Standard Operating Procedure CCTU/SOP006

The CCTU Archiving Process

1. Scope

This Standard Operating Procedure applies to staff working on Cambridge-Sponsored CTIMPs or trials managed by the CCTU.

This SOP can be used as guidance for research sponsored by external organisations that do not have alternative archiving arrangement in place.

2. Purpose

The purpose of this SOP is to ensure that archiving is carried out according to:

- The Data Protection Act 2018
- The Medicines for Human Use (Clinical Trials) Amendment Regulations 2006 Directive 2005/28/EC regulation SI 2006/1928
- CUH Policy Records: Preservation, Retention and Destruction

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 the University of Cambridge
Essential Documents	Essential documents is the collective term for those documents that individually or collectively permit the evaluation of the conduct of a trial and the quality of the data produced. Essential Documents include the Trial Master File (TMF), source documents, Case Report Forms (CRF), Investigator Site File (ISF), Sponsor File and the Pharmacy File (if applicable). A minimal list of documents for archiving can be found in ICH GCP E6 (R2) Section 8 this list is not exhaustive and is for guidance only
Trial Master File	The Trial Master File is a standard filing system which allows the effective storage and location of Essential Documents. The filing system can be in the form of a single project file or a number of files as deemed appropriate. The TMF encompasses Pharmacy, Laboratory, Data management, Randomisation & Statistics files that may be held separately. These are part of the TMF and will be archived with the TMF.
Investigator Site File	The Investigator Site File is a standard filing system which allows the effective storage and location of Essential Documents relating to

	the conduct of the study at the Participating Site. As with the TMF, the filing system can be in the form of a single project file or a number of files as deemed appropriate. The ISF may also encompass the Participating Site Pharmacy Files (if applicable).
Sponsor File	The Sponsor File comprises of a selection of Essential Documents which confirms compliance with sponsor's governance procedures and provides evidence of sponsor oversight and management of the trial. The Sponsor file also encompasses the sponsor pharmacy file (if applicable).
Pharmacy File	The Pharmacy File is a standard filing system which allows the effective storage and location of Essential Documents relating specifically to IMP Management and Dispensing Procedures (if applicable).
Trial Team	This term can refer to any member(s) of the research team. This can be but not limited to the : PI, CI, Coordinator, research nurses, admin staff, lab staff, data staff, statisticians.
Archivist	Person appointed by the Sponsor to be the point of contact for the archiving process.
IQM	Formally Q Pulse. An electronic Quality Management System storage system.
End of Trial Declaration date	The date officially declared to the review bodies (REC/MHRA/HRA) as the end of trial on the end of trial or end of study declaration form.
Sponsors end of trial confirmation letter	Letter sent by the CCTU Regulatory Team after regulatory reporting requirements are completed, and any closeout visit findings have been rectified.

3.2. Abbreviations

Abbreviation	Meaning
CI	Chief Investigator
CRF	Case Report Forms
CTC	Clinical Trial Coordinator
CTO	Clinical Trial Officer
EoT	End of Trial
PI	Principal Investigator
REC	Research Ethics Committee

4. Undertaken by

Staff trained to this SOP

5. Items Required

The relevant Checklists that together make up the TMF:

- CCTU/TPL032 TMF Index

  - CCTU/TPL063 Data Management Index
  - CCTU/TPL053 Randomisation Index
  - CCTU/TPL056 Statistics Index
  - CCTU/TPL080 Laboratory Index
  - CCTU/TPL034 Site Information File Index
- CCTU/TPL038 Local Pharmacy Site File Index
- CCTU/TPL033 Investigator Site File Index
- CCTU/TPL032A TMF for NON CTIMPS
- CCTU/TPL057 Sponsor File Index
- CCTU/TLP101 Site Closing Letter
- CCTU/FRM015 Archiving Box Label
- CCTU/FRM017 Archive Location Form
- CCTU/FRM109 Archive Box Tracking Log

6. Summary of Significant Changes

Change to how ISF destruction dates are calculated

7. Method

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

7.1. Regulatory Requirements

- Directive 2005/28/EC regulation SI 2006/1928
- Data Protection Act 2018
- The CUH Data Protection Policy and Procedure
- The CUH Records: Preservation, Retention and Destruction
- The CCTU acting on behalf of the Sponsor must have a named Archivist

7.2. Responsibilities

7.2.1. The Sponsor:

- Is responsible for ensuring that all records and documents regarding the trial are archived
- Will determine when a trial is ready for archiving
- Will determine the destruction date for the Sponsor File, TMF and ISF(s)
- Is responsible for archiving the Sponsor File and associated documents. For Cambridge Sponsored CTIMPs, this is delegated to the CCTU

7.2.2. Clinical Trial Officer:

- For CTIMP Trials, the Clinical Trial Officers are responsible for issuing the End of Trial Confirmation Letter on behalf of the Sponsor

7.2.3. Chief Investigator:

- Must ensure that the essential documents in the TMF and any participating site files (ISFs) are archived according to this SOP
- Must inform each site when these documents are no longer needed and to instruct the site to destroy them

7.2.4. Principal Investigator:

- Must ensure that the Investigator Site File at their respective site(s) are archived according to this SOP and any local requirements (as stipulated in the Participating Site Agreement)
- Ensure the location of the archive is documented (including electronic data) using CCTU/FRM017
- Ensure CCTU/FRM017 is returned to the lead site for inclusion in the TMF
- Ensure systems are in place for retrieval and destruction of the site file archive boxes

7.2.5. Named Archivist:

- A named Archivist is a legal requirement for CTIMPs
- The QA Manager is the Archivist for the CCTU, there can be named deputies; they are the point of contact for this archiving process
- The appointed CCTU Archivist takes responsibility for the management of archived boxes and the oversight of external archives, but takes no responsibility for completion of the archive checklist nor the physical preparation of archive boxes
- Where the CI cannot be traced and when contacted by a site, the named archivist will instruct sites to destroy documents when no longer needed

7.3. Archive Costs

The CCTU has no responsibility for any unscheduled or unapproved payments of archiving costs.

It is the responsibility of the CI or PI (as delegated) to review archiving costs and ensure that funds are available.

Archiving costs can include:

- Off-site archiving service providers
- Archiving materials, e.g. boxes, treasury tags, archiving bags, suitable fire proof lockable cupboard
- Trial staff resource

7.4. When to Archive

Documents can be archived as per the below process, once all the files are reconciled and are complete.

7.4.1. CTIMPs

- The Sponsor issued end of trial confirmation letter (EoT letter) signifies the end of all close out activities and regulatory reporting activities
- The CTC should send a copy of the EoT letter to the CCTU Archivist for the IQM archiving record
- The TMF can be archived from the date on the EoT letter
- The ISF can be archived once the site has received the CCTU issued site closing letter

7.4.2. Non CTIMPs

The trial documents can be archived one year from the date of the last correspondence to the REC/MHRA (whichever the latest).

The responsibility for archiving the Sponsor file for Cambridge Sponsored non-CTIMPs resides with the Cambridge University Hospitals R&D department.

7.5. Where to archive

- Archive facilities for the TMF and Sponsor files can be sourced either onsite or offsite
- The CCTU takes no responsibility for the financial implications of an appropriate archive solution
- Contact the CCTU Archivist if you are unsure whether the facilities identified for storage are appropriate
- If the CCTU recommended off site provider is not used, the sponsor should make an assessment of their suitability before use
- Archive facilities may be audited, as directed by the Sponsor appointed Archivist, to ensure the facility meets the following minimum requirements:
    - Restricted access
    - Elemental protection (including protection from fire & water damage)
    - Adequate space to host all boxes
    - Validation that boxes can be retrieved according to the agreement
    - Archive box tracking system
- The CCTU Archivist will maintain oversight of archive provider(s)
- For electronic systems please see section 7.8.4

7.6. What to archive

- Where the CI is responsible for the TMF and is also the PI for the site the ISF and the TMF can be archived together
- Where files are held in different locations e.g. pharmacy, statistics, randomisation, laboratory or data management they must be retrieved and archived with the appropriate file:
    - Sponsor File
    - Trial Master File
    - Investigator Site File

7.7. Archiving Checklists-Indexes

The sub-indexes collectively make up the TMF index. All the indexes have a section for archiving. This is used as a checklist to document the location of the documents that make up the files. Use of the checklist enables specific documents to be located if necessary.

For trials conducted before the index had an archive section, create a checklist by adapting the existing file index:

- Add a column to the index for the bag number the box number
- Add a tick box column the indicate the documents are present
- Create a sign off at the end of the checklist

7.8. How to Archive

Documents must to be stored in a way that preserves their integrity and readability. Trial documents must be legible and in their original format (wherever possible) for the full duration of the archiving retention period stated on the original application.

7.8.1. Best Practice

- Remove plastic wallets to prevent transfer of ink" sweating" onto the plastic
- Any documents which are prone to fading or wearing like waxed fax paper, ECG paper or overhead projector papers should be photocopied onto plain A4 paper for archiving purposes. If this is carried out, a member of the trial team should confirm the document as a certified copy (sign the new version, date and add a statement "true representative of the original version")
- Consider if any metallic administrative aids should be removed. Staples can remain in place where degradation is not likely to impair the text
- Contents of any one file should ideally be packaged together in large paper archiving envelopes or bags
- Plastic treasury tags (e.g. E-CLIPs) should be used to replace the metal ring binders/lever arch files to bind the documents together as one set
- It is good practice to create an index for the top of each bound paper pack, and number each bag as shown in the diagram
- Place a copy of the completed archiving checklist/index on top of the bags in the box

7.8.2. Personal Identifiable Information (PID)

- Any documents that contain PID above that which have been approved in the regulatory submissions, must be placed in separate sealed bags
- Seal securely and label with the document type e.g. (ECG printouts, recruitment logs) and mark as confidential
- Record as confidential on the checklist and bring to the attention of the archivist

7.8.3. Investigator Site Files (additional information)

- The Participating Site ISF should not be sent to the Sponsor organisation
- For single centre trials where the TMF & ISF have been maintained as a combined file, they can be archived together
- All documents must be collected and incorporated into the site file including:
    - The local pharmacy file (where applicable)
    - Source documents, if not part of the medical records (if source data is contained within the medical record, archiving should be carried out in accordance with the requirements of the host NHS Trust)
    - CRFs
- Participating sites (including CUH) are responsible for their own archiving in line with the Participating Site Agreement and their own Trust requirements
- Details of the Participating Site archiving location should be recorded using CCTU/FRM017 Archive Location Form and a copy sent to the lead site coordinator
- The lead site coordinator will:
    - File a copy in the TMF
    - Send a copy to the archivist for the IQM archive record
- In cases whereby the participating site ISF cannot be archived (e.g. inadequate facilities or insufficient funds), it is the responsibility of the CI to arrange for the ISF to be archived in collaboration with the lead site

7.8.4. Electronic Archiving

Where possible, electronic data should be printed and archived as part of the TMF. Where this is not possible, the data may be stored on electronic hardware/transportable media. If the data has been migrated to a new format for archiving, the transfer should be validated and fully documented, to ensure and demonstrate there has been no loss, change or corruption to the data or metadata, and to ensure that authenticity is maintained.

It is recommended more than one copy is retained (e.g. a back-up server) and consideration should be given to storing the data in different formats on different types of media. Access to the archived data must be restricted and protected from unauthorised changes to maintain authenticity.

This hardware/media is to be archived in suitably labelled boxes, the location recorded on the TMF checklist and in IQM.

Electronic records that cannot be printed can be stored according to CCTU/GD038 Storage and Access to Confidential Information.

7.9. Destruction Date

- TMF:
  - CTIMP: The destruction date is calculated from the agreed end of trial date as indicated in the Sponsor's End of Trial Confirmation Letter.
  - Non-CTIMP: The destruction date is calculated from the date of End of Trial Acknowledgment received from the REC.
- ISF: The destruction date is calculated from the End of Trial Declaration date, therefore the destruction date remains the same for all the ISF(s) even if some are archived earlier than others.
- The archive destruction date will be recorded on:
  - CCTU/FRM017 Archiving Location Form
  - CCTU/FRM015 Archive Box Label
  - IQM

Type	**TMF and Site Files**	**Sponsor Files**
CTIMP	5 years (unless otherwise stipulated in the end of trial confirmation letter)	25 years
Advanced therapies	30 years	30 years
Paediatric	Until the youngest participant reaches the age of 22 or for 5 years after the end of the trial, whichever the longer	25 years
Non-CTIMP Interventional Studies (Device trials, RCT or other clinical trial)	15 years	15 years
Non-interventional studies	5 years	5 years

7.9.1. Consolidating the Archive Boxes

Do not overfill or seal the boxes. The archive box lids should fit comfortably.

- Print the completed box label CCTU/FRM015 onto sticky backed paper and attach to the archiving box where indicated
- Place the completed checklist with the bag and box numbers recorded inside each box
- If the local department/theme is responsible for their own archiving, they will need to provide their own barcode labels for the CCTU recommended off site provider

7.10. Handover to the Archivist

Populate the following forms and send a copy to the CCTU Archivist:

- CCTU/FRM017 The Archive Location Form
- CCTU/FRM109 Archive Box Tracking Form
- Appropriate Index/Archive Checklist(s)

Once notified, the CCTU Archivist will create an archiving file in IQM according to CCTU/SOP066.

Once the archive boxes have been consolidated, notify the CCTU Archivist who will perform a check, seal the boxes and give CCTU authorisation for archiving.

If the archiving costs are included in the CCTU costing, the CCTU Archivist will take responsibility for the management of the collective boxed documents, provide the barcode labels and arrange for collection by the CCTU recommended off site provider.

If the local department/theme is facilitating their own archiving, they will inform the CCTU Archivist of the date of collection.

7.11. Access to Archived Documents

Access to Archives managed by the CCTU is restricted to the named CCTU Archivists.

Access to the ISF is restricted to delegated individuals at the site and must not be accessed by the CIs trial team or the Sponsor.

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

- MHRA, Good Clinical Practice "Grey Guide"
- Directive 2005/28/EC regulation SI 2006/1928
- Data Protection Act 2018
- Medicines for Human Use (Clinical Trials) Regulations 2004
- Medicines for Human Use (Clinical Trials) Amendment Regulations 2006

10. Associated Documents

Corporate Policy, Records: Preservation, Retention and Destruction
CCTU/SOP066 Archiving Retrieval and Destruction Process for Archivists

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.

Review date	2 years (or earlier in light of new evidence) from approval date
Owning department:	CCTU QA
Supersedes:	CCTU/SOP006 v9
Local reference:	CCTU/SOP006 v10