



THE UNIVERSITY
of NORTH CAROLINA
at CHAPEL HILL

Clinical Trial Quality Assurance Common Findings

Objectives

- Identify common findings found in research study reviews conducted by the CTQA Program
- Understand what findings require an action plan vs. a corrective and preventative action (CAPA) plan
- Explain what is needed to create an effective CAPA



Common Findings



Informed Consent Form

- Use of the incorrect version of a consent/HIPAA
- Lack of re-consent or providing new information when required by the IRB
- Inadequate documentation of consent/authorization
- Missing consent/HIPAA authorization
- Study procedures performed prior to obtaining consent



Site Regulatory Administration

- Missing essential documents, including but not limited to:

1572	Delegation of Authority Log
Financial Disclosures	CVs
Protocol(s)	Medical Licensure
Investigator Brochure(s)	Investigational Product Management Documentation
Clinical Trial Agreement	Monitoring/Auditing Reports
IRB Submissions/Approvals	Study Correspondence
IND/IDE approval by FDA, if applicable	Normal Value Range(s) for Laboratory tests
Subject Enrollment Log	Source Documents



Site Regulatory Administration Continued

- Untimely IRB submission of amendments to the protocol and/or investigator brochure (IB)
- Discrepancies between the protocol/IB and/or the informed consent form
- Missing or incomplete delegation of authority (DOA) logs
- Lack of site monitoring, if UNC/Investigator is considered the Sponsor



Staff Qualifications

- Lack of training documentation:
 - Site Initiation Visit/CRF completion/Investigational product management/Processing of specimens/GCP
 - Protocol amendments
 - Investigator Brochure amendments
 - Any other relevant training needed per protocol
- Delegation of study tasks to study personnel not licensed or qualified to perform those tasks



Protocol Compliance

- Missed visits
- Missed procedures
- Failure to follow the protocol required drug administration (e.g., dose reductions)
- Failure to report deviations

PROTOCOL



Subject Records

- Missing source documentation
- Incomplete questionnaires
- Incomplete assessments



Data Management

- Untimely data entry into Case Report Forms (CRFs) as specified by the protocol and/or Clinical Trial Agreement (CTA)



Documentation Practices

- Unsigned and dated notes to file
- Use of whiteout
- Documents signed by someone other than the subject or investigator
- ALCOAC Principles:
 - Attributable
 - Legible
 - Contemporaneous
 - Original
 - Accurate
 - Complete



Subject Protections and Adverse Events

- Lack of documentation of clinical significance of laboratory results by an investigator
- Lack of documentation of adverse event assessment and attribution by an investigator



Investigational Product

- Lack of patient drug diaries to determine patient adherence
- Lack of documentation addressing accountability:
 - Dispensing
 - Compliance by subject
 - Product returned
 - Discrepancies between product returned and product taken
 - Education and training (initially or ongoing)



Facilities and Equipment

- Lack of documentation of laboratory inspections/certifications
- Inadequate specimen handling (e.g., specimen left in public area overnight)
- Discrepancies in temperature logs and temperature excursions



Other

- Use of an external email account to discuss patient care (see UNC-Chapel Hill Individual Email Address Policy)
- Protected Health Information left on an answering machine (see UNC HCS Privacy Guidelines)
- Use of personal cell/smart phones to collect, store and transmit information poses additional HIPAA privacy concerns as these devices may not be properly secured to protect stored protected health information (e.g., text messages, photographs, or emails)



Action Plans



Observations Requiring Actions

- An observation which is a deviation and/or deficiency in compliance with applicable regulations and guidelines, the protocol, and/or university policies, or an observation which has the potential to impact patient safety, data integrity and or non-compliance with regulations.
- Examples may include:
 - Missing or incomplete delegation of authority (DOA) log
 - Missing training logs
 - Lack of documentation of significance of laboratory results by an investigator



Actions May Include:

- Completing a delegation of authority (DOA) log
- Removing tasks for study personnel that are outside of their licensure by lining through, dating and initialing the DOA log
- Providing training documentation for each person listed on the DOA



Observations Requiring a CAPA

- An observation considered by Clinical Trials Quality Assurance Program (CTQA) to:
 - Pose significant risk to the rights and/or safety of subjects
 - Jeopardize data integrity
 - Represent a major deviation from or deficiency in compliance with applicable regulations, guidelines, the protocol, standard operating procedures (SOPs) and/or policies



Examples of Actions Requiring a CAPA

- Incorrect drug or dose of drug administered
- Lack of investigational product management
- Study personnel did not obtain informed consent or re-consent a subject as required
- Excessive protocol deviations



Steps to Completing a CAPA

- Identify the problem
- Conduct a Root Cause Analysis (RCA) to identify the cause of the problem
- Develop an action plan to correct the problem and prevent recurrence
- Implement the plan
- Evaluate the effectiveness of the correction



Root Cause Analysis (RCA)

- By conducting an RCA, you will be able to identify the root causes of problems
- Some methods of RCA:
 - Brainstorming
 - The 5 Whys
 - Flowcharting
 - Fishbone Diagrams
 - Affinity Diagrams



CAPA Implementation May Include:

- Correcting or implementing revisions to the documentation
- Retraining study personnel
- Re-consenting study subjects
- Revising your department SOPs
- Reporting to the IRB/FDA or other agency, as required



Summary

- The best approach is to identify potential problems or risks and implement new processes to mitigate those risks as they are identified.
- Each event can be used as a teaching tool to prevent future recurrence.
- The CTQA program can assist with:
 - Setting up systems and processes at the beginning of a trial
 - Friendly compliance review during a study
 - Support prior to and during FDA inspections or Sponsor audits



Resource Links:

- ICH GCP E6(R2) dated 9 November 2016:

http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R2_Step_4.pdf

- Office of Clinical Trials - Links to internal and external resources (FDA, OHRP, NIH, Associations, Policies, etc.):

<http://research.unc.edu/clinical-trials/resources/>

- Office of Clinical Trials - Links to Forms/Templates (DOA log, SAE log, Start-up Checklist, Training log, etc.):

<http://research.unc.edu/clinical-trials/resources/forms/>



Resource Links:

- **UNC-Chapel Hill Individual Email Address Policy:**
<https://its.unc.edu/files/2014/08/email-address-policy.pdf>

- **UNC HCS Privacy Guidelines:**
<http://www.med.unc.edu/security/hipaa/documents/privacyguidelines-12-18-07.doc/view>

- **Cell Phone Usage and HIPAA Privacy Violations:**
<http://www.med.unc.edu/security/hipaa/documents/Cell%20Phone%20Usage.doc/view>



Thank you!

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