CONDUCTING COMPLIANCE ASSESSMENTS

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Agenda

- **Types of Assessments**
- **Objectives**
- **Selecting the Site(s) to Audit**
- **Investigator Site Audit & Follow-Up**
- **FDA Clinical Investigator Inspection**

Objectives

- **Ensure rights & safety of study subjects**
- **Ensure integrity of data**
- **Verify compliance with regulatory requirements**
- **Verify compliance with protocol requirements**

Selecting the Investigator Site To Be Audited

- Study Drug, Protocol or Project
- Number of Patients Accrued
- Complexity of Study
- Experience of the Investigator / Site
- History with the company (via monitors or audits)
- Experience of the monitor or CRO
- For Cause - concerns identified

Preparing for the Investigator Site Assessment

- Notify the internal clinical group (monitor / medical monitor)
- Discuss plans and process with internal clinical group
- Request data base, CRFs, regulatory documents
- Conduct In-House audit
- Request specific charts depending on the situation
- Clinical Group arranges the assessment visit
- Conduct the assessment

Conducting the Investigator Site Assessment

- Interview responsible site personnel - confirm no changes since last monitoring visit or study start
- Review regulatory study file
- Compare CRF entries to source records
- Confirm any deviations
- Assess Pharmacy - records, storage
- Assess any special requirements - freezer, diagnostic equipment

INTERVIEW STAFF

- **Verify involvement of the investigator**
- **Verify responsibilities delegated**
- **Review informed consent process**
- **Review other systems implemented at investigator site**

STUDY FILE REVIEW

- **Regulatory documents - FD1572, CVs, IRB composition, lab normals, financial disclosure statement ……..**
- **Most recent consent form and all versions**
- **IRB approval and appropriate reapproval(s)**
- **Current protocol and all amendments**
- **Signature log - site staff**
- **Monitor log and correspondence**
- **Study specific**
- **Financial payments usually not reviewed**

SOURCE RECORD REVIEW

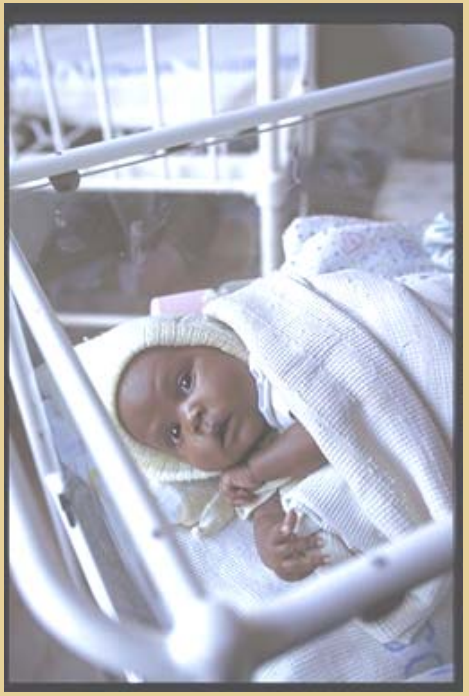
- **Verify involvement of the investigator**
- **Who is doing what (consent, randomize, exams, dose adjustments)**
- **Confirm source records support dates and data in CRF**
- **Confirm all sources for records identified**

PHARMACY REVIEW

- **Verify investigator involvement**
- **Verify records are maintained and up-to-date**
- **Verify drug only dispensed to study subjects**
- **Verify storage conditions are appropriate**
- **Review Inventory supplies**
- **Preparation area (if appropriate)**

RED FLAGS - The watch out

- Subject registered or examined on holiday/weekend
- Subjects seen when physician is not in the office
- New concomitant medicine; no new adverse event
- No corrective action for known problems
- SAEs not in CRF
- Consent form irregularity
- Lack of study drug accountability
- Lab results repeating or rounded
- Everything is too perfect ???



Post - Assessment & Follow-Up

- **Wrap-up discussion with site staff**
  - **summarize processes found in compliance**
  - **review anything requiring corrective action**
- **Audit report written and addressed to clinical area**
- **Action Plan to address findings in established time frame**
- **Open items followed by audit team until closure**

FDA INSPECTIONS

- NDA support vs. for cause
- Standard format / process
- Inspection results are available through FOI
- Warning Letters posted on the FDA Home Page
- FDA Compliance Program URL:
  www.fda.gov/ora/compliance_ref/bimo/7348_811/default.htm

QUESTIONS

&

DISCUSSION