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

Version No:	4	**Effective Date:**	17-Apr-2026
Description of changes:	Amendments relevant to the updates in the clinical trials regulations 2025 and updated GCP. Specific references to QPulse as the QMS have been removed. We now only refer to a QMS system.		

List of Abbreviations	
CAPA	Corrective and Preventative Action
CI	Chief Investigator
CRF	Case Report Forms
CtQ	Critical to Quality factors
GCP	Good Clinical Practice
IDMC	Independent Data Monitoring Committee
ISF	Investigator Site File
MHRA	Medicines and Healthcare products Regulatory Agency
PI	Principal Investigator
RA	Risk Assessment
RBM	Risk Based Monitoring
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 Master File
TMG	Trial Management Group
TSC	Trial Steering Committee

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	
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.
Non-conformance	Findings which do not conform with GCP, the research project protocol or applicable SOPs
Breach	Serious non-conformances that require expedited reporting.
Critical to Quality (CtQ)	Factors in clinical trials are the essential elements such as participant safety, informed consent, and primary endpoints that, if compromised, would undermine the study's integrity or results.
Risk based monitoring (RBM)	Monitoring that focuses efforts on high-risk, high-impact data points (identified as CtQ factors) rather than 100% data verification.

2. Background

Although the requirements of GCP do not apply to non-Clinical Trials of Investigational Medicinal Products (non-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 for the purposes of protecting the rights, safety and well-being of patients, Source Data Verification (SDV)/Source Data Review (SDR), to confirm the accuracy of data transcription, compliance with the protocol, GCP and applicable regulatory requirements and verification of the existence of participants.

It 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 (see STU-AD-TMP-035 Monitoring Plan template).

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 or other key documents.

Types of monitoring include:

- **On-site monitoring** of a project location e.g. hospital, GP practice, care home. This involves the monitor visiting the location in person to conduct checks and requires access to medical records and other source data pertaining to participants.
- **Remote monitoring** of a project location. This involves the monitor conduct checks by reviewing documents shared by the site in response to a monitoring request and typically replicates on-site monitoring activities where possible.
- **Central monitoring** involves an evaluation of accumulating data (or lack thereof), performed in a timely manner, supported by appropriately qualified and trained persons (e.g. data managers, statisticians, trial managers, data scientists). The aim of central monitoring is to mitigate specific risks defined in the trial Risk Assessment completed before recruitment commences and updated with the assessment of any new risks added as the trial progresses. It may be justifiable to use only central monitoring as a sole monitoring approach.

The UKCRC Monitoring of Clinical trials handbook provides additional detail on monitoring https://ukcrc-ctu.org.uk/clinical-trial-monitoring/.

4.1 Monitoring Plan

Where required, monitoring procedures must be clearly set out in a monitoring plan (STU-AD-TMP-035). 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.

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.

A Risk Based Monitoring (RBM) approach should be adopted when developing the Monitoring Plan. Critical to Quality (CtQ) factors must be identified (see STU-SOP-DMS-007) and a plan for monitoring them must be included in the Monitoring Plan. Monitoring tasks may include:

1) Checking recruitment and follow up rates
2) Checking that staff are conducting tasks in accordance with the delegation log
3) Checking that training requirements have been met
4) Confirming the eligibility and consent of participants
5) Confirming that the protocol and GCP requirements have been followed
6) Verifying source data e.g. participant diaries/questionnaires, lab results, prescriptions, scans, etc
7) Checking CRF accuracy and completeness, especially key data items such as primary outcomes and safety data
8) Reviewing protocol and GCP deviations reported
9) Reviewing safety reporting processes and forms e.g. SAE reports
10) Checking IMP management (for CTIMPs)

The contents of the ISF may be reviewed to ensure all current approved documentation is ready for use and older versions have been properly superseded.

For CTIMPs, Pharmacy files should be checked for IMP shipping and storage, documentation and labelling, randomisation, accountability and destruction.

Where laboratories or other vendors are used, they may need to be added to the monitoring plan.

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 (or other key document) change results 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 modifications 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.

If unblinded aspects of the project require monitoring, STU will nominate an independent member of staff to conduct a monitoring task designed by the TM or DM. The findings of the unblinded review will be held separately in the unblinded section of the TMF until the end of the trial (see STU-SOP-TM-002).

4.3 Monitoring personnel

Both the TM and DM should undertake monitoring activities but other STU staff may also be involved. Monitoring personnel must have knowledge of:

- research project protocol
- participant documentation
- STU SOPs and sponsor processes
- GCP
- all applicable regulatory requirements
- IMP information (for CTIMPs)

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

All required permissions to access medical records should be in place prior to reviewing medical notes (e.g. NHS Letter of Access).

4.4 Project Location Monitoring Process

4.4.1 Conducting Monitoring

The CI/PI of the project (or other departments, as appropriate) will be contacted by the Monitor to arrange a convenient time for an on-site or remote visit. The decision as to whether the monitoring task should be in person or remote will depend on the Risk Assessment and Monitoring Plan but may also be a triggered review not explicitly stated in these documents. The CI/PI will be available to meet with the Monitor as required. A monitoring visit may be split over multiple days and involve support departments such as pharmacy or laboratories.

Project location specific documents or logs may be requested from the project location team prior to the monitoring task and must be provided to the Monitor before the deadline issued.

For an on-site visit, a suitable, private location for document review must be arranged by staff at the project location. Any specific requirements by the Monitor should be requested as early as possible. 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 electronically or by post (sent

securely) in advance e.g. consent forms with names or other documentation with identifiable information.

All members of the project location team should be available at the beginning and the end of the monitoring task 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. Observations or recommendations will be classed as green.

All non-conformances will be highlighted to the project location 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.

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 STU Executive team should also be made aware of any Serious Breaches identified.

The Monitor will review the ongoing completion of CAPAs, before closing a finding, or referring to the project location 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 monitoring task taking place, unless further clarification or information is required. If the period between the trial location on-site monitoring visit and monitoring of other support departments (e.g. Pharmacy) exceeds 15 days, an updated report will be issued at a later date.

Monitoring reports should include findings requiring escalation, along with actions and resolutions.

The project location 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 project location 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 project location 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.

The completed monitoring report must be filed in the TMF and ISF.

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 Triggered monitoring

Triggered monitoring in clinical trials is a risk-based monitoring approach where triggers (derived from centralised reports and data, using predefined key risk and performance indicators) drive the nature, extent, timing and frequency of monitoring activity. The Monitoring Plan should detail the scenarios where triggered monitoring is required.

Triggered monitoring can be in the form of increased centralised or remote monitoring and where necessary an on-site visit. Monitoring activity may be triggered if/where:

- Information comes to light that suggests persistent non-compliance with the trial protocol, GCP or regulatory requirements at a particular project location.
- Issues have been raised from central monitoring activities that require further investigation at site level (e.g. appropriate storage of IMP supply).

4.6 Central Monitoring

Central monitoring analyses data collected by each project location and identifies whether any action is required. Some issues are noted by considering levels and thresholds and some by comparison between project locations.

Metrics are numeric measurements, mostly obtained and calculated from data held in the trial database, that are used to evaluate a project location's risk or performance.

It is often neither possible nor necessary to check all the data in a clinical trial. The data which will be subject to central monitoring will be defined by the Risk Assessment. As much of the monitoring as possible is performed by devising a metric which can be calculated using project location data to see if any action is required.

As risks can change throughout a trial, metrics and thresholds may also need to change.

Another sub-category of central monitoring is the identification and categorisation of protocol deviations (see STU-SOP-TM-001). A statistician may program the identification of protocol deviations from the data in the clinical database. Project locations may also notify the TM of local deviations. TMs, DMs or monitors may discover a protocol deviation throughout the course of their work.

The frequency of central monitoring depends on the trial parameters. Central monitoring should be frequent enough to improve the quality of trial data and conduct but with sufficient interval for actions identified previously to have been addressed. As central monitoring is a collection of tasks, each task needs to be completed at a frequency dependent on their individual risk.

4.7 Independent Monitoring

The independent data monitoring committee (IDMC) (see STU-SOP-TS-002) will review a summary of the monitoring achieved and may also review some data by project location (e.g. CRF return rate) within the IDMC report.

They may ask for information on particular project locations or may ask for particular project locations to have escalated monitoring. The IDMC is part of the monitoring framework.

4.8 Project Location 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 2025 - https://www.legislation.gov.uk/uksi/2025/538/contents
- ICH GCP E6 (R3) https://database.ich.org/sites/default/files/ICH_E6%28R3%29_Step4_FinalGuideline_2025_0106.pdf
- UKCRC Monitoring of Clinical trials: a handbook (Feb 2025) https://ukcrc-ctu.org.uk/clinical-trial-monitoring/

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	QMS
STU-AD-TMP-035	Monitoring Plan Template	QMS
STU-AD-TMP-036	Monitoring Report Template	QMS
STU-AD-GDN-009	Types of Monitoring Guidance	QMS
STU-AD-TMP-037	Source Data Location List	QMS
STU-AD-TMP-038	Medical Records Monitoring Checklist	QMS