Research and Enterprise

Standard Operating Procedure

Research Governance

Title:	**Monitoring of Research Studies**		
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Revision Log

Previous Version number	Date of Review/Modification	Reason for Review/Modification	New Version Number

1. Purpose

This Standard Operating Procedure (SOP) provides guidance for the monitoring of research studies that are sponsored by the University.

2. Scope

This SOP applies to all studies where the University is acting in the capacity of Sponsor/Lead Co-Sponsor. It applies to all members of University staff; both academic and support staff as defined by Statute 1, including honorary staff and students.

3. Responsibilities

3.1 Chief Investigator (CI)

The CI is responsible for the day-to-day monitoring of a study. This would include the following, that:

- Data collected are consistent with, and in adherence to, the study protocol;
- Case Report Forms (CRFs) are only being completed by authorised persons;
- No key data are missing;
- Review of recruitment rates, withdrawals and losses to follow-up (overall and by clinical site).

3.2 Site Principal Investigator (SPI)

In the event of a multi-centred clinical trial, the SPI is responsible for the day-to-day monitoring of a trial, as outlined for the CI in 3.1.

3.3 Sponsor

The Sponsor must ensure that studies are adequately monitored and will determine at the outset the extent and nature of the monitoring activity. Where a trial is co-sponsored with a Health and Social Care Trust, the co-sponsorship agreement will detail which organisation has lead responsibility for this process and the Memorandum of Understanding for Research Governance shall be adhered to.

4. Procedure

4.1 Extent and Nature of Monitoring

The decision regarding the extent and nature of monitoring a study should be in proportion to the objective, purpose, design, complexity, blinding, size and endpoints of the study (see Appendix 1). It must also be determined prior to the study commencing. Where there is a requirement for a study-specific monitoring plan this must be agreed by the Sponsor prior to study activation. The monitoring plan should clearly define the components of the study that require monitoring and the methods that will be used to monitor including on-site or remote monitoring. The monitoring plan should be amended if required, during the study and any changes agreed by the Sponsor.

4.2 Oversight Committees

There are a variety of approaches that can be employed to monitor a study. The procedures chosen should be determined at an early stage and reflect the complexity and risk involved in the study. The potential approaches include:

4.2.1 Trial Management Group

This Group is established to monitor all aspects of the conduct and progress of the study and it should include those persons with responsibility for the daily management of the study. Its purpose is to ensure adherence to the protocol and take any actions necessary to safeguard study participants. The need for a Trial Management Group and the membership should reflect the complexity and size of the study, though it may include the Chief Investigator (CI), research nurse, data manager, statistician, trial manager and data manager.

4.2.2 Trial Steering Committee

It is recommended that a Trial Steering Committee (TSC) is established for larger, multi-centred trials as they will provide overall supervision of the study and ensure that it is being conducted in accordance with the principles of Good Clinical Practice and in accordance with the legislative framework and relevant University Regulations. A TSC may include members who are independent of the investigators, and in particular it may have an independent chairperson.

A TSC should monitor the study's progress e.g. recruitment, data and ensure adherence to the protocol. Decisions about the continuation or termination of the study or substantial amendments to the protocol are usually the responsibility of the TSC.

4.2.3 Data Monitoring Committee

A Data Monitoring Committee (DMC) is established to review the accruing study data and to assess whether there are any safety issues that should be brought to participants' attention, or any reasons why the trial should not continue. The DMC should be independent of both the investigators and the Funder/Sponsor and should be the only group that has access to unblinded data.

4.2.4 Coordinating Centre

Daily monitoring is carried out by those responsible for running a trial.

4.2.5 Central Monitoring

Centralised or remote monitoring procedures can be used to confirm patient eligibility, to corroborate the existence of the patient and to determine the outcome. Examples of this might include the collection of pathology reports to substantiate a diagnosis, collection of an imaging investigation, central assessment of the results of an investigation, such as a X-ray or scan, investigation of study databases/completed case report forms, remote review of signed Consent Forms.

4.2.6 On-site monitoring

Arrangements for site visiting may vary from routine visits to all sites, visits to a random selection of sites or visits targeted at less experienced sites or those for which the central monitoring procedures suggest possible problems. On-site visits can include verification that study documents exist, assessment of the site's understanding of, and compliance with the protocol and study procedures, accountability checks for study supplies and checks of data quality and completeness, including source data verification.

4.3 Selection and Qualification of Monitors

Following the research study risk assessment and the establishment of an appropriate monitoring oversight committee(s) (e.g. Trial Management Group, Trial Steering Committee or Data Monitoring Committee), if required monitors should be appointed. It is the responsibility of the Sponsor/lead Sponsor to review and approve the monitoring plan. Where monitoring is being undertaken by a third party the Sponsor must conduct due diligence on the parties contracted to complete the monitoring for the study.

4.4 Monitor's Responsibilities

The Monitor(s) in accordance with the Sponsor's requirements must ensure that the study is conducted and documented properly by carrying out the following activities when relevant and necessary to the study and the study site, for example by the verification of:

- Investigators qualifications and resources;
- Supplies in respect of storage, supply, control, documentation and disposal;
- Adherence to the protocol and subsequent amendments;
- Written, informed consent was obtained, prior to the participant's participation;
- Only eligible participants are enrolled;
- Source document and other trial records are accurate, complete, kept up-to-date and maintained;
- Investigator provides all the required reports, notifications, applications, and submissions, and that these documents are accurate, complete, timely, legible, dated and identify the trial.

Ensuring that:

- Investigators and trial staff are adequately informed about the trial;
- Investigators receive all study supplies needed to conduct the trial properly and to comply with the applicable regulatory requirements;
- Participant recruitment is reported;
- Checking the accuracy and completeness of the CRFs, source documents and other trial-related records against each other;
- Informing the investigator of any CRF entry error, omission, or illegibility;
- Determining whether all adverse events (AEs) are appropriately reported within the required time periods;
- Determining whether the investigator is maintaining the essential documents;
- Communicating deviations from the protocol, SOPs, GCP, and the applicable regulatory requirements to the investigator and taking appropriate action designed to prevent recurrence of the detected deviations.

4.5 Monitoring Procedures

For monitoring that has been contracted to a third party and the Sponsor has agreed the third parties SOPs for monitoring may be used.

4.6 Monitoring Report

Reporting requirements to the Sponsor must be agreed as part of the monitoring plan established for the study.

Where significant issues at a study site have been identified during monitoring these must be raised with the Sponsor via a report and should include:

- Date, site, name of monitor;
- Name of the Investigator(s) or other individuals contacted;
- Summary of documents reviewed, along with a statement of findings, deviations, deficiencies, conclusions, actions taken or recommended to secure compliance.

Where a trial is co-sponsored, copies of monitoring reports should be received from / shared with the relevant party to enable any concerns or actions within their jurisdiction to be addressed.

Where issues have been identified the Sponsor shall engage with the CI to ensure these are resolved.

5. References

Ct-Toolkit (2004) Monitoring Procedures:
http://www.ct-toolkit.ac.uk/routemap/trial-management-and-monitoring/ (last accessed January 2022)

6. Appendices

Appendix 1: Monitoring Plan (Non-CTIMPs)

Monitoring Plan – Non-CTIMPs

Study Type	Risk Level	Audit Aim/Monitor	Determined by
Interventional Studies	High Eg invasive procedures, high risk population	Aim to audit 10% of interventional per annum High risk studies should be monitored within first 6 months of patient recruitment	Assessed on case by case basis
Human Tissue Studies	Medium Eg sample /Tissue collection studies	Aim to audit 10% of interventional per annum	Random selection from Human Tissue Database, unless triggered
Non-interventional	Low Eg Questionnaires Interviews Qualitative	3 studies per annum	Random selection from Sponsorship database, unless triggered