STANDARD OPERATING PROCEDURE FOR MONITORING CLINICAL TRIALS OF INVESTIGATIONAL MEDICINAL PRODUCTS (CTIMPs)

SOP NUMBER:	TASC SOP03 v11
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1. PURPOSE

This document describes the procedure for monitoring Clinical Trials of Investigational Medicinal Products (CTIMP) in accordance with the Medicines for Human Use (Clinical Trials) Regulations and the principles of Good Clinical Practice (GCP).

Monitoring is 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 (SOP), GCP and the applicable regulatory requirements.

2. SCOPE

This SOP applies to all members of staff involved with the CTIMP monitoring process. Monitoring duties may be delegated to a third party, but this must be documented in an agreement. This SOP may be used for Non CTIMPs where appropriate.

3. RESPONSIBILITIES

Research Governance: study risk assessment, review of monitoring plan.

Lead Clinical Trials Monitor/delegate: produce Monitoring Plan according to the risk assessment.

4. PROCEDURE

4.1 Monitoring Visits

4.1.1 Monitoring is undertaken by a TASC Clinical Trials Monitor (CTM) or a delegate on behalf of the Sponsor.
4.1.2 Monitoring can be onsite or remote e.g., by telephone or MS Teams.
4.1.3 The Monitoring Visit Log must be completed at each Monitoring Visit.

4.2 Monitoring Plan

4.2.1 Following the risk assessment, a monitoring plan (Doc Ref 039) will be produced.

4.2.2 A CTM will determine the monitoring visit schedule and requirements and detail these in the monitoring plan. The level of monitoring for individual trials should be determined by the Sponsor risk assessment so that those meeting multiple risk criteria are monitored more frequently than trials that are judged to be lower risk.

4.2.3 More frequent monitoring, including triggered visits, will be undertaken at the request of Sponsor.

4.2.4 The monitoring plan should document the types of monitoring visits required for the trial e.g., Site Initiation Visit (SIV), First Participant First Visit (FPFV), routine monitoring visit(s) during recruitment and follow-up, remote monitoring, and the close-out visit (COMV).

4.2.5 The monitoring plan will detail the level of Source Data Verification (SDV) and frequency and type of monitoring.

4.2.6 The monitoring plan should be filed in the Sponsor File, Trial Master File (TMF) Investigator Site File (ISF) and Pharmacy Site File (PSF).

4.2.7 The monitoring plan may be reassessed and modified, as per continuous risk assessment. Previous versions of the monitoring plan must be superseded and retained in the Sponsor File, TMF, ISF and PSF.

4.3 Conducting a Monitoring Visit

4.3.1 Prior to a Monitoring Visit

4.3.2 The CTM should familiarise themselves with the protocol and other study documents.

4.3.3 The CTM should arrange a date and time with a member of staff in the research team for the monitoring visit. The Chief Investigator (CI)/Principal Investigator (PI) may nominate an appropriate person e.g., a trial administrator or research nurse for the CTM to liaise with in order to arrange the monitoring visit.

4.3.4 Prior to the visit, the CTM should explain to the CI/PI (or other nominated individual) what will be covered in the visit and which documents will be reviewed during the visit. It is the CI/PI's responsibility to ensure that these documents are available.

4.4 Site Initiation Visit

4.4.1 The SIV will occur prior to the recruitment of the first participant at that site.

4.4.2 The purpose of the SIV is to ensure that the research site staff are trained on the protocol and study procedures and the site has all approvals in place in order for the trial to begin. These visits can be at site or remote.

4.4.3 During the SIV, as a minimum the following will be checked:

- Research staff know their responsibilities, are familiar with the protocol, study procedures and all essential documents.
- Research staff understand monitoring procedures.
- All approval documents are in place.
- Signature and delegation logs, CVs and GCP training certificates are in place.

- IMP accountability procedures.
- Serious Adverse Event (SAE) Reporting.
- Potential breach reporting.
- Review of the TMF, (ISF) and PSF.

4.5 Routine Monitoring Visits

4.5.1 The scheduling of the Routine Monitoring Visit will take place according to the monitoring plan. These visits can be at site or remote. The purpose of these visits is to check that the trial is being conducted in accordance with the principles of GCP. These visits can be at site or remote. As a minimum, the following, will be checked:

- Recruitment
- Informed Consent Forms
- Eligibility sign off by PI
- GP letter has been sent
- SDV of Case Report Forms (CRF)
- Approvals for study amendments
- Safety reporting
- SAEs
- Check for unreported breaches
- IMP accountability
- Review of the TMF or ISF and PSF.

4.6 Close Out Monitoring Visits

4.6.1 The COMV will take place once the last participant at that site has completed their last study visit. These visits can be at site or remote.

4.6.2 As a minimum, the following, will be checked:

- Informed Consent forms
- IMP accountability
- SAE reconciliation
- Safety Reporting
- Check for unreported breaches
- Sample storage
- CVs and GCP certificates.

4.6.3 The CTM will check that essential documents are complete and filed in TMF or ISF and PSF.

4.7 After the Monitoring Visit

4.7.1 The CTM should complete the monitoring report within agreed timelines. This report will include any actions to be completed by the CI, PI or delegate.

4.7.2 The monitoring visit report should be signed by the monitor and sent to the personnel identified in the monitoring plan within one calendar month of the visit taking place.

4.7.3 A copy of the signed monitoring report will be filed in the Sponsor File and TMF/ISF and PSF.

4.7.4 It is the CI/PI's responsibility to ensure resolution of actions within appropriate timelines. Repeated failure to comply within the agreed timelines will be reported to the CI and Sponsor.

4.7.5 The completed monitoring visit actions will be filed in the Sponsor File and TMF/ISF and PSF as applicable.

5. ABBREVIATIONS & DEFINITIONS

CI	Chief Investigator
COMV	Close Out Monitoring Visit
CTIMP	Clinical Trial of Investigational Medicinal Product
CTM	Clinical Trial Monitor
CRF	Case Report Forms
FPFV	First Participant First Visit
GCP	Good Clinical Practice
IMP	Investigational Medicinal Product
ISF	Investigator Site File
MA	Marketing Authorisation
PI	Principal Investigator
PSF	Pharmacy Site File
SAE	Serious Adverse Event
SDV	Source Data Verification
SIV	Site Initiation Visit
SOP	Standard Operating Procedure
TASC	Tayside Medical Science Centre
TMF	Trial Master File

6. ASSOCIATED DOCUMENTS & REFERENCES

Doc Ref 039: Monitoring Plan template

7. DOCUMENT HISTORY

History prior to 2021 is in the archived SOPs available from TASC Quality Assurance Dept.

Version Number:	Reviewed By (Job Title):	Effective Date:	Details of editions made:
10	Debbie Pankhurst (CTM) Heather Barclay (Pharmacovigilance Monitor)	03/12/2021	Scheduled review, text refreshed throughout, no changes to procedure made.
11	Marney Keiller (Lead Clinical Trials Monitor)	04/12/2023	Scheduled review, "review of monitoring plan" added as a Research Governance responsibility in section 3.

8. APPROVALS

Approved by:	**Date:**
Dr Valerie Godfrey, TASC Quality Assurance Manager, on behalf of TASC Clinical Research Guidelines Committee	29 Nov 2023