SOP-QA-28 V7

Title: Monitoring

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Document History

Version	Description of update	Date Effective
6	Reference to Log of Deviations at 3.19	26-11-25
7	Reference to SIVs at 1.2 Updated terminology at 3.2, 3.5, 3.20 & Appendix 1	28-04-26

1. Scope

1.1 This SOP applies to all NHS Grampian and University of Aberdeen Chief Investigators (CI) and Principal Investigators (PI) taking part in non-commercial Clinical Trials of Investigational Medicinal Products (CTIMPs), Medical Device Clinical Investigations (MDCIs) and any study deemed as requiring additional monitoring by Sponsor, which involve NHS Grampian staff, patients or resources. It also applies to NHSG R&D staff administering the process.

1.2 Although the requirements of ICH GCP only apply to CTIMPs it is best practice to apply the 'Principles of Good Clinical Practice' to **all** clinical studies and monitor them routinely. Monitoring includes Site Initiation Visits (SIV) and Close-Out visits. SIVs must not be requested until completion and acceptance of the SIV Request Template (TMP-QA-99) by QA.

2. Responsibilities

Research Monitors/CI	Prepare a monitoring plan.
CI, PI and trial team	Comply with all monitoring requests.

3. Procedure

3.1 The monitoring process is designed to ensure that active CTIMPs and MDCIs conform to the principles of Good Clinical Practice (GCP) and relevant legislation.

3.2 Effective monitoring is necessary to ensure that:

- The rights, wellbeing and safety of the trial participants are protected.
- Trial data is secure, high quality, accurate, complete and verifiable from source data.
- The conduct of the trial is in compliance with the currently approved protocol / modifications, and is conducted by approved personnel.
- Research misconduct and fraud is deterred and inadequate research practices are identified before they escalate to become research misconduct.
- GCP and Good Research Practice (see SOP-QA-34 - Good Clinical Practice/Good Research Practice training) are promoted, and compliance with the guidelines for research governance, including applicable regulatory requirements, is achieved.

3.3 For UoA-NHSG sponsored/co-sponsored CTIMPs, MDCIs and studies designated 'higher risk' by Sponsor, a Monitoring Plan, including site initiation and close-out visits, shall be prepared by QA staff, taking account of the Sponsor risk assessment (TMP-QA-16) and the monitoring risk adaption process (see Appendix 1). This shall be risk adapted, all studies being subject to the regular monitoring plan, unless additional information suggests that a reduced or increased monitoring plan is appropriate (see Appendix 1). The number and frequency of monitoring visits and level of Source Data Verification shall be determined by the plan and reviewed at regular monitoring schedule meetings involving QA and Research Governance.

3.4 A percentage of hosted non-commercial CTIMPs and MDCIs shall be monitored during the active phase, unless they have been recently monitored by the external Sponsor.

3.5 The monitoring plan may be amended (irrespective of who sponsors the trial) if:

- Concerns are raised regarding research practice.
- Monitoring of other projects has highlighted concerns.
- Information provided to the Sponsor is causing concern or is inconsistent.
- The trial is selected for regulatory inspection.
- Substantial modification and subsequent risk assessment indicate a change of risk.
- Audit or monitoring serious non-conformances are identified.
- There is a change in Principal Investigator or Chief Investigator.
- A Serious Breach is reported.
- An SAE/SADE or numerous SAE/SADEs are reported.
- A SUSAR or USADE are reported.
- Instructions are received from the Clinical Studies Oversight Group (CSOG).

3.6 If any of the events listed in 3.5 occur an additional risk assessment shall be undertaken using the same documentation as in 3.3 (see TMP-QA-59 – Monitoring Plan).

Monitoring Visit

3.7 Personnel may not carry out monitoring unless adequately trained. The CI/PI (or delegate) or other departments, as appropriate, shall be contacted by the Research Monitor to arrange a convenient visit, at which the CI/PI (or delegate) **shall be available** to meet the Research Monitor. Monitoring may, if required, be split over a number of days or conducted remotely.

3.8 Documents (including trial specific SOPs) may be requested from the research team prior to monitoring and must be provided to the Research Monitor(s) before the visit date. This may include arranging access to electronic records (including eTMF) during the monitoring visit.

3.9 An area, with sufficient space for document review, must be provided by the researchers to allow the Research Monitor(s) to conduct the visit.

3.10 The TMF and, if appropriate, source documentation (including a proportion of the medical records), all Case Report Forms (CRFs) and any other trial documentation must be available on the day of the visit, when applicable.

3.11 The PI/CI, and/or other members of the research team, as requested by the PI/CI, must be available for the closing meetings to answer any queries and to clarify and agree findings, Corrections and Corrective and Preventive Action (CAPA), as appropriate. Failure of a PI/CI to attend (or an appropriate delegate) may be considered a non-conformance.

3.12 If a finding does not comply with the principles of GCP, the trial protocol, or Sponsor/Trial specific SOPs (if applicable) it shall be reported as a non-conformance.

3.13 All non-conformances are considered as deviations, unless classed as a Breach. All non-conformances must be recorded on the Log of Deviations (TMP-QA-93) or Log of Breaches and Urgent Safety Measures (TMP-QA-51) by the research team.

3.14 A non-conformance that has affected (or has the potential to affect) the rights, wellbeing or safety of participants, or has affected (or has the potential to affect) the scientific integrity of a clinical trial shall be treated as a serious non-conformance, and may also be treated as a **Serious Breach** (see SOP-QA-25 – Deviations and Breaches). Findings shall be highlighted to the research team during the monitoring visit and, following further discussion and investigation, may be confirmed or downgraded. Non-conformances shall also be recorded on the appropriate Deviation Log (TMP-QA-93).

3.15 The Research Monitor shall review non-conformances (and any Corrections/CAPA) before closing a finding, or referring back to the auditee for further action.

3.16 Opportunities for improvement or a potential non-conformance are reported as observations.

3.17 Any concerns relating to Health & Safety or Environmental issues may also be raised as observations and referred to the appropriate department within either UoA or NHSG.

Monitoring Report

3.18 A monitoring report shall be issued electronically to the CI/PI (and other auditees as agreed) within **ten days** of the visit taking place, unless further clarification or information is required. If there is a delay between the monitoring visit to the research team and visits to support departments (eg Pharmacy) an additional report may be issued at a later date. Any correction and CAPA detailed in the monitoring summary report shall be as agreed and discussed at the closing meeting.

3.19 Auditees shall have a **maximum of 28 days** from the monitoring visit to close out findings and inform the Research Monitor. The CAPA Template (TMP-QA-80) and/or Log of Deviations (TMP-QA-93) may be used by the auditee to detail CAPA.

A shorter timescale may be implemented for serious findings.

3.20 The report shall include a summary table of any findings raised, including correction and CAPA agreed with the research team on the day of the monitoring visit. The report shall also include:

- Date reported (Printed)
- Monitoring visit reference number (assigned by Ideagen Quality Management system)
- Monitoring visit title and date of the monitoring activity
- Status ('performed' or 'closed')
- Monitoring visit type
- Lead auditor
- Scope
- Scheduled start date, end date and duration
- Actual start date, end date and duration
- Closed by and date (once closed)
- Accepted by and accepted on (once closed)

3.21 Findings shall be classified as non-conformances (NCs) or observations (OBS). NCs shall be colour coded as amber or red. Red shall indicate a serious non-conformance requiring immediate attention and such findings shall be referred to CSOG and the R&D Director. Observations are not colour coded.

3.22 If there are no findings raised this shall be indicated in place of the summary table.

3.23 Reports from all monitoring shall be reviewed by the Quality Assurance Manager and, for those sponsored by UoA and/or NHSG, the Research Governance Manager (or delegates) before issue.

3.24 Once all findings have been closed the Research Monitor shall assign the name of the auditee who has accepted the report and shall reissue the report to the CI/PI as 'closed'.

3.25 If necessary, a follow-up visit shall be carried out to review progress in ensuring previously agreed corrections and CAPA have been undertaken.

3.26 The research teams shall be given the opportunity to provide feedback on the monitoring visit and process (Snap Survey or by using TMP-QA-39). This shall be evaluated at Management Review Meetings in order to identify improvement opportunities in the monitoring process.

3.27 ⚠ Failure to complete CAPA within agreed timescales may be regarded as a serious non-conformance which may be reported as such to CSOG (see 3.20).

Non-compliance with the monitoring process

3.28 ⚠ If a PI/CI does not co-operate with the monitoring process then this may be escalated to CSOG, Sponsor, Research Ethic Committee, R&D and the appropriate line manager.

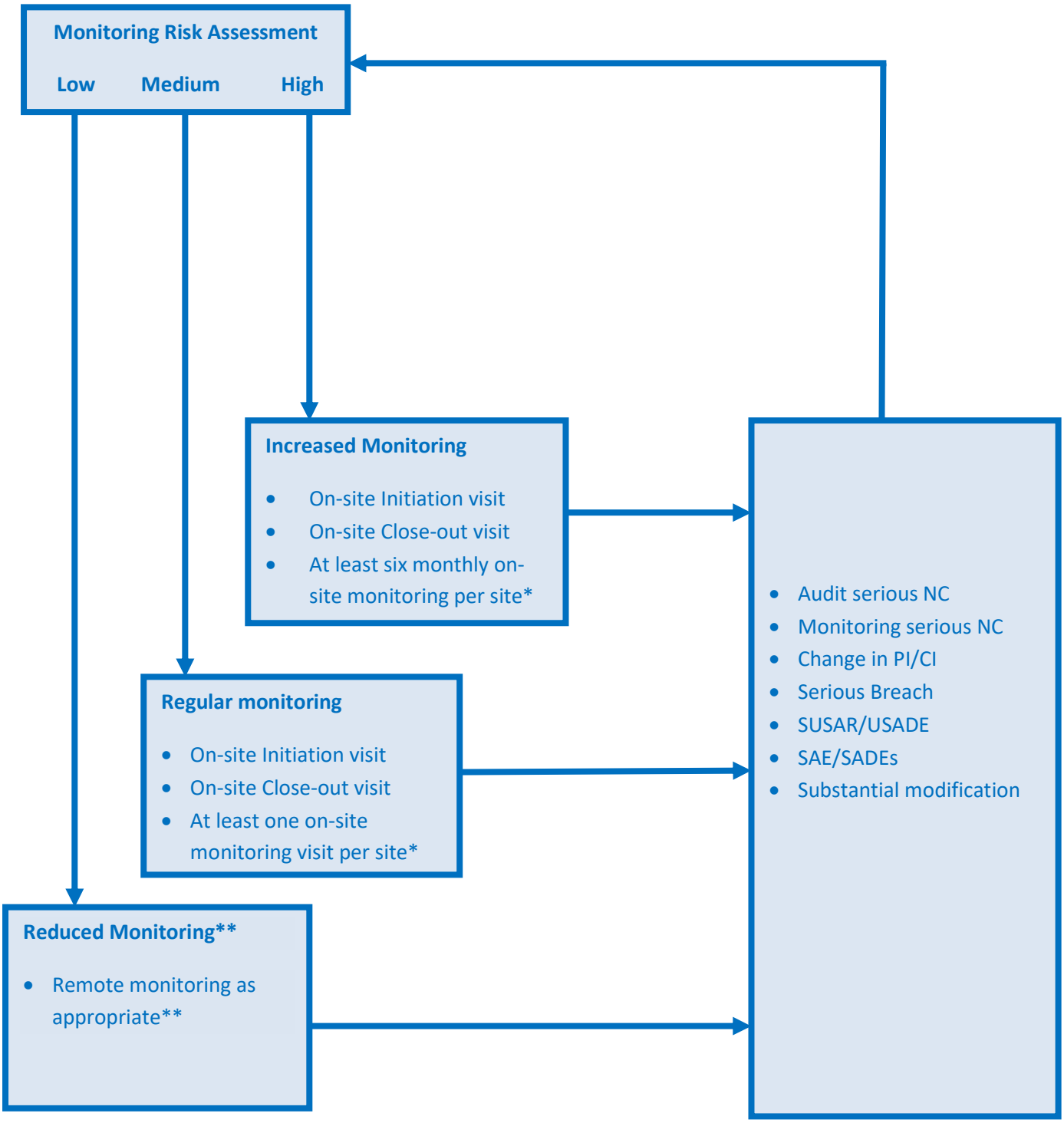
3.29 ⚠ For CTIMPs or MDCIs the MHRA shall be informed if the non-compliance with the monitoring procedure is considered a Serious Breach of GCP or the protocol (see SOP-QA-25 – Reporting and Managing Breaches).

4. Abbreviations and definitions

Correction	Action to correct an identified non-conformance
Corrective Action	Action to prevent recurrence of an identified non-conformance
Preventive Action	Action to prevent occurrence of a potential non-conformance
SUSAR	Suspected Unexpected Serious Adverse Reaction
USADE	Unanticipated Serious Adverse Device Effect

5. Related documentation and references

SOP-QA-25	Deviations and Breaches
SOP-QA-34	Good Clinical Practice/Good Research Practice training
UG-QA-3	Guidance document for monitoring
TMP-QA-16	Sponsor Risk Assessment
TMP-QA-39	Monitoring feedback form
TMP-QA-51	Log of Breaches and Urgent Safety Measures
TMP-QA-59	Monitoring Plan
TMP-QA-80	CAPA Template
TMP-QA-89	Log of Deviations
TMP-QA-93	Log of Deviations
TMP-QA-99	SIV request checklist



*** Unless it is identified during central monitoring/monitoring schedule meetings that further investigation and additional on-site monitoring visit is required. Where multi-site, this may be delegated by Sponsor to a Clinical Trials Unit and (if agreed by Sponsor) may take the form of reduced monitoring, unless on-site monitoring is triggered.**

****Reduced monitoring plan activities may be conducted on-site if appropriate.**

Risk Assessed Monitoring. (Agreed after initial risk assessment but subject to risk adaption)	Reduced Monitoring Plan**	Regular Monitoring Plan	Increased Monitoring Plan
Medical Device			
Review of SADEs recorded.		On-site	On-site (consider 100%)
Review AE records.		On-site	On-site
IMP			
Study dose assessed using eCRF (if possible).	Remotely	On-site	On-site
DSUR used to review and monitor AEs and provide oversight.	Remotely		
Review of SAEs recorded.		On-site	On-site (consider 100%)
IMP accountability reviewed by study team & pharmacy.	Remotely	On-site	On-site
Selection of patients' notes reviewed for batch number traceability from pharmacy.	Remotely	On-site	On-site
IMP storage temperature logs checked by study team and reported to Monitor.	Remotely		
IMP storage temperature logs checked.		On-site	On-site
Study dose checked against patients' notes, compared with randomisation documents.		On-site	On-site
Accountability check at pharmacy, if appropriate.		On-site	On-site
Review AE records.		On-site	On-site
Review of receipt, dispensing, return and destruction records.			On-site
Participants			
Review using eligibility checklist.	Remotely (if possible)	On-site	On-site
Source Data Verification of eligibility criteria.		On-site	On-site (consider 100%)
Review attendance data using eCRF (if possible) & non-attendance deviation log.	Remotely (if possible)	On-site	On-site (consider 100%)
Review informed consent forms.	Remotely (if possible)	On-site	On-site (consider 100%)
Medical notes reviewed to ensure correct documentation & staff correctly delegated.		On-site	On-site (consider 100%)
Study design & methods			
Data QC check using eCRF (if possible).	Remotely (if possible)	On-site	On-site
CRF checked using eCRF (if possible) or DMC for completeness/accuracy.	Remotely		
Deviation logs copied to Monitors regularly for review.	Remotely		
Deviation log reviewed.		On -site	On-site
Source Data Verification for primary and secondary endpoints.	Remotely (if possible)	On-site (100%)	On-site (consider 100%)
Paper CRF reviewed.		On-site	On-site
Study Organisation			
Review study team training in Sponsor SOPs, study specific SOPs and GCP.	Remotely (if possible)	On-site	On-site
Review recruitment levels against targets.	Remotely	On-site	On-site
Guidance on maintaining site file or Investigator TMF, as appropriate.	Remotely	On-site	On-site
Guidance on maintaining site delegation logs.	Remotely	On-site	On-site
Training needs assessment.		On-site	On-site
Screening and pre-screening data reviewed.		On-site	On-site
Delegation log reviewed.		On-site	On-site
Site file or Investigator TMF reviewed.		On-site	On-site

****Reduced monitoring plan activities may be conducted on-site if appropriate.**

Reduced Monitoring Plan

IMP

- Study dose assessed by Monitors using eCRF (if possible).
- DSUR used to describe AEs.
- IMP accountability conducted by delegated study team members and pharmacy (including checking of batch numbers, expiry dates and temperature monitoring), reported to Monitors.

Study Participants

- Confirmed remotely using eligibility checklists.
- Attendance checked using eCRF (if possible) and/or deviation logs noting non-attendance.
- Remote review of consent forms.

Study Design & Methods

- Remote data QC checks.
- CRF completion checked remotely using eCRF (if possible).
- Deviation logs copied to Monitors at regular intervals.
- Source Data Verification carried out remotely, where possible.

Study Organisation

- Confirm study team training in Sponsor SOPs, study specific SOPs and GCP/GRP.
- Recruitment monitored regularly.
- Guidance on maintaining site file or Investigator TMF, as appropriate.

Regular Monitoring Plan (Conducted on-site) As Reduced Monitoring Plan plus:

IMP

- Selection of patients' notes reviewed for batch number traceability from pharmacy (if applicable)
- Study dose checked against notes.
- Review of AE records.

Study Participants

- Medical notes reviewed to ensure correct documentation and staff correctly delegated.

Study Design & Methods

- Paper CRFs reviewed.

Study Organisation

- Training Needs Assessment.
- Screening and Pre-screening reviewed.
- Delegation log reviewed.
- Site file/Investigator TMF reviewed.

Increased Monitoring Plan (Conducted on-site) As Regular Monitoring Plan plus:

IMP

- Review records of receipt, dispensing, return and destruction.

Study Participants

- Increased number of consent forms reviewed (consider 100%).
- Increased number of medical notes reviewed (consider 100%).

Study Design & Methods

- Increased number of records checked for Source Data Verification (consider 100%).

Study Organisation

- Training Needs Assessment.
- Screening and Pre-screening reviewed.
- Delegation log reviewed.
- Site file/Investigator TMF reviewed.