Standard Operating Procedure CCTU/SOP015

Trial Master File/Site File - Essential Record Management

1. Scope

This standard operating procedure (SOP) applies to trial teams running Clinical Trials managed by the Cambridge Clinical Trials Unit (CCTU).

This SOP does not cover maintenance of Sponsor files - refer to Maintenance of Sponsor Files for CCTU Managed CTIMPs (CCTU/SOP010).

2. Purpose

To have a standard format for the management of essential records.

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
Essential Records	Documents which individually and collectively permit evaluation of the conduct of a study and the quality of the data produced. These records serve to demonstrate the compliance of the Investigator, Sponsor, and monitor with the standards of Good Clinical Practice (GCP) with all applicable regulatory requirements

3.2. Abbreviations

Abbreviation	Meaning
ALCOA++	Attributable, Legible, Contemporaneous, Original, Accurate, Complete, Consistent, Enduring & Available
CCTU	Cambridge Clinical Trials Unit
CI	Chief investigator
CPFT	Cambridgeshire & Peterborough NHS Foundation Trust
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
HRA	Health Research Authority
IB	Investigator's brochure
IMP	Investigational medicinal product
ISF	Investigator site file
MHRA	Medicines and Healthcare products Regulatory Agency
NIMP	Non-investigational medicinal product
PI	Principal investigator
PIS	Participant information sheet
PSF	Pharmacy Site File
REC	Research Ethics Committee
SIF	Site information file
SmPC	Summary of product characteristics
SOP	Standard operating procedure
TMF	Trial master file
UoC	University of Cambridge

4. Undertaken by

The clinical trial coordinator (CTC) and/or other designee(s)

5. Items Required

- CCTU/TPL032 Trial Master File Index
- CCTU/TPL033 Investigator Site File Index
- CCTU/TPL034 TMF Site Information File Index (SIF)
- CCTU/TPL038 Local Pharmacy Site File Index
- CCTU/TPL053 Randomisation File Index
- CCTU/TPL056 Statistics File Index
- CCTU/TPL063 Data Management File Index
- CCTU/TPL080 CCTU Lab File Index (subsection of the TMF)
- CCTU/SOP006 The CCTU Archiving Process
- CCTU/TPL081 CCTU Lab File Index for CCTU managed Trials

6. Summary of Significant Changes

Amendments throughout in response to the Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025, UKSI 2025/538

7. Method

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

7.1. Essential Record Management

- Essential records for the trial must be kept in hard copy and available for audit or inspection at any time except in exceptional agreed circumstances.
- Essential trial specific documentation must be prepared/collected and maintained:
    - In accordance with GCP
    - Before the trial commences and during the conduct of the trial
    - In the Trial Master File (TMF) and TMF Site Information File (SIF) and Pharmacy file if appropriate
    - In the Investigator Site File (ISF) and Pharmacy Site File (PSF) (if appropriate) at participating sites
- The TMF and essential documents must be kept up to date to ensure:
    - Compliance with regulatory, ALCOA++ and GCP requirements
    - Efficient trial management
    - Transparency and accountability

7.2. File Management

Files should be stored in a secure location and labelled with at a minimum:

- Trial title
- IRAS ID
- Volume number if there is more than one file (x of y)

Divide the file into appropriate sections according to the relevant index

- For TMF, use CCTU/TPL032
- For TMF SIF, use CCTU/TPL034
- For ISF, use CCTU/TPL033
- For PSF, use CCTU/TPL038
- For Lab Files, use CCTU/TPL081

- Sections that do not apply to the trial should be noted as not applicable in the 'comments' column or the section can be removed
- Trial specific sections may be added
- The documents in the file(s) should be arranged chronologically with the most recent documents at the front of each section
- Documents may be amended during the trial and it is important that amendment chronologies can be traced and are indicated
- Previous/superseded documents must be retained and labelled superseded (strike through sign and date)
- Any alterations must be traceable via an audit trail, including tracked changes, dates, version numbers etc.
- Where documents are stored in a separate location, document the location in the comments column of the index e.g. investigational medicinal product (IMP) and non-investigation medicinal product (NIMP) information details may be stored in the PSF rather than the ISF
- At the end of the trial any separately held documents/files must be merged in the appropriate main file prior to archiving. Refer to The CCTU Archiving Process (CCTU/SOP006).

7.3. Trial Master File (TMF)

- Prior to the start of a trial, a TMF should be prepared in accordance with the TMF Index (CCTU/TPL032)
- This does not include electronic copies of documents, documents must be printed and stored in hard copy except in exceptional agreed circumstances.
- The responsibility to hold and maintain an up to date TMF, including all superseded documents, is with the Chief Investigator (CI) but is usually delegated to the CTC
    - CV and GCP must be kept for the coordination team according to the staff on the delegation log
- All members of the trial coordination team should have access to the TMF
- Sub Sections of the TMF may be stored separately from the TMF during the trial but are archived as part of the TMF.
- These files have their own index which outlines the minimum documents expected to be included in each subsection:
    - CCTU/TPL063 Data Management File Index
    - CCTU/TPL056 Statistics File Index
    - CCTU/TPL053 Randomisation File Index
    - CCTU/TPL080 Lab File Index
    - CCTU/TPL034 Site Information File(s) in the TMF (SIF)

7.4. Site Information in the SIF (site information in the TMF)

- Prior to the start of a trial, a TMF SIF should be prepared in accordance with the TMF SIF Index (CCTU/TPL034) for each participating site
- If a new participating site is added during the course of the trial, a new TMF SIF should be prepared for each new participating site
- Documents in the TMF SIF are usually a copy of documents prepared or issued for the participating site
- GCP certificates and CVs should be kept for the Principal Investigator (PI) only
- An up to date delegation log for participating sites should be filed when there is a change of staff or change to delegated responsibilities
- At trial completion the TMF SIF(s) is/are archived together with the TMF. Refer to The CCTU Archiving Process (CCTU/SOP006)

7.5. Investigator Site File (ISF)

- An ISF contains essential records on the trial and forms/documents used by the individual participating sites for the duration of the trial
- The responsibility to hold and maintain an up to date ISF, including all superseded documents, is with the participating site. Electronic ISFs (eISFs) may be used if permitted by the local policy at each site. N.B. CUH do not permit the use of eISFs, CUH ISFs must be stored in hard copy
- The ISF Index (CCTU/TPL033) outlines the minimum documents expected to be filed in the ISF at each participating site. The ISF should be set up prior to opening a participating site

  - GCP certificates and CVs should be kept for all trial staff at a participating site according to the delegation log and local policies
- When new or amended trial documents become available (e.g. protocol, participant information sheet (PIS), investigator brochures (IBs)/summary of product characteristics (SmPCs), annual reports, etc.), it is the responsibility of the CTC to provide copies to the participating sites together with relevant Research Ethics Committee (REC), Health Research Authority (HRA) and Medicines and Healthcare products Regulatory Agency (MHRA) approvals as appropriate
- ISFs are archived by the participating site according to their local policy unless alternative arrangements are specified in the participating site agreement
- The location of the archived documents is recorded on the Archiving Details Location Form (CCTU/FRM017) and sent to the coordinating site for filing in the TMF

7.6. Pharmacy Site File (PSF) if required

- The Local PSF Index (CCTU/TPL038) outlines the minimum documents expected to be filed in the PSF at each participating site. The file should be set up prior to the start of a trial by the participating site or can be provided by the coordinating team according to the trial
- The responsibility to hold and maintain an up to date PSF ultimately lies with the PI at each participating site, but it is usually delegated to pharmacy
- During the trial initiation, the contents and maintenance of the PSF should be reviewed by the CTC with the lead trial pharmacist in attendance

7.7. Laboratory File if required

- If the trial is using laboratories for the storing, processing or analysing of trial samples it may be appropriate to provide them with a Laboratory File for their documentation.
- The Lab File Index for CCTU Trials (CCTU/TPL081) outlines the documents expected to be filed in this Laboratory File. This is a template and can be used as an index or as a guide.
- All documents pertaining to sample management must be retained by the laboratory.
- Some documents in the index may not be applicable, depending on the activities being conducted at the lab.
- Some documents may be held centrally by the lab, these centrally held documents must be accessible and retained for the full archiving period required for the trial.

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

NA

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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