SOP number	**53.010**	Version	**2.0**
Title	**Monitoring Clinical Research – Preparation and Management of a Monitoring Plan**		

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SOP category	NHS GG&C Sponsor Governance
Staff category:	

Staff Category	**R**	**A**	**C**	**I**
Lead Clinical Trial Monitor		x		
Clinical Trial Monitors	x			
Research Governance Manager	x			
University of Glasgow Governance Manager				x
Chief Investigator			x	
Pharmacovigilance			x	
R&I Coordinator				x
R&I Lead Sponsor Pharmacist			x	
R&I Pharmacy			x	
Project Managers			x	

1. Scope

This standard operating procedure applies to all NHS Greater Glasgow & Clyde Research & Innovation Clinical Trial Monitor(s) and applicable to staff working within the Glasgow Clinical Trials Unit (GCTU). Monitors may monitor trials out with the NHS Greater Glasgow & Clyde Sponsor team, agreements with external Sponsors should be made in writing prior to the use of this SOP. (Please refer to SOP 53.014)

2. Purpose

The purpose of this SOP is to describe the procedures that will be used by the Clinical Trial Monitors (CTMs) acting on behalf of the Sponsor, either internal or external as per agreement to prepare a Monitoring Plan for non-commercial clinical trials (CTIMPs, CIMDs and High Risk non-CTIMP) Sponsored by NHSGGC or on some occasions hosted trials (commercial and non-commercial) when asked to perform this function by an external Sponsor. The Monitoring Plan is an evolving document which should be updated throughout the course of the study as required. This SOP describes the measures taken by the CTMs preparing the plan and will also describe the procedures for updating the Monitoring plan.

3. Procedures

3.1. The Monitoring Risk Assessment

The type of Monitoring included in the plan will be determined by the risk rating of the trial and other risks documented on Form 51.004A – Risk Assessment Tool and the overall monitoring risk score which is determined through the use of Form 53.010B- Monitoring Risk Assessment. Once the trial protocol has been approved or close to approval and before the Sponsor green light approval happens the Monitor (CTM) will review the protocol and complete the NHSGGC Monitoring Risk Assessment (Form 53.010B) to determine the level and type of risks anticipated from a monitoring perspective. The table below is an example of the output from Form 53.010B and outlines an example of scoring a risk assessment for a high risk study. The example explores the risk encompassing the complex nature of the study design, primary and secondary endpoints, seriously ill or vulnerable population, inexperienced investigative site, a novel product and a high rate of missing data, transcription errors or protocol deviations. Four categories including alert, high, medium and low risk are employed depending on the level of risk and score from, Form 53.010B.

The levels of risk are outlined below:

- Low Risk is defined as a score < 13
- Medium Risk is defined as a score of greater than >=13 but less than<= 26
- High Risk is defined as a score > 26

n.b. Any alerts will add 3 points on to the risk assessment score, these will be based on a study by study approach. Any alerts which will adjust SDV selection and monitoring schedule including number of visits will be stated specifically in the Monitoring Plan, (Form 53.010A).

Below is an example of part of the scoring system used by the monitors to determine the risk of a study and how to mitigate risks. Regardless of the perceived initial risk of any study, all questions will be answered in the NHSGGC Monitoring Risk Assessment (Form 53.010B). In addition, the CTM will review the Sponsor Risk Assessment Tool (Form 51.004A) which is completed by the Research Coordinator, CI, Trial Team and Sponsor stakeholders at the start of any study, and determine if there are any issues which will impact monitoring. The Monitoring Risk Assessment (Form 53.010B) will be reviewed and approved by the Lead Clinical Trial Monitor/Research Governance Manager.

Table 1: Example of a Risk Assessment (Qu.1 to 5)

Question	Indicator	Alert = 3	High = 2	Med = 1	Low = 0	Running Total	Risk Mitigation
1	Phase I/ First In Human (FIH) / GMO	3				3	100 per cent SDV monitoring. Time of first monitoring visit when first patient recruited. Consider any potential issues / dose escalation timelines.
2	Study Design, complex study design with IMP dose escalation		2			5	100 per cent SDV monitoring. Time of first monitoring visit when first patient recruited.
3	Emergency Study with a number of different types of Consent		2			7	The monitor will risk assess the percentage of consents and aim to ensure these are reviewed in a timely fashion and give feedback to the site about their consents.
4	Novel Product (never used in humans before with dose escalation involved.)	3				10	First monitoring visit performed at first patient recruited.
5	Primary and Secondary Endpoints captured at a specific timeline/visit			1		11	Focus SDV on these endpoints and ensure timelines are queried within eCRF.

(Full Risk Assessment must always be performed and documented)

3.2. The Monitoring Plan

Based on both Risk Assessments, (Form 51.004A and Form 53.010B), and the definitions of the level of risk described in this form, the CTM will create a trial specific Monitoring Plan using the Monitoring Plan template (Form 53.010A). The Monitoring Plan template (Form 53.010A) will document the risk score and risk classification detailing if it is high, medium or low risk study based of the monitoring risk assessment. It will set out the main risks identified in both the sponsor and monitoring risk assessments, (Form 51.004A and Form 53.010B), and how to mitigate the risks. The objective timelines, detailing the type and number of visits required and the rationale for these visits and timelines will be based on the risk of the study. The visits may include but are not limited to; an initiation visit, a site compliance visit, full monitoring visit for both site and pharmacy, and site close out visit. The monitor will also consider any Laboratory or Imaging within the trial and whether or not it affects the primary endpoints of the study which may require an added objective to monitor or an extra visit. Each visit will be described within the plan detailing the objectives the monitor will aim to achieve based on trial specifications, assessment and mitigation of risks.

The monitor will also document the different types of monitoring which may be undertaken, i.e. remote monitoring, within the plan which may be due to costs or site circumstances.

At times there may be a requirement to draft an addendum to a Monitoring Plan, i.e. pandemic restrictions, a trial specific issue which requires a fast amendment to the plan. Any addendums to monitoring plans will be filed within the monitoring section of the TMF.

3.3. Review of the Monitoring Plan

Once the CTM has completed the Monitoring plan template (Form 53.010A), the plan will firstly be sent to the Lead Clinical Trial Monitor. The Lead Clinical Trial Monitor will review the monitoring plan to ensure risks relating to the trial activity have been incorporated and oversight planned for. The next step is to send the monitoring plan to the key stakeholders of the study including but not limited to, Project Manager, Sponsor Pharmacy, Pharmacovigilance and the Chief Investigator for review. Key Data which affects primary or secondary objectives will be documented within the plan and reviewed by the Chief Investigator and the Statistician. The CTM will set a date for the Monitoring Plan (Form 53.010A) to be reviewed by and the date it was sent to stakeholders will recorded on the document, any comments from the stakeholders addressed and incorporated with any relevant updates. If a stakeholder does not reply by the agreed review date, then the monitor will email the stakeholder a reminder giving them another five days to complete, if they do not reply after this date it will be documented as the stakeholder has no comments to make on the plan and the plan will be finalised. The Project Manager will also document the review in the TMG minutes of the study. After review by the key stakeholders, the Monitoring Plan will be reviewed and approved by the Lead Clinical Trial Monitor/Research Governance Manager. The final signed Monitoring Plan and Risk Assessment will be filed in the Monitors section of the Trial Master File. A copy of the final Monitoring Plan will be sent to the Chief Investigator (CI) for their information and site files.

3.4. Updating the Monitoring Risk Assessment and the Monitoring Plan

Over the course of the study, risks may change due to a protocol amendment, site compliance issues or other reasons. The Monitoring Plan and Risk Assessment must be updated and the monitor will complete the updated section of the Risk Assessment documenting the new risks, and updating the plan in regard to the new risk. After each monitoring visit, the monitor will also document on Q–Pulse visit checklist that the current monitoring plan template and risk assessment are appropriate and flag if an update is necessary. At every amendment the monitor must review the monitoring plan for any new risks to be documented, if the plan does not require to be updated, the monitor should document the evidence of this review on Form 53.010C. File Reviews are the responsibility of the named monitor for the study, this should happen at least once over the lifetime of the trial, however, may be performed more frequently to ensure the monitoring risk assessment and monitoring plan are up to date.

3.5. Compliance to the Monitoring Plan

Compliance to the Monitoring plan will be reviewed monthly at the Monitors meeting and all CTMs will update the monitoring status of each study and ensure Status tracker columns relating to compliance to the monitoring plan has been completed. An example of these columns is highlighted in Appendix 1 of this document. It is the responsibility of the study monitor to ensure the monitoring plan is adhered to, ensuring the detailed SDV has been performed and the relevant objectives have been achieved. A monitoring metrics report will be discussed at the meeting highlighting timelines for monitoring activity and reporting any non-compliances with site or pharmacy action, ensuring this has been escalated to the Governance Manager copying in the Sponsor Lead Pharmacist, as appropriate. Non-compliance will be documented and reviewed with the Lead Clinical Trial Monitor and/or Sponsor Governance Manager.

4. Referenced documents

- Form 53.010A - Monitoring Plan for a Clinical Trial of an Investigational Medicinal Product
- Form 53.010B - NHSGGC Monitoring Risk Assessment
- Form 53.010C - Research & Innovation Monitoring Plan Tracking Log
- Form 51.004A - Risk Assessment Tool.
- Form 51.016A - Sponsor TMF Index
- SOP 53.014 - External Sponsor Monitoring Arrangement

5. Related documents

- SOP 53.004 - Monitoring Clinical Research – Site Monitoring Visit
- SOP 56.001 - Site Set Up – Green for Go Process

6. Document History

Version	Date	Description
1.0	26/11/2020	First Release
2.0	18/06/2024	Significant updates to content, better reflect risk adaptation, oversight of compliance, review of amendments and change of Form numbers.

Appendix 1

Compliance Check - Monitoring Plan - Compliant Yes/No, add details as required	Compliance Check - Report timeline - Compliant Yes/No (as per SOP), please confirm if escalated	Compliance Check - Escalation follow up - Confirm if complete Yes/No