Standard Operating Procedure CCTU/SOP015

Trial Master File / Site File - Essential Document Management

1. Scope

This SOP applies to all trial teams running Cambridge Sponsored clinical trials of investigational medicinal products (CTIMPs) where QA and QC responsibility for Regulatory Oversight has been delegated or contracted to the Cambridge Clinical Trials Unit

2. Purpose

To have a standard format for all Trust-Sponsored CTIMPs for preparing, updating and maintaining all Essential Documents.

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

3.2. Abbreviations

Abbreviation	Meaning
CTIMPs	Clinical Trials of Investigational Medicinal Products
TMF	Trial Master File
ISF	Investigator Site File
SIF	Site Information File in the TMF
IMP(s)	Investigational Medicinal Product(s)

PIS	Participant Information Sheet
IBs	Investigator's Brochures
SmPCs	Summary of Product Characteristics

4. Undertaken by

The Trial Coordinator and/or other designee(s)

5. Items Required

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

6. Summary of Significant Changes

Index forms changed to templates

Clarification of TMF maintenance and archiving

Essential documents are kept in hard copy

7. Method

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

7.1. Essential Document Management

- Essential Documents for the Trial must be kept in hard copy Trial Master File (TMF), site specific documents are kept in a subsection of the TMF, referred to as TMF Site Information File, and in multicentre trials the participating sites should also maintain an Investigator Site File (ISF).
- All essential documentation should be maintained in the TMF, TMF Site Information File or ISF and pharmacy file
- These documents must be updated as appropriate throughout the trial
- Divide the file into appropriate sections according to the index
- Sections that do not apply to the trial should be noted in a file note as not applicable in the corresponding section
- Trial specific sections may be added
- The file should be arranged chronologically with the most recent documents at the front of each section

- Documents may be amended during the trial, it is important that amendment chronologies can be traced and are indicated
- Previous / superseded documents must be retained, labelled superseded (strike through sign and date) in the TMF, TMF Site Information File ,ISF and Pharmacy File
- Any alterations must be traceable via an audit trail, including tracked changes, dates, version numbers, etc
- Where documents are stored separately from the TMF or the ISF, a file-note should be kept in the appropriate section detailing where the document is stored e.g. IMP information details may be stored in the pharmacy file
- At the end of the trial any separately held documents / files must be merged in the appropriate TMF / ISF
- They must be made available to the Sponsor, trial monitors, representatives of Ethics Committee and Regulatory bodies upon request

7.2. Trial Master File: (TMF)

- The TMF contains all the essential trial specific documentation prepared/collected before the trial commences, during the conduct of the trial and at trial completion in accordance with Good Clinical Practice
- The content includes but is not limited to those documents outlined in the TMF Index CCTU/TPL032
- Prior to the start of a study, a TMF should be prepared in accordance with the TMF index CCTU/TPL032
- The responsibility to hold and maintain an up to date TMF, including all superseded documents, is with the Chief Investigator
- The TMF should be labelled on the spine with a minimum of Study name/title, EudraCT No., and stored in a secure location with restricted access
- There may be several volumes of the TMF, in which case, a TMF Volume number should be added to the label
- All members of the study coordination team should have access to the TMF
- At trial completion, the TMF is archived along with any files that were stored separately from the TMF during the trial. These files may include:
    - Data Management (CCTU/TPL063 Data Management File Index outlines the minimum documents expected to be filed in the Data Management File)
    - Statistics (CCTU/TPL056 Statistics File Index outlines the minimum documents expected to be filed in the Statistics File)
    - Randomisation (CCTU/TPL053 Randomisation File Index outlines the minimum documents expected to be filed in the Randomisation File)
    - Laboratory (CCTU/TPL081 Lab File Index for CCTU Managed Trials outlines the minimum documents expected to be filed in the Lab File)
- Refer to CCTU/SOP006 CCTU Archiving Process and CCTU/TPL051 Trial Master File Archiving Checklist

7.3. Site Information File(s) in the TMF (SIF):

- A TMF Site Information File (SIF) contains essential documents relating to an individual site and forms, it is a sub-section of the TMF
- The responsibility to hold and maintain an up to date TMF Site Information File, including all superseded document, is with the Chief Investigator
- The TMF Site Information File should be labelled on the spine with a minimum of Study Title, EudraCT No., Site number and name (volume no. if applicable), and stored in a secure location
- Prior to the start of a study, a TMF Site Information File should be prepared in accordance with the TMF Site Information File index CCTU/TPL034 for each participating site
- The content includes but is not limited to those documents outlined in the TMF Site Information File Index
- Documents in the TMF Site Information File are usually a copy of documents prepared or issued for the participating site, and must be maintained throughout the trial
- At trial completion the TMF Site Information File(s) is archived together with the TMF. Refer to CCTU/SOP006

7.4. Investigator Site File (ISF):

- An Investigator Site File (ISF) contains essential documents on the trial and forms/documents used by the individual site
- The responsibility to hold and maintain an up to date ISF, including all superseded documents, is with the Principal Investigator at each participating site
- When new or amended trial documents become available (e.g. protocols, PIS, IBs/SmPCs, annual reports, etc), it is the responsibility of the Trial coordinating team to provide copies to the Investigator Site together with relevant Ethics and MHRA approvals
- CCTU/TPL033 outlines the minimum documents expected to be filed in the ISF at each participating site, the file should be set up prior to the start of a study
- Investigator Site Files are archived by the Participating Site according to their local policy unless alternative arrangements are specified and documented in the TMF or participating site agreement

7.4.1. Local Pharmacy File

- The site pharmacy file constitutes part of the ISF and holds documents pertinent to the management of Investigational Medicinal Product(s) at the site
- The responsibility to hold and maintain an up to date Pharmacy File ultimately lies with the Principal Investigator at each participating site, but it is usually delegated to Pharmacy
- CCTU/TPL038 outlines the minimum documents expected to be filed in the Pharmacy File at each participating site, the file should be set up prior to the start of a study by the participating site or can be provided by the coordinating team

- During the trial initiation, the contents and maintenance of the Pharmacy File should be reviewed by the trial coordinator with the lead CT Pharmacist in attendance

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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