Royal Papworth Hospital
NHS Foundation Trust

Document Title: Gaining Regulatory Approval from the MHRA for CTIMPs

Document Number: PTUC SOP014

Staff involved in development: *Job titles only*	Senior R&D Manager, R&D Operational Manager, Clinical Project Managers
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Directorate:	Research and Development
Department:	Research and Development
For use by:	NHS Staff Trust-Wide
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Summary of Amendments

Version	Modification:
Version 4	Amended to be relevant for CTIMPs only. MHRA approval for devices to be covered in a new SOP
Version 4	Minor administrative changes throughout the document
Version 5	Amendments through

Key Points of this Document

- This document sets out the procedures to be followed by all Royal Papworth Staff who are involved in the initiation and set-up of projects managed by Royal Papworth Trials Unit Collaboration (PTUC) or sponsored by Royal Papworth Hospital NHS Foundation Trust which involve clinical trials of investigational medicinal products (CTIMPs) which require regulatory approval from the Medicines and Healthcare Regulatory Agency (MHRA).

- It provides guidance on how the necessary regulatory approvals should be obtained prior to commencement of the study to ensure compliance with the Trust's wider research policies.

1 Purpose and Content

a. This document defines the Trust's procedures for applying for and obtaining MHRA authorisation of clinical trials of investigational medicinal products (CTIMPs) which are managed by Royal Papworth Trials Unit Collaboration (PTUC) or sponsored by Royal Papworth Hospital NHS Foundation Trust (Royal Papworth).

b. Proof of approval for the study, as issued by the MHRA prior to the study commencing, must be filed in the Sponsor and Site Files as part of the study's essential documents as described in Good Clinical Practice

c. The document provides guidance on how approval should be obtained and recorded so as to comply with the Trust's procedures on Research Governance and Sponsor Files (Royal Papworth sponsored studies).

d. The subsequent gaining of Trust confirmation of capability and capacity for a research study is outside the scope of this SOP and is described in SOP034: Trust Approval and Research Governance.

2 Roles & Responsibilities

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

b. Staff involved in research trials concerning CTIMPs that are subject to MHRA regulation must comply with the requirements set out in section 4.

c. The Chief Investigator (CI), in conjunction with the Sponsor's representative, is responsible for applying for MHRA approval.

d. The Principal Investigator must ensure that a CTIMP has received regulatory approval from the MHRA (in addition to research ethics committee (REC) and the Health Research Authority (HRA) approval) prior to any study related activity being performed at Royal Papworth Hospital NHS Foundation Trust.

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

a. In line with the Medicines for Human Use (Clinical Trials) Regulations (and all applicable amendments) , all investigational medicinal products without marketing authorisation, or being used outside of indication, require authorisation by the competent authority (MHRA in the UK) in addition to a favourable opinion by an ethics committee. Medicinal trials are those in which an investigational medicinal product (IMP) is being assessed, e.g. to verify its efficacy or safety. If there is any doubt as to whether a trial should be classed as a CTIMP or not, please contact R&D (papworth.randdenquiries@nhs.net) who will be able to provide guidance.

b. The MHRA authorisation is granted in the form of a clinical trial authorisation (CTA). Therefore, no clinical activity can take place on a CTIMP study until written approval of the CTA has been received from the MHRA. A complete copy of the CTA application (including the covering letter) must be forwarded to the Research Governance Team and kept in the Sponsor File.

4.1 Making an application for Regulatory Approval

a. At the earliest opportunity an investigator should contact PTUC / the R&D Governance team, who will assign a Clinical Project Manager to give guidance on what is required to complete the application.

b. All applications for studies requiring sponsor authorisation from Royal Papworth Hospital NHS Foundation Trust (including REC) must be sent to the R&D Governance team via the R&D Enquiries inbox (papworth.randdenquiries@nhs.net) for review and agreement by the Trust, prior to submission to Ethics and any applicable regulatory bodies The CI, or their delegated representative, is responsible for ensuring the documentation is submitted to

the R&D Enquiries inbox in accordance with SOP048: Papworth Sponsorship of Research Studies.

c. Before submission to ethics and any applicable regulatory bodies, the application must be signed on behalf of the Trust by the Clinical Director of R&D, or their delegated representative.

d. A risk assessment must be undertaken by the investigators as preparation for the application to the MHRA and for running the study at Royal Papworth Hospital. This assessment, and actions put in place to mitigate any risks, should be documented accordingly and the outcomes of this assessment included in the CTA application. A template (FRM024: Risk Assessment Form of Royal Papworth Sponsored Clinical Trials of Investigational Medicinal Products) can be found on the intranet.

e. Pharmacy must be actively involved in the full development of the trial and must also complete the CTIMP risk assessment process. A full review of the pharmacy requirements for the proposed trial must be conducted as part of the application process.

4.2 Completing the application

a. As of 1st January 2022 all new CTIMPs, not previously submitted to the MHRA or REC for review, are submitted through combined review in order to obtain both MHRA and REC approvals in parallel. Combined review is accessed via a new part of IRAS and details of this process can be found online: Step by step guide to using IRAS for combined review - Health Research Authority (hra.nhs.uk)

b. The combined review requires allocation of the trial team to different roles within the new part of IRAS:

    a. Project deputy: access and editing rights to the project (essential allocation and only one permitted per study)

    b. Chief Investigator: access and editing rights to the project (essential allocation)

    c. Collaborators: any number permitted and have more limited editing access than deputy or CI

    d. Sponsor: The sponsor group is made up of the organisations that contribute to the management of the project.

c. Step by step guidance on completion of the application forms is given within IRAS and via the link above. Once you have completed your application and followed the steps outlined

to obtain the status of "content verified" next to each of the question sets, you will be able to click the "request review" button. The dataset and application will be transferred to the Sponsor for review and electronic confirmation for the application.

d. The application will then allow booking of the ethics (REC) review. NB: although guidance refers only to the booking of a REC review this will encompass parallel review by both the REC and MHRA.

e. A notice of valid submission will be sent within 3 days of booking the REC review.

f. If any requests for further information (RFI) are required, requests will be sent to the person initially submitting the application and will appear in their task list in IRAS. Any RFI must be responded to within 14 days of the request being made, unless you require additional time in which case, an application must be made via email to the MHRA: clintrialhelpline@mhra.gov.uk

g. A clearly written Clinical Trials Authorisation (CTA) application will mean the MHRA is more likely to approve the application without requesting further information or conditions. The application must include:

1. A detailed covering letter to explain the application and to justify any exclusions.
2. A clear description of the IMP, its use and certification
3. A clinical trial protocol
4. An Investigator Brochure or Summary of Product Characteristics, including reference to the Reference Safety Information (RSI) to be used in all expectedness assessments of any Serious Adverse Reactions (please refer to SOP079: Reference Safety Information).
5. Labelling which complies with Annex 13, EudraLex Volume 4
6. Authorisations for all EU sites of manufacture and assembly, and Qualified Person (QP) release
7. Any further scientific advice
8. If available, the REC opinion

The investigator must ensure consistency between all the submitted documents.

4.3 After MHRA Approval

a. The CI is responsible for ensuring that a copy of the MHRA approval letter is forwarded to PTUC (papworth.ptuc@nhs.net) and the Research Governance Team in R&D (papworth.randdenquiries@nhs.net).

b. Documentary evidence that the conditions for a CTA have been met is required prior to Trust Confirmation of Capacity and Capability and Sponsor Green Light for a study being issued.

c. All subsequent amendments must be addressed in line with SOP037: Amendments to 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 Sponsor and Site Files.

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

PTUC SOP014 – Gaining Regulatory Approval from the MHRA

Further Document Information

Approved by: *Managment/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 Need to site all applicable SOPs here: Trust CCC Amendments RSI

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Groups	Disability	Race	Gender	Age	Sexual orientation	Religious & belief	Other
Yes/No	NO	NO	NO	NO	NO	NO	NO
Positive/Negative							

Review date:	June 2025

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

DocuSigned by:
Dr Patrick Calvert
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19-Jun-2022

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

Date