Fourth Annual Medical Research Summit

Concurrent Session 4.05 – Managing CROs and SMOs from a Compliance Perspective

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Aprill 23, 2004

Agenda for Concurrent Session

- Introductions
- Industry Background
- An Approach to Managing CROs and SMOs
- FDA Inspections
- Fraud and Abuse in Clinical Trials
- Questions & Answers

Industry Background

Industry Background

Complex Scenario

- Intensive regulatory process
- Demand for higher quality clinical data
- Competition for clinical investigators
- Shortage of human subjects
- Global clinical research programs
- Co-development partnerships
- Reliance on outsourcing to service providers (e.g., CROs and SMOs)

Industry Background

Outsourcing is not a new concept

- Estimated that 42% of all pharmaceutical drug development expenditures in 2004 will be committed to outsourcing
- Skyrocketing growth of the CRO market
  - 1992 – approximately $1 billion
  - 2002 - > $8 billion
  - 1992 – 7 million subjects
  - 2001 – 20 million subjects
- Rapidly evolving business of SMOs for managing multi-site clinical trials
- CROs and SMOs – competitors, partners or both?

Industry Background

Basic premise for this presentation under 21 CFR 312.52 *Transfer of obligations to a contract research organization.*

Sponsor → CRO

Sponsor → SMO

Sponsor → CRO → SMO

CROs = SMOs

Industry Background

FDA Compliance Program 7348.810 - Sponsors, Contractors, and Monitors of Clinical Investigations

- Responsibilities of sponsors:
  - Obtain agency approval for clinical studies
  - Manufacture and label investigational drug
  - Initiate, withhold, discontinue clinical trials
  - Select qualified investigators and monitors
  - Evaluate and report adverse experiences
  - Maintain records
  - Submit progress reports and the final results of studies

Industry Background

FDA Compliance Program 7348.810 - Sponsors, Contractors, and Monitors of Clinical Investigations

- Sponsors may transfer responsibilities to a Contract Research Organization (CRO):
  - Written agreement specifying transferred responsibilities
  - CROs are subject to same regulatory actions as sponsor

Approach to Managing CROs and SMOs

Approach to Managing CROs and SMOs

- Consider compliance-related implications when selecting, managing, evaluating, retaining and dismissing CROs and SMO
- Proposal – Follow the OIG Compliance Program Guidance for Pharmaceutical Manufacturers published in April 2003
- Rationale:
  - Seven elements of an effective compliance program
  - Based on U.S. Sentencing Commission's organizational sentencing guidelines
  - Communicated in OIG CPG and Corporate Integrity Agreements

Approach to Managing CROs and SMOs

- Seven elements of an effective corporate compliance program
  - Standards and Procedures
  - Oversight Responsibility
  - Education and Training
  - Lines of communication
  - Monitoring and auditing
  - Enforcement and Discipline
  - Response and Prevention

Approach to Managing CROs and SMOs

Seven elements of compliance programs applied to CROs and SMOs

- Standards and Procedures – Has the organization established written standards and procedures for the regulatory obligations assumed under 21 CFR 312.52? What about KPIs?
- Oversight Responsibility – Have individuals with the appropriate experience been assigned responsibility to oversee compliance with established standards?
  - Prior experience in Phase I through IV studies including numbers of studies, subjects, sites, etc.
  - Professional qualifications for monitors, project managers and CRAs
  - Average years of employment of monitors by the organization

Approach to Managing CROs and SMOs

Seven elements of compliance programs applied to CROs and SMOs (continued)

- Education and Training – Does the organization conduct training programs and document employee participation?
  - Orientation training for new hires
  - Ongoing training for experienced personnel
- Lines of Communication – Does the organization take steps to communicate its standards to employees and sponsors?
  - KPIs for trip reports, completion of CRFs, QA audits and findings
  - Hotline for reporting suspected violations

Approach to Managing CROs and SMOs

Seven elements of compliance programs applied to CROs and SMOs (continued)

- Monitoring and Auditing – Does the organization take reasonable steps to achieve compliance with its standards by routinely using monitoring systems?
  - % of clinical sites audited by QA; qualifications of auditors
  - Process for reporting audit findings and corrective action to the sponsor
  - Results of FDA audits

Approach to Managing CROs and SMOs

Seven elements of compliance programs applied to CROs and SMOs (continued)

- Enforcement and Discipline – Standards should be enforced consistently through appropriate disciplinary mechanisms.
  - Describe a situation where the organization had to remove a CRA from a study for performance issues.
  - What is the procedure for replacing study personnel?

Approach to Managing CROs and SMOs

Seven elements of compliance programs applied to CROs and SMOs (continued)

- Response and Prevention – Does the organization have a process for investigating suspected violations of standards, taking reasonable steps to respond appropriately, and to prevent further similar offenses?
  - Assigned responsibility for conducting investigations
  - Procedure for documenting findings
  - Review/approval of corrective and preventive action plans

FDA Inspections at CROs and SMOs

FDA Inspections

Suggestions to enhance readiness for inspection by regulatory agencies:

- Assign responsibility for managing an inspection to key individuals and identified designees
- Assign responsibilities for inspection tasks to individuals and designees (note-taking, retrieving documents, accompanying inspectors, etc.)
- Address logistics (meeting room, equipment, contact list, etc.)
- Review results of past sponsor and CRO audits
- Prepare and train through mock inspections

Fraud and Abuse in Clinical Trials

Fraud and Abuse in Clinical Trials

Fundamental concerns about the pharmaceutical marketplace

- Is money – or anything of value – interfering with independent clinical/formulary decisions?
- Is misleading, inaccurate, or other inappropriate information influencing independent clinical/formulary decisions?
- Are inappropriate marketing practices leading to increased federal/state/private expenditures?
- Are these or any other practices placing patient safety and interests at risk?

Questions & Answers

For More Information

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