# STU-SOP-TM-009 – Standard Operating Procedure on Monitoring

## 1. Purpose and Definitions

This Standard Operating Procedure (SOP) describes the procedure of monitoring research projects to ensure these studies comply with regulations, GCP, sponsor requirements and delegated STU duties.

| Definitions | |
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| **Monitoring** | 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 requirement(s). |
| **Case Report Form (CRF)** | A printed, optical or electronic document designed to record all research project protocol-required information to be reported to the Sponsor on each research project participant. |
| **Source Documents** | Original documents, reports, images, data and records. Source documents are the first place where data are recorded. The CRF may be the source for some research project data (i.e. data may be recorded directly onto CRFs with no prior written or electronic record of data). The research project protocol should document the identity of any data recorded directly onto the CRFs. |
| **Source Data Verification (SDV)** | The process by which information reported by an investigator or authorised site personnel is compared with source documents to ensure that it is complete, accurate and verifiable. |
| **Hazard** | Anything that could cause harm. This includes hazards to the participant, research, organisation or the researcher. |
| **Risk** | Probability that harm will be caused by a hazard. |

## 2. Background

Although the requirements of GCP do not apply to non-Clinical Trials of Investigational Medicinal Products (CTIMPs), it is best practice to apply GCP principles to all interventional research projects.

Monitoring is the act of overseeing the progress of a research project.

Monitoring is an integral process in the quality control of any research project and should be designed to assure the quality of the research project. Central monitoring in conjunction with procedures such as investigator training, meetings and extensive written guidance can assure appropriate conduct of the research project in accordance with GCP. In addition, monitoring may be initiated as a result of identified issues (see STU-AD-GDN-009 Types of Monitoring).

# 3. Roles and Responsibilities

The **Sponsor** has responsibility for ensuring a research project has a monitoring plan and should have oversight of the review process.

The **Chief Investigator (CI)** is responsible for ensuring that agreements are in place, a monitoring plan has been written, is regularly reviewed and that the local site Principal Investigator (PI) complies with monitoring requests.

**STU** are responsible for securing an agreement and monitoring when this task has been delegated by the sponsor. Monitoring is usually performed by Trial Management personnel.

The **Trial Manager (TM)** support the CI to draft the monitoring plan and determine which tasks can be delegated to STU regarding monitoring and sponsor oversight.

The **Data Manager (DM**) is usually involved in supporting the TM and CI to draft the monitoring plan with regards to central monitoring of research project data.

The **Monitor** is responsible for assessing whether the research project is conducted and documented to the requirements of GCP, the monitoring plan and relevant standard operating procedures (SOPs) and legislation as applicable.

**External use of SOP**: this SOP and Associated Documents (AD) may be used for research projects not adopted by STU where Swansea University (SU) staff and associated NHS organisations require guidance. In such instances, oversight responsibility for any associated tasks will not be the responsibility of STU.

# 4. Procedure

Research projects assessed as low risk or non-interventional must still consider monitoring requirements and arrangements which should be documented in the project protocol. Such studies will not usually require a detailed monitoring plan.

For CTIMPs and other high-risk interventional research projects, a monitoring plan will be drafted by the research team and agreed with the Sponsor.

Monitoring plans are subject to annual review and should also be assessed following substantial changes to the protocol.

## 4.1 Monitoring Plan

Where required, monitoring procedures must be clearly set out in a monitoring plan. This document is in addition to the protocol and must document the nature and extent of monitoring required. This is determined by the completion of the research project Risk Assessment (RA) Proforma (STU-AD-TMP-049), unless a sponsor template is provided. Guidance on the types of monitoring for research projects can be found in STU-AD-GDN-009.

If a sponsor template is provided, the plan should include all elements outlined in the Monitoring Plan Template (STU-AD-TMP-035).

Where required, a Source Data Location List (STU-AD-TMP-037) will be included as part of the monitoring plan. The plan will be written by the TM, with input from the research team and agreement by the CI.

#### 4.1.1. Determining the extent and nature of monitoring

The reach of the monitoring plan and frequency of any visits will satisfy the risk category of the individual project calculated using the RA Proforma. The resulting plan will be agreed by the sponsor.

#### 4.1.2 Changes to the monitoring plan

The monitoring plan should be reviewed when a protocol change result in a change to the objective, purpose, design, complexity, risk, blinding, sample size or endpoints of the research project.

The monitoring plan may also be amended during the project if:

- Concerns are raised regarding research practice
- Substantial amendments and subsequent risk assessment indicate a change in risk
- Serious non-conformances are identified during audit or monitoring
- A change of CI
- A breach of the protocol or GCP has been assessed as serious
- Serious Adverse Event (SAE) or Suspected Unexpected Serious Adverse Event Reaction (SUSAR) reporting raises concerns

### 4.2 Considerations for blinded studies

For double-blinded studies, involvement of blinded personnel (usually TM) in monitoring activities should be considered and detailed within the plan to maintain the blind.

### 4.3 Monitoring personnel

Both the TM and DM may undertake monitoring activities.

Monitoring personnel must have knowledge of:

- research project protocol
- participant documentation
- STU SOPs and sponsor processes
- GCP
- all applicable regulatory requirements

Personnel must not conduct on-site monitoring until they have had appropriate training for the research project.

All required permissions to access medical records should be in place prior to reviewing medical notes (e.g. NHS Letter of Access). STU-SOP-TM-016 (Letters of Access) indicates how to obtain a letter of access, honorary contract or research passport.

### 4.4 Site Monitoring Process

#### 4.4.1 Conducting Monitoring Visit

The CI/PI of the project (or other departments, as appropriate) will be contacted by the Monitor to arrange a convenient time for an onsite or remote visit. The CI/PI will be available to meet

with the Monitor as required. A monitoring visit may be split over multiple days and involve visiting support departments such as pharmacy or laboratories.

Site specific documents or logs may be requested from the site team prior to the monitoring visit and must be provided to the Monitor before the visit date.

For an onsite visit, a suitable location for document review must be arranged by the Monitor to conduct the visit. The Trial Master File (TMF), source documentation (including medical records), all CRFs and any other required documentation must be available during the visit if requested. For remote visits, redacted documents may be requested in advance.

All members of the site team, as requested by the CI/PI, should be available at the beginning and the end of the visit to answer queries, and to clarify monitoring findings and Corrective and Preventative Actions (CAPA) as appropriate. Failure of a CI/PI or delegate to attend visit meetings will be considered a non-conformance.

### 4.4.2 Breaches and Non-conformance

Findings which do not conform with GCP, the research project protocol or applicable SOPs will be reported as non-conformances and follow a traffic light system.

Findings that can or have the potential to affect the rights, wellbeing or safety of participants or the scientific integrity of a research project will be classed as a serious non-conformance (red). All other non-conformances which will be classed as amber. All non-conformances will be highlighted to the site team during the monitoring visit with opportunity to correct minor non-conformances when appropriate. Where required, further discussion and investigation following the monitoring visit, may result in the downgrade from red to amber as appropriate. Observations or recommendations will be classed as green.

For CTIMPS, any non-conformance classed as a Serious Breach would require the completion of appropriate documentation and expedited reporting to the Sponsor, REC and MHRA as a minimum. Further information detailed within STU-SOP-TM-011.

The Monitor will review the ongoing completion of non-conformances, corrections and CAPAs, before closing a finding, or referring to the site team for further action.

Any opportunity for improvement of a potential non-conformance will be recorded. Any concerns relating to Health & Safety or Environmental concerns will be recorded and referred to the appropriate department.

### 4.4.3 Monitoring Report

A signed monitoring report (STU-AD-TMP-036 Monitoring Report Template) will be issued electronically to the CI/PI within 15 working days of the visit taking place, unless further clarification or information is required. If the period between the site monitoring visit and visits to support departments (e.g. Pharmacy) exceeds 15 days, an updated report will be issued at a later date.

The site team will usually have a maximum of 30 calendar days from the monitoring visit to action all non-conformances and inform the Monitor. A shorter timescale will be implemented for serious non-conformances.

The report will include a summary table of any findings raised, including corrections and CAPAs agreed with the site team. Where medical records checks have formed part of the monitoring visit, a Medical Records Monitoring Checklist (STU-AD-TMP-038) should also be included with the report.

The site team can correct minor non-conformances during the visit. These corrections will be recorded in the monitoring report but not usually raised as findings (green). A monitoring report will be issued should no findings be recorded.

If necessary, follow up monitoring will be carried out to review progress in ensuring previously agreed corrections and CAPAs have been completed.

#### 4.4.4 Non-compliance with the monitoring process

If a CI/PI does not comply with the monitoring process, the research sponsor, REC, R&D and their line manager will be notified.

Failure to complete corrections and CAPA within agreed timescales will result in sponsor notifications and may result in revocation of sponsor approval.

For CTIMPs, the MHRA will be notified if the non-conformance with the monitoring process is considered a Serious Breach of GCP.

### 4.5 Site Closure

Prior to closure, the Monitor must ensure that all data queries have been resolved, all outstanding CAPA actions have been completed and that the ISF and supporting files contain all necessary documentation (detailed in STU-SOP-TC-002).

## 5. References

- Health Research Authority website (HRA) - http://www.hra.nhs.uk/
- Medicine and Healthcare products Regulatory Agency website (MHRA) - https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency/services-information
- UK policy framework for health and social care research (2017) - https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/
- UK Medicine for Human Use (Clinical Trials) Regulations 2004 - http://www.legislation.gov.uk/uksi/2004/1031/contents/made

It is assumed that by referencing the principal regulations that all subsequent amendments are included in this citation.

## 6. Associated Documents

| Number | Title | Location |
|---|---|---|
| STU-AD-TMP-049 | RA Proforma | Q-Pulse |
| STU-AD-TMP-035 | Monitoring Plan Template | Q-Pulse |

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|---|---|---|
| STU-AD-TMP-036 | Monitoring Report Template | Q-Pulse |
| STU-AD-GDN-009 | Types of Monitoring Guidance | Q-Pulse |
| STU-AD-TMP-037 | Source Data Location List | Q-Pulse |
| STU-AD-TMP-038 | Medical Records Monitoring Checklist | Q-Pulse |

## 7. Abbreviations

| List of Abbreviations | |
|---|---|
| **CAPA** | Corrective and Preventative Action |
| **CI** | Chief Investigator |
| **CRF** | Case Report Forms |
| **GCP** | Good Clinical Practice |
| **ISF** | Investigator Site File |
| **MHRA** | Medicines and Healthcare products Regulatory Agency |
| **PI** | Principal Investigator |
| **RA** | Risk Assessment |
| **SAE** | Serious Adverse Event |
| **SAR** | Serious Adverse Reaction |
| **SDV** | Source Data Verification |
| **SUSAR** | Suspected Unexpected Serious Adverse Reaction |
| **SOP** | Standard Operating Procedure |
| **STU** | Swansea Trials Unit |
| **TM** | Trial Manager |
| **TMF** | Trial/Project Master File |
| **TMG** | Trial Management Group |
| **TSC** | Trial Steering Committee |

## 8. Appendices

### Appendix 1: Document History

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| **Version No:** | 3 | **Effective Date:** | 20 Jun 2024 |
| **Description of changes:** | Clarification of procedure | | |