FDA Guidance of Clinical of Research; Risk-Based Monitoring Plans: The Current Status

AAAAI 2013 Annual Meeting
Kathy L. Pinzone, RN, CCRC, AE-C
pinzone@email.chop.edu
• No Conflict of Interest

• No Financial Disclosures
Objectives

- Define monitoring and the focus of “risk-based monitoring”
- Discuss FDA Draft Guidance issued in August 2011
- Discuss the process of combining monitoring activities to effectively oversee a study
- Review approaches to developing a protocol-specific monitoring plan
FDA Draft Guidance

Guidance for Industry
Oversight of Clinical Investigations–
A Risk-Based Approach to Monitoring
August 2011
Introduction

- FDA guidance acknowledges “One-size-fits-all” approach in oversight of clinical research is not ideal
- Describes strategies for monitoring activities reflecting a modern, risk-based approach
Monitoring Guidance

- ICH E6 GCP guidelines define monitoring as:
  “The act of overseeing the progress of a clinical trial, and of ensuring that it is conducted, recorded, and reported in accordance with the protocol, Standard Operating Procedures (SOPs), Good Clinical Practice (GCP), and the applicable regulatory requirements”

- Monitoring is a requirement set forth in the federal regulations pertaining to IND and IDE research (21 CFR 312 and 21 CFR 812)

- The Sponsor is responsible for providing monitoring
  - 21 CFR 312.53(d)Selecting monitors. A sponsor shall select a monitor qualified by training and experience to monitor the progress of the investigation.

- Routine Monitoring differs from a Data Safety Monitoring Board (DSMB)
Monitoring

FDA’s approach to alternative monitoring
Withdraw of the January 1988 FDA Guidance, Guideline for the Monitoring of Clinical Investigations

- Technology has

• Development of the modern, risk-based approach included in the recent August 2011 draft guidance
Types of Monitoring

- On-Site Monitoring
  An in-person evaluation carried out by the sponsor personnel or representative(s) at the site(s) at which the clinical investigation is being conducted.
  Identify data entry error–discrepancies between source documents and CRFs
  Missing data or assurance data exists
Types of Monitoring: On–Site

- Assesses study staffs adherence to the protocol, required procedures, and investigational product accountability
- Assesses critical study data and processes, evaluates for significant risks and potential for site non-compliance
- On–Site is critical early in a study, especially with complex protocols and novel procedures.
Types of Monitoring

- Centralized Monitoring
  A remote evaluation conducted by sponsor personnel or representative(s) at a location other than the site(s) at which the clinical investigation is being conducted.
  Provides many of the capabilities of On-Site monitoring.
Types of Monitoring; Centralized

- Monitors activities such as standard checks of range, consistency, and completeness of data and checks for unusual distributions of data within and between study-sites.
- Monitor data quality through routine review of submitted data in real-time to identify missing data, inconsistent data, data outliers and potential protocol deviations.
Types of Monitoring

- Target on-site monitoring by identifying higher risk clinical sites—sites with a higher frequency of data anomalies or data errors, protocol violations, or dropout rates relative to other sites
Types on Monitoring

- Augment on-site monitoring by performing monitoring activities that can only be accomplished using centralized monitoring;
  - Identify data trends which are not easily detected by on-site monitoring
Development of Monitoring Plan

- Monitoring Plan should be based on:
  - Investigator experience
  - Complexity of protocol
  - Level of Risk
  - Subject population
  - Disease Entity
  - Trial Phase
  - Plans for data management
Development of Monitoring Plan

- Monitoring Plan should be based on:
  - Scope of services to be provided
  - Tools – SPOs or MOPs
  - Include a guide of responsibility for reporting to federal agencies, fiscal and regulatory sponsors, institutional officials and applicable IRBs.

Monitoring plans need to be flexible and dynamic in order to respond changes within the protocol.
Development of Monitoring Plan

- Though not prohibited by regulations, a sponsor-investigator may perform monitoring services, however, segregating these duties is important to maintain trial integrity.
- If possible, Contract Research Organizations (CROs) or risk-based monitoring from within a sponsor-investigators institution is recommended.
Development of Monitoring Plan

- Academic Medical Centers—Most engage in Translational Research and recognize that responsible clinical research programs involve more than IRB review.
- Research Compliance program at institutional level should address needs of sponsor-investigators:
Development of Monitoring Plan

- Monitoring services
- Centralized databases
- Development of metrics to collect, track, and trend issues
- Education and training for sponsor–investigators & staff on regulatory requirements, best practice trial management
- Develop monitoring plans with emphasis on human subject protection and data integrity
Development of Monitoring Plan

- Thank you