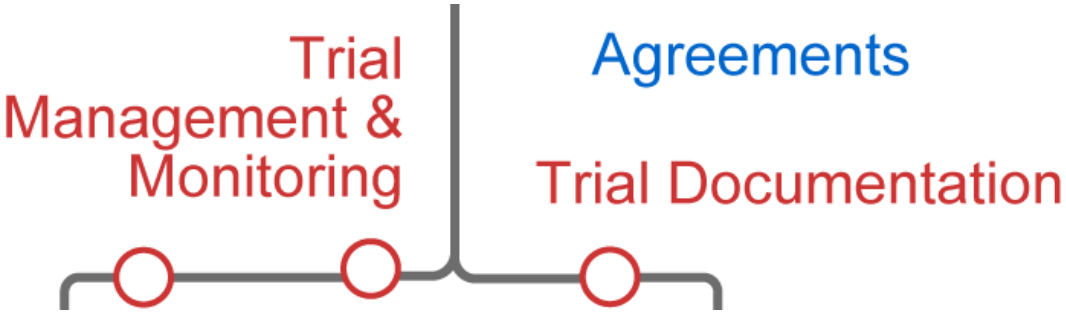
Routemap

Trial Management & Monitoring



Trial Planning Phase

Trial Management & Monitoring follows the Protocol Development station and precedes the Trial Documentation station. Trial Management & Monitoring is a legal requirement which is relevant to all trials. This station is part of the 'trial planning phase' group of stations.

Appropriate planning before the trial and adequate oversight and monitoring during the trial will help ensure that trial subject safety is maintained throughout the trial and that there is accurate reporting of results at its conclusion.

The sponsor is responsible for ensuring that robust trial management systems are put in place. The monitoring of a trial is one of the key activities undertaken as part of the trial's management. The MHRA accepts a risk-adapted approach to trial management and the advice specific to trial monitoring can be found in Appendix 2 of The Risk-adapted Approaches to the Management of Clinical Trials of Investigational Medicinal Products (pdf) (.PDF).

Risk-adapted trial management addresses the question:

What are the critical processes and critical data for this trial and how best can any risks and/or vulnerabilities identified in these areas be mitigated?

This question should be considered early in the protocol design stage so that processes to proactively manage those aspects of the trial that are critical to quality can be put in place. The US Clinical Trials Transformation Initiative (CTTI)

have produced a Toolkit including Quality by Design principles (.PDF) that provides a useful framework for this process.

Where trial management activities are contracted out to third parties, the sponsor must implement procedures to ensure appropriate **oversight** of all delegated functions. This can be achieved by:

- Assessing that individuals or organisations delegated trial management functions are appropriately qualified and competent to perform those functions.
- Ensuring all parties are aware of their roles and responsibilities (for example by clearly defining them in contracts and agreements).
- Maintaining lines of communication to ensure the obligations of all parties are being met (for example by receiving progress reports).

Documentation should be in place to describe all key processes. This ensures that those performing tasks have a clear plan of *what, when* and *how* trial activities are undertaken and also enables auditors/inspectors to historically reconstruct all trial management activities.

The following provide further information and guidance on trial management:

- The Summary of Trial Management Systems Workstream Document gives an overview of the activities associated with trial management as well as the requirement for oversight and documentation of those activities.
- The Monitoring Procedures Workstream Document gives further information on the types of monitoring a sponsor may implement (for example on-site monitoring or central statistical monitoring) and the documentation of all aspects of the monitoring process. Further examples of risk adaptation are also provided in the following Joint Project Workstream Documents:
    - Trial Scenarios in Monitoring which illustrates the approach to monitoring applied to five very different trials
    - NIHR Learn provides training to support staff involved in clinical trials, including GCP training and training for staff in service departments such as pharmacy and laboratories.
- The MHRA GCP Guide outlines the expectations for trial management and monitoring and provides a detailed description of all key processes and many examples of risk adaptation.
- The Trial Managers Network (TMN) is a source of practical support and guidance on the trial management process and has published comprehensive guidance: A Guide to Efficient Trial Management.

- The MRC-NIHR TMRP host a series of webinars on trial conduct including Monitoring trials efficiently: The role of central statistical monitoring.
- Consolidated Standards of Reporting Trials (CONSORT) reporting guidelines recommend that an accurate record of patients considered for RCT participation is maintained. The SEAR (Screened, Eligible, Approached, Randomised) framework (.PDF) provides a systematic way to record the flow of potential participants through the recruitment process to support better recruitment practices in clinical trials.
- Guidance on maximising the impact of qualitative research in feasibility studies for RCTs was developed to help researchers consider the full range of contributions that qualitative research can make in relation to their particular trial.
- The use of qualitative methods to inform Delphi surveys in core outcome set development (.PDF) identifies some issues for COS developers to consider.
- Developing and using progression criteria for internal pilot studies: Avery et al. (2017) (.PDF) outlines the key issues to consider in the optimal development and review of operational progression criteria for RCTs with an internal pilot phase.
- The UKCRC Registered CTU Network - Monitoring of clinical trials: a handbook, provides information on the theory of monitoring, tips on conduct and real life examples that may help to explain and support possible monitoring approaches and their application.

Further reading:

- The GCP Inspectors Working Group have published a number of documents relating to trial processes:
  - Reflection paper for laboratories that perform the analysis or evaluation of clinical trial samples (PDF, 135 KB) (.PDF)
  - Reflection paper on expectations for electronic source data and data transcribed to electronic data collection tools in clinical trials (PDF, 127) KB (.PDF)
- Several funders and journals require that Individual Participant Data from clinical trials are made available on reasonable request. Tudur Smith et al describe the development of the MRC Hubs for Trials Methodology Research (HTMR) guidance on Good Practice Principles for Sharing Individual Participant Data from Publicly Funded Trials.
- Guidance for researchers and study coordinators on the General Data Protection Act can be found on the HRA website.

- Khin et al. Data Integrity in Global Clinical Trials: Discussions from Joint US Food and Drug Administration and UK Medicines and Healthcare Products Regulatory Agency Good Clinical Practice Workshop. Clinical Pharmacology & Therapeutics, Volume 108, Issue 5.