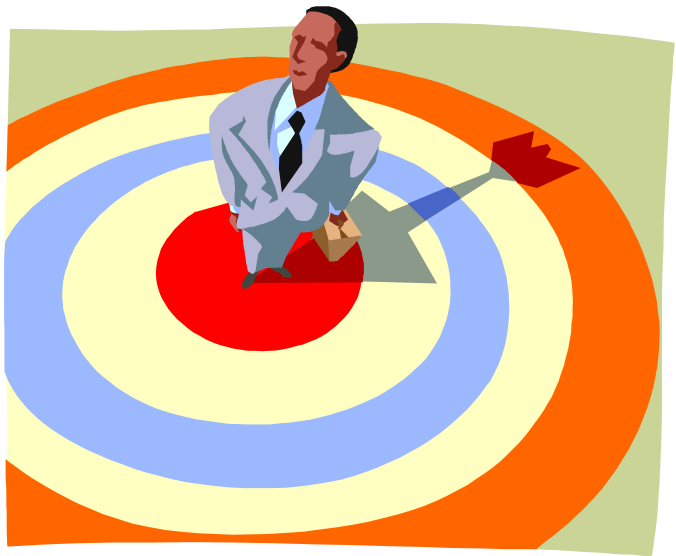
Preparing for an FDA Inspection

Why does the FDA conduct inspections?

- Ensure the rights, safety, and welfare of participants are being protected.
- Ensure adherence to regulations.
- Assess quality and integrity of data submitted in support of products pending FDA approval.

What might make an investigator (or a study)more susceptible to an audit?

- Large number of studies
- Lapses in IRB approval or IRB suspension
- Reports of superior efficacy for a drug/device
- Significantly fewer reports of AEs than other sites.
- Complaints



What can the FDA look at?

- The regulations require that sponsors and investigators grant authorized FDA employees access to the following:
  - Any location where drugs/devices are stored.
  - Any location where devices are manufactured, processed, packed, installed, used, or implanted.
  - Study documents including but not limited to: list of studies performed by the PI, 1572, lab certificates, copies of IRB documentation, delegation of duties log, monitoring log, source documents, records of drug/device use and results, etc.
- The regulations also allow copying of all records relating to an investigation.

Types of Inspection

- Study-Oriented (Not for Cause)
  - Routine surveillance
- Investigator-Oriented (For Cause)
  - Complaints, Termination of study, Multiple reports of serious or continuing noncompliance

How to Prepare (before the call)

- Conduct regular internal compliance checks
- Identify potential weak spots.
  - Disorganized or incomplete binders
  - Opportunities for drug/device mix-up or unauthorized use
- Keep up with Children's Policies and Procedures.
- Provide adequate training for study staff (including study specific, CITI, and GCP).
- Ask for help when you need it.

ALWAYS BE PREPARED!

How to Prepare (when you receive the call)

- Call the IRB and Research Compliance Offices.
- Call the FDA to schedule/confirm the appointment.
- Approach this as a learning opportunity.
- Identify roles (point person, someone to help with copying filing).
- Prepare adequate workspace for inspector.
- Prepare all study staff for interview.
- The PI must make time to prepare.

During the Inspection

- The Inspector must present credentials and a Notice of Inspection (Form FDA 482).
- The PI and point person should arrange to attend ALL interviews.
- If the Inspector is agreeable, schedule close-out summary meetings at the end of each day.
- Escort the Inspector.
- Be responsive and cooperative.
- Clarify any unclear questions.
- Don't blame-shift.
- Keep a record of questions the inspector asks.
- Provide (and record) requested documents.

What are they looking for?

- Delegation of duties.
- Inclusion criteria met.
- Process for obtaining informed consent.
- Condition of source documents.
- Documentation that subjects existed and came to appointments.
- How drugs/devices are controlled and accounted for.
- Monitor evaluations.
- Missing information (dates, signatures, lab results, etc.).

What do they usually find?

- Informed Consent process and documentation issues.
- Problems with accuracy and completeness of study records.
- Eligibility criteria not recorded or not met.
- Improper AE review and reporting.
- Issues with drug/device accountability.
- Poor regulatory site documentation.
- Failure to address monitor findings.
- Inadequate PI oversight.

After the Inspection

- Exit Interview
- Discuss the findings and issue an FDA Form 483 (Inspection Observations).
- Establishment Inspection Report (EIR)

Post-inspection Activities

- A corrective action plan should be developed and sent to the Inspector's district office.

  The FDA issues two types of letters when deviations are found:

  - Voluntary Action Indicated (VAI)
  - Official Action Indicated (OAI)

Responding to the Findings

- The response should be from the PI.
- Include an explanation and provide documentation of any mistakes or misunderstandings.
- For all other findings, ACCEPT RESPONSIBILITY, evaluate the errors, and provide a corrective action plan.
- Request your response be included with any release of the 483.

Focus of recent audits

- Consents
- Adverse event reporting
- Delegation logs

Recent findings

- Lapse in approval
- Inadequate drug disposition logs
- Failure to provide FDA with file annual report
- Failure to provide FDA with IND safety report

FDA Warning Letters

http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/default.htm