SOP number	**53.004**	Version	**7.0**
Title	**Monitoring Clinical Research – Site Monitoring Visit**		

Prepared by Signature	Sheila M^{c}Gowan	Date
Approved by Signature	Caroline Watson	Date
Released by Signature	Chloë Cowan	Date

SOP category	NHS GG&C Sponsor Governance

Staff category

Staff Category	**R**	**A**	**C**	**I**
Research Governance Manager		X		
Clinical Trial Monitors	X			
Lead Clinical Trial Monitor	X			
Project Managers			X	
R&I Sponsor Pharmacists			X	
R&I Sponsor Research Co-Ordinators			X	
R&I Quality Assurance Manager			X	
Chief Investigators				X
Glasgow University – Research Regulation & Compliance Manager				X

1 Scope

This Standard Operating Procedure applies to all NHS Greater Glasgow and Clyde Clinical Trial Monitors, working within the Glasgow Clinical Trials Unit (GCTU).

2 Purpose

The purpose of this SOP is to describe the procedures that will be used by the NHSGGC Clinical Trial Monitors, acting on behalf of the Sponsor, to monitor non-commercial clinical trials, including CTIMPs, high risk Non-CTIMPs and medical device studies which are Sponsored or Co-Sponsored by NHS Greater Glasgow and Clyde (NHSGGC). The SOP also covers activity undertaken if contracted by an external sponsor as detailed in SOP 53.014.

3 Procedures

3.1 Study Design

The Clinical Trial Monitors (CTM) will be made aware of new trials by the R&I Sponsor Research Co-Ordinators and/or Lead CTM. The CTMs will be asked for their input in the protocol development process (SOP 51.001), Patient Information Sheets/Consent forms and will attend trial set up meetings to offer advice and guidance to the trial team on the design and conduct of the trial and conduct eCRF user acceptance testing in line with SOP 50.020. Additionally, the Lead CTM/CTM will provide financial input into study costings for the grant application or funding in line with SOP 51.010. The CTM/Lead CTM will also attend the Sponsor Risk Assessment and provide monitoring-specific guidance and mitigations, as appropriate. The site monitoring visit/remote monitoring visit forms part of the overall monitoring strategy for the trial and the monitoring responsibility of other stakeholders will be detailed within the Risk Assessment (SOP 51.004) and monitoring plan.

3.2 Monitoring Plan

Once the trial protocol has been approved or close to approval and the Sponsor Risk Assessment has been undertaken, the Monitors will review the protocol and complete the NHSGGC Monitoring Risk Assessment (Form 53.010B) as detailed in SOP 53.010. Based on this Risk Assessment, and the definitions of level of risk described in this form, the CTM will create a trial specific Monitoring Plan using the Monitoring Plan template (Form 53.010A) as per SOP 53.010. In addition, the CTM will review the Sponsor Risk Assessment Tool (Form 51.004A) and determine if there are any issues which will impact monitoring. The Monitoring Plan will be peer reviewed by the Trial Management Group, as described in SOP 53.010 and approved by the Lead Clinical Trial Monitor/Research Governance Manager. Compliance to the monitoring plan is detailed in SOP 53.010. The monitoring plan will only include the responsibility of the LCTM and CTMs. Responsibilities for other stakeholders within the overall strategy will be documented within the Risk Assessment (Form 51.004A) and other appropriate trial documentation.

3.3 Types of Visit

There are 4 main types of visit that will be carried out within the life cycle of a trial and as applicable to each trial type. The details and nature of what visits are required for each trial will be available in the monitoring plan which is developed in accordance to SOP 53.010.

- Site Initiation Visit
- Site Monitoring Visit
- Pharmacy Monitoring Visit
- Site Close Out Visit

Site Monitoring Visits and Pharmacy Monitoring Visits are detailed within this SOP and may take place as separate visits or during the same visit. Each visit type has its own structure and checklist available in Q-Pulse which is used to identify what visits have taken place for each site in a trial. Site Monitoring Visits and Pharmacy Monitoring Visits may also take place at the same time as a Site Close Out Visit in some instances.

All visits may be conducted as remote visits rather than on site, this will be detailed if applicable within the monitoring plan and recorded as such in Q-Pulse. This is detailed in section 3.11.

3.4 The Site Monitoring Visit

The purpose of the site monitoring visit (MV) is to ensure the trial is being conducted in accordance with the protocol, GCP, and applicable regulations, the rights and well-being of trial participants are being protected, and data derived from the trial is accurate and verifiable. A list of participants will be selected, with consideration of the type of trial, risks that have been identified and detailed with the monitoring plan, to represent an appropriate percentage of participants for SDV. The site will be notified of the participants selected for SDV prior to the visit to allow sufficient time to retrieve the relevant medical notes/Investigator Site File (ISF) or to set up access to Electronic Health Records (EHR).

The core monitoring tasks for the MV are:

- Ensure that the Investigator Site File has been maintained appropriately (including amendments, safety updates, version changes and staff changes).
- Ensure the site resources remain adequate to conduct the study (including laboratories, equipment, and staff).
- Ensure the Investigator qualifications remain adequate and training is up to date.
- Ensure any dose and/or therapy modifications are well documented and concomitant medications are reported.
- Ensure Adverse Events are recorded and reported appropriately.
- Ensure visits the participants fail to make, tests that are not conducted and examinations that are not performed are reported and recorded clearly in the source documents.
- Ensure all stopped and/or withdrawn participants are documented and correctly entered in CRF/eCRF.
- Ensure the Informed Consent process is being followed.
- Ensure key data (eligibility, safety, primary and secondary endpoints) derived from selected subjects are accurate and complete/verifiable and inform the Investigator of any errors identified during the visit.
- Ensure any deviations and non-compliances identified at monitoring visits are correctly documented and inform the Investigator of any deviations identified during the visit.
- Ensure trial activity is adequately documented in case records, trial logs and forms (e.g. file notes, deviation reports).
- Ensure that data that is reviewed by the Monitor at visits is verifiable, through the checking of case notes, laboratory results and any other relevant reports.
- Ensure each subject selected for review meets all inclusion/exclusion criteria as per the protocol.
- Ensure the safety reporting process is being followed.
- Ensure trial staff are conducting tasks as delegated by the PI (Principal Investigator) and that they have been adequately trained to do so.
- Ensure the accuracy of the accountability of any Investigational Medicinal Product (IMP)(s).
- To resolve outstanding issues raised at the SCV.
- Ensure PI oversight during SDV of participant data, especially bloods, scans are reviewed in the participant notes and review is documented.
- Perform SDV of key lab data (eligibility, safety, primary or secondary endpoints, etc.)
- Ensure any Investigative Medical Devices (IMD) are appropriately stored, and used as per Protocol.
- Ensure any Device Deficiencies are correctly reported and recorded.
- Archiving – ensure the site/pharmacy have a process is in place for the end of the trial.

3.5 The Pharmacy Monitoring Visit

The purpose of a Pharmacy visit is to ensure that any Pharmacy department involved with all or any of the procurement, supply, storage, preparation, dispensing or destruction of an IMP and/or associated medicines used in a NHSGGC Sponsored or Co-Sponsored trial can and does achieve this in accordance with the protocol and all applicable laws and regulations.

The core Pharmacy monitoring tasks are:

- Ensure that the Pharmacy file is maintained in accordance with guidance provided by the Sponsor Pharmacist(s)
- Ensure the file contains, or refers to current CVs and GCP certification for key staff
- Ensure the Pharmacy is handling and managing the IMP(s) and/or associated medicines in accordance with the sponsor guidelines
- Ensure the procurement, receipt, storage, handling, preparation, dispensing and disposal of the IMP and/or associated medicines adhere to the protocol/Investigator Brochure(s)/Summary (ies) of Medicinal Product Characteristics, as appropriate, and that this is evident in the documentation.

3.6 Visit Documentation

3.6.1 Preparation for the Monitoring Visit

Prior to any monitoring visit the CTM will familiarise themselves with the protocol and all essential/trial-specific documents, including the Source Data plan. The CTM will review the eCRF for any data inconsistencies or unresolved queries and will review reported Serious Adverse Events (SAEs) for the site. The ICFs will also be reviewed prior to the visit if the patient has consented to the upload of their data to the eCRF (secure area with restricted access, not part of data capture). The CTM will check the correct ICF and PIS have been used for the subject, examine any re-consent if applicable, correct version date, consistent with ethical and local approval and the ICF was taken before any trial specific activity. The CTM will also check the person who took consent is delegated on the log, with relevant CV and GCP and the patient has printed their name, signature and date correctly, the handwriting is legible and the subject has confirmed by initialling boxes throughout the ICF. The CTM can also review visit dates prior to ensure protocol compliance. The CTM will also contact the Pharmacy Sponsor staff to check if there are any issues prior to the pharmacy visit.

The Monitors will contact the Principal Investigator, the Lead Pharmacist at the site (if appropriate) and other key site staff, by email, to arrange a suitable date and time for the visit. During the visit, the site should be represented by the PI or Lead Site Pharmacist, but another member of the site or Pharmacy team may attend in the absence of the CI/PI or Pharmacist, as appropriate. All relevant communication regarding site visits will be stored in the in the Monitor section of the trial master file (Form 51.016A – Section 12). Any relevant communication by telephone will be recorded in the Telephone Contact form (Form 53.004E), if not followed up by email. The Monitors will confirm with the PI or site representative whether the site use paper or electronic case records and ask site to ensure access whilst on site. If the site fail to respond to several emails or telephone attempts to arrange a visit, the Monitor will contact the CI. If the CI fails to resolve the lack of response from the site, the Monitor will escalate the lack of involvement in the monitoring process to the Lead Clinical Trial Monitor/Research Governance Manager.

A Monitoring Visit Agenda (Form 53.004F) will be completed and sent to the PI and site representatives by the Monitor recording the tasks to be undertaken at the visit. This will be sent by email prior to the visit ensuring the site have enough time to prepare for the upcoming visit. It should include the participants who have been selected for SDV, ICFs and the ISF for both the pharmacy and the site depending on the type of visit, and any SAEs to be reviewed; as per the monitoring plan objectives. The agenda will also be uploaded as an attachment to the corresponding visit record in Q-Pulse.

The visit will be recorded in Q-Pulse using the audit wizard set up, detailing the trial, site name, PI, and have the appropriate checklist applied the date of the visit, refer to Guideline 53.004A.

3.6.2 During the Visit

The Monitor will meet the PI or site representative, and the Pharmacy representative if undertaking a pharmacy visit, at the start of the visit to ensure all documentation required is available, suitable space has been provided to conduct the visit and clarify any local arrangements. Any issues encountered can be escalated, as appropriate to the PI/CI, Sponsor Pharmacist, Lead Pharmacist Clinical Trials R&I, Research Governance Manager or Lead Clinical Trial Monitor. The Monitors will endeavour to meet with the representative again before leaving the site, to discuss any findings or questions. At each visit the monitor will complete the Site Monitoring Visit Log which requires site sign off and will be filed in the Monitoring section of the Trial Master File (TMF) (Form 51.016A) and ISF, if required the CTM can request a copy from site.

If applicable, some of these tasks may be conducted by remote and/or central monitoring. This will be detailed in the Monitoring Plan (Form 53.010A).

During the visit, if the Monitor identifies any findings which may require an urgent safety measure the PI/CI will be notified immediately and the finding handled as per SOP 53.001. If the Monitor has concerns regarding poor quality and/or fraud in a trial they will handle their concerns according to SOP 53.002 and detailed in section 3.10.

3.7 Visit Reporting and Action Resolution

3.7.1 Visit Findings

Non-compliance issues and potential Serious Breaches will be categorised and handled in accordance with SOP 51.008 and SOP 51.009, as described below.

Any minor findings (grade 1 & 2 issues) may be resolved during the visit when discussed with the site representative. This resolution will be noted in the monitoring report. Any findings categorised 1 and 2 will be addressed in the standard follow up letter, if applicable.

Any findings categorised serious (grade 3 issues) or critical (grade 4 issues) will be formally documented and reported using the appropriate form outlined in SOP 51.008. A copy will also be sent by email to the Research Governance Manager and/or Lead Pharmacist Clinical Trials R&I and, if applicable, the Sponsor Pharmacist, Sponsor Research Co-Ordinator, Project Manager and CI.

There may be occasions when as a result of a finding included in the follow up actions to a visit, that a further finding is discovered, such as site being unable to locate a document that is missing from the ISF. In this instance, a new finding can be raised and details should be gathered in order to discuss appropriate timescales with Lead CTM/QA Manager.

3.7.2 Visit Report

The monitor will update the associated Monitoring Record in Q-Pulse as described in Guideline 53.004A. This will involve completing the visit checklist and uploading any documentation including relevant email trails associated with the visit, documents sent out to site in advance of the visit such as checklists and agenda, documents sent by site to the CTM for review prior to the visit and the monitoring visit log Form 53.004G (if remote visit option), the follow up letter and the actions resolution document. The CTM can download a copy of the appropriate Q-Pulse checklist as a visit guide/aid if required. If applicable, this checklist should be saved and can be provided to another CTM if required i.e. leave cover/handover. When the report is complete, it will be reviewed by the Lead Clinical Trial Monitor, Governance Manager or other member of the Governance Team. Once approved, the approver will add a note to Q-Pulse to say "Approved" and the Follow Up letter and Actions Resolution Document will then be sent to site with a turnaround time from visit date to approval of 15 working days, if the timeline is not met then this must be documented on the report in the note section in Q-Pulse e.g. annual leave.

3.8 Follow Up Letter

A Follow Up letter (Form 53.004H), summarising the Monitoring Visit, and an Actions Resolution document (ARD) generated from the Q-Pulse report listing all actions arising from the visit, including action resolution timelines, will be sent to the CI/PI by email or post within 15 working days unless documented otherwise. A copy of the Follow Up letter will be sent by email to the Research Governance Manager, the NHSGGC Sponsor Research Co-Ordinator, the Lead Clinical Trial Monitor and, if applicable, the Project Manager. A copy of the letter will retained in the Monitoring section of the TMF and uploaded to Q-Pulse prior to review.

If the Pharmacy Visit is part of the Site Visit, the Follow Up letter (Form 53.004H) to the PI will incorporate the Pharmacy section. Where the Pharmacy Visit is a separate, standalone visit, the Follow Up letter (Form 53.004H) will be sent to the Lead Site Pharmacist and the Sponsor Pharmacist, copying the PI, the Research Governance Manager, the NHSGGC Sponsor Research Co-Ordinator and, if applicable, the Project Manager. In both cases, the letter will be e-mailed to the named parties, a hard copy of the letter will be posted to the Lead Site Pharmacist or asked to print, and a copy retained in the Monitoring file.

3.9 Resolution of Action Points

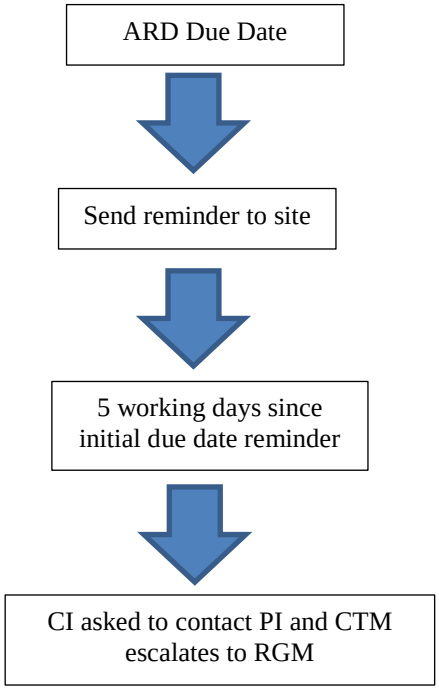
The PI will be asked to confirm resolution of the action points by signing the Actions Resolution document and returning the completed document to the Monitors within 30 calendar days from the date the FU letter/ARD were sent to site, unless otherwise stated. The Action Resolution Document will be generated from Q-Pulse and so the CTM must ensure that the due date reflected in this document is 30 calendar days from the date it will be sent to sites, this can be achieved by updating the dates of the finding records in Q-Pulse and printing out the ARD. Receipt of the completed document will be confirmed by the Monitors signing the Actions Resolution document and a copy returned to the site for their site files. Resolution of any Pharmacy actions will be confirmed by the designated pharmacy team member and signed by the PI Resolution of action points will be updated in Q-Pulse also providing the date when the action was completed. A reminder email can be sent 5 working days before the 30 calendar day timeline, if applicable.

3.10 Escalation Process

The monitors will employ an escalation process when there is no, or incomplete resolution of actions. If the PI does not return the completed Actions Resolution Document confirming resolution of all actions points by the date of the first resolution timeline, the Monitor will send a reminder email on or close to the due date, depending on CTM availability e.g leave/travelling. If there is no response to the reminder email, a final reminder will be sent by the monitor after 5 working days. The Monitor will request that the CI contact the local PI and escalate to the Research Governance Manager. The R&I Research Co-Ordinator may also be asked to contact the local site R&I contact regarding the non-compliance to the completion of monitoring actions.

When the University is Co-Sponsor the Research Regulation & Compliance Manager or appropriate designee will be included in the correspondence regarding the monitoring visits, follow up letters, actions and escalations, for their information.

All escalation documents will be filed in the Monitoring section of the TMF and/or uploaded to the Q-Pulse report, including adding to the note section in Q-Pulse



3.11 Remote Monitoring Visit

There may be times when face to face on-site monitoring visits are not possible, or planned within the monitoring plan, and a remote visit can take place instead. These visits can be arranged via email or telephone/video conference. The aim is the same as for a monitoring on-site visit and will rely on the integrity of the site staff to confirm and verify the presence and correctness of the SDV. The monitor will review and confirm that the ICF allows for remote viewing of participant data prior to the visit taking place.

The remote visit can take several forms depending on local access privileges to EHR at site. Microsoft Teams may be utilised for this purpose if appropriate and data security is essential. If a site require further confidentiality, then Clinical Trial Monitor Remote Monitoring Agreement Form 53.004P can be used or local site equivalent.

All routine preparation, documentation and reporting apply to remote visits.

3.12 Additional Monitoring reporting

On occasion, ad-hoc monitoring may be required, which will be detailed in the updated monitoring plan, for issues such as – Serious Breach, PID/screening logs, ICF review etc. or any issue which requires immediate action out with the monitoring plan timeline. This will be documented in Q-Pulse and the follow up letter. Site compliance will be measured by grading monitoring issues detected into category 1, 2, 3 or 4, as per SOP 51.008. Glasgow Health Science Partnership Regulatory Affairs Group (GHSP RAG) will be informed of any Serious (grade 3) and Critical (grade 4) as described in SOP 51.008. Compliance to monitoring timelines, both by sites and the monitoring team will be reported to GHSPRAG in the event of non-compliance.

4 Referenced documents

- Form 53.004E - Monitoring Telephone Contact Form
- Form 53.004F - Monitoring Visit Agenda Template
- Form 53.004G - Site Monitoring Visit Log
- Form 53.004H - Follow Up letter
- Form 53.004P - Clinical Trial Monitor Remote Monitoring Agreement
- Guideline 53.004A - Q-Pulse guidance for Monitoring visit
- SOP 53.014 - External Sponsor Monitoring Arrangement
- SOP 50.020 - eCRF User Acceptance Testing (Glasgow Clinical Trials Unit)
- SOP 51.010 - Preparation and Review of Grant Applications and Costs
- SOP 51.004 - Risk Assessment
- SOP 53.010 - Monitoring Clinical Research – Preparation and Management of a Monitoring Plan
- SOP 51.001 - Protocol Development
- SOP 51.008 - Handling non-compliance with Good Clinical Practice (GCP) and/or the trial protocol in clinical research sponsored, co-sponsored or hosted by NHS Greater Glasgow and Clyde
- SOP 51.009 - Notification of serious breaches of Good Clinical Practice or the trial protocol for clinical trials of investigational medicinal products
- SOP 53.001 - Handling urgent safety measures for clinical trials of investigational medicinal products
- SOP 53.002 - The Handling of poor quality and fraud in clinical research
- Form 53.010A - Monitoring Plan for a Clinical Trial of an Investigational Medicinal Product
- Form 53.010B - NHSGGC Monitoring Risk Assessment
- Form 51.016A – Sponsor TMF Index
- Form 51.004A - Risk Assessment tool

5 Related documents

- SOP 51.016 - Preparation and maintenance of a Trial Master File
- SOP 56.001 - Site Set Up – Green for Go Process

6 Document History

Version	Date	Description
1.0	11/09/2008	Release of Version 1.2 (for review)
1.1	18/06/2009	Minor clarifications
1.2	12/07/2010	Release of version 1.2
2.0	27/11/2013	Release of version 2.0 (Update to monitoring processes)
3.0	19/01/2015	Release of version 3.0 clarification of monitoring processes and timelines.
4.0	17/6/2016	Renumbered SOP. Transfer of author.
5.0	08/01/2019	SOP name updated and transfer of author; addition of staff category; addition of Guide for Q-Pulse
6.0	26/11/2020	SOP Site compliance visit and close out visit removed to separate new SOPs and referenced documents, forms and guidelines revised and updated Change of Author.
7.0	29/10/2024	Routine review with the following updates - Escalation detail added, Late action timeline, report checks, PI oversight and SDP review prior. Removal of obsolete forms and a guideline.