Objectives

- Describe practical considerations and approaches to developing an internal quality assurance program for human subject research
- Identify and prioritize potential risks
- Discuss strategies for overcoming challenges when implementing an internal audit program

...the road to establishing an internal Quality Assurance Program
Key Questions

“I never learn anything talking. I only learn things when I ask questions.” Lou Holtz

FREQUENTLY ASKED QUESTIONS

• Why do we need an internal quality assurance program?
• What are the risks and concerns?
• Who will be our target audience/stakeholders?
• How to plan for effective implementation of an internal quality assurance program?
• How to effectively disseminate information and provide quality feedback?
• What are the thresholds for corrective actions?
• What are some strategies to overcome challenges and positively impact the research community?
What is the purpose?

• Why do we need an internal quality assurance program?
  • Patient safety
    – Protection of Human Subjects
  • Monitor compliance
    – IRB, regulatory requirements (FDA) and GCP guidelines
  • Monitor the conduct of the study
  • Perform over-site review of all new, existing and continuing trials (IND/IDE)
  • Preparation for internal sponsor audits, NIH/FDA audits

• Assure study data is accurate, complete and verifiable
• Identify strengths and target areas for quality improvement initiatives
• Provide educational resources and guidance for best practice
• Assure validity and completion of data

Attributable Risks

• What are the risks and concerns?
  – Risks to institution, investigator, research subject
  – How many Investigator-initiated studies?
    • Investigational New Drug (IND)
    • Investigational Drug Exemption (IDE)
  – How many studies lack external monitoring?
    • NIH, DOD, Foundation(s) sponsored studies
Who are the Stakeholders?

- Research community
- Research Administration
- Ethics Board (Institutional Review Board)
- Researchers
- Study team members
- Research subjects
- Industry collaborators
- Regulatory agencies
- Funding agencies

Organizing an Internal QA Program

- What are the priorities?
  - Quality assurance
  - Quality control
  - Quality improvement
Organizing an Internal QA Program

• Program structure?
• How to identify gaps?
• Who will be accountable?
  — Reporting relationships
    • Corporate Compliance
    • Research Administration
  — Developing corrective actions
    • Minimize and manage risks

Program Structure Goal

Supportive and educational
- Preventative
- Assessment/Identification of findings
- Corrective Actions

Organizing an Internal QA Program

• What are the standards?
  — Policies and procedures
  — Training
  — Implementation
  — Reporting requirements
....the great debate

Quality Assurance

vs.

Quality Control

Are they the same?

Quality Control (QC) Monitoring

“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.”
Quality Assurance (QA) Auditing

“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.”

QA vs. QC Are they the same?

QC is **NOT** QA

Quality Review Plan

- Monitor compliance
  - Regulations & GCP standards
- Monitor the conduct of the study
- Perform over-site review of all new, existing and continuing trials (IND/IDE)
- Preparation for internal sponsor audits, NIH/FDA audits
What are the types of QA reviews conducted?

• For cause reviews:
  – a request from the IRB, Research Administration or some other group has raised concerns and issues related to the conduct of the research.

• Routine reviews:
  – process of randomly selected review of IRB approved studies.

What types of research studies are reviewed?

• Any active clinical research study
• All disciplinary areas
• Generally, no outside monitor

Quality Review Plan

• When?
  – Before (pre-study review)
  – Randomly
  – Annually
Quality Review Plan

• What to Audit?
  – Protocol
  – Informed Consent
  – Case Report Forms (CRF’s)
  – Compliance with eligibility criteria
  – Adverse Event Reporting
  – Compliance to FDA/ICH Guidelines
  – Documentation for compliance to IRB, FDA (GCRC, NIH, if applicable)

• What do we review?
  • 100% review of essential documents (regulatory files)
  • Informed consent documents
  • Study Documents
    • Study management tools
    • Subject study records (10%)  
    • Case Report Forms (data collection tools)
    • Source documents

QA Review Process

• Study identified
• Principal investigator (PI) notified
• Brief meeting with PI and study team
• Review conducted
• Exit interview
• Written report of findings: regulatory issues and best practice recommendations
What do we look for?

- Regulatory compliance
- Protocol compliance
- Adherence to institutional policies and procedures
- Areas of potential risk
  - Human subject risk
  - Institutional risk
- Identify strengths and opportunities for improvement
- Assess resources as well as educational needs

How will information be disseminated?

- Oral and written communication
  - Regulatory and professional obligation
  - Opportunities for improvement
- Training and education

How are QA review findings documented?

- QA Summary Monitoring Report using the following categories:
  - Regulatory/Source Data/Documentation
  - Informed consent
  - Protocol adherence/Eligibility
  - Financial Considerations
  - Unanticipated problems/SAE reporting
  - Data Security

Note: Investigator-Initiated studies (IND/IDE)
  - Review of Investigational product accountability
What are some common QA review findings?

- Incomplete documentation of consent;
- Inclusion/exclusion criteria not met;
- Deficiencies in maintaining documentation;
- Lack of and limited documentation of delegated responsibilities;
- Lack of source data/documents and
- Incomplete or missing data collection tools (including questionnaires, surveys, case report forms (CRFs)).

How are findings communicated?

- Oral and written communication provided
  - Principal Investigator/Study Team
    • Address regulatory and professional obligations
  - IRB (as applicable)
    • Reportable event
      - Protocol deviation
      - Significant non-compliant findings

Findings: Regulatory Issues

- Any break with regulatory compliance as it relates to study management and the IRB approved protocol and/or federal regulatory requirements
- Finding is reported to the PI of the study and IRB is notified
- The IRB has the regulatory authority to review, make determinations about non compliance and report to the appropriate federal regulatory agency
- IRB determines seriousness of finding
- IRB sets corrective action
- Collaborative effort to confirm completion of corrective actions
Findings: Best Practices

• Any finding that indicates a need for improvement in study management or study documentation
• Best practice recommendations provided to study team in the form of standard operating procedures, templates, policy

Findings: Best Practices

• Best practice issues and solutions are presented in workshops and incorporated into study coordinator trainings
• Note: these are not regulatory findings
• Minimal risk studies, unlike clinical trials, do not have best practice standards and thus we are developing them

Overcoming Challenges

• Changing the culture
• Support from leadership
• Engaging leadership and research community
• Resources
• Planning and implementing changes
• Disseminating policies and procedures
How to make a positive impact?

• Be proactive
• Be transparent
• Determination, commitment and perseverance
• Focused, coordinated and consistent approach to monitoring and reporting
• Effective and consistent communication
• Knowledgeable, skilled and professional staff

What Resources are Available?

– Research QA Policy and Procedure
– Research QA Monitoring and Audit Preparation Tools
  • Preparing for regulatory agency site visit
  • Self-audit checklist
– Research QA Frequently Asked Questions (FAQs)

Final Thoughts

• Strategies for implementing an effective internal QA program
  – Ensuring safety and compliance
  – Demonstrate internal control
  – Minimize and manage risks
  – Develop educational activities
  – Process improvement
“Dreams are today's answers to tomorrow's questions.”

Edgar Cayce
References

- Department of Health and Human Services Regulations (HHS)
  http://www.hhs.gov/policies/index.html
- Food and Drug Administration (FDA)
  www.fda.gov
- ICH Guidelines E6 Good Clinical Practice:
- Office for Human Subject Protections (OHRP)
  http://www.hhs.gov/ohrp/
- ORCRA Intranet
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Thank You!

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