Audit Readiness

BLANCA PERNIC
QUALITY ASSURANCE OFFICER
Purpose of audit

- To verify compliance with federal regulations for the protection of human research subjects
Difference between Monitoring and Auditing

Monitoring:
The act of overseeing the progress of the clinical trial, and ensuring that it is conducted, recorded, and reported in accordance with the protocol, SOP, GCP and applicable regulatory requirements.

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 recorded, analyzed and accurately reported according to the protocol, sponsors SOPs, GCP and applicable regulatory requirements.
Pre-inspection activities

After receiving a call from an auditing body, notify the relevant stakeholders:

- Sponsor
- Sponsor Investigator
- Principal Investigator
- Sub-Investigator
- Study Coordinators
- Medical records

- IRB
- Investigational Pharmacy
- Clinical Laboratories
- Reception Area Staff
- Quality Assurance
Pre-inspection activities

Identify
- Identify a staff member to be the Audit Escort to accompany the auditor during the inspection.

Designate
- Designate a staff member to take notes during the audit.

Designate
- Designate a staff member to photocopy any exhibits being subjected to inspection and keep a log of those materials.
Pre-inspection activities

- When an Auditor asks you to make a copy of a document...
  - Stamp copy with “Copy” stamp & sign your first initial and last name next to the stamp.
  - If the document contains any patient information (name, MRN, DOB, next of kin names, SSNs, patient study initials, etc.) redact this information with a redaction pencil.
  - Keep a log of what you gave the auditor or make an extra copy of what was given to auditor.
Assemble the following documents:
- Protocol
- Investigator’s Brochure and IND Safety Reports
- IRB correspondence, including approval documentation and final report to IRB and Sponsor
- IRB-approved Informed Consent form
- IRB-approved advertising
- Study-related correspondence, excluding investigator agreement and financial information
- Monitor sign-in Log
- Laboratory certification documents
- Drug accountability records
- Each subject’s signed informed consent
- Assess the support areas (pharmacy, lab) to be sure they are properly prepared
Do’s and Don’ts

- Be friendly and courteous but don’t offer free meals, just beverage
- Show the inspector where the restrooms are, emergency exits, etc.
- Answer all questions honestly, succinctly and factually
- Answer only the questions asked by Inspector
- Request clarification before answering unclear questions
- Focus on facts related to the study only. Do not comment on other sites
- Do not offer opinions, speculations or suppositions
- Ensure PI and key research personnel are available at all times during inspection
- Provide a friendly work environment for the inspector, (phone, desk, chair)
- Take notes when possible
- Offer assistance to the auditor in making copies, software assistance, etc.
Do’s and Don’ts

- Do not answer questions you do not know the answer to
- Say you do not know the answer and defer to the Subject Matter expert
- Do not fill the silence
- Do not make jokes
- Do no become defensive or emotional
AUDIT DAY
Inspection activities

Protocol

- Make sure all versions of the clinical protocol are available
- Confirm all signatures are present and dated
- Make sure all protocol amendments and memorandums are available
Inspection activities

Documents

- Investigator’s brochures
- IND Safety Reports
- Consent forms
- IRB Approval for original protocol
- IRB Approval for protocol amendments
- IRB Approval for revised Informed Consent forms
- IRB approval for any subject compensation and documentation of payments
Inspection activities

Correspondence from Investigator to IRB

- Submission of all versions of protocols
- Including investigators brochure
- Annual reports
- Final report
- Notification of premature discontinuation from trial
- Clinical holds
- Package insert for that drug
- All IND safety reports
- All site Adverse Events
Inspection activities

Correspondence from Investigator to Sponsor / Sponsor investigator
- Adverse events
- Documentation of telephone conversations regarding trial
- Hard copies of emails
- Notes to file
- Memoranda
- Letters from the Monitors
Inspection activities

**LOGS**

- Enrollment logs: Confirm it is current, legible, and available for inspection
- Delegation of Authority – DOA logs: Confirm name and signature of all staff authorized to make entries in case report forms
- Trial initiation monitoring visit report is available for inspection
- Signed and dated monitoring visit log
Inspection activities

Study Team

- Documentation of staff protocol training
- Good Clinical Practice / Human Subject Protection training documentation
Inspection activities

<table>
<thead>
<tr>
<th>Pharmacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>✔ Study team - CV’s, licenses of key pharmacy personnel</td>
</tr>
<tr>
<td>✔ Log records</td>
</tr>
<tr>
<td>✔ Investigators brochures</td>
</tr>
<tr>
<td>✔ Certificates of Analysis</td>
</tr>
</tbody>
</table>
HIPPA – Patient Confidentiality

“According to your HIPAA release form I can’t share anything with you.”
Good Documentation Practices

- Ensure traceability between two or more documents.
- Use indelible ink.
- Do not use pencils.
- Legible handwritten entries.
- Do not use white out.

Handling omitted data: Clearly indicate the date the activity was performed and the date the activity is recorded on the documentation.

Document an explanation to substantiate the entry and the reason for the delay in recording.

Sign and date the change.

Do not use post-it notes.
### Adverse Event

<table>
<thead>
<tr>
<th>AE #</th>
<th>SAE</th>
<th>Start Date mm/dd/yy</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>Anomaly</td>
<td>2/14/17</td>
</tr>
<tr>
<td>18</td>
<td>Headaches</td>
<td>12/10/15</td>
</tr>
<tr>
<td>20</td>
<td>Fatigue</td>
<td>2007</td>
</tr>
<tr>
<td>30</td>
<td>Hyperpigmentation</td>
<td>9/2011</td>
</tr>
<tr>
<td></td>
<td>Hand-foot syndrome</td>
<td></td>
</tr>
</tbody>
</table>

**Notes:**
- No initial, date or explanation.
- Better with initial and dates but no explanation.
- Lots of date corrections.
- No scribbling out. Must be single line cross through.
Clinical Research Documentation

ALCOA-C CHECKLIST

If it wasn’t documented, it wasn’t done.

Having its roots in the federal regulations governing good laboratory practice for non-clinical laboratory studies, or 21 CFR 58.180 (c), ”ALCOA” remains the practice of FDA auditors and quality assurance professionals regarding clinical practices. This checklist reflects the recently updated guidelines (ICH GCP E2 Rev2) and how clinical research professionals should apply them to their study.

Attributable
- It should be obvious who created a record, and when it was created.
- If a record was changed, it should be obvious who made the change, when the change was made, and why.

Legible
- The research record should be easily read.

Contemporaneous
- Study evidence/results should be recorded as they are observed.
- All signatures/initials should be attached to a date indicating when the signature was added to the document.

Original
- Study records should be original, not photocopies.

Accurate
- Study records should have a high level of integrity and honesty to what was truly observed, give a full accounting of the research process.
- Study records should be thorough and correct; work should be double checked for unintentional errors.

Complete
- Investigators and institutions should maintain adequate, accurate and complete source documents.
Common deficiencies

- Failure to follow investigational plan
- Protocol deviations (and failure to properly document and report deviations)
- Failure to ensure that informed consent was obtained in accordance to 21 CFR 50
- Failure to maintain accurate, complete and current records
- Lack of appropriate accountability for investigation agent
- Failure to obtain IRB approval
Common questions asked during an audit

- Provide an overview of the study including background, objectives, study design, duration of the study, subject population, number of subjects, etc.
- How are potential research subjects identified?
- Who screens and recruits' subjects?
- Were all advertisements used for recruitment IRB approved?
- Who verifies inclusion and exclusion criteria?
Common questions asked during an audit

Who obtains informed consent/assent?

Were screening and enrollment logs used and maintained during the conduct of the study?
Use the audit as a learning opportunity

- Are we following best practices?
- Can we improve a particular process?
- Do we need more training in a particular area?
Your success is our goal!