Royal Papworth Hospital
NHS Foundation Trust

Document Title: Set-up and Project Management of Research Studies

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Staff involved in development: *Job titles only*	Senior R&D Manager, R&D Operational Manager, Clinical Project Managers
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Summary of Amendments

Version:	Modification:
7.0	Amendments throughout
8.0	Amending Title of SOP and clarifying financial responsibilities
9.0	Minor amendments made throughout

Key Points of this Document

- This document sets out the procedures to be followed by all staff who are involved in the set-up and project management of research studies managed by Royal Papworth Trials Unit Collaboration (PTUC) or sponsored by Royal Papworth NHS Foundation Trust.

- It provides guidance on managing study set up and study conduct to ensure compliance with the Trust's policies.

1 Purpose and Content

a. This document defines the project management responsibilities as part of the overall management of research projects managed by Royal Papworth Trials Unit Collaboration (PTUC) or sponsored by Royal Papworth Hospital NHS Foundation Trust.

b. The document details the requirements for project management to help ensure compliance with 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').

2 Roles & Responsibilities

a. This SOP should be read in conjunction with SOP055: Roles and Responsibilities for the Conduct of Research Studies and Clinical Trials including CTIMPs (Clinical Trials of Investigational Medicine Products), which defines the overall responsibilities of the Sponsor, The Chief Investigator and Principal investigators when conducting clinical research studies.

b. All staff managing research projects managed by Royal Papworth Trials Unit Collaboration (PTUC) or sponsored by Royal Papworth NHS Foundation Trust must comply with the requirements set out in section 4.

c. The conduct of clinical research studies is the responsibility of the Sponsor, the Chief Investigator (CI) and the Principal Investigator (PI) at each participating site. The management duties that need to be completed as part of a clinical research study can be delegated but not the responsibility. This delegation needs to be clearly documented on the Sponsor delegation of duties log (FRM040: Delegation of Sponsorship responsibilities). Evidence of ongoing Sponsor oversight of delegated duties must be filed in the TMF.

d. The management roles to be delegated by PTUC, the Sponsor and CI will include the roles of overall Project Manager, Data Manager and Study Monitor. For smaller studies some of these roles may be combined into a single role or conducted by several trained staff. This delegation needs to be clearly documented on the Project Management delegation of duties log (FRM042: Project Management Delegation Log).

3 Policy

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

4 Procedure

4.1 Study Set-up

a. Once a potential Investigator wishes to proceed with a research idea they must contact Royal Papworth Trials Unit Collaboration (contact details provided on the web-site and intranet).

b. A Clinical Project Manager (CPM) will be assigned to each project. The CPM will meet with the researchers to discuss the study idea.

c. The CPM will then draw together a Project Team/ Trial Management Group to discuss the study design, funding implications, potential funding sources, patient population, fit of the study with patient pathway, and other trial related considerations.

The frequency of project team meetings and their constitution must be agreed before the study starts. All project team meetings must be documented and the minutes filed in the Sponsor File.

d. This team must include all parties required to ensure successful set-up of the study and is dependent on the type of study. This may include a sponsor representative (for PTUC studies); PTUC representative, Statisticians, Data Management, Health Economists, Pharmacy and service department representatives. For a proposed Clinical Trial of an Investigational Medicinal Product (CTIMP) a Pharmacy representative must be on the project team.

e. Roles and responsibilities of the project team members should be agreed, clearly defined using FRM042: Project Management Delegation Log

f. The PTUC representative (Senior R&D Manager or Clinical Project Manager) will provide advice on the set-up and management of the research study. The study must be appropriately funded and the research team must ensure that funding has been agreed prior to Trust Confirmation of Capacity and Capability.

g. For studies that require grant funding:

1. The Team needs to identify a suitable funding source.
2. A writing committee needs to be established with responsibility delegated to complete the various sections of the form and timescales set.
3. A lead must be identified to lead the application process.
4. If the study is deemed to be multi-centred, potential sites and co-applicants must be identified and be invited to the project team.
5. Patient & public involvement (PPI) must be discussed and, if required, suitable representatives invited to assist with the work-up of the study. Researchers can contact appropriate PPI groups for support and advice e.g. the Eastern Clinical Research Network, INsPIRE (which is a local patient and public involvement group in health and social care).
6. Sufficient time needs to be allowed prior to grant submission for the Sponsor to review costings and obtain the required Sponsor signatures.

h. Costing of the study must be done in accordance with "Attributing the costs of health and social care Research & Development (AcoRD, DH 2012) and support from Papworth Trials Unit Collaboration must be sought and the CTU Costing template must be used (TPL040 CTU Costing Template).

i. During the set-up of the study all decisions must be agreed by the Trial Management Group, fully documented in either meeting minutes, email correspondence or file note/s, and filed in the Trial Master File, including but not limited to:

1. Protocol design.
2. Trial supply (IMP) management – CTIMPs only.
3. The RSI must be identified for any IMP and referenced in the protocol – CTIMPS only see SOP079.
4. Completion of regulatory and ethical application forms (as applicable to the type of study), and portfolio adoption form (to apply to go on the NIHR portfolio).
5. Completion of pragmatic risk assessment (SOP065: Risk-Adapted Approaches to the Management of Clinical Trials of Investigational Medicinal Products) – CTIMPs only.
6. Informing R&D Governance of the study and requesting the study receive registration and a P0 number (for studies which will be recruiting at Papworth only)
7. Ensuring the study is presented to the Research Governance Project Approval System (RGPAS) Committee to obtain Trust agreement to become study Sponsor.
8. Administrative duties including set-up and maintenance of the Sponsor File (see SOP013: Sponsor Files).
9. Remit for patient & public involvement in the study.
10. Communication plan.

11. Data Management including design of paper or electronic case report forms and ongoing Data Management (and development of the Data Management Plan).
12. Development of the Statistical Analysis Plan.
13. Preparation of periodic safety reporting (e.g. Development Safety Update Report (DSUR)) and annual progress reports (APR).
14. Management of the study including site initiation (see SOP015: Site Recruitment and Initiation).
15. Registering and keeping update study details on a publicly accessible website
16. writing of final reports.
17. Archiving responsibilities
18. Delegation of Sponsor duties to the CI using FRM028 Sponsorship Responsibilities Agreement.
19. Requirement for outsourcing any of the study set-up activities including, but not limited to, Pharmacy subcontractors to repackage and Qualified Person (QP) release of study material, Statistical and Health Economics support or use of PTUC or an alternative Clinical Trials Unit. The team must delegate who will be responsible for choosing the subcontractors and ongoing oversight of these contractors.
20. Setting-up of contracts with the subcontractors (see PTUC SOP066: Subcontracting of Research Activities).
21. Requirement for a Trial Steering Committee (TSC) and /or a Data Monitoring Committee (DMC). The constitution, remit and frequency of meetings must be agreed by the point of the site initiation visit. All CTIMPs and external grant funded studies should have a TSC. As a minimum, a TSC should be formed of an independent physician Chair, the PIs from each site and a Sponsor representative. The requirement for having a DMC needs to be agreed on a study by study basis. Trials involving subjects with life-threatening illnesses, vulnerable populations, significant risk of harm, or unknown or uncertain risks will usually require a DMC. As a minimum, a DMC must be formed of two independent physicians (one of whom must be the Chair) and a Statistician.
22. Frequency of checking for updates to the 'Summary of Product Characteristics' (SmPC) / Investigator Brochure (IB) (CTIMPS only) and how changes to the SmPC/IB will be notified to the wider project team. The frequency needs to be in relation to the risk profile of the drug and study. For example a licensed drug used within indication may require checks every 6 – 12 months, whereas an unlicensed drug or a drug being used outside of its indication may need to be checked every 12 weeks.
23. Study timelines including recruitment targets.
24. Selection of site/s and the type of site assessment that is appropriate for the trial and site (e.g., pre-qualification questionnaire vs on-site visit). For CTIMPs this will be documented in the risk assessment form (see SOP065: Risk-adapted Approach to the Management of Clinical Trials of Investigational Medicinal Products).
25. Frequency and type of study monitoring. For example, 10% of all data monitored on-site; or central monitoring; or 100% baseline / inclusion data to be monitored. This

must be documented in the Monitoring Plan and filed in the Sponsor File (see SOP016: Monitoring Research Studies).

26. Training requirements for study personnel. If trial specific training is required it should be documented on the trial specific training log which should be filed in the site file.
27. Type of site initiation visits. Do these have to be face-to-face (i.e. on-site or via a virtual meeting) or can they be completed using a study specific slide deck.
28. or CTIMPs – assign users to be able to access ICRS for reporting of SUSARs and submission of the DSUR.
29. Arrange to have a Research Account created (see SOP092 Research Account Management).
30. SOPs and Study Team – All CTU and Operational staff affiliated to the study must be SOP compliant prior to green light being given.

4.2 Data Management

a. During study set up, the case report forms and database will be designed and a Data Manager and study Statistician should be involved (see SOP077 Data Management Overview). A study specific Data Management Plan should be documented in the Trial Master File.

The Data Management Plan should include:

1. Details of the personnel involved,
2. Timelines,
3. Database Specification including Hardware and Software locations,
4. Database Structure,
5. Coding Dictionaries,
6. Data entry processes,
7. Database lock process,
8. Database archiving.

b. The CRFs should be piloted prior to the study starting.

4.3 Site Initiation

a. PTUC SOP 015: Site Recruitment and Initiation for PTUC and Royal Papworth Sponsored Studies must be followed.

b. b. Test emergency un-blinding and code-breaking procedure (if relevant) in accordance with PTUC SOP069: Emergency Un-blinding & Code-breaking of Clinical Trials.

4.4 Issuing Sponsor Green Light

a. Upon completion of the above, receipt of site approvals (Regulatory, Ethical, NHS R&D (i.e. Trust Confirmation of Capacity and Capability)) and necessary documentation (e.g. Site Delegation Log etc), the Sponsor teams should then issue Sponsor Green Light to the site to open to recruitment.

b. Sponsor Green Light should be notified to the site by email (see TPL037).

4.5 Study Conduct

a. Following Trust Approval, the project team will carry out the following activities:

1. Review recruitment, withdrawals and follow-up at pre-agreed intervals which must be at least every 6 months.
2. Receive Serious Adverse Event (SAE) and Suspected Unexpected Serious Adverse Reactions (SUSARS) reports, as per PTUC SOP012: Adverse Event Reporting, and report them as per the required timelines (and AE reports if applicable).
3. Manage the study budget ensuring it is in line with the contract. All variances from the forecast and budget must be reported to the Papworth Trials Unit Collaboration Management Oversight Committee.
4. Complete annual reports to the funding committee. For NIHR studies this includes completing an ASTOX report in conjunction with the R&D Finance Manager.
5. Hold Project team meeting, at the frequency agreed during study set-up, to check study status and address performance/clinical issues.
6. Arrange TSC and DMC meetings at the pre agreed time intervals. Circulate agendas prior to the meeting and summary notes/minutes after the meeting including agreed actions.
7. Update project team members on changes to the study design or timelines.
8. Review the Investigator Brochure (IB)/ Summary of Product Characteristics (SmPC) / RSI at the agreed intervals.
    i. If there are changes to the IB/SmPC/RSI these must be reviewed against the current protocol and patient information sheet and changes made if required.
    ii. The decision as to whether an amendment to the study is required must be formally documented.
9. Obtain REC and Competent Authority/MHRA approval when an amendment to the protocol or study documentation is required, and that approval/authorisation is received before the changes are implemented (unless there is an urgent safety issue). (See PTUC SOP037: Amendments to Research Documents).
10. When an amendment is required, it must be reviewed by the project team to ensure that any necessary changes are made to Data Management and / or the Statistical Analysis Plan.

11. Ensure all sub-contractors e.g. Pharmacy subcontractors are provided with updates to the protocol and study documentation (see PTUC SOP066: Subcontracting of Research Activities).
12. Ensure that all mandatory reports are issued within agreed timescales.
13. Ensure correct accruals to the National Institute of Health Research (CPMS) database if adopted onto portfolio.
14. Carry out staff training as required for both new and existing staff and document this in the TMF.
15. Ensure that staff have access to the necessary study documentation.
16. For staff that join after the Site Initiation visit, ensure they have all the required training and this is documented in the trial specific training log, the Trial Master File and that the delegation log is updated.
17. Ensure monitoring is completed according to the schedule agreed at the start of the study (following SOP016: Monitoring Research Studies)
18. Ensure that the data are managed in accordance with PTUC SOP077: Data Management Overview.
19. The agendas for the TSC and DMC meetings must be agreed with the meeting Chair and circulated with the minutes of the previous meeting at least 1 week before the meeting.

4.6 Study closure, Data analysis, Final reporting and Publication

a. After the completion of the 'last patient, last visit' for the research study the project team is responsible for (in accordance with PTUC SOP021: Trial Closure and End of Trial Reporting; PTUC SOP017: Statistics Input in Clinical Trials; PTUC SOP011: Archiving and PTUC SOP077: Data Management Overview.):

1. Ensure all outstanding monitoring and data queries are resolved at each site.
2. Undertake a close-out visit at each study site.
3. Liaise with Pharmacy, if applicable, regarding the return of unused IMP, the destruction of the IMP and archiving of the code break envelopes.
4. Complete end of trial forms for ethics, regulatory authorities and funders following database lock.
5. Carry out final checks of Sponsor File and governance files.
6. Complete a final budget reconciliation and complete funding final reports (including FSTOX for NIHR funded studies).
7. Data Analysis.
8. Arranging a meeting of TSC to agree and finalise the publication and dissemination strategy, and produce an action plan. It is the CI's responsibility to ensure that this is carried out, but the Clinical Project Manager will monitor progress and arrange further discussions as necessary.
9. Review the publications and presentation plan.

10. Publish the data within 12 months of the database lock. If a journal article is not possible then a report must be filed on a publicly accessible website.
11. Arrange archive of study documentations as per PTUC SOP011: Archiving of Research Studies.

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 (2018)
Key related documents:	

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:	July 2026

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

Patrick Calvert 10-02-2024

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