Inspecting Sponsors and Contract Research Organizations

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APEC GCP Inspection Workshop
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Sponsors -1-

- Responsible for general conduct of clinical trials – important to understand process and quality controls
- In direct communication with regulatory authorities and must provide adequate information to investigators
  - Required communication must be accurate, timely, and complete
Sponsors -2-

- Handle study data – from time it leaves the investigator site until it is communicated to regulatory authorities
- Handle and account for investigational product – including control of shipping and receipt by investigator(s)

Sponsors -3-

- Duties and functions can be contracted to others – commonly Contract Research Organizations (CROs)
- FDA regulation governing investigational pharmaceuticals (drugs and biologics) addresses transfer of regulatory responsibilities
- FDA device regulation does not include such language
- Sponsor ultimately responsible for conduct of studies
Sponsor/CRO Inspections -1-

- May be issued
  - On receipt of marketing application/submission
  - Upon receipt of a complaint/concern
  - For general surveillance
- Usually study-specific
- Usually pre-announced

Sponsor/CRO Inspections -2-

- Inspection includes
  - Notice of inspection and credentials
  - Opening interview (and secondary interviews as appropriate)
  - Records inventory and audit
    - Data audit – where appropriate
    - Records of research subject protection
    - Control of investigational product(s)
  - Documentation of objectionable findings (exhibits)
  - Close-out discussion
Elements of a Sponsor/CRO Inspection -1-

- Organization and Personnel
  - Key research processes: Where and by whom (organizational structure and staffing) are these conducted by the sponsor
  - What (if any) sponsor duties and functions are contracted
    - Contracted to whom
    - Written documentation (contract)
    - Sponsor oversight of contracted duties

Elements of a Sponsor/CRO Inspection -2-

- Selection of/communication with investigators
  - Criteria for evaluating investigator qualifications and training
  - Correspondence with and provision of adequate information to investigator(s)
    - Investigator’s Brochures; safety updates, etc.
  - Identification of any GCP noncompliant investigators and corrective actions taken to secure compliance or terminate
### Elements of a Sponsor/CRO Inspection -3-

- Monitors and Monitoring
  - List of all monitors for the selected study
  - Qualifications, selection, training of monitors
  - SOPs for study monitoring (FDA investigational device regulation requires written SOPs; also in ICH E6 5.18.6)
  - Review of monitoring/site-visit reports
  - Follow-up to corrective actions identified in monitoring reports

### Elements of a Sponsor/CRO Inspection -4-

- Adverse event reporting
  - Review of systems for tracking adverse events, ensuring the receipt of information from investigators and relay to regulatory authorities (and other study sites/IECs as required)
- Data handling/data audit
  - SOPs for data handling; following these SOPs
  - Audit of data quality/integrity from source (investigator site) through data listings/analysis to submission in applications/reports
Elements of a Sponsor/CRO Inspection -5-

- Control of investigational product(s)
  - Integrity from manufacture to receipt by the investigator, including integrity of “blinding”
  - Accountability through final disposition
- Review of automated (computerized) processes
  - Procedures
  - Validation; change controls
  - System security
  - Audit trails

Elements of a Sponsor/CRO Inspection -6-

- Recordkeeping
  - Record storage and security
  - Availability of records for inspection
- Multiple regulated studies
  - While the inspection assignment is usually focused on a single selected study, additional regulated studies may be identified and reviewed during the course of a sponsor/CRO inspection
  - Emphasis is on process implementation and quality
**Most Common Deficiencies**

- Inadequate monitoring
  - Lack of qualified monitors
  - Lack of documentation of monitoring visits
  - Lack of adequate procedures
- Failure to bring investigators into compliance
- Inadequate accountability for the investigational product

**FY’07 Sponsor Inspections**

**Classified**

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FY’07 Sponsor Inspections
Classified – All Centers

Sponsor Exercise
Disclaimer:

The information within this presentation is based on the presenter's expertise and experience, and represents the views of the presenter for the purposes of a training workshop.

What This Lecture will Address/Review

- Key Activities in a Clinical Trial
  - The Process Approach
- Brief History of GCP (U.S. and international)
- Goals and Principles of GCP
- Roles and Responsibilities Under GCP
  - Investigators
  - Sponsors/Contract Research Organizations
  - Ethics Committees