

Clinical Quality Management Plans Policy

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Purpose

To outline the process for creation and implementation of Clinical Quality Management Plans (Plans) in Duke Clinical Research Units (CRUs) and Oversight Organizations (OOs).

The following entities are covered by this policy:
Duke University School of Medicine and School of Nursing

Overview

Performing clinical monitoring under this policy includes the development of a Plan, designating a trained Quality Management (QM) reviewer, conducting QM reviews according to the Plan, and reporting results. Plans define methodology to ensure implementation of quality measurements during the conduct of clinical research. Plans should accurately reflect all applicable protocol, Principal Investigator (PI), sponsor, Sponsor-Investigator, CRU/OO and Institutional Review Board (IRB) requirements, while aligning with all Duke Health policies, procedures and guidelines, Code of Federal Regulations and International Council on Harmonisation Guidelines for Good Clinical Practice (ICH-GCP). The purpose of QM reviews is to identify issues and trends for key quality indicators (KQI) governing the conduct of clinical research.

Determining which Studies Require a Plan

1. The Clinical Quality Management Program (CQMP) central office is responsible for evaluating each study's complexity level and determining if a Plan is required. The complexity levels are as follows:

| Complexity Level | Study Type Examples |
|------------------|---|
| High | Prospective Phase I–III interventional procedure, device, and/or drug studies (novel product or indication). All studies under an IND or IDE with the FDA. |
| Medium | Studies using FDA-approved drugs, devices, or biologics for their approved indication. Other studies that do not meet high complexity but are more than minimal risk (e.g., behavioral intervention, complex observational, tissue collection). |
| Low | Studies using procedures generally considered to be minimal or low-risk (e.g., blood sample collection, imaging not using sedation, questionnaires, and behavioral surveys). |

2. A Plan is required for clinical research studies conducted at a local Duke-affiliated site or community location that are not externally monitored (or operating under an established monitoring plan), with the exception of the following types of low-risk studies:
 - Approved as Exempt by the Duke Health IRB

- Retrospective only
- Waiver of informed consent or waiver of documentation of informed consent
- Low complexity and internally-funded only
- Surveillance registries with minimal risk and interaction with the participant*
- Study design is limited to focus group interviews and/or surveys about perceptions, feasibility, or refinement of a tool or implementation strategy*

*Studies of this nature are evaluated on a case-by-case basis to determine if monitoring is needed

3. The Research Practice Manager (RPM) or designee is responsible for providing additional information (upon request by the CQMP central office) to assist in the complexity and CQMP requirement determination, including external monitoring plans, when applicable, to ensure alignment with the Policy objectives.
4. The RPM or designee is responsible for communicating any substantial study modifications to the CQMP central office whereby the study needs to be re-evaluated for the Plan requirement and complexity level.

Establishing and Maintaining a Plan

1. Each CRU/OO's RPM is responsible for developing a Plan as part of the Institutional Approval process. The task may be delegated to the QM Reviewer assigned to monitor the study or other CQMP qualified designee.
2. Plans include required training, KQIs applicable to the study, role and responsibilities of the QM Reviewer, frequency of QM reviews, reporting requirements, and the process for implementing Corrective and Preventive Action (CAPA) Plans based on review findings. Traditional 100% source data verification of research data is not a required component of the CQM Plan. QM Reviewers are encouraged to take a risk-based approach where the focus is on critical variables that may impact the integrity and reliability of study outcomes (i.e., primary and secondary endpoints) and procedures that are at high risk for error or relevant to participant safety.
3. The frequency for ongoing QM reviews is dependent on the study's complexity level; and the number of participant chart reviews required each period is based on the cumulative enrollment rate, as follows:

| Complexity Level | Regulatory Reviews | Participant Chart Reviews – by Cumulative Enrollment | | |
|------------------|--------------------------------|--|------------------------------|--------------------------|
| | | 1-39 | 40-99 | ≥100 |
| High | Quarterly (every three months) | Quarterly 3 records | Quarterly 10% of records | Quarterly 10 records |
| Medium | Bi-annually (every six months) | Quarterly 3 records | Quarterly 10% of records | Quarterly 10 records |
| Low | Annually (once per year) | Biannually 3 records | Biannually 10% of records | Biannually 10 records |

Regulatory file reviews must be completed at this frequency (at a minimum) based on the institutional approval date. Participant chart reviews must be conducted at this frequency (at a minimum) based on the first participant enrollment date. Reviews may be conducted more frequently at the request of the PI, CRU/OO or CQMP central office. The number of participant chart reviews required at each monitoring visit may be reduced in unique circumstances at the request of the CRU/OO and with the approval of the CQMP central office (e.g., excessive percentage of participants being monitored when using cumulative enrollment to calculate number of reviews in relation to study design and rate of incremental accrual).

4. The Plan must be created using the Clinical Quality Management Plan Template (Appendix A) according to the Clinical Quality Management Plan Template Instruction Sheet (Appendix B). Plans may initially be developed on the Word Template or directly in the Clinical Quality Management (CQM) Database in REDCap. However, the Plan must ultimately be entered into the CQM Database prior to final approval.
5. The CQMP central office is responsible for reviewing each Plan, providing feedback, and final approval.
6. The RPM or designee is responsible for signing and marking the Plan as complete in the CQM Database before Institutional Approval will be granted.
7. The assigned QM Reviewer is responsible for making updates to the Plan throughout the life of the study, as needed. Each CRU/OO is encouraged to review all Plans at least annually.

Designating a QM Reviewer

1. Each CRU/OO is responsible for designating a trained QM Reviewer(s), who is independent of the study under review, to conduct QM reviews. The name(s) of the QM Reviewer(s) must be included on the Plan.
2. The CQMP central office provides QM Reviewer Training for all designated QM Reviewers. This training focuses on the purpose of QM reviews, developing Plans, metrics for reviews, the CQM Database, and how to use the QM tools. This training is required for all individuals developing Plans and performing QM reviews. QM Reviewers are also encouraged to attend the Ongoing Educational Series facilitated by the CQMP central office.

Conducting QM Reviews & Sending Reports

1. QM reviews may be conducted and entered directly into the CQM Database, or by using the most current version of the QM review tools available for download from the CQM Database File Repository in REDCap or CQMP website: Regulatory File Review Tool & Instruction

Sheet (Appendix C) and Participant Chart Review Tool & Instruction Sheet (Appendix D). All reviews must ultimately be entered into the CQM Database, even if initially captured on the Word version of the review tools.

2. The QM Reviewer is responsible for scheduling ongoing reviews in accordance with the frequency specified in the Plan. The required number of participant chart reviews at each monitoring visit is based on cumulative enrollment (i.e., number of consented participants) from the onset of accrual to the first day of the monitoring window for the review period. See frequency [table](#) for details.
3. Prior to conducting a review, the QM Reviewer should meet with the appropriate study personnel to ensure access to all study documents and research data required to perform the review.
4. In order to capture the most data, ongoing QM reviews should be completed and entered into the CQM Database within the designated monitoring window (30 days after the end of the review period according to the respective study complexity level). Monitoring window start and end dates are displayed on the Regulatory Review and Participant Chart Review Key Dates forms in the CQM Database for each review period.
5. Reviews completed prior to the monitoring window do not fulfill the policy for an ongoing review. Therefore, an additional review will be required unless the early review was approved by the CQMP central office in advance. Reviews submitted after the monitoring window will be considered late unless otherwise approved by the CQMP central office.
6. The following guidance should be used when selecting participants for participant chart reviews:
 - The first three participants enrolled (i.e., consented) in the study must be reviewed.
 - The first three participants with whom a new study team member (e.g., PI, CRC, CRNC) has significant interactions or interventions for research purposes must be reviewed.
 - The remaining participants should be a representative sample across the enrollment period (early or recently enrolled) taking study design and identified risks into account.
 - When possible, prioritize the selection of participants who have not been previously reviewed to achieve the maximum, representative sample of charts for review.
 - Participants who were partially reviewed at a previous monitoring visit may be re-selected for studies with multiple visits/encounters or extended follow-up when re-consenting and/or long-term safety events or clinical outcomes are identified as a risk. Only new study activities since the last review need to be evaluated for those participants.
7. The QM Reviewer is responsible for reporting discrepancies (if found) in the CQM Database, ensuring actions are resolved, and sharing the final QM review report with the study team (i.e., PI, CRC, Regulatory Coordinator, RPM).
8. The study team is responsible for addressing all discrepancies specified by the QM Reviewer within the agreed-upon schedule stated in the Plan (e.g., 30 days).

9. CAPA plans should be created to address issues identified during QM reviews and mitigate their recurrence.
10. The QM Reviewer is responsible for notifying and providing the CQMP central office with applicable information when QM reviews may no longer be required for a study.
11. The CQMP central office is responsible for routinely monitoring issues identified by QM Reviewers and may report issues to the Office of Audit, Risk & Compliance (OARC), as required.
12. On a quarterly basis, the CQMP central office provides a unit-specific summary report to CRU/OO leadership (e.g., CRU Director, Research Quality Officer, RPM) containing high-level results and trends. On a biannual basis, the CQMP central office provides a summary report to School of Medicine (SOM) leadership.

References:

[Code of Federal Regulations \(CFR\) Title 21 Parts 50: Protection of Human Subjects](#)
[Code of Federal Regulations \(CFR\) Title 21 Parts 312: Investigational New Drug Application](#)
[Code of Federal Regulations \(CFR\) Title 21 Parts 812: Investigational Device Exemptions](#)
[International Council on Harmonisation \(ICH\)-Guidelines for Good Clinical Practice \(GCP\) E6\(R2\)](#)
[Title 45 Code of Federal Regulations \(CFR\) Part 46 Protection of Human Subjects](#)
[U.S. Department of Health & Human Services: Office for Human Research Protections](#)

Appendices:

[Clinical Quality Management Plan Template \(Appendix A\)](#)
[Clinical Quality Management Plan Template Instruction Sheet \(Appendix B\)](#)
[Regulatory File Review Tool & Instruction Sheet \(Appendix C\)](#)
[Participant Chart Review Tool & Instruction Sheet \(Appendix D\)](#)
[RCA and CAPA Plan Documentation \(Appendix E\)](#)

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| Policy Owner: | Vice Dean and Associate Vice Provost for Scientific Integrity (Clinical Quality Management Program) |
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