Inspector's Preparation for a CI Inspection: FDA Compliance Program & the Records Inventory

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Compliance Program Guidance Manuals (CPGMs) -1-

- FDA's SOPs for the conduct of inspections
- Developed and periodically updated by agency work groups
- Describe
  - Preparation and planning
  - Conduct of the inspection
  - Report and documentation of findings
- Allow FDA investigator/inspector flexibility to expand the inspection dependent on observations

CPGMs -2-

- BIMO CPGMs cover
  - Clinical investigators
  - Sponsors/Monitors/Contract Research Organizations (CROs)
  - IRBs/IECs
  - Bioequivalence (and bioavailability) studies
  - Nonclinical laboratories (GLPs)

CI CPGM

- Current version available at http://www.fda.gov/ora/ftparea/compliance/48_811.pdf
- Includes
  - Objectives & administrative authority
  - Assignments
  - Conduct of inspection -- including specifics of what and how to inspect (with product-specific information)
  - Reporting
  - Administrative and regulatory follow-up
  - Pertinent references and contacts

Conduct of the Inspection

- Clinical investigator inspections are usually study specific
- Compliance program describes minimal scope; assignment specifics may augment; inspectional findings may require further expansion
- Majority of on-site inspection time consists of records review
- Need to determine early in the inspection what study records are available on site – determine if any essential records need to be “retrieved”

Records Inventory -1-

- FDA inspectional emphasis = data audit
- Essentially an assessment of data quality and integrity
- Includes confirmation of adherence to study protocol and regulatory compliance
- Inspectional approach – comparison of source data with CRFs, and data submitted in support of marketing application when appropriate

Records Inventory -2-

- Identification of source data and source documents
- Copy of completed CRFs
- Safety reports, if applicable
- Identify what should be there --- and what is available for each subject

Records Referenced in FDA's CI Compliance Program

- Agreement with sponsor (Form FDA 1572, investigator agreement)
- IEC/IRB and sponsor correspondence
- Protocol and amendments
- Subject case histories – source documents and case report forms (CRFs) – includes informed consent documents
- Investigational product accountability
- Required reports

ICH E6 As a Guide to Records Inventory

- Section 8 of the ICH E6 guideline defines “Essential Documents” that should be retained at the investigator (and sponsor) sites
- Lists documents to be available at the initiation of the study, during the conduct of the study, and after completion of the study

Clinical Investigator (CI) Records -1-

- Investigator’s Brochure, including updates
- Protocol, amendments, revisions
- Information given to the study subjects
  - Informed Consent form – revisions, if appropriate
  - Any other written information
- (Financial aspects of the study)
- (Insurance statement – where required)

CI Records -2-

- Signed agreements between involved parties
  - Investigator and Sponsor
- Dated, documented IEC approval(s)
  - Protocol
  - Amendments
  - Informed Consent form
  - Other written information to subjects
  - Recruitment materials
  - Subject compensation

CI Records -3-

- (IEC composition)
- (Regulatory authority authorization[s])
- Curriculum vitae
  - Clinical Investigator
  - Subinvestigators/site staff (List of duties)
- (Laboratory information; normal values at study initiation, with any necessary updates during the course of the study)

CI Records -4-

- Shipping records for investigational product and study-related materials
- Appropriate labeling of investigational product
- Instructions for handling investigational product
- Decoding procedures for blinded studies
- (Study initiation monitoring report, monitoring visit reports, close-out report)

CI Records -5-

- Relevant communications with sponsor
  - Letters
  - Meeting notes
  - Records of calls
- Signed and dated Informed Consent forms
- Source documents
- (Signed) completed CRFs
- Documentation of CRF corrections

CI Records -6-

- Notification to sponsor (and IEC) of serious adverse events
- Notification by sponsor to CI re: important safety information
- Interim reports to IEC
  - Supporting IEC's continuing review
  - Timeliness

CI Records -7-

- Subject Screening "Log"
- Subject Enrollment "Log"
- Investigator product accountability at the site
  - Documentation of return or destruction at end of study
- (Signature sheet: Authorized signatures)
- Study reports

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