

Standard Operating Procedure CCTU/SOP047

CTIMP Start-up/Set-up Procedures for Trial Teams

1. Scope

This SOP describes the procedures from funding award to Lead Site Activation to be followed by all trial teams running CTIMPs where QA and QC responsibility for Sponsor oversight has been delegated or contracted to the Cambridge Clinical Trials Unit (CCTU).

2. Purpose

To ensure that trials are organised and opened in accordance with CCTU, Regulatory, Research Governance and GCP requirements.

To ensure that Investigator's are fully informed of their responsibilities and that staff involved in the set-up of a CTIMP are aware of the trial requirements.

3. Definitions and Abbreviations

The headings below contain the definitions of terms and meaning of abbreviations used within the document.

3.1. Definitions

Term	Definition
Cambridge Sponsored	Sponsored by Cambridge University Hospitals NHS Foundation Trust (CUH); or the University of Cambridge (UoC); or jointly by CUH and UoC OR Sponsored by: Cambridge University Hospitals NHS Foundation Trust (CUH) or CUH jointly with the University of Cambridge or Cambridgeshire & Peterborough NHS Foundation Trust (CPFT) or CPFT jointly with the University of Cambridge
Sponsor	An individual , company, institution or organisation which takes responsibility for the initiation, management and/or financing of a clinical trial
Trial Team	Generally includes the Chief Investigator (CI), Principal Investigator (PI), Clinical Trials Coordinator (CTC), Data Manager (DM) Research Nurse at the coordinating site as identified and delegated by the CI and/or Sponsor
Regulatory Team	Includes the Clinical Trials Officers (CTOs), Regulatory and Quality Manager, Clinical Trials Monitors (CTMs) and the Pharmacovigilance (PV) Officer(s)

3.2. Abbreviations

Abbreviation	Meaning
ARSAC	Administration of Radioactive Substances Advisory Committee

Cambridge Clinical Trials Unit Box 401

C&C	Capability & Capacity
CCTU	Cambridge Clinical Trials Unit
CI	Chief Investigator
CRF	Case Report Form
CTA	Clinical Trial Authorisation
CTIMP	Clinical Trial of Investigational Medicinal Product
CTM	Clinical Trials Monitor
CTO	Clinical Trials Officer
GCP	Good Clinical Practice
HRA	Health Research Authority
IMP	Investigational Medicinal Product
IRAS	Integrated Research Approval System
LIP	Local Information Pack
MHRA	Medicines and Healthcare products Regulatory Agency
NIHR	National Institute for Health Research
PI	Principal Investigator
PV	Pharmacovigilance
R&D	Research and Development
REC	Research Ethics Committee
SAF	Study Assessment Form
SOE/SOECAT	Schedule of Events/ Schedule of Events Cost Attribution Tool

4. Undertaken by

Members of the Trial Team as delegated by the CI

5. Items Required

- R&D/SOP001 CTIMP Delegation of Roles and Responsibilities
- CCTU/SOP040 Risk Assessment Process for CTIMPs
- CCTU/SOP045 Use of Vendors
- CCTU/GD029 CTIMP Submission Checklist
- CCTU/TPL001 Protocol Template
- CCTU/TPL002 Patient Information Sheet and Consent Template
- CCTU/TPL017 Patient Information and Consent Template 11-15 Year Olds
- CCTU/TPL014 Participant ID Card Template
- CCTU/TPL015 GP Letter Template
- CCTU/TPL070 GP Letter Pregnant Partner Template
- CCTU/TPL079 Pregnant Partner PIS & ICF Template
- Study Assessment Form (available from the Cambridge R&D Department)

6. Summary of Significant Changes

More clarification regarding approval processes and lead site activation
Changes in responsibilities for:

- The generation of the initial submission documentation
- Notification of the trial to reviewing departments
- Who can authorise and sign the IRAS application

7. Method

The following sections provide a description of the processes to be followed when implementing this document's procedures.

7.1. Initial Notification

- Once a trial has received funding, the following departments should be notified of the start of trial set-up activities:
 - CCTU
 - Pharmacy
 - Relevant Legal Team (R&D and/or University)
 - Any other essential department involved in the set-up of the trial (e.g. laboratories)

7.2. Documentation Generation

- The relevant SOPs, templates, forms and guidance documents to enable the generation of trial level documentation are available in Q-Pulse:
- Templates listed in Section 5 are mandated for Cambridge Sponsored trials as appropriate. Editable copies can be requested from the CCTU for staff without access to Q-Pulse
- The trial team are responsible for developing the essential documents using the templates provided and interacting with the relevant departments/staff as necessary to ensure that the relevant information is included (e.g. radiology for timing and duration of scans etc.)
 - CCTU/GD029 CTIMP Submission Checklist should be used as a guide for the documentation required for CTIMPs
 - An R&D Number should be requested from the relevant R&D contact email R&D Enquiries if you are unsure
- Where required, insurance provision must be sourced by the trial team and confirmation of provisional cover provided as part of the submission
- Where appropriate, the CCTU Statistician will provide statistical information required for the protocol and IRAS application
- Where appropriate, the relevant pharmacy department should provide input into the IMP sections of the protocol, IRAS application and IMP labels
- The Accord Specialist will provide advice and must authorise the final cost attribution detailed in SOE/SOECAT, as required
- The Study Assessment form (SAF – available from Trust R&D) must be signed by the appropriate Divisional Lead for the CI/PI department(s)

7.3. Protocol Peer Review

- The scientific quality of the trial should be reviewed by an expert in the field who is not involved in the trial

- The trial team will liaise with the R&D Department to arrange for a suitable peer review of the protocol if not already completed by external funders charities or sponsors
 - Please note that review of the trial as part of a programme grant does not constitute sufficient peer review of the protocol and an additional peer review will be required
- The R&D Department will facilitate the Peer Review and liaise with the Trial Team directly
- Peer review can take up to 6 weeks to complete
- Peer review should happen in advance of CCTU review of the submission documentation, however it can happen in parallel if appropriate

7.4. Trial Supplies, Agreements & Contracts

- Refer to CCTU/SOP045 Use of Vendors
- Once a supplier has been identified, the trial team must liaise with the relevant legal team to ensure that the required service level agreements are negotiated and implemented (including technical agreements, etc.)
- The CTO requires a copy of all draft agreements and any relevant site-level documents (e.g. Organisation Information Document) as part of the review process
- All funding agreements relating to the supply of IMP, equipment, services and facilities must be reviewed by the relevant legal team
- Only a representative of the relevant legal team can negotiate agreements on behalf of any trial conducted through the CCTU
- Only an authorised signatory as confirmed and obtained by the relevant legal team can sign any trial related agreements
- A copy of all final executed agreements should be provided to the CTO by the trial team

7.5. Initial Submission Review

- The trial team should contact any reviewing departments prior to submission to the CCTU so they are prepared to answer any queries which may arise during the Regulatory Team review process as appropriate e.g. Laboratories, Clinical Engineering etc.
- Once the Collaborative Research Letter has been signed and executed by all parties the CTO will begin the review process
- The CTIMP Submission Checklist CCTU/GD029 should be used as a guide for the documentation required by the regulatory team for review
- All submission documentation must be submitted as a single package, to allow essential cross-checks to be conducted
 - If any document listed in the submission checklist isn't required, this should be indicated and where relevant explained in the submission email to the CTO
 - HRA Technical Assurance review documentation should also be submitted to the CTO (pharmacy & radiation)
 - Appropriately signed SAF for CI/PI department(s) should also be submitted to the CTO

- Once all documentation is submitted, a submission validation email will be sent to the trial team, confirming the documentation received, version numbers, dates and the timelines for review and feedback
- The documentation will be reviewed:
 - For regulatory compliance (MHRA, REC, HRA and ARSAC)
 - Against recent Grounds for Non-Acceptance and reported Serious Breaches (MHRA) in other trials
 - Against recent HRA and REC concerns and released guidance
 - With a view to incorporating risk mitigation early in trial documentation
- All changes required following the regulatory team review will be written, where possible, using tracked changes to allow the trial team to review and agree changes in a timely manner
- Once any agreed alterations are made, the CTO will provide authorisation for the submission to the regulatory authorities

7.6. Risk Assessment

- During/following initial review of the trial documentation the CTO will commence the risk assessment and mitigating action process in accordance with CCTU/SOP040

7.7. NIHR Portfolio Application

- The PAF can be submitted at any time after review and does not require any signatures
- The trial must send confirmation to the CTO once their trial has been adopted into the NIHR Portfolio

7.8. HRA/REC Submission

- The HRA/REC submission can only be made once:
 - The CTO has confirmed that the review is complete and all required changes have been made
 - The CTO has electronically signed the sponsor declaration page of the HRA/REC IRAS application form
 - All necessary documents have been signed by the relevant parties
- Copies of all final signed and submitted documents must be provided to the CTO by the trial team normally within 5 working days of submission
- Copies of all correspondence with the HRA and the REC should be forwarded to the CTO in a timely manner
- Any changes required by the HRA and the REC to the submitted documents must be reviewed and agreed for re-submission by the CTO

7.9. MHRA Submission

- The MHRA submission can only be made once the CTO has confirmed that the review is complete and all the required changes have been made
- The final CTA Form for the MHRA can be signed by the CI, unless otherwise stated by the Sponsor

- The CTO will make the MHRA Submission via the relevant portal and provide submission confirmation to the Trial Team for inclusion in the TMF
- Copies of all correspondence with the MHRA should be forwarded to the CTO in a timely manner
- Any changes required by the MHRA to the submitted documents must be reviewed and agreed for re-submission by the CTO

7.10. ARSAC Submission

- The ARSAC submission can only be made once:
 - The CTO has confirmed the review is complete
 - The necessary signatories have electronically signed the ARSAC form in IRAS

The submission must be copied to the CTO via CCTU@addenbrookes.nhs.uk

7.11. CRF Design, Trial Database & Randomisation System

- The trial team are responsible for engaging the Data Manager/ Programmer as appropriate for the generation of the trial specific CRF, database and/or randomisation system
- The Data Manager/Coordinator/Programmer, as appropriate will work with the trial team to generate and finalise the CRF and randomisation system in advance of the trial initiation meeting
- The Data Manager/Programmer as appropriate is responsible for the generation of the trial specific database and associated documentation in accordance with CCTU SOPs and the timelines set out in the risk assessment mitigating actions

7.12. Site-specific Document Submission

- Upon receipt of the MHRA & REC validation letters and the HRA initial assessment letter, the trial team must submit the Local Information Pack (LIP) to the relevant Cambridge R&D Department
 - In addition to the LIP, the signed SAF for the CI/PI department(s) must be submitted
- The LIP should not be sent to participating sites until after the lead site submission has been made

7.13. HRA/REC, MHRA & ARSAC Approvals

- Once received, all approval documentation must be forwarded in a timely manner to the CTO for inclusion in the Sponsor file
- Please note: A requirement of REC approval is that the trial must be registered on a publicly accessible and searchable database
 - For all phase 2, 3 and 4 CTIMPs this will be automatically included as part of the MHRA approval on the www.clinicaltrialsregister.eu website
 - For trials included on the NIHR portfolio the trial will automatically be included as part of the adoption process on the www.crn.nihr.ac.uk website

- The trial team must send confirmation to the CTO once their trial is registered and available on this and any other suitable website (e.g. www.clinicaltrials.gov)
- Some disease indications may have specific websites where the trial should also be registered

7.14. Pre Initiation

- Lead site C&C Approval will be provided by directly to the trial team by the R&D Department
- Prior to the planned initiation meeting the CTO will provide the initiation documentation to be completed by the trial team refer to CCTU/SOP024 Initiation Meetings for Sponsored CTIMPs
- This documentation must be completed and returned to the CTO as soon as possible to allow the pre-initiation checks to be completed
- Documentation generated as part of the risk assessment mitigating action requirements must be sent to the CTO for review and confirmation in advance of the initiation meeting – ideally at least 2-3 weeks in advance of the initiation meeting
- The CTO must be provided with confirmation from the CI/PI acknowledging compliance with the implementation timelines for all mitigating action requirements which are due for completion following the initiation meeting
- Once all mitigating action documentation is agreed the initiation meeting can proceed
- The PV Officer will generate and provide the trial specific PV forms (e.g. Serious Adverse Event Reporting form, CCTU FRM001, Pregnancy Reporting Form, CCTU FRM003)
- The CTM will contact the trial team and arrange trial master file, investigator site file and pharmacy file review approximately 2 weeks prior to the initiation meeting
- Any outstanding documentation for the sponsor file will be requested and must be provided prior to the initiation meeting in order for the meeting to proceed

7.15. Initiation Meeting

Refer to CCTU/SOP024 Initiation Meeting for Sponsored CTIMPs

7.16. Lead Site Activation

- The CTO will provide the trial team with the Sponsorship Letter and email confirmation of site activation when all pre-trial procedures and initiation requirements have been met
- No trial activities can be undertaken until the activation confirmation has been provided by the CTO

8. Monitoring Compliance with and the Effectiveness of this Document

a. Process for Monitoring Compliance and Effectiveness

As part of routine monitoring visits, audit and inspection

b. Standards/Key Performance Indicators

This process forms part of a quality management system and is reviewed according to CCTU procedures. Standard Operating Procedures are reviewed every two years.

9. References

The Institute of Clinical Research, Abbreviations used in Clinical Trials.
MHRA, Good Clinical Practice "Grey Guide"

10. Associated Documents

R&D/POL003 International Studies Policy
CCTU/SOP024 Initiation Meetings for Sponsored CTIMPs
CCTU/SOP027 Data Management
CCTU/SOP049 Overview of Data Management Tools and Procedures
CCTU/SOP041 Green Light Procedure for IMP Release
CCTU Collaborative Research Letter
CCTU FRM001 Serious Adverse Event Reporting Form
CCTU FRM003 Pregnancy Reporting Form

11. Equality and Diversity Statement

This document complies with the Cambridge University Hospitals NHS Foundation Trust service equality and diversity statement.

12. Disclaimer

It is the user's responsibility to check against the electronic library that this printed out copy is the most recent issue of this document.

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