Portsmouth Hospitals NHS
NHS Trust

Standard Operating Procedure (SOP) for the Monitoring of Research Studies Sponsored by PHT

For Completion by SOP Author	
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For Completion by Research Dept., SOP Controller	
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The definitive versions of all Portsmouth Hospitals Trust SOPs, Templates and Forms for Research are online at http://www.porthosp.nhs.uk/research-department

If you are reading this SOP in printed form then you are reading an uncontrolled document. You must therefore verify that the version number and date given below are the most recent, by cross-checking with the Trust research website before proceeding with implementation.

Portsmouth Hospitals NHS Trust is committed to ensuring that, as far as is reasonably practicable, the way we provide services to the public and the way we treat our staff reflects their individual needs and does not discriminate against individuals or groups on any grounds. This SOP has been assessed accordingly

CONTENTS

1. INTRODUCTION

Monitoring is a quality control function designed to ensure that the study is run to a high standard and that all study related activities are fulfilled. It is defined by ICH GCP as the act of overseeing the progress of a clinical trial, and of ensuring that it is conducted, recorded, and reported in accordance with the protocol, Standard Operating Procedures (SOPs), Good Clinical Practice (GCP), and the applicable regulatory requirement(s).

The purpose of monitoring is to verify that:

- The rights and well-being of human subjects are protected.
- The reported trial data are accurate, complete, and verifiable from source documents.
- The conduct of the trial is in compliance with the currently approved protocol/amendment(s), with GCP, and with the applicable regulatory requirement(s).

This SOP should be read in conjunction with the following SOPs:

1. SOP for the Risk Assessment of Studies Sponsored by PHT
2. SOP for Developing a Monitoring Plan for Studies Sponsored by PHT
3. SOP for the Initiation and Management of Corrective and Preventative Action Plans (CAPA) for Studies Sponsored by PHT

2. PURPOSE

The purpose of this document is to describe the SOP for carrying out monitoring activities of research studies, sponsored by Portsmouth Hospitals NHS Trust (PHT).

3. SCOPE

This SOP is designed to be used by the members of the Research & Innovation (R&I) Office and the study teams who are delivering PHT sponsored research.

This SOP applies to studies, sponsored by PHT, that have a requirement for monitoring. It describes the process of preparing, conducting and reporting monitoring activities.

The Trust recognises that some external sponsors, networks, funders and employers may require the use of their own SOPs for the good governance of research. In such cases it is the responsibility of the PHT user (including those individuals contracted to work on behalf of the Trust), to ensure that the external SOP is compatible with the procedure outlined below. If the external SOP contradicts the Trust's procedure then approval must be sought in writing from the Research and Quality Manager.

In the event of an infection outbreak, flu pandemic or major incident, the Trust recognises that it may not be possible to adhere to all aspects of this document. In such circumstances, staff should take advice from their manager and all possible action must be taken to maintain ongoing patient and staff safety.

4. ABBREVIATIONS & DEFINITIONS

Abbreviation	Meaning
CAPA	Corrective and Preventative Action plan
CI	Chief Investigator
CTIMP	Clinical Trial of Investigational Medicinal Product

CTA	Clinical Trials Assistants
ICH GCP	International Conference on Harmonisation-Good Clinical Practice
PHT	Portsmouth Hospitals NHS Trust
PI	Principal Investigator
RC	Research Coordinator
RF	Research Facilitator
RGG	Research Governance Group
R&I	Research & Innovation (Office)
SIV	Site Initiation Visit
SOP	Standard Operating Procedure
TMF	Trial Master File

Term	Definition
Monitoring	The act of overseeing the progress of a research study and of ensuring that it is conducted, recorded, and reported in accordance with the protocol, SOPs, GCP, and the applicable regulatory requirement(s).
PHT Sponsored Studies	Studies that PHT have ultimate responsibility for the initiation, management and financing of. The Trust take primary responsibility for ensuring that the design of the study meets appropriate standards and that arrangements are in place to ensure appropriate conduct and reporting.
Study Team	The individuals involved in the conduct of a research project. There may be different research teams for the project at different sites.
Minor Non-Compliance **(Deviation)**	Minor non-compliance is a departure from one or more of the protocol, SOP, GCP or regulatory requirements that have been identified retrospectively, which is neither critical or major and so not likely to effect to a significant degree: • The safety or physical or mental integrity of the trial participant • The scientific value of the trial For example: • Errors in applying the inclusion/exclusion criteria • Lab time points missed or late • Missed data points in CRF's as a result of error (rather than an intention to mis-record information) • Missed follow up visits due to unforeseen circumstances.
Major Non-Compliance **(Breach)**	Major non-compliance is a significant and unjustified departure from the protocol, SOP, GCP or regulatory requirements that may not have developed into a critical issue but may have the potential to do so unless addressed. Where there are a number of instances of minor non-compliance within a single area of responsibility, this indicates a systematic quality assurance failure and so should be collectively treated as major non-compliance. For example: • Significant and unjustified non-compliance with relevant legislation or Good Clinical Practice (ICH GCP) • A number of breaches or legislation or GCP within one area, indicating systematic quality assurance failure • A failure to comply with legislative requirements including annual reporting requirements
Serious Breach	A 'serious breach' is defined by the Medicines for Human Use (Clinical Trials) Regulations 2004 as a breach which is likely to affect to a serious degree:

(Critical Non-Compliance)	• The safety or physical or mental integrity of the subjects of the trial; and/or • The scientific value of the trial. For example: • The safety, well being or confidentiality of participants has been jeopardised or has the potential to be jeopardised • Reported data are unreliable or absent • Inappropriate, insufficient or untimely corrective action has taken place regarding major non compliance • Where there are a number of Major non-compliances across areas of responsibility, indicating a systematic quality assurance failure • Lack of adequate documentation available to reconstruct the study or failure to maintain an appropriate Trial Master File (TMF) Examples of serious breaches notified to the MHRA are provided in Appendix 1.

5. DUTIES AND RESPONSIBILITIES

Role	Responsibilities
Sponsor	▪ A member of the R&I office will carry out any monitoring duties or arrange any remote monitoring activities ▪ Where specialist monitoring is required (e.g. statistical analysis) the R&I office will identify a suitable monitor ▪ Report findings and implement a CAPA.
Chief Investigator (CI)	▪ Accommodate and support monitoring activities as agreed in the monitoring plan ▪ Ensure availability, as required, during monitoring visits ▪ Review monitoring findings and manage any CAPAs

6. PROCESS

6.1. Monitoring Plan & Types of Monitoring

The monitoring plan describes the agreed monitoring activities that will take place, during the lifetime of the study. This SOP should be followed once the monitoring plan has been agreed.

Monitoring activities are actions taken to oversee the clinical study and may include any of the following:

- site selection and site initiation visits
- On site monitoring
- Central monitoring
- Statistical monitoring
- Trial management group meetings

- Oversight committees such as data monitoring committees, data safety monitoring boards or trial steering committees
- Close out monitoring

Monitoring is not limited to this list; any activity that provides oversight of a study may be considered a Monitoring activity.

6.2. Preparing for Monitoring

A monitor will be identified and assigned by the R&I office.

The Monitor will:

- Familiarize themselves with the study to be monitored, ensuring they have a full understanding of the protocol and all the study procedures, GCP and any relevant regulatory requirements.
- Make themselves aware of the current versions of the study documents in use. For example, but not limited to, the protocol, participant information sheet, consent form, case report forms, eligibility checklists and pharmacy accountability logs.

The monitor will also review:

- Previous monitoring activities and recent site correspondence to identify issues requiring follow-up or resolution during the monitoring visit.
- the current recruitment status of the study

Where required, the monitor will identify any patient medical notes that need to be requested for monitoring. If patient notes need to be randomly sampled, the randomisation process does not need to be formal however the patient selection must be made by the monitor, not the researcher.

6.3. Arranging a monitoring visit

The monitor will arrange the monitoring visit with the study team and identify any attendance requirements. Usually at least one member of the core study team will be required to attend for an onsite monitoring visit.

For onsite visits the monitor and study team will identify an appropriate working space for the monitoring to take place. This may be within the R&I offices, the study department or alternative meeting room.

The monitor will advise the study team of any medical notes or other study documentation that will be required. Sufficient time should be allowed as retrieval of medical notes can take up to 3 weeks. It will be the responsibility of the study team to ensure all requested documentation is made available for the monitoring visit.

6.4. Conducting the monitoring visit

During an onsite visit, the monitor will record their name, signature, date and nature of the monitoring visit on the Monitoring and Audit Visit Log and ensure that an appropriate member of the study team also signs the log.

The monitor will complete monitoring forms as appropriate to evaluate and record the conduct and delivery of the study to date. E.g. the template site initiation checklist or the template onsite monitoring form. If non-compliance is identified, this will be recorded in the monitoring report and subsequent CAPA.

The monitor will verify that outstanding issues from any previous visits are addressed, documented and followed to resolution.

At the end of the monitoring visit the monitor will discuss any findings and expected next steps.

6.5. Documenting the monitoring visit

All monitoring visits should be documented as evidence of study oversight. Monitoring activities will be documented in a manner appropriate to the nature of the monitoring visit.
For example:

- An site initiation visit will be documented using a 'site initiation checklist'
- An onsite monitoring visit will be documented using an 'onsite monitoring form'
- Minutes will be taken during any oversight committee meetings
- Statistical reports will provide evidence of statistical analysis carried out
- Close out monitoring will be documented using a 'close out monitoring form'

Monitoring documents must make it clear the nature of the monitoring activity, the personnel present, what was monitored, any findings and any required corrective and preventative actions (CAPA).

Monitoring documents should be signed and dated by the Monitor and where applicable the Research Manager or member of the study team.

The monitoring visit will be reported promptly to the study team. Where possible, this should be sent within **1 week** of the visit taking place.

Any monitoring findings will be captured as per the SOP for CAPA management (PHT/RDSOP/020) and using the CAPA template.

Monitoring findings will be categorised as minor/major non-compliance or serious breach, as per the definitions for non-compliance described in the SOP for Non-Compliance and Serious Breaches (PHT/RDSOP/002). See section 4 for full definition.

All monitoring documentation must be filed in the TMF and the R&I study file.

6.6. Monitoring Follow Up

The monitor and study team are both responsible for tracking the resolution of any monitoring findings and timeframes will be described in the CAPA.

The study team must inform the monitor of steps taken to resolve any actions and when actions have reached a resolution.

The monitor may arrange a follow up monitoring visit, if deemed necessary, to confirm all actions have been resolved.

Non-compliance will result in the implementation of the SOP for Non-Compliance and Serious Breaches (PHT/RDSOP/002).

Monitoring activities and a summary of any findings will be presented at an RGG meeting to ensure the wider department is aware of all monitoring activity taking place.

7. TRAINING REQUIREMENTS

The following must evidence training in this SOP:

- Members of the R&I Office staff who are conducting monitoring activities on PHT sponsored studies.
- Chief Investigators and delegated members of their study team who are supporting monitoring of any PHT sponsored studies.

"The Research Dept., will endeavour to notify staff of SOP developments that may be relevant to them. SOPs are available on the Research department website. Updates on SOPs will feature in Research newsletters and communications and disseminate at local research meetings. It is the responsibility of all research active staff to ensure that they read the issued updates that may be relevant to them.

When a new SOP is authorised, or when an existing SOP is revised, self directed training must be carried out by all staff to which the SOP is relevant and this training documented in their training record. A template is provided to support this process. A study specific SOP training plan will be developed for investigators on high risk PHT Sponsored studies.

Staff should take time to read and fully understand the SOP and relevant documents, ensuring that they are able to implement the SOP when required. If clarification is needed then the trainee should approach their line manager and the SOP Controller who will arrange additional training. All staff should complete their training prior to the published implementation date which will normally be between 2-6 weeks after publication.

All staff are responsible for maintaining their own SOP Training Records and copies must be made available to line managers, the SOP Controller or study monitors on request."

8. REFERENCES AND ASSOCIATED DOCUMENTATION

Associated Documents

- Template – Monitoring and Audit Log
- Template – Onsite monitoring form
- Template – Site Initiation Checklist
- Template – GCP Tool (Self Monitoring)
- Template – CAPA
- SOP for the Risk Assessment of Studies Sponsored by PHT
- SOP for Developing a Monitoring Plan for Studies Sponsored by PHT
- SOP for the Initiation and Management of Corrective and Preventative Action (CAPA) Plans for Studies Sponsored by PHT (PHT/RDSOP/020)
- SOP for Reporting and Managing Non-Compliance and Serious Breaches in Clinical Research (PHT/RDSOP/002)

References

- ICH Guideline for GCP E6 (R2), Step 4, 9th November 2016
- The MHRA Good Clinical Practice Guide 2012

9. VERSION HISTORY LOG

This area should detail the version history for this document. It should detail the key elements of the changes to the versions.

Version	Date Implemented	Details of Significant Changes
1.0	01/07/2012	Made Obsolete in November 2014 when replaced by the Monitoring Work Instruction
2.0	16/01/2020	SOP rewritten to replace work instruction

10. APPENDICES

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CONFIRMATION OF SOP TRAINING RECORD

A copy of this record may be kept in your personal training file to confirm your training in a specific SOP. If required by a study Sponsor a record may also need to be kept in the Trial Master Files (TMF) or Investigator Site Files (ISF)

SOP Details: To be completed by the SOP Controller	
Title of SOP	Standard Operating Procedure (SOP) for the Monitoring of Research Studies Sponsored by PHT
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Personnel Details	
Name	
Job Title & Research Role	
Date of Training	
Nature of Training	Self Directed/Delivered by etc
Records of any meetings to clarify details in SOP	

Signatures
I confirm that I have read and consider myself to be sufficiently trained in the above Standard Operating Procedure with regards to my individual roles and responsibilities Signature of Trainee …… Date ……
I confirm training in the above SOP was delivered as recorded above and that the trainee may be considered sufficiently trained in their roles and responsibilities Signature of Trainer …… Date ……

Additional Notes & Signatures
Signature of Trainer (where appropriate) I confirm training in the above SOP was delivered as recorded above and that the trainee may be considered sufficiently trained in their roles and responsibilities Signature of Trainer …… Date ……..