What Could Go Wrong? ICH E6 R2, Investigative Sites and Risk Assessment

Module 2 of a 4 Part Series

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What Could Go Wrong? ICH E6 R2, Investigative Sites and Risk Assessment

- Summary:
  - Experienced sites have encountered trials that have gone poorly for various reasons.
  - With real-time discussion about trial challenges and delays, we aim to help sites think differently about RBM.
  - We will present different perspectives on ICH E6 R2, explore the implementation of a risk-based approach, and how key risks are identified.
  - We'll also examine engagement with sponsors and CROs during protocol and clinical trial risk assessment.

Quality Management & Protocol Risk Assessment

What it is

5. SPONSOR

ADDENDUM

5.0 Quality Management

The sponsor should implement a system to manage quality throughout all stages of the trial process.

Sponsors should focus on trial activities essential to ensuring human subject protection and the reliability of trial results. Quality management includes the design of efficient clinical trial protocols and tools and procedures for data collection and processing, as well as the collection of information that is essential to decision making.

The methods used to assure and control the quality of the trial should be proportionate to the risks inherent in the trial and the importance of the information collected. The sponsor should ensure that all aspects of the trial are operationally feasible and should avoid unnecessary complexity, procedures, and data collection. Protocols, case report forms, and other operational documents should be clear, concise, and consistent.

The quality management system should use a risk-based approach as described below.

INTEGRATED ADDENDUM TO ICH E6(R1):
GUIDELINE FOR GOOD CLINICAL PRACTICE

E6(R2)

What it is ***not***

- Assessment of site performance
- Intended to add complexity to trial operations
- Standardized (yet!)

Polling question #1

- Which one of the following is a key contributor to trial conduct challenges for sites?
  a. Complex protocol procedures
  b. Difficult inclusion & exclusion criteria
  c. Over estimated recruitment rate expectations

Quality Risk Management Example

ICH GCP E6 ADDENDUM FOR RBM

5.0.1 Critical Process & Data ID

- Processes and data that are critical to assure human subject protection and reliability of study results

Primary endpoint in a trial is improvement in cognitive rating scales, so critical data is cognitive rating scale values and critical process is collection/conduct of cognitive rating scales

5.0.2 Risk Identification

- Risks to processes and data (SOPs, systems, personnel, trial design, data collection, informed consent process)

Risks to cognitive rating scales (what could go wrong?):site not using certified rater, not using same rater within a subject, subject not having eaten prior to scale, incomplete scales, scales completed out of order

5.0.3 Risk Evaluation

- Likelihood of occurrence, detectability / sufficient controls in place, impact to trial / patient

Per Medical Monitor and statisticians, any deviation in requirements for cognitive scales could have significant impact to data

5.0.4 Risk Control

- Reduce risks: protocol design, monitoring plans, roles & responsibilities, training

- Add instruction in protocol to set expectations around cognitive scale conduct/collection, include training at Inv meeting for raters
- Ensure data management plan has edits for scales out of range or missing data
- Ensure monitoring plan has expectations for CRAs to look for continuity in raters and protocol deviations
- Ensure centralized monitoring plan has trending of cognitive rating scales scores to identify anomalies that could signal potential transcription errors or protocol deviations

Poll Question #2

- In what ways can sites provide feedback on trial challenges (as part of the protocol risk assessment process)?
  a. Provide protocol risk assessment feedback on the site information forms (feasibility questionnaire)
  b. Investigator meeting
  c. Sponsor site advocacy group meetings
  d. During site qualification visits by monitors

How will the sites learn about the sponsor & CRO protocol risk assessment outcomes?

- During Investigator meeting
  - Protocol review and training on critical data and processes
- Site initiation visit
  - On-site and off-site monitoring strategy discussion
  - Review of critical data and processes for collection
- Interim and remote monitoring
  - Feedback on emerging risks, risk mitigation impact, and early course corrections

In a one, two, or three word phrase, where/how/when ca you effectively contribute to the risk assessment discussion?

Respond at **PollEv.com/riskassessment**

Text **RISKASSESSMENT** to **22333** once to join, then text your message

If your response is longer than one word, use a hyphen or underscore instead of a space when you text in! (ex: investigator-meetings or investigator_meetings). Multiple entries are encouraged!

Don’t miss the final two webinars in this series!

April 5 at noon ET:

Module 3 - What’s behind the curtain? Centralized Monitoring Unveiled

April 12 at noon ET:

Module 4 - An Exploration of Risk Based Monitoring from the Site Perspective

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