Standard Operating Procedure CCTU/SOP039

Set up and Activation of Participating Sites for Cambridge Sponsored CCTU Led Clinical Trials

1. Scope

This SOP applies to Cambridge Sponsored CCTU Led Clinical Trials for

- Sites approved in the original application
- Sites approved by the amendment process
- Sites approved in England and the Devolved Nations

This SOP does not apply to international trials

2. Purpose

This SOP describes the process of setting up and activation of participating sites (PSs) in accordance with Good Clinical Practice (GCP), CCTU procedures and applicable legislation

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 Cambridgeshire & Peterborough NHS Foundation Trust (CPFT); or CPFT jointly with UoC
Clinical Trial of an Investigational Medicinal Product (CTIMP)	An investigation in human subjects which is intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of one or more medicinal products. Identify any adverse reactions or study the absorption, distribution, metabolism and excretion, with the object of ascertaining the safety and/or efficacy of those products. This definition includes pharmacokinetic studies.
Devolved Nation	Scotland, Wales, and Northern Ireland
Investigator Site File	The investigator site file (ISF) contains trial and site specific essential documents and is located at the site and maintained by the local Principal Investigator (PI) and local site research team.
Multi-centre Trial	A clinical trial conducted according to a single protocol but at more than one site, and therefore, carried out by more than one investigator.

Non-CTIMP	A research study in humans that does not involve an investigational medicinal product (IMP) and does not fall in the scope of the Medicines for Human Use (Clinical Trials) Regulations 2004. Non-CTIMPs can include observational studies, interventional studies, randomised controlled studies, and device studies.
Participating Site	The location(s) where trial related activities are conducted (referred to in this SOP as the site or PS).
Site Activation	The point at which a site is opened for recruitment.
Site Information File	The site information file (SIF) is a sub-section of the TMF and contains Sponsor essential documents relating to an individual site.

3.2. Abbreviations

Abbreviation	Meaning
CCTU	Cambridge Clinical Trials Unit
CI	Chief Investigator
CPFT	Cambridgeshire & Peterborough NHS Foundation Trust
CTA	Clinical Trials Authorisation
CTC	Clinical Trial Coordinator
CTIMP	Clinical Trial of an Investigational Medicinal Product
CUH	Cambridge University Hospitals NHS Foundation Trust
CV	Curriculum Vitae
GCP	Good Clinical Practice
GP	General Practitioner
HRA	Health Research Authority
HSC	Health and Social Care
IB	Investigator's Brochure
ICF	Informed Consent Form
IMP	Investigational Medicinal Product
IRAS	Integrated Research Application System
ISF	Investigator Site File
LIP	Local Information Pack
MHRA	Medicines and Healthcare products Regulatory Agency
OID	Organisation Information Document
PI	Principal Investigator
PIS	Patient Information Sheet
PS	Participating Site
PSA	Participating Site Agreement
PSF	Pharmacy Site File
REC	Research Ethics Committee
R&D	Research and Development
SmPC	Summary of Product Characteristics
SIF	Site Information File
SOP	Standard Operating Procedure
SoE/SoECat	Schedule of Events/Schedule of Events Cost Attribution Template

TMF	Trial Master File
UoC	University of Cambridge

4. Undertaken by

Principal Investigators (PIs), Clinical Trial Coordinators (CTCs), and other delegated members of the coordinating and site trial teams

5. Items Required

- CCTU/SOP081 Identification and Feasibility Assessment of Participating Sites for Cambridge Sponsored CCTU Led Clinical Trials
- R&D/SOP005 Management of Contracts for Research Projects
- Participating Site Agreement (PSA) from Trust R&D
- CCTU/SOP024 Initiation Meeting for CTIMPs
- CCTU/SOP076 Initiation Meeting for CCTU led Non CTIMPs
- CCTU/SOP015 TMF and Site File Essential Document Management
- CCTU/SOP071 Selection of Laboratories for Analysis of Research Samples
- CCTU/TPL058 Delegation of Roles and Responsibilities and Signature Log (Delegation Log)
- CCTU/FRM051 Trial Specific Training Record
- CCTU/TPL087 Out of Hours Test File Note
- CCTU/TPL066 Pharmacy Manual template
- CCTU/FRM064 Participating Site Activation Checklist
- CCTU/TPL028 Participating Site Activation Letter

6. Summary of Significant Changes

Clarification that for CTIMPs FRM064 must be sent to the Regulatory Team for review prior to site activation

7. Method

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

Refer to the Health Research Authority (HRA), Integrated Research Application System (IRAS), and/or the Medicines and Healthcare products Regulatory Authority (MHRA) websites for any further information or clarification.

7.1. Identification and Feasibility Assessment of Sites

- Refer to CCTU/SOP081 Identification and Feasibility Assessment of Participating Sites for Cambridge Sponsored CCTU Led Clinical Trials

7.2. Setting up NHS Sites in England and the Devolved Nations

- The site must be listed on the initial HRA/Research Ethics Committee (REC) and Clinical Trials Authorisation (CTA) application forms. Additional sites can only added via the amendment process

- Following submission to REC/MHRA/HRA, trial-related documents can be sent to the site to begin their set-up process
- The Local Information Pack (LIP) will be sent to the relevant department for the site refer to the IRAS guidance by the CTC

NOTE:

- Receipt of the LIP by the site may trigger their locally reportable timeline to recruit their first participant. The CTC should discuss this with the site R&D department and research team prior to submission of the LIP
- The LIP will typically include the following (always check IRAS guidance for updates):
    - Copy of the submitted IRAS Form
    - Submitted protocol
    - Submitted participant information sheet (PIS) and informed consent form (ICF) (without local logos/ headers)
    - Relevant NHS model agreement
    - Completed Organisation Information Document (OID)
    - Schedule of Events (SoE)/Schedule of Events Cost Attribution Template (SoECAT)
    - A copy of HRA Initial Assessment Letter (if one is issued)
    - A copy of the HRA Approval Letter and final documents
    - Any other documents to support the set up and delivery of the trial
- The relevant approval letters together with any revised trial documents will also be sent to the site (PI, local research team, local R&D office and local Clinical Research Network (where relevant)) by the CTC
- The site will confirm their capacity and capability to deliver the trial by exchanging signed agreements and/or agreeing the OID

7.3. Setting up non-NHS/HSC sites

(e.g. University sites or GP surgeries)

- For CTIMPs:
    - All non-NHS/Health and Social Care (HSC) sites should be listed in the appropriate section of the IRAS form
    - A non-NHS/HSC site assessment form should be completed and submitted for all non-NHS/HSC sites
    - Additional documentation should be included with the application, including the following (always refer to the IRAS guidance for updates):
        - Short CV for PI
        - Evidence of insurance or indemnity (if required)
        - Local versions of documents (if significantly different to the main version)
- For all other study types:
    - All non-NHS/HSC sites should be listed in the appropriate section of the IRAS form, and no additional documents/forms are needed.

7.4. Participating Site Agreement

A Participating Site Agreement (PSA) between the Sponsor and each site will be issued, signed and filed. Refer to R&D/SOP005 Management of Contracts for Research Projects.

- The draft agreement should be sent to the R&D department of the site for their review before signatures are obtained
- If the R&D department of a site has any issues with the PSA, this must be resolved between the solicitors and/or contract managers of the Sponsor and the PS R&D department
- For CTIMPs: A pharmacy appendix to the PSA will also be completed and signed by the site Pharmacy Department

7.5. Site File Preparation

- For each site, the CTC will prepare an ISF (and for CTIMPs, a Pharmacy Site File). Refer to CCTU/SOP015 TMF and Site File Essential Document Management
- These files are sent to the site prior to the site initiation visit as they contain trial and site related essential documents
- The CTC will prepare and maintain a Site Information File (SIF) for each site, as a part of the Trial Master File (TMF)
- Any updated trial related documentation sent to site are filed in the ISF (and/or PSF as appropriate) by site staff

7.6. Documents Managed by Participating Site(s)

- The participating site(s) must complete:
    - The Delegation of Roles and Responsibilities and Signature log CCTU/TPL058 (also referred to as 'delegation log')
    - Trial Specific Training Log CCTU/FRM051
    - All participant documentation (PIS, ICF, GP letter, etc.) with site specific logos/contact details (as required) and send copies to the CTC for checking and filing in the SIF
- The PI must sign and date the delegation log to confirm staff suitability for their delegated responsibilities
- The completed delegation log, CV and GCP certificates for all site staff will be filed in the ISF at the site

During the course of the trial site staff are responsible for:

- Keeping the delegation log up to date
- Keeping the out of hours contacts up to date
- Keeping CVs and GCP certificates for site staff up to date in accordance with their local policy
- Keeping training records up to date

Sending to the CTC updated copies of:

- Updated out of hours contacts so the test can be repeated
- The updated delegation log
- Updated training records

- Current or updated GCP and CV evidence for the PI only

7.7. Laboratory and Pharmacy Documents

The site must provide the CTC with:

- Accreditation documents for the laboratories that the site will be using for the trial, with their normal reference ranges
- A lab questionnaire for non-accredited laboratories refer to CCTU/SOP071 Selection of Laboratories for Analysis of Research Samples
- Copies of local SOPs (e.g. pharmacy) and policies that differ from those described in the trial protocol

7.8. Drug/IMP Supply System (if applicable)

The Sponsor's Clinical Trials Pharmacist (Oncology or Central Pharmacy) will be involved in the preparation of the trial specific drug/IMP management guidelines known as the pharmacy manual. Refer to CCTU/TPL066. This must cover as a minimum the following topics:

- Procedures for drug supply/ordering
- Instructions for drug storage
- Instructions for preparation and administration of drug
- Drug labelling (if relevant)
- Procedure for temperature deviations
- Quarantine procedure
- Drug accountability and form completion
- Drug destruction instructions
- List of pharmacy forms provided by the Sponsor
- Pharmacy staff training requirements
- Electronic-prescribing (if relevant)

The trials pharmacy at the site will be responsible for receipt, storage and accountability of the drug and for issuing the green light for the drug to be used at the site.

The CTC will supply sites the following as required:

- Trial specific drug/IMP management guidelines (pharmacy manual)
- The current Investigator's Brochure (IB) and/or Summary of Product Characteristics (SmPC) for the medicinal product(s) to be used (for pharmacy IMP management purposes)
- Trial specific prescriptions and forms for drug/IMP accountability (the site may use their own versions, but a copy must be provided by the site to the CTC and approved prior to use)
- Delegation log, patient log etc. for the Pharmacy Site File

7.9. Local Service Agreements

Local resources and/or agreements should be in place in good time before site initiation to avoid delays in activation.

The CTC should remind PIs at sites that they must liaise with local service departments involved in trial specific procedures (e.g. radiology, pharmacy, laboratories) as soon as the site start-up process commences.

7.10. Participating Site Initiation

Site initiation can only take place:

- After the lead site has been activated
- Before the site is activated

The site initiation process is described in detail in:

- CCTU/SOP024 Initiation Meeting for CTIMPs
- CCTU/SOP076 Initiation Meeting for CCTU led Non CTIMPs

7.11. Participating Site Activation all trials

After the lead site has been activated, approved participating sites can be activated when:

- The local R&D department has provided the fully executed PSA and confirmation of their capacity and capability
- Site initiation has been completed

The CTC will:

- Check that the Participating Site Activation Checklist CCTU/FRM064 has been completed and signed, and copies of all site related documentation have been received
- Ensure that the site PI is aware that he/she must provide relevant protocol training to all new staff joining the trial team after the site initiation and that the Trial Specific Training Log CCTU/FRM051 is updated
- Perform out of hours testing
    - Complete the Out of Hours Test File Note CCTU/TPL087 for the SIF and provide a copy to the site for the ISF

Additional procedures for CTIMPs:

- Ensure the Participating Site Activation Checklist CCTU/FRM064 has been completed and signed, and sent to the CCTU regulatory team for review and authorisation before site activation
- The CTC has authorised the release of IMP to the site (if applicable)
- The site pharmacy has given the green light for the IMP to be used
- Arrangements for IMP receipt, storage and accountability are in place

Confirm that the site is open to screening and recruitment by issuing the activation letter CCTU/TPL028 to:

- The site
- Other relevant parties (e.g. randomisation office, contracted service providers)

7.12. Addition of Sites

Further sites not included in the original IRAS application must be identified and processed according to CCTU/SOP081 Identification and Feasibility Assessment of Participating Sites for Cambridge Sponsored CCTU Led Clinical Trials

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"

HRA website: www.hra.nhs.uk

IRAS website: https://www.myresearchproject.org.uk/

10. Associated Documents

CCTU/SOP041 Green Light Procedure for IMP Release

CCTU/SOP005 Test of Out of Hours Medical Cover Arrangements

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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