

Results and Recommendations:

Effective and Efficient Monitoring as a Component of Quality Assurance in the Conduct of Clinical Trials

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Effective and Efficient Monitoring Project*

■ Goal

- ◆ Identify best practices and provide sensible criteria to help sponsors select the most appropriate monitoring methods for a clinical trial, thereby ensuring reliable and informative trial results and human subjects' protection

■ Objectives

- ◆ Workstream 1: Describe the range of current monitoring practices and examine factors that drive their adoption
- ◆ Workstream 2: Define key quality objectives for monitoring clinical trials
- ◆ Workstream 3: Examine ways to build quality into trials to enable more focused and efficient monitoring

*<https://www.trialstransformation.org/projects/effective-and-efficient-monitoring/>

Results: Survey of Monitoring Practices*

Results consistent with hypotheses:

- **Wide variety of monitoring practices in use**
- **Choice of monitoring approach correlates with type of organizational sponsor**
- **Rationale for using any specific monitoring approach does not appear to be evidence-based**

***Poster of results on CTTI Website:**

<https://www.trialstransformation.org/projects/effective-and-efficient-monitoring/monitoring-project-workstream-1>

Results: Range of Monitoring Practices

- **On-site monitoring**
 - ◆ **Industry and CROs: 80% or more**
 - ◆ **Academic coordinating centers/cooperative groups/
government organizations combined: less than 33%**
- **Despite availability of central data, 33% or less use centralized data monitoring to guide, target, or replace site visits**

Results: Key Quality Objectives

Major quality objectives are to:

- **Protect participant rights, safety and wellbeing**
- **Ensure the reliability of the study results**
- **Maintain adherence to the protocol**

Also noted that monitoring provides:

- **An opportunity for focused training**
- **Feedback that can improve study processes**

Results: Building Quality into Trials

- **Primary focus should shift from post-hoc monitoring/inspection to incorporation of quality into the scientific and operational design of a trial**
- **No single monitoring approach is appropriate or necessary in all circumstances**
- **Monitoring approach for a given clinical trial should be tailored to the needs of that trial and may combine several methods**

Results: Building Quality into Trials

Focus on what is important:

- **Importance of proper randomization**
 - ◆ **no foreknowledge of likely treatment allocation**
 - ◆ **minimize post-randomization withdrawals**
 - ◆ **minimize loss to follow-up**
- **Sufficient numbers of relevant clinical outcomes**
- **Unbiased ascertainment and analysis of study outcomes**

Results: Building Quality into Trials

Oversight should focus on those errors most likely to adversely affect trial quality:

- **Data elements vary in their impact on the safety of participants or on the reliability of trial results**
- **Single-minded focus on checking/ensuring accuracy of every data point is misguided**
- **Sponsors and regulators should agree up front what data points are critical and need to be verified**
- **Sponsor should institute metrics to prospectively ensure the quality of critical data**

Primary Recommendation

■ Build quality into the scientific and operational design and conduct of clinical trials

◆ Focus on what matters

- “Quality” is defined as the absence of errors that matter (*i.e., errors that have a meaningful impact on patient safety or interpretation of results*)
- Determine what matters for the specific trial

◆ Develop a quality management plan

- Initiate in parallel with protocol development
- Focus on areas of highest risk for generating errors that matter
- Seek regulatory review of plan

◆ Assess performance in important parameters

- Prospectively measure error rates of important parameters
- Monitoring approach (e.g., site visits, central, statistical) should be tailored to the trial design and key quality objectives

◆ Improve training and procedures

- Based on measured parameters

◆ Report findings of quality management approach

- Issues found, actions taken, impact on analysis and interpretation of results
- Include in regulatory submissions and publications
- Encourage inclusion in ICMJE requirements

Ancillary Recommendations

■ Share knowledge and experiences

- ◆ Collaboration between academia, industry, and regulators to share methodologies and data

■ Encourage appropriate regulatory guidance

- ◆ Emphasize key principles of quality trials
 - i.e., human subjects protection, reliable results, protocol adherence
- ◆ Encourage risk-focused oversight of trials

■ Promote education and awareness

- ◆ Audience: those involved in design, implementation, analysis, interpretation, regulation, inspection, and publication of clinical trials
- ◆ Also include users of results (e.g., health care providers, doctors, and patients)

■ Seek international adoption and harmonization

- ◆ Facilitate global adoption of proposed changes