be updated?**
11. Does the CQMP require modification? If yes, describe: