USF UNIVERSITY OF SOUTH FLORIDA

Preparing for an IRB Audit

Goals

- Describe the USF RIC Evaluation Process
- Help you prepare if you are chosen for a study review
- Prevention of typical findings

Overview

- What is an evaluation or “audit” ?
- For Cause vs. Routine
- Types of Evaluations (Full, IC, AE)
- Components of the QA Evaluation
- Top Findings
- How to prepare for your QA Evaluation
- USF RIC QA Evaluation Process

Oh No!!!
I've just been told …..
my study is being audited!

- Don't Panic
- Remain calm
- Notify the study team
- Are you prepared?
  - Gather & organize your study documents

What an audit isn't…

- A fact finding mission to destroy you
- A finger pointing session to ruin your professional reputation
- A quest to destroy the integrity of your data
- A last ditch effort to rid the world of scientific progress

What an audit really is ….

- An opportunity to fine-tune your study and improve its conduct and the data it generates
- An opportunity to collaborate with the IRB to ensure subject safety is being maximized
- An opportunity for you to teach the IRB about your important research
- An opportunity to learn from each other

Definitions

- Audit
  - “A systematic and independent examination of trial-related activities and documents to determine whether the evaluated trial-related activities were conducted, and the data were recorded, analyzed, and accurately reported according to
    - the protocol
    - sponsor's standard operating procedures (SOPs)
    - good clinical practice (GCP), and
    - the applicable regulatory requirement(s).”

– ICH GCP Definition

Definitions continued

- Monitoring
  - The act of overseeing the progress of a clinical trial, and of ensuring that it is conducted, recorded, and reported in accordance with
    - the protocol
    - standard operating procedures (SOPs)
    - GCP, and
    - the applicable regulatory requirement(s).

– ICH GCP Definition

Definitions continued

- USF Quality Assurance (QA) Evaluation
  - Routine Monitoring or for cause audit evaluation of a research protocol to ensure compliance with applicable rules, regulations, laws, and policies and procedures.

Types of QA Evaluations

- For Cause
- Routine
- Full Review
- Informed Consent Process and/or Documentation Review
- Unanticipated Problem/AE Event Review
- Requesting a *Consult*

For Cause

- Requested by the IRB
- IRB requests the type of review (Full, IC, AE)
- PI is notified that the IRB has requested the evaluation
- Can result during IRB review of
  - Reportable Events (SAEs, deviations, noncompliance, etc.)
  - Continuing Review
  - Amendments
  - Concern/Complaint Report

Routine

- Study chosen at random from the pool of IRB approved research or selected by RIC administration
- QI Program will contact PI to schedule monitoring visit

Informed Consent Process and/or Documentation Review

- IRB can request specific aspects be reviewed to answer questions they have about the conduct of the research
- IRB can request a full IC audit

Unanticipated Problem/AE Event Evaluation

IRB can request specific aspects of AE reporting be reviewed

- All SAE submissions or just those from a specific time period
- Specific types of SAEs
- All SAE submissions from a specific Sponsor, Investigator, Site, Hospital etc.

QA Review – What will be reviewed

- Depends on the type of review:
  - Full Review
  - Informed Consent Review
  - Unanticipated Problem/AE Review

Components of a Full Review

- Informed Consent Documentation
  - All ICDs or a just a subset of ICDs
  - HIPAA Authorizations
  - Documentation of the IC Process

- Adherence to the IRB approved Protocol
  - All protocol versions with enrolled subjects
  - Subject research charts/medical records
  - CRFs
  - Pharmacy Records, if applicable

Full Review continued

- Adverse Event Reporting
  - All SAE reports to the IRB
  - IRB SAE reports for selected subjects
  - AEs recorded in research chart/medical records

- Regulatory Record Review
  - IRB Documentation
  - Key Personnel Documentation
  - Sponsor Documentation, if applicable
  - FDA Documentation, if applicable

Components of an Informed Consent Review

- IC Documentation and/or process Review

- IC Documentation
  - Original ICDs and supporting documentation
    - All ICDs or a subset of ICDs
      - 100 % ICD review or random selection of 10-20%
  - Documentation of the IC process

- IC Process
  - witness the IC process

Components of an Unanticipated Problem/AE Review

- All AEs and SAEs for randomly selected subjects
- All Unanticipated problems reported to the IRB
- AE contact information in the ICD

Common Review Findings

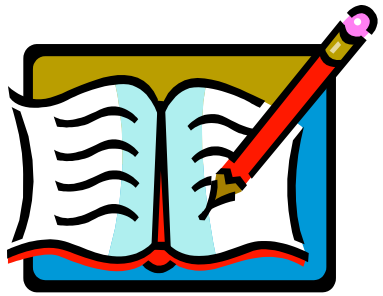
1. Incomplete Informed Consent Documentation
2. Non-Adherence to the IRB approved Protocol
3. Incomplete Documentation of Eligibility
4. Incomplete Regulatory Documentation
5. Unreported Deviations
6. Incomplete Recording of AEs

Incomplete IC Documentation

- ICD incomplete
  - Missing date of signature
  - Missing witness (if applicable)
  - Missing signatures
  - Missing initials or check marks (contraception, storage etc)
  - Markings, cross outs, corrections
  - No source documentation of consent process
- Wrong version of ICD used
- Unstamped version of ICD used

Non-Adherence to the IRB approved Protocol

- Missing procedures or laboratory testing
- Procedures or laboratory testing conducted out of window
- Procedures conducted by individuals not approved by the IRB



Incomplete determination and documentation of eligibility criteria

- Unable to verify subject met eligibility criteria
  - Missing assessments (procedures, labs) needed to assess eligibility
  - Missing PI determinations on eligibility (life expectancy, grading pre-existing conditions)
  - Records of eligibility kept in multiple locations
- Prove the subject is eligible and document the proof in the subject's study file.

Incomplete Regulatory Documentation

- Regulatory files unorganized or difficult to follow/find items
- Regulatory files incomplete – missing documents
- Regulatory files kept in multiple locations
- Multiple volumes without labels
- Empty sections without explanation

Unreported Deviations

- HRPP Policy # 18.2 – Deviations in Human Subjects Research

- Protocol Deviation = Any departure or inadvertent act in study activity from the currently-approved protocol.
  - **Serious Deviation** = a deviation that affects subject safety, rights, welfare, and/or data integrity.
  - **Non-serious Deviation** = a deviation that does not affect subject safety, rights, welfare, or data integrity.

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HRPP Policy – When to Report Deviations

- **Serious Deviations** – PI report to the IRB within 5 business days whenever the deviation results in or has a potential to increase risk(s) to subjects or decrease benefit or has the potential to recur.

- **Non-serious Deviations** – PI report to the IRB at the time of Continuing Review on a protocol deviation log.

What to Report – Deviations

- Study Identifiers – IRB #, PI name, Title
- Detailed description of the event(s)
- Description of changes to protocol or corrective actions
- Description of actions take to prevent future recurrence

❖ *provide details and a complete description of your CAPA plan*

How to Report – Deviations

- Serious Deviations – electronic studies
  - ARC – eIRB
- Non-Serious Deviations – deviation log at Continuing Review (or Final Report)

Incomplete Recording of AEs

- AEs in study charts inconsistent with medical record
  - Start/stop dates
  - Grade of event
  - AEs in medical record, including lab abnormalities, not recorded in study chart
- Documentation of assessment of AEs by PI or other investigator for severity & causality

How to Prepare for a QA Review

- Best preparation
  - Start to prepare at the initiation of the trial
  - Know the protocol and its required procedures, testing, inclusion/exclusion criteria
  - Develop a plan to organize all study documents and implement it before the trial begins – be consistent
    - Regulatory binder, Regulatory folder
    - Subject study records, CRFs
    - Sponsor documents and submissions

How to Prepare for a QA Review

- Keep a complete & up-to-date list of all subjects screened and enrolled
- Keep a complete & up-to-date list of all study personnel and include their delegated responsibilities

Catherine's study team had changed so many times, she'd done more staff inductions than site initiations!

How to Prepare for a QA Review

- Create and use a protocol deviation log
- Perform internal “self” audits periodically throughout the life of the study

What if you've inherited an existing trial?

- Get to know the trial when you take it over
  - Read the Protocol, IRB applications, and ICD
  - Speak with the PI and existing study personnel, ask questions
  - Perform an internal "self" audit

What if you've inherited an existing trial continued

- Review the Regulatory Binder
  - Are any documents missing? If missing, locate them. If unable to find them create a note-to-file.
- Review the Subject records
  - ICD, Clinical notes, CRFs
- Review the Pharmacy records, temperature logs, accountability records, product storage condition

❖ *Tool available to help you perform self-assessment*

Your review is coming …

- Gather study materials
  - Regulatory Binders
    - IRB Documentation – Applications, Approvals, Correspondence
    - ICD – all approved ICDs
    - Protocols – all approved copies of protocol
    - Key Personnel list, CVs, and HSP education certificates

Gather, Gather, Gather …

- Subject Study Records
  - ICD
  - CRFs
  - Source Documents
  - Medical Records
  - Adverse Event/Unanticipated Problem documents
- Sponsor Documents
  - Correspondence
  - Monitoring Logs/Reports
  - CRFs (if applicable)

If applicable

- FDA Studies – IND & IDE
  - Correspondence
  - Test Article Accountability
  - Laboratory Documentation – Certifications, Normal Ranges, CV of Director
- IND Studies
  - 1571
  - 1572
  - Investigator's Brochure
- IDE Studies
  - Investigator's Agreement

Pre-Review Meeting

- 15-20 minutes
- PI
- Key Study Personnel (Study personnel involved in day-to-day conduct of the trial)
- Opportunity to get overview of the study, gain a better understanding of site specific logistics and answer any questions about the review process

Day of the Review is here

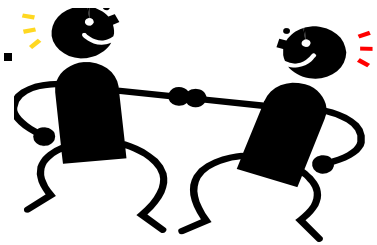
- Place to work – quiet, out of your way
- 15-20 minutes at the start of the day to provide study documents, orientation to the location
- Will work independently but helpful if available for questions
- Conduct an exit meeting at the end of the day provide a summary
- Some reviews can last multiple days depending on the size of the study

Post-Review

- Will receive a QA Report for your comments & response
- Send a response letter to the IRB addressing any findings
- QA Report and PI response will be reviewed together

Things to keep in mind

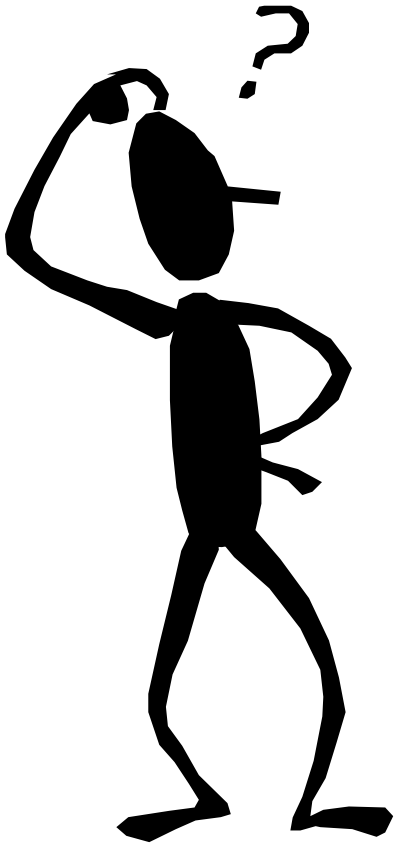
- The process is mostly painless
- The process is intended to be educational for both sides
- QA reviewer and the site work together to ensure the study is running in compliance with applicable regulations
  - If someone else would audit your study after a USF review you'd feel confident you'd be o.k.



Always Remember

- Do not stress
- Do not panic
- Call/email if you have any questions

Questions?



Thank You

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