Royal Papworth Hospital
NHS Foundation Trust

Document Title: Handling of Protocol Non-Compliance

Document Number: PTUC SOP050

Staff involved in development: *Job titles only*	Senior R&D Manager, R&D Operational Manager, Clinical Project Managers
Document author/owner:	Senior R&D Manager
Directorate:	Research and Development
Department:	Research and Development
For use by:	NHS Staff Trust-Wide
Review due:	February 2024

Summary of Amendments

Section(s):	Modification:
5.0	General review and update
6.0	General review and update

Key Points of this Document

- This document sets out the procedures to be followed by all Staff who are involved in research in identifying, recording and reporting cases of non-compliance from the trial protocol, Standard Operating Procedures or regulatory requirements.

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1 Purpose and Content

1. This document defines the Trust's procedures for determining the nature and extent of non-compliance in Research Studies and Clinical Trials of Investigational Medicinal Products (IMPs) or non-CE marked devices managed by Royal Papworth Trials Unit Collaboration (PTUC) or sponsored by Royal Papworth NHS Foundation Trust.

2. The document states the procedures to be followed to protect patients, maintain the integrity of the trial and comply with legal and Good Clinical Practice guidelines (GCP: 'a standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected').

3. The appropriate documentation, assessment and reporting procedures that should be used are specified in section 4.0.

4. The management of serious breaches of protocol or GCP in CTIMPs is outside the scope of this SOP and is described in SOP051: Serious Breach of Protocol or GCP in CTIMPs and non-CE marked device studies.

2 Roles & Responsibilities

a. This Policy applies to all personnel who are conducting research at the Trust.

b. Staff working on research studies must comply with the requirements set out in section 4.0.

c. The Chief or Principal Investigator must ensure that they, and their study staff, comply with the requirements set out in section 4.0.

3 Policy

a. This SOP is mandatory and, non-compliance may result in disciplinary procedures.

4 Procedure

4.1 Definition of a non-compliance/deviation:

a. A non-compliance/deviation is defined as a departure from the protocol that has been identified retrospectively. A non-compliance/deviation is one that **may impact** the participant safety or affects the integrity of the study data.

4.2 Identification of a non-compliance/deviation and immediate reporting requirements:

a. Non-compliance/deviations may be identified by anyone involved in the conduct, management or monitoring of the trial.

b. Members of the study team may also receive information relating to potential non-compliance/deviation directly or indirectly from whistle-blowers or complainants from within or outside the study site.

c. Once a non-compliance is suspected the event should be reported to the PI (or CI) within 24 hours of knowledge of the event.

d. When non-compliance is suspected, further information should be gathered detailing the nature and extent of the episode. Any information used in detailing the nature and extent of the episode must be retained and filed alongside the documentation of the non-compliance/deviation.

e. The PI (or CI) must then refer to the MHRA guidance in order to assess whether the non-compliance constitutes a serious breach. If a serious breach is suspected, then SOP051 must be followed.

f. The completed non-compliance form (FRM038) or entry in OpenClinica must be signed by the PI (or CI) and forwarded to the trial sponsor using the safety reporting mailbox – NB: for trials utilising the electronic forms within OpenClinica for recording of all trial non-compliances, this notification system is automated.

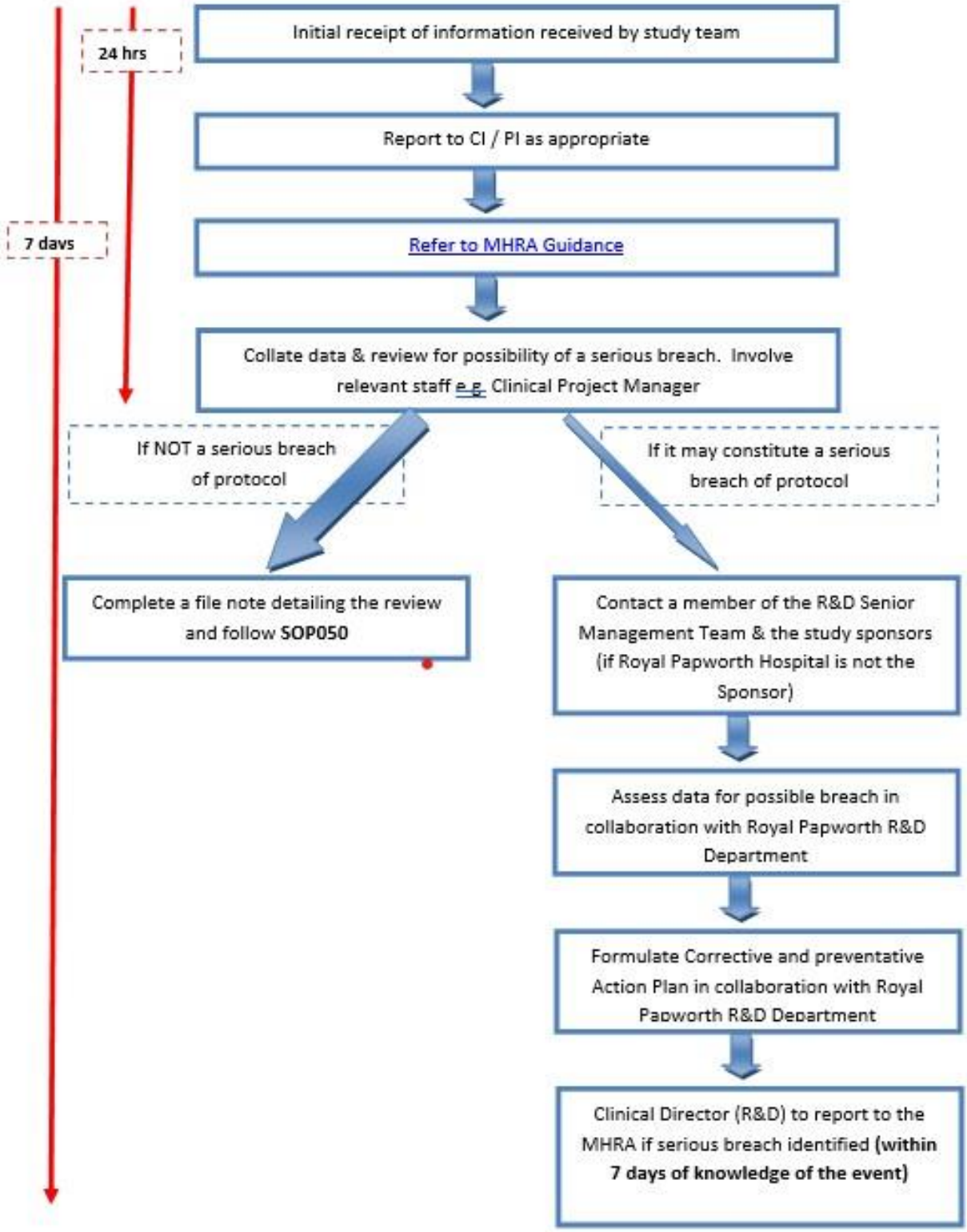
g. All non-compliances are reviewed by the QA team which constitutes sponsor representation for the purpose of non-compliance oversight for Royal Papworth sponsored studies and trials. If the sponsor deems the non-compliance to be a serious breach then SOP051 must be followed.

h. It is the sponsor's responsibility to ensure that a detailed log of all non-compliances is maintained throughout the trial. Where OpenClinica is being used for the electronic

recording of non-compliance the fully auditable log will be accessible via the trial database.

i. **Medical Devices Non-compliance**: In addition to the above, all protocol non-compliance ***in trials of medical devices*** must be reported to the MHRA as soon as they have been made aware of them. Details about the nature of the deviation, when it occurred, where it occurred, and any proposed corrective and preventative actions should be provided. An Excel template link can be found here https://www.gov.uk/guidance/notify-mhra-about-a-clinical-investigation-for-a-medical-device. The excel template should be kept as a "live" document so that new deviations can be added. This will enable the sponsor and the MHRA to have a complete overview each time the spreadsheet is submitted. The spreadsheet should be sent to the MHRA email at info@mhra.gov.uk.

Appendix 1 Summary of Assessment and Reporting for Trial Related Non-Compliance and Serious Breaches



5 Risk Management / Liability / Monitoring & Audit

1. The R&D SOP Committee will ensure that this SOP and any future changes to this document are adequately disseminated.

2. The R&D Department will monitor adherence to this SOP via the routine audit and monitoring of individual clinical trials and the Trust's auditors will monitor this SOP as part of their audit of Research Governance. From time to time, the SOP may also be inspected by external regulatory agencies (e.g. Care Quality Commission, Medicines and Healthcare Regulatory Agency).

3. In exceptional circumstances it might be necessary to deviate from this SOP for which written approval of the Senior R&D Manager should be gained before any action is taken. SOP deviations should be recorded including details of alternative procedures followed and filed in the Investigator and Sponsor Master File.

4. The Research and Development Directorate is responsible for the ratification of this procedure.

Further Document Information

Approved by: *Management/Clinical Directorate Group*	Research and Development Directorate
Approval date: *(this version)*	[Current active version approved date]
Ratified by Board of Directors/ Committee of the Board of Directors:	STET
Date:	N/A
This document supports: *Standards and legislation*	Medicines for Human Use (Clinical Trials) Regulations 2004 and all associated amendments. UK Policy Framework for Health and Social Care Research (2018)
Key related documents:	Trust Research Policy SOP051: Serious Breach of Protocol or GCP in CTIMPs and non-CE marked device studies

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Equality Impact Assessment: Does this document impact on any of the following groups? If YES, state positive or negative, complete Equality Impact Assessment Form available in Disability Equality Scheme document DN192 and attach.							
Groups	Disability	Race	Gender	Age	Sexual orientation	Religious & belief	Other
Yes/No	NO	NO	NO	NO	NO	NO	NO
Positive/Negative							
Review date:			February 2027				

I certify the contents of this SOP has been reviewed and ratified

Patrick Calvert

11-03-2024

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Signed by Dr Patrick Calvert, Clinical Director of R&D

Date