Plymouth Research and Development

NHS University Hospitals Plymouth NHS Trust

Standard Operating Procedure

Please refer to https://www.plymouthhospitals.nhs.uk/research-sops to ensure the latest version of this document is in use. Printed copies are uncontrolled.

Title:	Monitoring		
Approver		Document No:	QA2
Name:	Chris Rollinson	Version No:	3.1
Signature:		Effective Date:	Feb-2022
Date:	18-Feb-2022	Review Date:	Feb-2025

1. Purpose

To describe the minimum monitoring procedure for all Trust sponsored research studies. For the purposes of this Standard Operation Procedure (SOP), the term monitor will be used to refer to any member or committee designated by the Sponsor to undertake a specific monitoring task.

2. Scope

This SOP relates to Trust sponsored studies and where required internal monitoring of hosted studies.

3. Responsibilities

Sponsor must ensure on-going activities (i.e. monitoring) are in place to oversee the progress of a study, and ensuring it is conducted, recorded, and reported in accordance with the protocol, SOPs, Good Clinical Practice (GCP), and the applicable regulatory requirement(s).

Research Governance Manager (RGM) and Assistant Clinical Trials Manager will conduct monitoring visits or by a suitable trained delegates, for example to a Clinical Trials Unit (CTU) on behalf of the Sponsor.

Monitors must not conduct independent visits until they have had adequate training and experience, demonstrating their ability to carry out the tasks involved correctly and in a professional manner. Visit must be accompanied by an established monitor.

Principal Investigator (PI) and study team must facilitate monitoring by the Sponsor, ensuing documents are made available and act on any issues identified.

4. Documents needed for this SOP

- Work Instruction (WI) WI2 Remote Monitoring Visits
- Monitoring Report Template

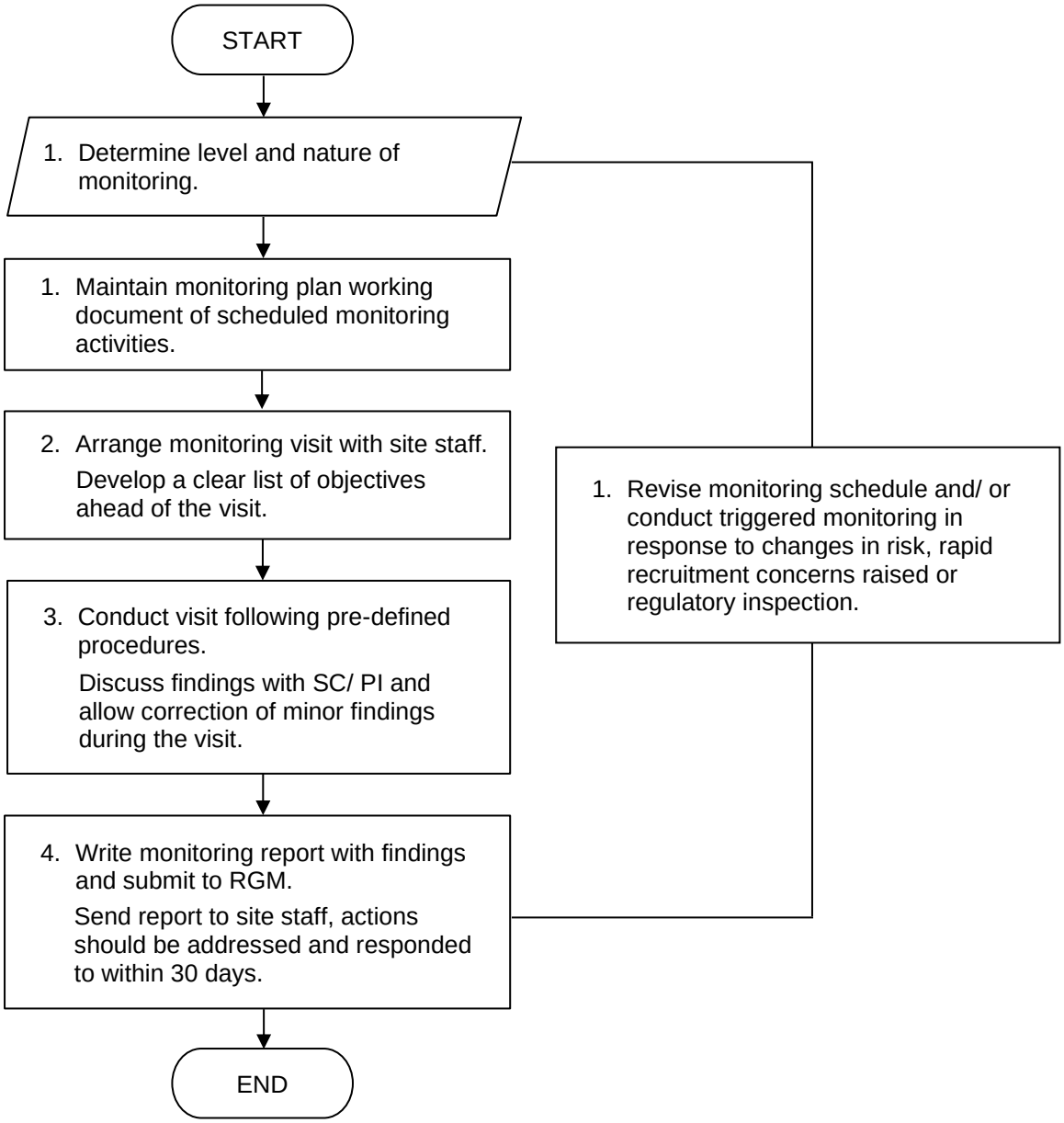
5. Related documents

- Monitoring Plan Working Document
- SOP P6 Risk Assessment
- CAPA Plan Template

6. Acronyms

CAPA: Corrective and Preventive Actions
CI: Chief Investigator
GCP: Good Clinical Practice
MHRA: Medicines and Healthcare products Regulatory Agency
CTU: Clinical Trials Unit
PI: Principal Investigator
QC: Quality Control
R&D: Research and Development
RGM: Research Governance Manager
SC: Study Co-ordinator
TMG: Trial Management Group
TSC: Trial Steering Committee
SIV: Site Initiation Visit

7. Process map(s)/ flow chart(s)



8. Procedure

Step	Action	Responsibility
1	Determine level and nature of monitoring as described in appendix 1 and 2, and by risk assessment; proportionate to the objective, purpose, design, size, complexity, blinding, endpoints and risks of the study. Maintain oversight as study Sponsor by: **Committee meetings** - Sponsor represented on Trial Management Group (TMG) and Trial Steering Committee (TSC). **Central monitoring** - Review number of data queries, timeliness of data returned, and missing/ spoiled data. - Pharmacovigilance signal detection. - Documents and reports. - Statistical review of data from the study. **Remote monitoring** *(must be focused to minimise site burden)* - Regular communication with site staff (phone call/ email). - Access to redacted scanned data files *via* EDGE or other secure platform. - Video visits showing non-redacted data *via* MS Teams screen sharing. - Scanning and emailing. - Feedback from questionnaires/ checklists sent to investigators. **On-site monitoring** - In-person evaluation at the site. Schedule monitoring activities over the calendar year in a monitoring plan working document, not inclusive of studies where a specific monitoring plan is set. Elect a risk based approach ensuing higher risk studies, are monitored first. Perform Site Initiation Visit (SIV) as required i.e. multi-site studies. The Chief Investigator, Co-investigator(s) or monitor may lead the pre-study visit. Conduct first monitoring visit for all sponsored studies (where monitoring has not been devolved to a vendor) within approximately 30 days of local Research and Development (R&D) Confirmation of Capacity and Capability. Revisions to the monitoring schedule can be made if concerns are raised, study risk has changed or the study is selected for a regulatory inspection.	RGM, Assistant Clinical Trials Manager and monitor.

Step	Action	Responsibility
	Undertake triggered/ for cause visit for both Trust sponsored and hosted studies in response to, for example rapid recruitment or concerns raised by R&D personnel, internal/ external individuals, departments/ agencies. In some cases, a Quality Control (QC) check may be used to review a specific aspect of a study/ group of studies. QC checks can be made within teams by a senior member of staff.	
2	Discuss study status and any identified issues i.e. recruitment rate, with the PI and Study Coordinator (SC), at regular intervals during the study. Contact SC, PI and Pharmacy (if applicable), giving reasonable notice of the intention to conduct a monitoring visit, type of visit (on-site/ remote), documentation required and personnel to be available. Develop a clear list of objectives ahead of the visit by reviewing last monitoring report, recent correspondence with the site and safety report, if applicable.	Monitor.
3	Follow pre-defined procedures during the monitoring visit as outlined below. **Consent process** ✓ Participants are being consented appropriately. ✓ A consent form has been completed for all participants. ✓ All consent forms have been completed correctly. **Protocol adherence** ✓ Eligibility criteria met for all participants. ✓ Study procedures, sample handling and storage have been followed. ✓ Withdrawals recorded as per the protocol. ✓ Randomisation procedures followed. ✓ AEs/ SAE as recorded as per the protocol. ✓ Protocol violations are recorded as per the protocol. ✓ Study amendments implemented correctly. **Data Quality** ✓ CRF/ eCRFs completed fully in a timely manner. ✓ Data has been recorded accurately. ✓ Results reviewed, signed and dated by an investigator. ✓ Errors corrected as per GCP by authorised site personnel.	Monitor.

Step	Action	Responsibility
	✓ Adequate data management procedures i.e. data entry, handling of data discrepancies and data back-up. **Drug Accountability** ✓ Storage conditions of the investigational medicinal product are acceptable. ✓ Stock levels, dispensing and accountability, and participant compliance is acceptable. **Site File** ✓ Complete monitoring visit log. ✓ Site file kept up to date and is in good condition. ✓ Delegation of duties are appropriate, current and all staff have a valid GCP certificate and CV. ✓ Participant screening/ enrolment log has been completed and recruitment rate on track Discuss each potential finding with the SC and/ or PI at close of visit to clarify if a finding is valid, agreeing appropriate Corrective and Preventive Actions (CAPA). Correction of minor findings should be provided to the study team during the visit.	
4	Record all findings using the monitoring report template promptly following the visit and submit to RGM for review. Following RGM approval, send monitoring report to the SC, PI and Pharmacy. Address and respond to reported findings within one calendar month unless otherwise agreed.	Monitor, RGM, study site.

9. Changes from last revision

Minor changes to the pre-defined monitoring visit procedures and minimum SDV requirements in Appendix 1.

Appendix 1: Guidance for risk based monitoring strategy for studies regulated by the Medicines and Healthcare products Regulatory Agency (MHRA)

Risk Level	Examples of Clinical Trials	Minimum Monitoring	Minimum SDV
Type A: No higher than that of standard medical care	Trials involving medicinal products licenced in the EU member state if: • They relate to the licensed range of indications dosage and form, or • if they involve off-label use (such as in paediatrics and in oncology etc.) if this off label use is established practice and supported by sufficient published evidence and/or guidelines e.g. Phase 4 studies	• SIV • 1st study monitoring 30 days after approval • Interim monitoring visits after first 3 patients recruited • Close Out	100% consent 10% safety & concomitant medication reporting A minimum of 10% SDV on eligibility and primary endpoints
Type B: Somewhat higher than that of standard medical care	Trials involving medicinal products licensed in any EU member state if: • Such products are used for a new indication (different patient population/disease group), or • Substantial dosage modifications are made for the licence indication, or • If they are used in combinations for which interactions are suspected Trials involving medicinal products not licensed in any EU member state if: • The active substance is part of a medicinal product licensed in the EU (A grading of TYPE A may be justified if there is extensive clinical experience with the product and no reason to suspect a different safety profile in the trial population) e.g. Phase 3, Phase 2b studies (may include some phase 1 /2a studies of licensed products in new indications)	• SIV • 1st study monitoring 30 days after approval • Interim monitoring visits after first 1-2 patients recruited • Close Out	100% consent 10% safety & concomitant medication reporting A minimum of 10% SDV on eligibility and primary endpoints
Type C: Markedly higher than that of standard medical care	Trials involving a medicinal product not licensed in any EU Member State. (A grading other than Type C may be justified if there is extensive class data or pre-clinical and clinical evidence) e.g. Phase 1, phase 2a studies	• SIV • 1st study monitoring 30 days after approval • Interim monitoring visits after 1st patient recruited • Close Out	100% consent 100% safety reporting 100% eligibility A minimum of 10% SDV on eligibility and primary endpoints IMP accountability and storage conditions

N.B. Capacity for monitoring multi-centre studies will be ascertained on a case by case basis during sponsor review.

Appendix 2: Guidance for risk based monitoring strategy for studies not regulated by the MHRA

Type of study	Risk Level	Examples of studies	Minimum Monitoring	Minimum SDV
Non-interventional	Low	• Questionnaires • Interviews • Qualitative • Data Collection	• 1st study monitoring 30 days after approval • Interim study monitoring annually, unless stated otherwise in study risk assessment • Close Out	100% consent 10% safety reporting A minimum of 10% SDV on eligibility and primary endpoints
Interventional Tissue	Medium	• Sample /Tissue collection studies	• 1st study monitoring 30 days after approval • Interim study monitoring visits annually, unless stated otherwise in study risk assessment • Close Out	100% consent 10% safety reporting A minimum of 10% SDV on eligibility and primary endpoints
Interventional Procedure	High Medium Low	• High e.g. Invasive procedure, high risk patient population • Medium e.g. Invasive procedure, Low risk patient population • Low e.g. Non-invasive procedure, diagnostic procedures	• SIV (multi-site studies) • 1st study monitoring 30 days after approval • Interim study monitoring visits after 1st patient recruited. Further monitoring dictated by initial monitoring and risk assessment. As a minimum high/ medium risk interventional studies will be monitored 6 monthly • Close Out	100% consent 10% (100% high) safety reporting 10% (100% high) eligibility A minimum of 10% SDV on eligibility and primary endpoints

N.B. Risk level ascertained during sponsor review and documented in the risk assessment.