# Standard Operating Procedure CCTU/SOP039

# Set up and Opening of a Participating Site for Cambridge Sponsored Clinical Trials

## 1. Scope

This SOP applies to multi-centre Cambridge Sponsored clinical research trials both CTIMPs and non-CTIMPs. For non-CTIMPs, sections on MHRA are not relevant. This SOP does not apply to commercially sponsored trials or research sponsored by an external non-commercial organisation.

## 2. Purpose

This SOP describes the process of setting up and opening a Participating Site (PS) for participant recruitment in accordance with GCP and applicable legislation.

## 3. Definitions and Abbreviations

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

Common abbreviations and definitions can be found in CCTU/INF001 Common Abbreviations and Definitions.

### 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 |
| Multicentre 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 |
| Participating Trial Site | The location(s) where trial related activities are conducted (referred to in this SOP as the site) |
| Site Information File | The site information file is a sub-section of the TMF and contains Sponsor essential documents relating to an individual Participating Trial Site. |
| Investigator Site File | The investigator site file contains trial and site specific essential documents and is located at the participating site and maintained by the local Principal Investigator and local site research team |
| CTIMP | A clinical trial is 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. |

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| Non-CTIMP | A research study in humans that does not involve an IMP and does not fall in the scope of the Medicines for Human Use (Clinical Trials) Regulations 2004Non-CTIMPs can include observational studies, interventional studies, randomised controlled studies, device studies. |

## 3.2. Abbreviations

| Abbreviation | Meaning |
|---|---|
| CCTU | Cambridge Clinical Trials Unit |
| CI | Chief Investigator |
| CLRN | Comprehensive Local Research Network |
| CRF | Case report From |
| CUH | Cambridge University Hospitals NHS Foundation Trust |
| DN | Devolved Nation (Scotland, Wales, Northern Ireland) |
| CTA | Clinical Trial Authorisation |
| CTC | Clinical Trials Coordinator |
| CV | Curriculum Vitae |
| GCP | Good Clinical Practice |
| GP | General Practitioner |
| HRA | Health Research Authority |
| IB | Investigator 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 |
| 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 |
| RoIF | Registration of Interest/Feasibility Template |
| SmPC | Summary of Product Characteristics |
| SOP | Standard Operating Procedure |
| SoE | Schedule of Events |
| SoA | Statement of Activities |
| SSA | Site Specific Assessment |
| SSI | Site Specific Information |
| TMF | Trial Master File |
| UoC | University of Cambridge |

# 4. Undertaken by

Chief Investigators (CI), Principal Investigators (PI), Clinical Trial Coordinators and other delegated members of the trial team.

# 5. Items Required

CCTU/TPL028- Participating Site Activation Letter
CCTU/TPL033- Investigator Site File Index
CCTU/TPL034- Site Information Index in the TMF
CCTU/TPL038- Local Pharmacy Site File Index
CCTU/TPL058 Delegation of Responsibility and Signature Log
CCTU/FRM051 Trial Specific Training log
CCTU/TPL065 Registration of Interest/Feasibility Assessment Template
CCTU/FRM064 Participating Site Initiation Check List
CCTU/FRM086 Participating Site Initiation Form
CCTU/SOP014 Amendment Management of CTIMPS by Trial Teams
CCTU/SOP024 Initiation Meeting for CTIMPs
R&D/SOP005 Management of Contracts for Research Projects
Participating Site Agreement (PSA) from Trust R&D

# 6. Summary of Significant Changes

- Changes to site set-up procedure due to the new HRA approval process
- The need to carry out site feasibility prior to commencing a site set-up
- Clarification added for frequency of GCP refresher training at participating sites
- Clarification that a participating site can only be opened after the lead site has opened

# 7. Method

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

## 7.1. Identification and Feasibility Assessment of New Sites

- Potential participating sites and Principal Investigators approached or expressing an interest in participating in the trial will be asked to complete a registration of interest/ feasibility assessment form (CCTU/TPL065) in order to establish their site's suitability
- The CI and CTC will review the completed TPL065 to establish:
    - The ability of the site to identify a suitable number of potentially eligible participants
    - If the site has sufficient resources and staff with the relevant skills, expertise and time to conduct the trial procedures
    - If the site has appropriate equipment and facilities

  - If the site is participating in other clinical trials that are competing for the same trial population
  - If there are any financial implications or other factors that may affect the conduct of the trial at the site
- The CTC will confirm in writing to the PI whether their site can become a participating site (PS). If the site is unsuitable to host the trial the CTC will explain the reasons for the decision
- A copy of the RoIF CCTU/TPL065 and any related correspondence will be filed in the TMF for both accepted and sites declined
- A list of proposed participating sites including the PI name and qualifications will be included in the IRAS application forms for submission to HRA/REC and MHRA.
- Following HRA/REC and MHRA approvals for the trial the addition of further sites (not included in the original submissions) will require:
  a substantial amendment for (CTIMPs)
  a non-substantial amendment (non-CTIMPs) see section 7.11

## 7.2. Setting up NHS Sites in England

- Following submission to REC/MHRA/HRA trial related documents can be sent to the PS to begin their set-up process
- The Local Information Pack (LIP) will be sent to the site by the CTC with either the HRA Initial Assessment Letter or the HRA Approval Letter (depending on timing of PS set up).
  **PLEASE NOTE:**
  Receipt of the LIP by the PS will trigger their 70 day timeline to recruit their first patient. Please discuss this with the participating site R&D department and research team prior to submission.
- The LIP will typically include the following (always check HRA guidelines for updates to the required contents of the LIP)
  - Copy of the IRAS Form (combined REC and R&D form) as submitted for HRA approval
  - Current protocol
  - Participant information and consent documents (without local logos/ headers)
  - Relevant NHS model agreement
  - Statement of Activity and Schedule of Event templates obtained from the HRA website (including known information)
  - Any other documents that the sponsor wishes to provide to the site to support the set up and delivery of the trial
  - Copy of HRA Initial Assessment Letter (if one is issued) and (when issued) HRA Approval Letter and final documents
- When HRA approval has been issued:
  - The PS (PI, local research team, local R&D office and Local Clinical Research Network (where relevant)) will be sent the relevant approval letters together with any revised trial documents

- The PS will confirm their capacity and capability to deliver the trial by exchanging signed agreements and/or agreeing the Statement of Activities

## 7.3. Setting up NHS sites in the Devolved Nations and non-NHS sites

- Site Specific Information (SSI) forms will be used for setting up NHS sites in the devolved administrations (DAs) as well as non-NHS sites (e.g. university sites or private hospital).
- The CTC will generate the SSI form for each PS within IRAS (guidance is available within IRAS)
- The SSI is an integrated form for use for both NHS and non NHS sites. The answer to the question within IRAS stating the participating sites to be included in the trial will determine whether the site is NHS or non NHS and generate the appropriate SSI form

For NHS sites:

- The CTC will transfer the SSI form to an appropriate member of the trial team at the PS for completion and submission to the local R&D department for approval
- Each NHS Trust will be responsible for obtaining authorisations from relevant local NHS departments
- When submitting final SSI forms R&D departments will consider the 70 day timeline (i.e. the first patient recruited to the trial within 70 days of the submitted SSI being validated)

For Non NHS Sites

- SSI and other relevant documents should be submitted to the main REC responsible for favourable opinion.

## 7.4. Participating Site Agreement

- A Participating Site Agreement (PSA) between the Sponsor and each PS will be issued, signed and filed in accordance with R&D/SOP005 Management of Contracts for Research Projects
- The draft agreement should be sent to the R&D department of the PS for their review before signatures are obtained
- If the R&D department of a PS has any issues with the PSA, this will 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 be completed and signed by the participating site Pharmacy Department
- For non-UK sites the CUH contracts officer should be contacted for advice on the required agreements

## 7.5. Site File Preparation

- For each participating site an Investigator Site File (ISF) will be prepared according to CCTU/TPL033 Investigator Site File Index *(ensure that the approved version of the Reference Safety Information (RSI) applicable for the trial is included as detailed in the index)*
- For CTIMPS, a Pharmacy Site File (PSF) should also be

prepared according to CCTU/TPL038 Local Pharmacy Site File Index

- These two files are sent to the PS prior to the Site Initiation as they contain trial and site related essential documents
- The CTC will also prepare and maintain a Site Information File section of the TMF for each PS according to CCTU/TPL034 – Site Information Index in the TMF
- Any updated trial related documentation sent to PS's should be filed in the ISF or PSF as appropriate by the participating site trial staff

## 7.6. Trial Documents generated by the Participating Site

- The participating site must complete a Delegation of Responsibility and Signature log CCTU/TPL058 provided to them by the CTC listing personnel involved in the trial at the site (PI and any Co-Investigators, Research Nurses, Pharmacist(s), Trial Coordinators, Data Managers etc, as applicable)
- Each person listed on the site Delegation of Responsibility and Signature log will list the duties being delegated to them with a start date and sign and initial the log
- The PI will sign and date every entry on the delegation log to confirm the staff suitability for their delegated responsibility
- At the point of the site opening for recruitment, a current CV (signed and dated) and confirmation of GCP training must be provided for all relevant staff involved in the trial
- GCP training should be updated every two years or in accordance with the PS local policy. Local policy also applies to non UK sites
- A copy of all participant documentation (PIS, ICF, GP letter etc) with site specific logos must be sent back to the CTC for checking and filing in the Site Information File of the TMF
- The completed Delegation of Responsibility and Signature log, CVs and GCP certificates will be filed in the ISF at the PS with copies sent to the CTC for filing in the Site Information section of the TMF
- Trial staff at the PS will be reminded that they are responsible for keeping the delegation log, CVs and GCP certificates up to date during the course of the trial and sending copies of all updated documents to the CTC

## 7.7. Laboratory and Pharmacy Documents

- The Participating Site should provide the CTC with:
    - Accreditation documents for the laboratories that the site will be using for the trial, with their normal reference ranges
    - 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 CTC will supply all PS's the following as required:
    - Trial specific guidelines on the drug/IMP management

  - The current IB and/or SmPC for the medicinal product(s) to be used (for pharmacy IMP management purposes)
  - Trial specific prescriptions and forms for drug/IMP accountability
  - Delegation of Responsibilities and Signature log, patient log etc for the site pharmacy trial file (PSF)
- The Sponsor's Clinical Trials Pharmacist (Oncology or Central Pharmacy) will be involved in the preparation of the trial specific drug/IMP management guidelines. These 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)

PLEASE NOTE: The trials pharmacy at the PS 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.

## 7.9. Local Service Agreements

The CTC should remind PIs at participating sites that they must liaise with any local service departments needed for trial specific procedures (e.g. radiology, pharmacy, laboratories) as soon as the participating site start-up process commences. This will ensure resources and/or agreements are in place in good time before site initiation and avoid delays in site opening.

## 7.10. Site Initiation

- Site initiation of a PS can only take place after the lead, sponsor site has opened
- PS initiation must be conducted before the site opens for recruitment. Its purpose is to explain all aspects of the trial to key personnel at the site (PI, Research Nurse(s), Pharmacist, Trial coordinators, Data Managers etc) and to clarify any issues that they may arise
- The site initiation process is described in detail in CCTU/SOP024: Initiation Meeting for CTIMPs)
- The PS must be listed on the initial HRA/REC and CTA application forms. Additional sites can only added via the amendment process (section 7.12)

## 7.11. Site Opening

A site can officially be opened to recruitment when:

- After the lead, sponsor site has been opened

- The local R&D department has provided the fully executed PSA and confirmation of their capacity and capability
- All items on the site initiation checklist (CCTU/FRM064) are in place and copies of all site related documentation have been sent to the CTC for checking and filing in the Site Information section of the TMF
- Site Initiation has been completed and the Participating Site Initiation form (CCTU/FRM086) has been signed by the PI and CTC
- For CTIMPs/trials involving drug, the CTC will need to authorise the release of drug to the PS and the site pharmacy must give the green light for the drug to be used before the site is activated
- Arrangements for IMP receipt, storage and accountability are in place

The CTC will:

- Issue and send an activation letter (CCTU/TPL028) to the PS to inform them that their site is officially open to participant screening and recruitment
- Inform other relevant parties (e.g. randomisation office, contracted service providers) of the new PS opening; for CTIMPs the CTC will inform the IMP supplier to authorise release of IMP to the new site
- Ensure that the site PI provides relevant training on the trial protocol and procedures to all new personnel joining the trial team after the site initiation and that the Trial Specific Training Log (CCTU/FRM051) is updated

The Participating Site must provide the CTC with:

- Updated site specific documents when they become available (e.g. updated Signature and Responsibility log
- CV's
- Evidence of GCP training
- Lab ranges and accreditation
- Confirmation of continued capacity and capability
- Amendments
- Amended PIS on headed paper
- Trial specific training logs etc

## 7.12. Addition of Investigator Sites

- Following HRA/REC/MHRA approval any further Participating Sites not included in the original IRAS application must be notified to the HRA/REC as an amendment
- For CTIMPs the addition of new sites must be submitted to the HRA/REC as a substantial amendment refer to CCTU/SOP014 - Amendment Management of CTIMPS by Trial Teams. There is no requirement to notify the MHRA
- For non-CTIMPs, addition of new sites is submitted as a non-substantial amendment to hra.amendments@nhs.net

For further guidance check the HRA/IRAS websites.

# 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. Documents are reviewed every two years

# 9. References

The Institute of Clinical Research, 2008, Abbreviations used in Clinical Trials.

HRA website: www.hra.nhs.uk

# 10. Associated Documents

CCTU/SOP015 Trial Master File/Site File – Essential Document Management

CCTU/SOP041 Green Light Procedure for IMP Release

# 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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