Quality Management in Clinical Research

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Objectives

- Identify responsibility for oversight of research

- Specify the purpose and goals of Quality Management in research

- Implement internal auditing system for Quality Management

- Discuss components of a QM Plan for research teams

- Understand how to utilize tools, report findings and develop corrective plans

Oversight

- Principal Investigator

- Sponsor (Industry or Investigator)

- Institutional Review Board

- Institution

- OHRP / FDA
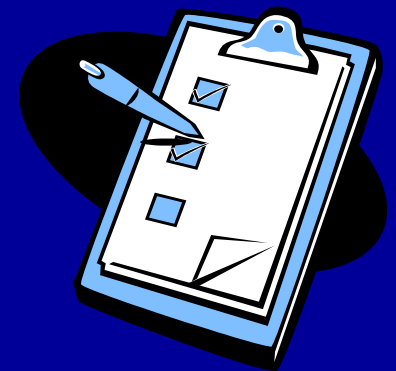
Quality Management Program

A plan or system, including structure and defined responsibilities, which provides a framework for all quality management activities, including quality control, quality assurance, quality improvement and the reporting of these activities

ICH E6 Guideline for Good Clinical Practice

Principles of ICH GCP

Systems with procedures that assure the quality of every aspect of the trial should be implemented.

ICH GCP 2.13

ICH GCP Guideline

Investigator:

The investigator should ensure the accuracy, completeness, legibility, and timeliness of the data reported to the sponsor in the CRFs and in all required reports.

ICH GCP 4.9.1

PI Responsibility

The Principal Investigator is ultimately responsible for all study related activities.

Goals of Quality Management

- Ensure adequate protection of research participants

- Improve quality of study conduct

- Improve quality and scientific validity of collected data

- Increase compliance with regulatory requirements

Goals of Quality Management

- Improve documentation practices

- Ensure adequacy of informed consent

- Provide early identification of problems and provide process improvement

- Identify areas where education and training efforts should be focused
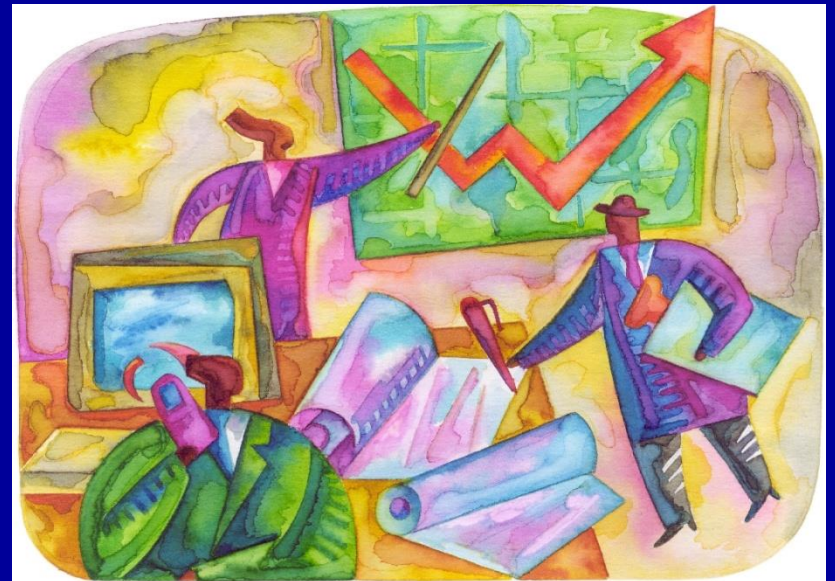
How is this Accomplished?

- Self assessment

  http://www.umaryland.edu/hrp/for-researchers/study-conduct/

- Team work

- Communication

- Education

Quality Management for the Research Team

- Defined responsibilities

- Reporting

- Education

Components of a Quality Management Plan

- Quality Control
  - Real time, systemic checks of protocol and regulatory adherence

- Quality Assurance
  - Interval auditing

- Quality Improvement
  - Evaluation and Education

Quality Control

The operational techniques and activities undertaken within the quality assurance system to verify that the requirements for quality of the trial-related activities have been fulfilled.

ICH GCP 1.47

Quality Control

- Systematic checks of compliance

- Performed at every step of the research process

- Ongoing, concurrent

- Assuring adherence to the approved protocol and protocol procedures

- Documentation

Quality Control

- Performed by members of the research team

- Ideally, 100% chart review

- Collaboration between staff to get a "second set of eyes" on all records

- 'Real time' correction of deficiencies

What to Review

- Informed Consent documents

- Inclusion and Exclusion criteria verification

- Completed source documents and CRFs

- Study procedure records/worksheets

- Study drug and concomitant med records

- Specimen collection and laboratory results

- Drug accountability and management

- Safety and efficacy documentation

- Deviations and adverse events reporting

Example

Quality control checklist for informed consent document and inclusion/exclusion criteria

Quality Assurance

All those planned and systematic actions that are established to ensure that the trial is performed and the data are generated, documented (recorded), and reported in compliance with GCP and the applicable regulatory requirements.

ICH GCP 1.46

Quality Assurance

- Validates effectiveness of quality control

- Prioritize

- Done retrospectively

- Sample size

What to Review

- Protocol adherence

- Informed consent documentation

- Clinical endpoints

- Treatment discontinuation

- Regulatory documents

- Compare source documents and case report forms for accuracy

- Documentation practices

DATE OF VISIT:_____ CICERO #:_____SUBJECT ID #:_____

DATE OF AUDIT:_____PERSON COMPLETING AUDIT_____

Verify the following for **EACH** page.

1. Participant ID on EVERY page
2. All source documents are signed and dated
3. Entries in black ink
4. No blank entries
5. Entries are legible
6. No white out
7. Errors corrected with single-line, dated & initialed
8. Entries can be verified with source document
9. Able to identify who wrote all entries

10. Correct spelling used
11. Only approved abbreviations are used
12. Units of measure clearly marked
13. Time 24 hour clock or am/pm marked
14. Entries are original - no copies
15. No space between signature and entry
16. No ditto marks indicating repeat entry
17. No charting for another staff member
18. Leading 0"s when applicable, i.e., 0.5ML

Record ALL instances of documentation deficiencies. Record in the first column the # of the type of deficiency.

Deficiency Type (#)	Visit, form and/or page #	Details – if necessary	Responsible Clinician	Correction Completed

Consent Version	Date Signed	Dated correctly	Signatures correct	Problems	Correction Completed

Outcome

- Quality assurance activities often result in finding deficiencies and identifying problems.

  - What now?
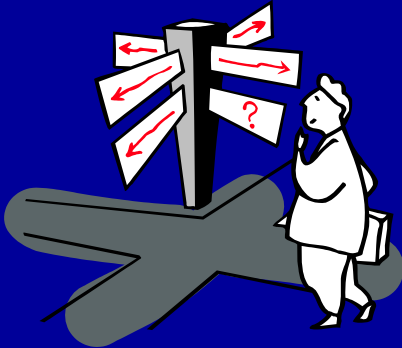
Deficiencies

- Communication of activities and findings
  - Research team members
  - Clinical staff
  - Investigator

- Develop a corrective action plan

- Implement that plan

- Learn from the deficiencies

- Educate

Corrective Action Plan

- The corrective action must be achievable and verifiable.

- The person(s) responsible for its implementation must be clearly identified.

- The timeframe for implementing the corrective action must be specified.

Remember……

- Errors and problems will be identified

- Knowing mistakes made in the past can help prevent making the same mistake in the future

- Identifying problem areas $\rightarrow$ identifies areas of educational needs

Quality Improvement

- Continuous

- Evaluation

- Education

- Best Practices

Prior to Initiation

- Qualifications of Investigator and research staff, IRB submission

- Site/Facilities vs. Protocol requirements

- Protocol vs. Informed Consent

- Protocol vs. Case Report Form or Data collection instrument

During the Study

- Source documents vs. CRF's
- Regulatory File
- Data Correction Forms/Query forms
- IRB Correspondence
- Sponsor/Monitor Correspondence
- Study Product Accountability
- Serious Adverse Events/Unanticipated Problems

End of Study

- Database review
- CRF's vs. Total number of participants
- Clinical Study Reports
- Safety and Efficacy Summary
- SAE's
- Final Report

Human Research Protections Office

- Quality Management
 - * Quality Control
  - * Quality Assurance

Quality Control & Quality Assurance Activities	Indicators	Responsible Individual	Month/Year	Month/Year
	HRPO Director at all IRB meetings	Responsible individual		
QC	Pre-review of ICD (QC 10%)	Responsible individual		
QC	IRB Minutes (QC-100%)	Responsible individual		
QC	IRB Letters of determination (QC-100%)	Responsible individual		
QC	Modifications Required to Secure Approval (QC-100% Confirmation Convened IRB)	Responsible individual		
QA	Modifications Required to Secure Approval (QA-10 % Non-committee review)	Responsible individual		
QC	Reportable New Information Determination letters Fullboard (100%)	Responsible individual		
QA	Pre-reviews (QA-10% Convened IRB)	Responsible individual		
QA	Non-committee reviews (QA- 10 %) Exempt Expedited	Responsible individual		
QA	Full committee reviews (QA -10%)	Responsible individual		
QA	Contracts – ORD (QA-10/quarter)	Responsible individual		
QA	Investigational Drug Service (QA-Spot audit	Responsible individual		
QA	Emergency Use of a test Article in a Life Threatening Situation (QC 100%)Worksheet 317/SOP 023 and 027)	Responsible individual		
QA	Waivers of Informed Consent (QA-10%)	Responsible individual		

Summary

- Quality Management activities often identify issues

- Corrective action plans should be devised and implemented to address issues

- Principal Investigator and research staff should receive additional education in areas of identified issues

Conclusion

- Goal of QM: Protect research participants, Regulatory compliance

- Strengthens credibility

- Quality Management is team effort

- Continuous process

- Education and improvement are vital
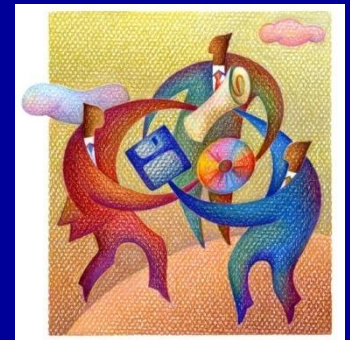
Resources

UM: HRPO Website, Investigator Toolkit:

HRP-430 - CHECKLIST - Investigator Quality
   Improvement Assessment