University of Hertfordshire

ARCHIVING ESSENTIAL DOCUMENTS

Clinical Trials Support Network (CTSN)

Standard Operating Procedure for Archiving of Clinical Trial Data and Essential Documentation in clinical research studies

SOP Number: gSOP-17-02	**Effective Date:** 28th July 2022
Version Number: 2.0	**Review Date:** 3 years (or as required)

1.0 BACKGROUND

This is a University of Hertfordshire (UH) standard operating procedure (SOP). Where there are potential conflicts between different collaborating organisations' SOPs, project level working instructions should be developed, to determine precedence.

2.0 PURPOSE

This document describes procedures for the archiving of essential clinical trial documentation and ensures that the process is carried out according to The Data Protection Act 2018 and The Medicines for Human Use (Clinical Trials) Amendment Regulations 2006 Directive 2005/28/EC regulation SI 2006/1928. It covers Clinical Trials of an Investigational Medicinal Product (CTIMPs), interventional and non-interventional trials sponsored/co-sponsored and those adopted by the UH CTSN. Archiving is a legal requirement which is relevant to all trials. All essential documents should be archived, and this includes essential documents held by investigators, sponsors and others involved in the conduct of a clinical trial (including services departments such as pharmacy, laboratories and radiology). For externally sponsored multi-centre trials, archiving requirements should be outlined in the contract.

Medical notes will be archived in accordance with standard care guidance and are not covered by this SOP.

3.0 APPLICABLE TO

This SOP applies to all staff involved with clinical research that is UH sponsored/co-sponsored or adopted by the UH CTSN including, but not limited to, Chief Investigators (CI), Principal Investigators (PI), Co-investigators, Research Fellows, Statisticians, Trial Manager, the Clinical Trial Support Network Management Group (CTSNMG) & Data Managers.

4.0 RESPONSIBILITIES

4.1 <u>The Sponsor</u>:

- Is responsible for ensuring that all records and documents regarding the trial are archived in compliance with legal requirements.
- Will determine the requirements for retention of materials, their retention periods and location prior to trial start and formally document in the contract.

- Will determine when a trial is ready for archiving and the destruction date for the Sponsor File, the TMF and the ISF(s).

4.2 The CTSN:

- For those studies adopted by the CTSN, the CTSN will take on the specific Sponsor responsibilities as detailed in the Division of responsibilities log for all externally sponsored projects.

4.3 Chief Investigator:

- Must ensure that the essential documents in the Trial Master File (TMF) and the Investigator Site File(s) (ISF) are archived in accordance with this SOP.
- Must inform each participating site when these documents are no longer needed to be retained in archive and when to destroy those documents.

4.4 Principal Investigator:

- Must ensure that the ISF at their respective site(s) are archived in accordance with this SOP and any local requirements stipulated in the Participating Site Agreement.
- Must ensure that the location of the archive is documented and ensure systems are in place for the retrieval and destruction of the documents.

4.5 Named Archivist:

- Is responsible for the management of archived boxes and the oversight of external archives but does not take responsibility for completion of the archive checklist nor the physical preparation of archive boxes.
- At the University of Hertfordshire, the named Archivist is the University Records Manager.

5.0 PROCEDURE

5.1 Preparation for Archiving

5.1.1 Clinical trial related documentation can only be archived once the trial has been officially completed and all files are reconciled and complete.

5.1.2 Ahead of archiving, a Clinical Trial Monitor/Delegated Individual (DI) will organise a close out visit (see gSOP-21) and make sure the study database has been locked (see gSOP-46). Where documents require archiving before the study database is locked, e.g. a large longitudinal study, essential documentation on earlier study participants who have completed that trial may be archived off site to deal to preserve space then recalled to gain access.

5.1.3 Once all issues are resolved following the close out visit(s) a Declaration of End of Trial form should be submitted by the CI/DI to the CTSN, R&D, REC and MHRA where appropriate (see gSOP-21).

5.1.4 Once the End of Trial Acknowledgement Letter has been received, this signifies the end of all close out and regulatory reporting activities. If archiving is delegated to the CTSN, the End of Trial Declaration letter will be issued by a member of the CTSN.

5.1.5 Documents can be archived from the date on the End of Trial Acknowledgement letter. The retention period is calculated from the date of End of Trial on the letter.

5.1.6 Prior to archiving documents, the study protocol and related contracts/agreements are to be referred to, to ensure that the documents are archived in accordance with Sponsor requirements.

5.2 Documents to be archived

5.2.1 Essential documents are those which individually and collectively permit evaluation of the conduct of a trial and the quality of the data produced.

5.2.2 All essential documents retained within the TMF and/or ISF should be archived alongside the Case Report Forms (CRFs) and the Pharmacy Clinical Study Files. The CI/DI is responsible for archiving the TMF. For single centre trials where the TMF and ISF have been maintained as a combined file, they can be archived together.

5.2.3 Any essential trial documentation that has been kept elsewhere e.g. pharmacy, statistics, randomisation, laboratory or data management should be returned to the CI/DI after the study is finished so that all documents can be archived together.

5.2.4 The participating site(s) ISF should not be sent to the Sponsor organisation. The ISF can be archived once the site has been informed that the trial is closed. Participating sites are responsible for their own archiving in line with the Participating Site Agreement and their own Trust requirements. Site archiving arrangements should be recorded, and a copy sent to the CTSN (uhclinicaltrialsupportnetwork@herts.ac.uk) for their records.

5.2.5 A list of documents to be archived can be found in ICH GCP E6 Section 8. This list is not exhaustive and is for guidance purposes only.

5.3 Retention times of essential documents

5.3.1 Essential documents must be retained (archived) for sufficient periods to allow for audit and inspection by regulatory authorities and should be readily available upon request.

5.3.2 For trials not intended to support marketing authorisation applications (or variations), documents contained, or which have been contained in the Trial Master File (TMF) are retained for 5 years after the completion of the trial. Medical files of trial participants must be retained for 5 years after the conclusion of the trial.

5.3.3 For trials intended to support marketing authorisation applications (or variations), essential clinical trial documents (including Case Reports Forms (CRFs)) other than participant's medical files, should be kept by the owners of the data:

i. for at least 15 years after completion or discontinuation of the trial,

OR

ii. at least 2 years after the granting of the last approval of a marketing application. These documents should be retained for a longer period if required by the applicable regulatory requirement(s) or by agreement with the sponsor,

OR

iii. for at least 2 years after formal discontinuation of clinical development of the investigational product.

iv. When the trial involves minors (under 18 years of age) essential documents must be retained until the youngest participant reaches the age of 22 OR for 5 years after the end of the trial, whichever the longer.

5.3.4 For non-CTIMP research, the archive time period is 5 years, unless otherwise stipulated.

5.3.5 For sponsored non-interventional trials, relevant documentation should be in accordance with the information submitted for ethical approval.

5.4 The archiving process

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

5.4.2 In line with the University records storage procedures and the archiving process map (see Appendix 2), study documents should be prepared for archiving using an archiving checklist (see TP-62) and following the below process:

5.4.3 For hard copy documents:

i. Remove plastic wallets to prevent transfer of ink “sweating” on to the plastic.

ii. Any documents which are prone to fading or wearing 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 the statement *“true representative of the original version”*).

iii. Consider if any staples should be removed – they can remain in place where degradation is not likely to impair any text.

iv. Pack the files into standard archiving boxes. Contents of any one file should ideally be packaged together.

v. Complete the Records Deposit Form, retaining a completed copy within the archiving box (See appendix 3).

vi. A signed copy of the Records Deposit Form should be sent to the records manager (dataprotection@herts.ac.uk) . A copy should also be sent to the CTSN (uhclinicaltrialsupportnetwork@herts.ac.uk).

vii. A unique barcode will be provided for each box and an index created on the University Document Management System (DMS) for tracking and retrieval purposes.

viii. When archiving is complete, and the boxes are ready to be collected liaise with the UH records manager to arrange delivery to the UH offsite storage facility.

ix. The UH records manager will ensure that the archiving database, which is the Document Management system, is updated.

5.4.4 For electronic documents i.e. eTMF

i. Request for a project folder to be set up in the Electronic Document and Records Management System (EDRMS) via edrmsupport@herts.ac.uk, providing the following information:
   a. Project code
   b. Short name of project
   c. Project start and end date
   d. Chief Investigator
   e. Access requirements, i.e. names of those requiring access to the project documents.

ii. Upload the electronic files to the EDRMS and remove from any other local or shared area. The EDRMS' audit facility will allow monitoring of access and activity. Please notify the CTSN (uhclinicaltrialsupportnetwork@herts.ac.uk) once this has been completed.

iii. If access is needed to a previously created project folder please request access using the "Request for access to Document Management" form.

5.5 Retrieval of archived documents

5.5.1 Materials that have been archived may, on occasion, need to be retrieved, e.g. for regulatory inspection.

5.5.2 Retrieval of hard copy documents

i. The CI, DI or CTSN should request the correct box or boxes through the Document Management system. The system will keep an audit of all requests and locations. The required boxes will be identified by the UH records manager who will check the requester identity and request the boxes from the offsite storage company.

ii. Once returned to the University they will be delivered to the requestor.

iii. The Document Management System will keep an audit trail of requests, requesters and delivery locations.

5.5.3 Retrieval of electronic documents

i. Contact with the CTSN should be made to find out who has access to the documents on the EDRMS.

ii. The archivist/DI should access the EDRMS to retrieve any electronic archived documents.

iii. The EDRMS' audit facility will track who accessed the information and when. In addition an email to log this activity is to be sent to the CTSN.

5.6 Return of archived boxes to storage

5.6.1 Once the requester has finished with all information in the box, they will need to put in a request for collection through the Document Management System.

5.6.2 Boxes should not be returned incomplete unless the information is to be permanently removed or destroyed. In which case, the Records Manager needs to be made aware.

5.6.3 The Records Manager will arrange for collection and return to storage.

5.7 Destruction of all archived study documents

5.7.1 The reasons for destruction of essential documents should be documented and signed by a person with appropriate authority (Sponsor, Contract Research Organisation (CRO), Investigator or Host Institution), in accordance with the study protocol requirements and Sponsor SOPs.

5.7.2 The Records Manager should be informed via an email that the information can be destroyed. The destruction date will be noted in the Document Management System and the Records Manager will get the permission of the CI, DI or CTSN before confidentially destroying the information.

5.7.3 The signed record of destruction should be retained for a further five years from the date that the essential documents were destroyed.

6. RELATED DOCUMENTS

- UH gSOP-14 Writing Research Protocols
- UH gSOP-22 End of Trial Procedures
- UH gSOP-46 Database Lock and Data Extract Authorisation
- UPR IM11 Records Management and the archiving and retention of prime documents and business records
- Request for access to Document Management form

7. APPENDICES

- Appendix 1 – Definitions
- Appendix 2 – Archiving Process Map
- Appendix 3 – Example Records Deposit Form

8. AUTHORSHIP & APPROVAL

Author

Signature **Date 23 June 2022**
Megan Smith

Pro-Vice Chancellor (Research & Enterprise) Approval

Signature **Date 16 June 2022**
Professor J M Senior

9. VERSION HISTORY/REVISIONS

Version Number	Effective Date	Reason for Change
2.0	**28th July 2022**	Review

10. AGREEMENT

Please detach and retain within <u>your training files</u>

I have read and understood the contents and requirements of this SOP (ref SOP-17-01) and accept to follow University policies implementing it.

Recipient
Signature: ……Date: …….
Name & Position: ……

Please retain copy of the signed form for your reference in your training file

Appendix 1 - Definitions

Archive
The material storage area, including its operation, necessary for the secure retention and maintenance of material.

Archive Details Form
Document which must be completed for each clinical study archived. The form contains study details, investigators details, box contents and the destruction date. A copy should be in each box archived, one sent to the CTSN and a copy, signed as receipted by the named archivist, with the research team.

Case Report Form (CRF)
A printed, optical, or electronic document designed to record all of the protocol required information to be reported to the Sponsor on each trial subject.

Chief Investigator (CI)
A registered Physician, Dentist, Pharmacist or Nurse who has overall responsibility for the conduct of the trial.

Clinical Trial
A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or control) to evaluate the effects of those interventions on health outcomes.

Clinical Trial of Investigational Medicinal Product (CTIMP)
A study that looks at the safety or efficacy of a medicine/food stuff/placebo in humans as defined by the Medicines for Human Use Regulations (2004).

Essential Documents
Essential documents are those documents which individually and collectively permit evaluation of the conduct of the trial and the quality of the data produced. Essential documents include the Trial Master File (TMF), source documents, Case Report Forms (CRFs) and the pharmacy documentation relating to the trial which should have all accountability and destruction records for the study drugs.

Investigational Medicinal Products (IMP)
A pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical trial. This includes a medicinal product which has a marketing authorisation but is, for the purposes of the trial -

- used or assembled (formulated or packaged) in a way different from the form of the product authorised under the authorisation,
- used for an indication not included in the summary of product characteristics under the authorisation for that product, or
- used to gain further information about the form of that product as authorised under the authorisation

Named Archivist
Person responsible for ensuring archiving requirements are met as required in the regulations.

Principal Investigator (PI)
A registered Physician, Dentist, Pharmacist or Nurse who has responsibility for the conduct of the trial at a host site.

Site File
Site Files are held by the PI at sites and contain copies of the essential documents, local approvals, signed consent forms and completed data forms.

Source Documents
Source documents are original documents, data, and records (e.g. hospital records, clinical and office charts, laboratory notes, memoranda, subject's diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate copies, microfiches, photographic negatives, microfilm or magnetic media, x-rays, subject files, and records kept in pharmacy, at the laboratories and at the medico-technical departments involved in the clinical trial).

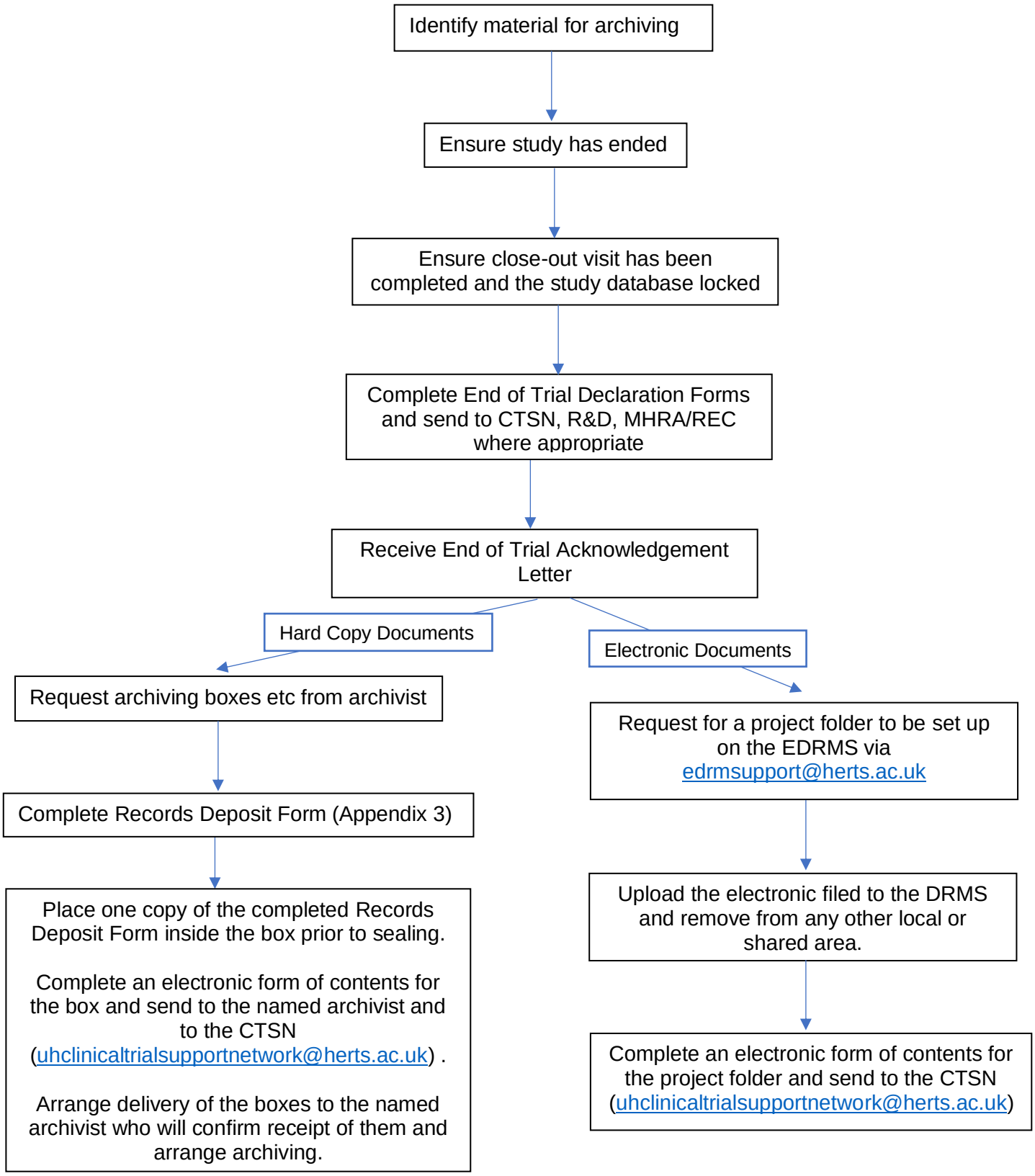
The Medicines & Healthcare products Regulatory Agency (MHRA)
UK competent authority responsible for regulation of clinical trials.

The Regulations
Medicines for Human Use (Clinical Trial) Regulations 2004 transposed the EU Clinical Trials Directive into UK legislation, as Statutory Instrument 2004 no 1031. This became effective on the 1st May 2004. An amendment to implement Directive 2005/28/EC was made to the Regulations as Statutory Instrument 2006 no 1928.

Trial Master File
The Trial Master File (TMF) will be held at the principal site by the Sponsor, Chief Investigator or at the co-ordinating centre. The TMF should contain all essential documents defined as documents which individually and collectively permit evaluation of the conduct of a trial and the quality of the data produced. A TMF should be set up at the beginning of a trial and maintained up to date throughout the trial until trial conclusion. Where electronic Trial Master File (eTMF) is used, this refers to an electronic filing system.

For trials currently running, it is recommended that Section 8 of the ICH-GCP Guideline is followed as guidance in order to meet statutory requirements. However, some of the documents listed may not be available or applicable in many non-commercial trials. The appropriate documentation will vary according to the trial and sponsor requirements.

Appendix 2: Archiving Process Map



Appendix 3 Example Record Deposits Form

An excel version of this form is available to download from HertsHub – Records Deposit Form *which should be used to facilitate completion. Further guidance can be found on in the Documents and Records Management section under Legal and Compliance. This form should then be submitted to Abi Tomlinson: (*a.tomlinson@herts.ac.uk).

I would like to deposit the following boxes:

Name:
Department/ SBU:
Location:
Contact No.

Dept Box No	Record Type	Title/Contents	Description	Date From	Date To	Destruction Date	Department/ Faculty/ School

PRINCIPAL INVESTIGATOR:	**PROTOCOL NO:** **IRAS NO:**
DATE OF ARCHIVING:	**BOX NO: (OF)**
BOX CONTENTS: **Archive until:** **(Do not destroy without Investigator authorisation)**	
SIGNATURE ……..……..…… **(CI, designated person or CTSN representative)** **NAME (PRINT): ……..……**	

Please place one copy of this form in the box prior to sealing and send a copy to the CTSN. Retain a copy of this form once receipt is acknowledged.

Acknowledgement of receipt of sealed archive box:-

Signed:……..

Name:……

Date: …../……../…….