Guidance Document

Preparation of a Monitoring Plan

This guidance accompanies SOP RI/QMS/SOP/014 Monitoring

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Document Version History

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1. PURPOSE AND SCOPE

This guidance document describes the factors to consider when preparing and reviewing a monitoring plan for CTIMPs sponsored by NBT, including the activities to be undertaken by R&I and the study team. The guidance also outlines the procedures to follow in preparation for, during and following the monitoring.

Although this guidance focuses on CTIMPs sponsored by NBT, the principles in the SOP apply to all research sponsored by NBT.

2. DEFINITIONS/ABBREVIATIONS

AE	Adverse Event
CI	Chief Investigator
CRF	Case Report Form
CTIMP	Clinical Trial of Investigational Medicinal Product
ICH GCP	International Conference on Harmonisation Guidelines for Good Clinical Practice
IMP	Investigational Medicinal Product
NBT	North Bristol NHS Trust
PI	Principal Investigator
PD	Protocol Deviation
R&I	NBT Research & Innovation Office
SOP	Standard Operating Procedure
ICH GCP	International Conference on Harmonisation Guidelines for Good Clinical Practice
Sponsor	The individual, company, institution or organisation, which takes on ultimate responsibility for the initiation, management (or arranging the initiation and management) of and/or financing (or arranging the financing) for that research

3. WHO SHOULD USE THIS GUIDANCE

This guidance is applicable to all investigators, research staff, monitors, service support teams, monitors, and R&I staff involved in research.

4. WHEN SHOULD THIS GUIDANCE BE USED

This guidance should be used alongside the SOP on Monitoring (RI/QMS/SOP/014) when determining the frequency and type of monitoring required for NBT sponsored CTIMPs.

The guidance should also be used when monitoring is being undertaken, in order to determine the procedure for preparing for, completing, and following up the monitoring.

5. MONITORING PLAN REQUIREMENTS

5.1. Monitoring schedule

Following a suitable risk assessment the Sponsor and research team should confirm a monitoring schedule for the duration of the study.

As an example, the monitoring schedule may include:

(a) Site initiation visit, focusing on review of investigator site file.

(b) Visit after the 1st patient is recruited, focusing on CRF completion, protocol compliance, source date verification, and informed consent.

(c) Visit(s) during the recruitment period, focusing on CRF completion, protocol compliance, source date verification, and informed consent.

(d) Close-out visit, focusing on investigator site file, archiving arrangements, and trial reporting requirements.

5.2. Monitoring plan checks

A monitoring plan should be created so that all pertinent areas are checked in line with Protocol and legislative requirements.

The monitoring plan should incorporate the following checks:

(a) There should be clear documented evidence of CI/PI oversight for the entire duration of the study. CI/PI decisions should clearly outline the rationale for the outcome; decisions which fall under other delegated staff should demonstrate CI/PI awareness and approval.

(b) Data management checks and a review of the Data Management Plan (DMP) for the study, including:

- how the eligibility of participants is assessed and documented.
- how the provision of trial related information is documented.
- how study related activity is undertaken and documented.

Where applicable, the monitoring plan will include checks of the documentation required for activities undertaken by impartial witnesses (where permitted). Please see SOP on Data Management (RI/QMS/SOP/017) for further guidance.

(c) A review of the arrangements for storage and accountability of IMP and the management of samples.

(d) A review of the provision of services (including monitoring plans for vendor services, where necessary). Please see SOP on Vendor Management (RI/QMS/SOP/016) for further guidance.

(e) A review of study-specific procedural documents (such as work instructions, flowcharts, SOPs) including their approval, implementation and the management of superseded study-specific procedural documents.

5.3. **Type of monitoring**

Once the checks to be included in the Monitoring Plan have been determined then it should be decided how these will be completed. Not all checks require Sponsor onsite monitoring and the research team may be delegated certain tasks.

Examples of the monitoring approaches that may be adopted include:

(a) Trial Management Meetings

Trial management meetings between the Sponsor and Trial Manager are held approximately every two months. A trial management report (in a format agreed with the Sponsor) should be submitted to the Sponsor at least two working days before the trial management meeting for discussion at the meeting. The CI should attend the trial management meeting, but if this is not possible then the CI should submit the report to the Sponsor to confirm that they have ratified the content.

(b) Self-Monitoring

PIs are sent a self-monitoring form to check recruitment, safety, and trial progress. This type of monitoring is an opportunity for PIs to identify any issues with the trial at their site, and for R&I to raise any concerns.

(c) Site File Review

Site files are reviewed to ensure essential documentation is available to enable the trial to run in accordance with ICH GCP.

(d) On site Monitoring

Representatives from the Sponsor team may conduct planned or triggered on site monitoring visits to review overall trial conduct and regulatory compliance. Key aspects of Protocol/ICH GCP compliance are assessed, for example:

- Verifying that the approved protocol and approved amendments are being followed;
- Reviewing the consenting process, including contemporaneous signature of the individual receiving consent and appropriate impartial witnesses where permitted;
- Verifying that only eligible participants are enrolled, and that consent has been given in accordance with ethical approval;
- Confirming that approved site specific SOPs are in place;
- Reviewing CRF entry error, omission, and illegibility, ensuring any changes are made, explained (if necessary), and initialled as necessary;
- Checking CRF accuracy and completeness of CRF entries, other trial documents, and source data against each other, to ensure that:

- The data required by the protocol is reported accurately on the CRFs and is consistent with the source documents;
- Any dose and/or therapy modifications are well documented for each of the trial participants;
- Adverse Events (AEs), concomitant medications and illnesses are reported in accordance with the protocol;
- Visits that participants fail to make, tests that are not conducted, and examinations that are not performed are clearly reported as such on the CRF;
- All withdrawals of enrolled participants from the trial are reported and explained on the CRFs;
- Only delegated investigators sign off the CRF;
- Determining whether all AEs are appropriately reported within the timescales specified by the Sponsor and regulations;
- Verifying, for Investigational Medicinal Products (IMPs):
  - That storage temperature and conditions are acceptable, and that sufficient supplies are in place throughout the trial;
  - That the IMP(s) are supplied only to the participants who are eligible to receive it and at the protocol specified dose(s);
  - That participants are provided with necessary instruction on properly using, handling, storing, and returning the IMP(s);
  - That the receipt, use, and return of the IMP(s) is controlled and documented;
  - That the destruction of unused IMP(s) complies with applicable regulatory requirements and is in accordance with the protocol;
- Checking archiving arrangements;
- Confirming appropriate training has been undertaken by staff for their delegated activities;
- Verifying that all relevant study activity has been undertaken;
- Checking systems are in place to ensure compliance with data protection; and
- Checking the transportation and storage arrangements for any samples taken as part of the protocol.

(e) <u>Central (off site) Monitoring</u>

Not all monitoring requires monitoring on site, certain elements of monitoring may be completed remotely, where documentation is available to allow for this. The Sponsor can review a number of aspects of the study remotely, for example:

- Appropriate AE and PD reporting.
- Participant recruitment rates.
- Vendor engagement and conduct.

6. RELATED SOPS AND DOCUMENTS

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

RI/QMS/SOP/014	Monitoring SOP