Audit Findings in Clinical Trials: Avoiding the Pitfalls

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Top Clinical Trial Audit Finding Areas

- Informed Consent Process & Documentation
- Accurate and Complete Study Records
- Determination and Documentation that Eligibility Criteria are Satisfied
- Adverse Event Review and Reporting
- Drug/Device Accountability
- Protocol Adherence
- Poor Regulatory Site Documentation
- Failure to Address Monitor Findings
- Sponsor-Investigator Trials

Informed Consent Process and Documentation

- Incorrect consent version
- No source documentation of consent process and fact that subject was provided a copy of consent
- Consent not dated by subject
- Check boxes left blank; pages not initialed by subject
- No HIPAA Authorization
- Original consent missing
- Not re-consented when required
  - Long lag time between signed consent and start of participation

Solutions

- Include a note regarding consent process -- how it was conducted; whether questions were asked/answered; fact that signed copy was provided
- Before starting consent process, check to make sure you have latest approved version from IRB
- NEVER fill out consents in advance
- REMEMBER – Informed Consents aren't the same as HIPAA Authorizations
- Watch your times – Goldilocks Rule
  - Not too much, not too little – Just Right!

Accurate and Complete Study Records

- Discrepancies between CRFs and medical records/source documents
- Incomplete CRFs
- No documentation of PI review of CRFs
- Improper Error Correction
  - NO WHITE OUT; NO PENCIL

Solutions

- Read the protocol and CRF forms carefully before starting the study to make sure:
  - CRF captures necessary study data
  - Source document captures necessary study data
- Set up a regular research team meeting time to review study data
- Avoid Messy CRF Build-Up
  - Complete forms in real time – not just before the next monitoring visit

Determination and Documentation that Eligibility Criteria are Satisfied

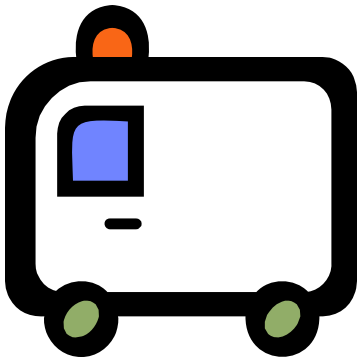
- Eligibility checklists incomplete
- No source documentation confirming eligibility criteria
- Failure to conduct all tests needed to satisfy eligibility criteria
- No documentation that PI has reviewed and signed eligibility checklist
- No documentation of sponsor waiver of eligibility requirement or waiver by PI when protocol specifically states that no waivers are allowed

Solutions

- Set up a process for PI review/signature of eligibility checklist
- Document any waivers from sponsor
- REMEMBER – don't confuse treatment with research
  - Protocol may call for tests within a certain window for eligibility determination even though in a treatment context those tests might not be required

Adverse Event Review and Reporting

- Conflict between CRFs and source documentation, e.g., AE noted in medical record but not on CRF, or vice versa
- AEs not signed/graded/attributed in a timely manner
- Failure to follow reporting requirements



Solutions

- Evaluate AEs in real time
- Review the reporting requirements
  - IRB Policy & Procedure 64 – Investigator Reporting Obligations to IRB
  - Clinical Trial Agreement

Drug/Device Accountability

- No documentation that oral drug was provided to subject and/or returned by subject with pill count
- Poor documentation regarding drug diaries
- Poor prescription practices

Solutions

- Document reminders to subjects to complete pill diaries and return diaries/drug
  - Phone call before visit and after visit
  - Letter seeking return of drug
- Improve script practices
  - Make sure all are signed by physician
  - Print name and phone number under signature
  - Provide IDS with list of authorized prescribers and their signatures

Protocol Adherence

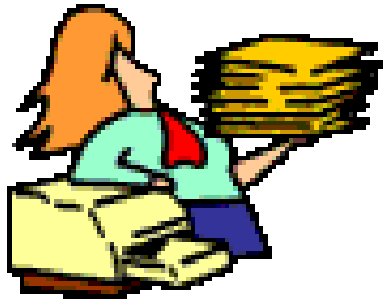
- Changes made in protocol without first obtaining IRB approval for reasons other than immediate patient safety
- No documentation of reason for missed tests, schedule changes, etc.

Solutions

- Read protocol BEFORE starting the trial to make sure it is realistic and to identify differences between what protocol requires and what would typically be done in a treatment situation
- Don’t confuse treatment and research
- If a protocol deviation occurs more than once, determine if protocol modification is appropriate
- Document deviations a[illegible]vare of reporting requirements

Poor Regulatory Site Documentation

- No delegation of duties log
- No up-to-date folder with CVs, licensing info, etc.
- No SOPs
- Missing records and poor record storage

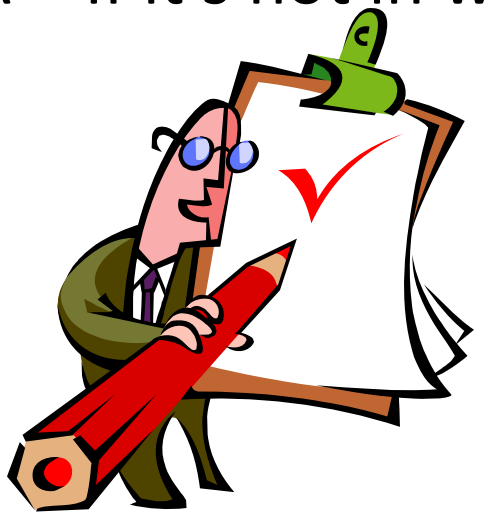


Solutions

- Start every study with a delegation of duties log and review with all study team members
- Look at your Clinical Trial Agreement for record retention requirements
  - Remember to negotiate for funds to cover document maintenance costs

Failure to Address Monitor Findings

- Ignore sticky notes at your peril.
- Solution: Don't let it wait – set rigid timetable for addressing all monitor findings and documenting how they were addressed
  - REMEMBER – If it's not in writing, it didn't happen



Sponsor-Investigator Trials

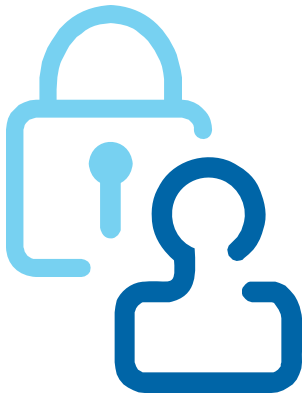
- Investigator must meet BOTH Investigator and Sponsor Responsibilities
- Watch out for multi-site trials
- Solution – ASK YOURSELF:
  - Can I do this?
  - Do I have the resources to do this?
  - Do I want to take on this responsibility?

Re-Sponsorbilities Checklist

- IND
- Annual Reports
- Protocol Amendments
- PI Selection & Obtaining:
  - CV, 1572, financial disclosure
- Investigator Brochure
- Monitoring Trial
  - Selection of Monitor
  - Documented transfer of any obligations to be carried out by CRO
- Safety reports on AEs/risks to all investigators and FDA
- Ensure FDA compliance by all investigators
- Evaluate safety and effectiveness data
- Drug accountability records
- Labeling

Bonus Feature: New HITECH HIPAA Rules on Breach Notification

- Effective Sept. 23, 2009
- Covers “Unsecured PHI”
- Breach Notification is required if the unauthorized disclosure, use, acquisition or access compromises the security or privacy of the protected health information by posing a significant risk of financial, reputational or other harm to the individual
  - Notice by Mail - Always
  - Notice in broadcast media - Sometimes
- Encryption is the key!



Questions ?

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