Document Title: Research Protocol Design

Document Number: PTUC SOP019

Staff involved in development: *Job titles only*	Senior R&D Manager, R&D Operational Manager, Clinical Project Managers
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For use by:	NHS Staff Trust-Wide
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Summary of Significant Change(s) (for this version only)

Section(s):	Modification:
	Minor administrative changes only

Key Points of this Document

- This document sets out the procedures to be followed by all Staff who are involved in the preparation of protocols for research studies which are managed by Royal Papworth Trials Unit Collaboration (PTUC) or sponsored by Royal Papworth NHS Foundation Trust.

- It provides guidance on what a research protocol should contain, who should be involved in its formulation, and what level of review it must undergo to ensure compliance with the Trust's research policies.

1 Purpose and Contents

a. This document defines the Trust's research procedures for the writing and preparation of research protocols for use in Research Studies and Clinical Trials managed by PTUC or sponsored by Royal Papworth NHS Foundation Trust.

b. The document describes the requirements for a research protocol to comply with section 6 of the Good Clinical Practice: Consolidated Guidance (ICH E6) 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').

c. The subsequent approval of the study protocol in terms of obtaining Trust sponsorship is outside the scope of this SOP and is described in SOP048: Royal Papworth Sponsorship of Research Studies.

d. The approval of the study protocol by the hosting NHS Trust, the regulatory authorities and ethical review board are outside the scope of this SOP and is described in SOP009: Project Management of Research Studies;SOP034: Trust Confirmation of Capacity and Capability to Conduct Research Studies; SOP005: Ethics Approval of Research Studies and (if applicable), SOP014: Gaining Regulatory Approval from the MHRA

2 Roles & Responsibilities

a. This Policy applies to all personnel that are involved in advising on, writing or reviewing study protocols for research that will seek sponsorship from Royal Papworth Hospital or studies managed by Royal Papworth Trials Unit Collaboration.

b. The Chief Investigator (CI) is responsible for the preparation of the research protocol.

c. The CI must ensure that if they delegate the role of writing the research protocol (or aspects of the protocol) to another member of the research team, that they have sufficient knowledge and expertise, and are aware of GCP procedures.

3 Policy

a. This SOP is mandatory and, as per the Trust's Research Governance framework, non-compliance with may result in disciplinary procedures.

4 Procedure

4.1 Protocol Development

a. A protocol is an essential document which details the study plan. It must provide clear direction to a person (of suitable training and skills) who may be naive to the study, to be able to set-up and undertake the study correctly and in line with the required standards and regulations.

b. A protocol should be written in accordance with the requirements described in the ICH GCP guidelines (http://ichgcp.net/6-clinical-trial-protocol-and-protocol-amendments).

c. The protocol should describe the background and rationale, objective(s), design and methodology, the statistical and data analysis plan, and organisation of the study. For further information and guidance, particularly for interventional studies, refer to the SPIRIT 2013 guidelines available online (http://www.spirit-statement.org/). The HRA has also provided examples which can be used to check that the protocol captures all necessary elements prior to submission (https://www.hra.nhs.uk/planning-and-improving-research/research-planning/protocol/).

d. Templates are available from the R&D department website for the following study types:

1. Clinical Trial Protocol for a Clinical Trial of an Investigational Medicinal Product (CTIMPs). CTIMPs to be considered for Royal Papworth sponsorship should be presented using this template. This template requires investigators to detail their monitoring and publication plans for the trial. If an alternative template is to be used, agreement must be sought from the Senior R&D Manager.

2. Clinical Trial Protocol for non-CTIMPs.

3. Service Evaluations or research with no material ethical issues. For further information visit: https://www.hra.nhs.uk/approvals-amendments/what-approvals-do-i-need/

e. The protocol should be developed by a multi-disciplinary project team with experience commensurate with the nature, complexity and magnitude of the research, including clinical procedures and risks. This team must include all parties required to ensure successful set-up of the study and may include:

1. The CI. For multi-centre research, the Trust recommends that Principal Investigators (PIs) at each proposed site are given the opportunity to contribute.
2. A sponsor representative (usually a Clinical Project Manager - CPM)
3. Statistician
4. Health Economist
5. Pharmacy. For a proposed CTIMP a pharmacy representative must be involved.
6. Service department representatives e.g. pathology, radiology, immunology.
7. A patient / lay representative
8. Other subsidiary groups e.g., risk and information governance.

f. A robust mechanism for protocol drafting should be agreed and recorded. This should include:

1. Assignment of defined responsibilities e.g. process oversight, coordination, and records management
2. Method for archiving drafts and recording comments from the individuals in the team, including justification for any comments not incorporated in the final version.

g. The protocol should be version-controlled according to SOP060: Version Control of Study Documentation.

h. The project team must arrange independent expert peer review of the protocol in line with SOP034: Confirmation of Capacity and Capability to Conduct Research Studies.

i. The final version of the protocol must be sent to the key members involved in the trial to request confirmation they are in agreement so that the protocol can be finalised. This evidence should be stored in the Trial Master File (TMF).

j. For CTIMPs, the final version of the protocol must have the signature of the CI or academic supervisor and be stored in the TMF.

4.2 Review & Updates to the Protocol

a. In the case of urgent safety measures the protocol can be changed with immediate effect. Refer to SOP037: Amendments to Research Studies and SOP071 Urgent Safety Measures

b. The CI is responsible for the review of the protocol. The process and timelines for review of the protocol should be agreed and documented at time of writing. Evidence of this review process should be stored in the TMF.

c. Any decision to make a change to the protocol must be formally documented in writing with the reasons for the change(s). Changes to the protocol must be reviewed and approved by the appropriate personnel e.g. trial pharmacist for changes relating to the drug. A record of the decision for the change, the amendment/s and evidence of the relevant approvals should be kept and stored in the TMF. SOP037: Amendments to Research Documentation must be followed.

d. For CTIMPs, any subsequent finalised versions of the protocol must have the signature of the CI or academic supervisor and stored in the TMF or equivalent locations.

5 Risk Management/Liability/Monitoring & Audit

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

b. 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).

c. 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.

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

Approved by: *Management/Clinical Directorate Group*	Research and Development Directorate
Approval date: *(this version)*	Current approved version 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
Key related documents:	Trust Research Policy [Insert list of linked or relevant documents to this SOP]

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:	June 2022

Version Control

Version	Date effective	Valid to	Approved by	Date of approval
1.0	5 August 2009	July 2011	RDD	5 August 2009
2.0	8 November 2013	July 2016	RDD	11 October 2013
3.0				
4.0				

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

..... 4th June 2019

Signed by Dr Ian Smith, Clinical Director of R&D — Date

SOP release date: 13th June 2019