Portsmouth Hospitals NHS
NHS Trust

Standard Operating Procedure (SOP) for the Initiation and Management of Corrective and Preventative Action Plans (CAPA) for Studies Sponsored by PHT

For Completion by SOP Author	
Reference Number	PHT/RDSOP/020
Version	V1.0, 16 Dec 2019
Document Author(s)	Toni Baker, Research Facilitator
Document Reviewer(s)	Anna Cunnington, Research Support Officer

For Completion by Research Dept., SOP Controller	
Name of Responsible Committee	Research Governance Group, (12 Dec 2019)
Issue Date	16 Dec 2019
Implementation Date	16 Jan 2020
Review date	16 Dec 2022
Electronic location	Research and Development - Research Office\Policies and SOPS\# Active SOPS

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....3
2. PURPOSE....3
3. SCOPE....3
4. ABBREVIATIONS & DEFINITIONS....3
5. DUTIES AND RESPONSIBILITIES....5
6. PROCESS....5
   6.1. Completion of the CAPA....5
   6.2. Progressing the CAPA....6
   6.3. Non-Compliance....6
7. TRAINING REQUIREMENTS....6
8. REFERENCES AND ASSOCIATED DOCUMENTATION....7
9. VERSION HISTORY LOG....7
10. APPENDICES....7

1. INTRODUCTION

Adherence to the study protocol is a fundamental part of the conduct of a research study. ICH GCP E6 (R2) states that studies must be conducted in compliance with the protocol agreed by the Sponsor, the Research Ethics Committee (REC), Health Research Authority (HRA) giving a favourable opinion and, if required, by the Competent Regulatory Authority (in the UK this is the Medicines and Healthcare products Regulatory Agency, (MHRA)).

Non-compliance can take the form of a protocol breach or deviation and whether intentional or accidental, it is important that it is identified and dealt with appropriately. Efforts should be made to determine how the breach or deviation occurred and how it will be managed going forward.

A Corrective and Preventative Action Plan (CAPA) is a tool used to record breaches/deviations and outline what actions will take place to correct the specific breach/deviation and the steps that will be taken to prevent re-occurrence.

2. PURPOSE

The purpose of this document is to describe the Standard Operating Procedures (SOP) for initiating, and managing a CAPA to resolve breaches and deviations within a research study.

3. SCOPE

This SOP applies to all research studies sponsored by Portsmouth Hospitals NHS Trust (PHT).

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 Portsmouth Hospitals NHS Trust 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
GCP	Good Clinical Practice
MHRA	Medicines and Healthcare products Regulatory Agency
PHT	Portsmouth Hospitals NHS Trust
PI	Principal Investigator
R&I	Research and Innovation (Office)
REC	Research Ethics Committee
RGG	Research Governance Group
SOP	Standard Operating Procedure

Term	Definition
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 **(Critical Non-Compliance)**	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: • 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.

PHT Sponsored Studies	Studies which Portsmouth Hospitals NHS Trust have ultimate responsibility for the initiation, management of and financing for. They 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.
Research Study Team	The people involved in the conduct of a research project. There may be different research teams for the project at different sites.

5. DUTIES AND RESPONSIBILITIES

Role	Responsibilities
Individual	▪ Report any non-compliance they identify
PI / Research Study Team	▪ Ensure the CAPA is completed within the deadlines stated
PHT R&I Office	▪ Coordinate and track completion of the CAPA ▪ Escalate any issues as required to the Research Governance Group

6. PROCESS

Non-compliance may be identified by any individual. An individual does not have to be associated with a research study to identify and escalate non-compliance.

In accordance with the Non-Compliance SOP (PHT/RDSOP/002), on finding the non-compliance the individual must notify the R&I Office in the first instance, who will then notify the Sponsor representative.

It is expected that the CAPA template is used unless specific reporting arrangements have been made with the R&I office in advance of a breach being identified.

6.1. Completion of the CAPA

The identified non-compliance must be documented as clearly as possible. It may be necessary to split the breach/deviation up into smaller parts, particularly where it is a complex issue. It is important to be clear, concise and factual.

On first identifying the non-compliance the CAPA must be opened. The R&I Office will categorise the non-compliance, and will adhere to the definitions as per the non-compliance SOP (repeated on previous page for convenience). Breaches/deviations will be categorised as minor/major non-compliance or serious breach.

Each section of the CAPA template must be completed. Corrective actions will be described to address the actual breach and preventative actions will be proposed to address any systemic failures that may allow re-occurrence of the breach. The root cause should be explored when considering preventative actions.

Timeframes

Serious Breach must be addressed urgently and within **7 days**
Major non-compliance must be addressed promptly and within **30 days**
Minor non-compliance must be addressed within **60 days**

6.2. Progressing the CAPA

Progress during completion of the CAPA will be monitored by the R&I Office. The lead individual/PI will be responsible for ensuring that all actions identified are completed by the deadlines stated in the CAPA.

Updates on CAPAs will be provided during routine RGG meetings to maintain sponsor oversight.

6.3. Non-Compliance

Failure to comply will result in the non-compliance SOP (PHT/RDSOP/002) process being implemented. A final version of the CAPA must be sent to the R&I Office to close the breach.

7. TRAINING REQUIREMENTS

- R&I Office staff involved in developing CAPAs for PHT studies must be trained in this SOP.
- It is advised that Chief Investigators and delegated members of their study team based at the lead site/coordinating centre for any PHT Sponsored Studies read this SOP. Training is not essential

"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 – CAPA Plan
- SOP for Reporting and Managing Non-Compliance and Serious Breaches in Clinical Research (PHT/RDSOP/002)

Reference

- ICH GCP E6 (R2)
- University Hospitals of Leicester NHS Trust Support Office SOP S-1012, Management and production of CAPAs for studies sponsored by UHL

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	16/01/2020	New document

10. APPENDICES

There are no appendices

Portsmouth Hospitals NHS
NHS Trust

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 Initiation and Management of Corrective and Preventative Action Plans (CAPA) for Studies Sponsored by PHT
Reference Number	PHT/RDSOP/020
Version	V1.0, 16 Dec 2019
Issue Date	16 Dec 2019
Implementation Date	16 Jan 2020

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 …….