Monitoring

Division: Trust-Wide

Specific staff groups to whom this policy directly applies	Likely frequency of use	Other staff who may need to be familiar with policy
Staff employed by North Bristol Trust who directly or indirectly work on Clinical Research within the Trust	Role Dependant	Staff not employed by North Bristol NHS Trust who are working on Research studies sponsored or hosted by NBT

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Consultation:	R&D Sponsorship Team
Approval Authority (Committee/ Group/ Lead Clinician):	R&D Senior Team
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Version:	RD/QMS/SOP/014 Version 3.1
KEYWORDS:	Risk proportionate monitoring, CAPA report, Audit Trail, Direct Access, TMF, ISF,
Summary of changes since the previous version	Changed format to align with NBT SOP template Changed R&I to R&D Update on wording to clarify Direct access to monitors, and sponsor to ensure audit trails for documentation are provided as needed. Added information in relation to responsibilities when working with Clinical Trials Units. Change the naming convention of R&D SOPs

	Editorial amendments have been made to sentence structure and wording to improve clarity, flow, and consistency across the R&D SOP's.

1. Purpose	This SOP describes the risk-based procedures that will be used by R&D to monitor CTIMPs sponsored by NBT, including oversight of essential records and trial conduct. The SOP also outlines the procedures to follow in preparation for, during and following the monitoring. .
2. Key Messages	Monitoring is a core sponsor responsibility and a key quality control activity designed to verify the protection of participants' rights, safety and well-being, and the reliability and integrity of trial data, in accordance with ICH GCP E6(R3). North Bristol NHS Trust (NBT), as Sponsor, applies a risk-proportionate monitoring approach for CTIMPs, based on a documented sponsorship risk assessment and a study-specific monitoring plan. Monitoring may be conducted using a range of methods, including on-site visits, central or remote review, self-monitoring, and site file or compliance review, proportionate to the risks and complexity of the study. The monitoring plan must define the type, scope, and frequency of monitoring required before, during and after the trial and must be reviewed at least annually, or sooner where risks are identified or the trial is modified. Investigators and participating sites must provide timely and direct access to trial-related records, including source data, for authorised monitors, auditors and regulatory authorities, while ensuring participant confidentiality and compliance with data protection requirements. Monitoring findings must be documented, communicated, and followed up in a timely manner, with corrective and preventative actions (CAPA) implemented and tracked to resolution. Although this SOP primarily applies to CTIMPs sponsored by NBT, the principles of risk-based monitoring described may also be applied to other NBT-sponsored research, where appropriate **Terminology Note:** The term "participating site" is used throughout and should be read interchangeably with "trial location" where applicable for clinical trials of investigational medicinal products, in line with the Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025

Abbreviations

AE	Adverse Events
CAPA	Corrective and Preventative Action
CI	Chief Investigator
CRF	Case Report Form
CTIMP	Clinical Trial of an Investigational Medicinal Product
CTU	Clinical Trials Unit
ICH GCP	International Conference on Harmonisation Guidelines for Good Clinical Practice
IMP	Investigational Medicinal Product
ISF	Investigator Site File
NBT	North Bristol NHS Trust
PI	Principal Investigator
PD	Protocol Deviation
R&D	Research and Development
SOP	Standard Operating Procedure
TMF	Trial Master File

3. Relevant Policies & Guidance

Policies and Guidance:

Guidance for Good Clinical Practice ICH GCP (E6) R3 - ICH
https://database.ich.org/sites/default/files/ICH_E6%28R3%29_Step4_FinalGuideline_2025_0106.pdf

Medicines for Human Use (Clinical Trials) Regulations 2004, as amended by the Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025

The following NBT documents are available on the R&D website:
www.nbt.nhs.uk/research

Associated SOPs and Templates:

RD QMS SOP 007 Applying for NBT Sponsorship

RD SOP 007c Delegation of Responsibilities

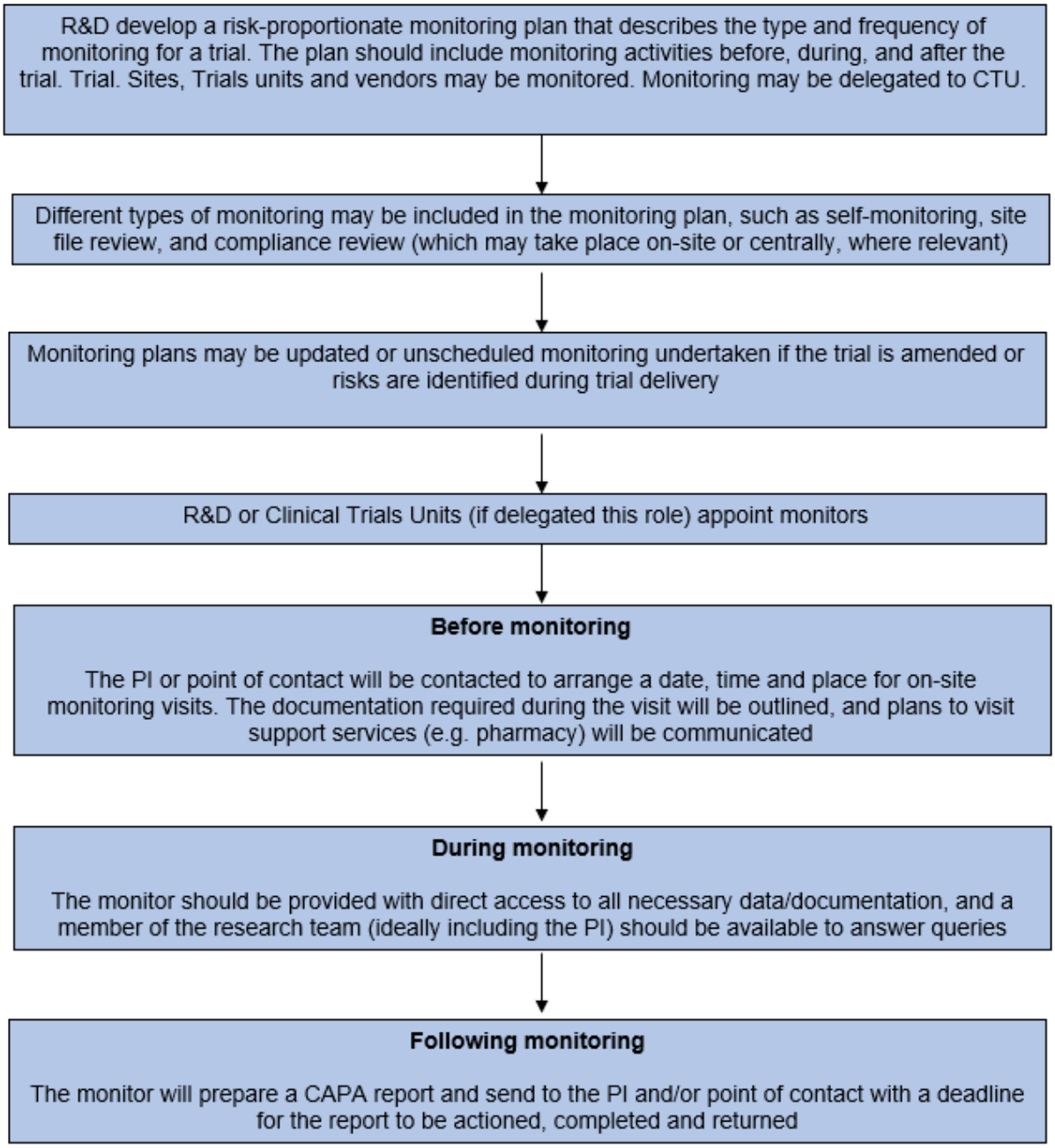
	RD QMS SOP 014a Preparation of a Monitoring Plan RD QMS SOP 012 Managing Breaches of Good Clinical Practice or the Protocl.
4. Operational Areas Included	This SOP applies to all research studies sponsored by North Bristol NHS Trust (NBT), as well as studies that are externally sponsored and hosted by NBT. For NBT-sponsored CTIMPs, this SOP must be used to determine the type, scope, and frequency of monitoring required. For externally sponsored studies hosted by NBT, this SOP provides guidance to research teams on their responsibilities in facilitating and supporting sponsor-led monitoring activities, including preparation for monitoring visits, granting access to trial-related records, and responding to monitoring findings, in line with applicable agreements and regulatory requirements.
5. Operational Areas Excluded	None
6. Who should read this	This SOP applies to all investigators, research staff, monitors, service support teams, and R&D staff involved in the conduct, management, or monitoring of research studies sponsored or hosted by North Bristol NHS Trust (NBT). When collaborating with external stakeholders, such as Clinical Trials Units, on NBT-sponsored projects, it may be appropriate to utilise external SOPs to ensure proper project governance and the fulfillment of delegated roles and responsibilities. In such instances, both the external stakeholder and the NBT sponsorship team must ensure that the external SOP aligns with the procedures outlined in this SOP. If there is a conflict between the external SOP and NBT's procedures, the NBT SOP will take precedence, except in exceptional cases where approval is obtained from the Research Operations Manager or the Deputy Director of Research.
7. Roles responsible for carrying out this procedure	**Chief Investigator (CI)** The Chief Investigator (CI) is responsible for ensuring that a risk-proportionate monitoring plan is developed for the study. This responsibility may be delegated (for example, to a trial manager or Clinical Trials Unit); however, the CI remains responsible for ensuring that the monitoring plan is compiled and submitted to the Sponsor for review and approval prior to implementation. **Principal Investigator (PI)**

	The Principal Investigator (PI) must ensure that authorised monitors are provided with timely and direct access to all relevant study documentation and essential records, including source data and trial-related records, in accordance with applicable regulatory requirements. The PI is responsible for ensuring that appropriate facilities are available at the organisation to support monitoring activities, including provision of adequate workspace and access to relevant systems and records. During monitoring activities, the PI should ensure their own availability, where possible, and must facilitate access to appropriately delegated study staff and relevant support departments (for example Pharmacy or laboratories), as required to support the effective conduct of monitoring. **NBT Sponsorship Team** NBT, as Sponsor, is responsible for ensuring that appropriate monitoring arrangements are established and maintained to oversee the conduct of the trial and the reliability and integrity of its data. The Sponsor must implement a proportionate, risk-based monitoring approach, ensure that appropriately qualified monitors are appointed, and maintain adequate oversight of any monitoring activities that are delegated to third parties, including Clinical Trials Units. The Sponsor is responsible for ensuring that monitoring activities verify: The rights, safety, and well-being of participants; Compliance with the approved protocol and applicable regulatory requirements; and The accuracy, completeness, and integrity of trial data and essential records. The Sponsor must also ensure that monitoring findings are appropriately documented, communicated, and followed up in a timely manner, including the review and oversight of corrective and preventative actions (CAPA), where required. **Monitor** The Monitor is responsible for conducting monitoring activities in accordance with the approved monitoring plan, applicable SOPs, and regulatory requirements. The Monitor must document monitoring findings accurately, communicate these to the appropriate members of the research team and Sponsor, and follow up on corrective and preventative actions (CAPA) within agreed timelines. The Monitor must escalate significant issues or risks to participant safety, data integrity, or protocol compliance to the Sponsor without delay.

	Clinical Trials Unit (CTU) ***(where monitoring activities are delegated)*** Where monitoring activities are delegated to a Clinical Trials Unit (CTU), the CTU is responsible for undertaking the delegated monitoring activities in accordance with the approved monitoring plan, the approved SOPs, and applicable regulatory requirements. The Sponsor retains overall responsibility for monitoring oversight, including review of monitoring outputs and follow-up of identified issues.

8. Procedure:

SOP Flowchart



8.1 Monitoring Plan

All CTIMPs sponsored by NBT will be subject to a sponsorship risk assessment, which must be completed prior to regulatory submission (see *Applying for NBT Sponsorship*, RD/QMS/SOP/007). Based on this assessment, the Sponsor, through R&D, will determine a risk-proportionate monitoring plan for each trial.

The monitoring plan must document the monitoring methods to be used and the frequency of monitoring. As a minimum, the plan must describe the monitoring activities required before, during, and after the trial. The approved monitoring plan will be communicated to the Chief Investigator (CI).

The monitoring strategy must ensure appropriate Sponsor oversight of trial conduct and should take account of site capability and the potential burden of monitoring. The plan must focus on aspects critical to trial quality, including participant safety, protocol compliance, and the reliability and integrity of trial data and essential records. The monitoring plan must reference the Sponsor's applicable policies and procedures.

The specific requirements of the monitoring plan will be determined on a case-by-case basis. Not all monitoring activities are required to be conducted on-site; therefore, a proportionate approach must be taken when developing the monitoring plan, which may include central, remote, or triggered monitoring. Further guidance is provided in *Preparation of a Monitoring Plan* (RD/QMS/GD/014a), available on the NBT R&D website.

The monitoring plan and sponsorship risk assessment must be reviewed by the Sponsor at least annually throughout the trial and updated where necessary, for example following trial modifications or the identification of new or emerging risks during trial conduct. Any updated monitoring plan will be communicated to the CI.

Where a formal review of the monitoring plan and risk assessment is not required, the Sponsor may nevertheless undertake unscheduled or additional monitoring where necessary to ensure ongoing participant safety, protocol compliance, and data quality, in addition to the monitoring activities specified in the approved monitoring plan.

8.2 Monitors

R&D will appoint monitors who are appropriately trained and who have appropriate experience or knowledge to monitor the trial adequately, in accordance with the approved monitoring plan and applicable regulatory requirements.

The Sponsor may delegate certain monitoring activities to the research team or to trial managers, for example where the study is managed by a CTU, The Sponsor retains ultimate responsibility and accountability for monitoring oversight, including reviewing monitoring outputs and follow up of any identified issues.

8.3 On-Site Visits

When on-site monitoring visits take place, the following will apply:

(a) <u>Before the visit:</u>

i. The monitor will notify the PI (or the point of contact, where the monitoring visit is to take place at non-recruiting establishments such as trials units).

ii. A date for the visit will be agreed by the monitor. This will usually be a minimum of two weeks in advance (except where critical risks are identified that need urgent mitigation, where triggered monitoring may be required sooner).

iii. Prior to the visit, the monitor will confirm exactly what documentation they will need available (e.g. site files, medical records)

iv. The monitor will confirm prior to the visit whether any other departments (e.g. Pharmacy) will be visited.

(b) <u>During the visit:</u>

i. The PI or other point of contact should ensure that an appropriate space is booked for use by the monitor during the visit. The monitor will require a quiet space where they can review the documentation.

ii. Investigators and trial sites must permit timely and direct access to all trial-related records, including source data and source documents, for the purposes of monitoring, auditing, and regulatory inspection, in accordance with ICH GCP E6(R3).

iii. Such access must be granted to authorised representatives of the Sponsor (for example, monitors and auditors) and to applicable regulatory authorities, to enable verification of trial conduct and data integrity. Access must be provided in a manner that ensures data are attributable, legible, contemporaneous, original, and accurate, while maintaining the confidentiality and privacy of trial participants in line with applicable data protection requirements.

iv. The research staff should identify if any documentation requested for review is in electronic format, and ensure the monitor has relevant access to these during the visit. If electronic data access is required by the monitor during the visit, the research staff should ensure that someone is available during the visit to provide any necessary training and ongoing Information Technology (IT) support.

v. A member of the research team should be available to meet the monitor during the visit and to assist with any queries.

vi. Where possible, the PI should be available for at least part of the monitoring visit.

vii. ICH GCP E6(R3) places responsibility on the Sponsor to ensure the reliability and integrity of trial data and the traceability of all data changes.

   a. Sponsors must ensure data changes are justified, documented, and traceable, with appropriate audit trails for paper and electronic records.

   b. Any post-hoc or post-unblinding changes must:

viii. Be exceptional and significantly justified

ix. Be authorised by the sponsor prior to implementation

x. Be fully documented including the rational for the change

xi. captured in the audit trail for the relevant record or system

xii. Be reported in the clinical trial report, where applicable

(c) Following the visit:

Following completion of any monitoring activities, the Monitor will prepare a written monitoring report and submit this to the Principal Investigator (PI) and/or other relevant members of the research team.

Where self-monitoring has been undertaken, feedback may be provided in the form of written email feedback, as appropriate.

Where monitoring has included a site file review or compliance review, the Monitor will issue a Corrective and Preventative Action (CAPA) report, which will be distributed via email. The CAPA report will include:

- Details of what was reviewed
- Any significant findings, including identified deviations or deficiencies
- Actions required and/or recommendations to secure compliance.

The PI and research team must review the CAPA report and ensure that all actions are addressed promptly and within the agreed timelines. The Monitor will specify a deadline for completion of actions. The PI is responsible for documenting the actions taken within the CAPA report and returning the completed report to the Monitor by the agreed deadline.

9. Dissemination and Training

SOPS will be distributed in accordance with the SOP on Preparation of R&D Research SOPs (RD/QMS/SOP/001). This SOP and any associated templates and forms will be uploaded to the NBT website (www.nbt.nhs.uk/research) shortly after having been released.

All staff whose activities are subject to this SOP should ensure that they read and understand the content of this SOP.