## 1. Introduction

This Standard Operating Procedure (SOP) describes the requirements for archiving of all research sponsored by the University Hospitals of Leicester NHS Trust (UHL). Its purpose is to ensure that Trial Master Files (TMFs) for studies are readily available at all reasonable times for inspection by Regulatory Authorities or any person appointed by the Sponsor to audit the study.

Retention of the TMF (including the Investigator Site Files) for Clinical Trials of Investigational Medicinal Products (CTIMPs) and the medical records of subjects involved is a legal requirement. The Sponsor and Chief/Principal Investigator (CI/PI) must ensure that the documents contained, or that have been contained in the TMF, as well as the medical files of trial subjects are retained for at least 5 years after the conclusion of a study and that they are complete and legible. Studies where the data are used to support a marketing application have further requirements as per Directive 2003/63/EC or the prevailing relevant legislation at the time. Subjects' medical records must be retained for at least 5 years in their original format and in accordance with the maximum period of time permitted by the institution to whom they belong.

Arrangements for retention of documents for non-CTIMP studies must be appropriate to the requirements for each individual study.

## 2. Scope

This SOP applies to all research studies that are sponsored by the UHL. At the time of writing (September 2020) there are no studies sponsored by UHL which use 100% electronic TMF so this SOP refers only to paper and hybrid filing systems. NB Hybrid format refers to where both paper documents, copies of documents scanned or held electronically and electronic platforms e.g. e-CRF are used.

Electronic format refers to a dedicated 100% electronic system e.g. an electrical system being used to record and store all clinical trial information.

## 3. Definition

Clinical trial information must be stored in such a way that it can be accurately reported, interpreted and verified. The TMF is a collection of the documentation that allows the conduct of a clinical trial, the integrity of the trial data and the compliance of the trial with GCP and applicable regulatory requirements to be evaluated. SOP S-1015 UHL, Essential Documents and Trial Filing for Research Sponsored by the University Hospitals of Leicester NHS Trust, provides more information on the requirements for the TMF.

## 4. Individual Responsible for Archiving

At UHL Head of Research Operations is the named person responsible for archiving of CTIMP documentation and for ensuring that access is restricted to themselves, their delegate, auditors and inspectors. The CI is responsible for the completeness and the quality of the documentation that makes up the TMF.

## 5. Archiving Arrangements

For all studies the Sponsor will inform the investigator(s)/institution(s) in writing of the need for record retention (appendix 7). The Sponsor delegates responsibility for notifying the Head of

Research Operations, the investigator(s)/institution(s) in writing to the Chief Investigator (CI) when the trial related records are no longer needed and can therefore be archived.

The provisional arrangements and costings (if applicable) for archiving the TMF will be agreed between the CI and the Sponsor during the initial Sponsor review process. Costs for archiving are the responsibility of the CI and where possible must be included in an application for funding.

The TMF may be filed locally if suitable facilities are available or alternatively off-site through a Sponsor-approved external archiving facility.

The length of time required for archiving depends on the type of research activity. Appendix 5 provides an Archiving Guideline of required length of time.

For multicentre studies, each participating site will be responsible for archiving their Investigator Site File (ISF). The Sponsor (UHL) is not responsible for archiving participating sites' essential documents.

The Archiving Workflow in EDGE must be completed to detail the archiving arrangements. The Workflow will include: the data format (electronic and/or paper), date of archiving, the exact location of archived study data (including any relevant references e.g. Stor-a-File barcode, box numbers etc.), the expected date of destruction and the required method of destruction.

### 5.1 On Site Archiving

For all research including CTIMPs archived on site the proposed archiving area will be assessed by the Sponsor to ensure it is suitable unless the facilities and storage conditions are already known and approved by the Sponsor. This assessment must be documented using the UHL Archiving Assessment Checklist (Appendix 1). It is possible that at the start of a study facilities may not be 100% ready to be used for Archiving, but there must be a plan of action to ensure that by the time the study is ready for Archiving the facilities are fit for purpose. Each iteration of the Archiving Assessment Checklist must be saved to show progress and will form part of the TMF and audit trail.

Before the TMF is archived, it is recommended that it is checked to ensure that it is complete and that all necessary documentation has been filed. This check should be comprehensive as described in SOP S-1024 UHL.

A checklist to aid the archiving process can be found at Appendix 2. This final check will usually be undertaken by the trial manager but may also be undertaken by other appropriate personnel. Preparation for archive is expected to be completed by the study personnel.

Before archiving, the contents of the TMF should also be assessed for any records that could be disposed of (for example, duplicates) and those that may be subject to rapid deterioration and will therefore require transferring to a more robust media prior to archiving.

Patient medical records will be subject to arrangements within the NHS Organisation that owns them, but clear identification that the patient has been involved in a Clinical Trial must be evident, e.g. a sticker on the front of the records. In addition, it must be clear if the record must be retained and not destroyed before a specified date.

It is important that where centralised records have been held – for example – staff training records or CVs, that these are considered in the arrangements for archiving and retention as they may be required to be produced in addition to the TMF to demonstrate compliance.

Documentation and records from supporting services i.e. laboratories are required to be archived alongside the TMF, where appropriate.

In addition, pharmacy records and records of vendors or other agents of the Sponsor also form part of the TMF and appropriate arrangements must be made to ensure this documentation is stored appropriately for the required length of time and is retrievable if required.

The ultimate responsibility for the documents to be retained by the investigator or institution resides with the investigator or institution. If the investigator becomes unable to be responsible for their essential documents (for example due to retirement) the Sponsor should be notified in writing and informed to whom the responsibility has been transferred.

Where electronic systems for activities such as data management (e-CRFs), statistical analysis and storing scanned copies of documents are being utilised, the electronic data /documentation needs to be retained. The data may be on a server or transportable media. It is recommended that more than one copy of the data is retained (e.g. a back-up server or back up media stored in a separate location) Consideration should be given to storing the data in differing formats on different types of media or even on the same media from different manufacturers.

Access to archived data must be suitably restricted, either by user access levels to the archive area of a server or by controls to access the storage area where the media are retained. Additionally the electronic documents or data that have been archived must be protected from unauthorised changes to maintain authenticity.

It is important to consider the most appropriate media for archiving electronic documentation. The selected medium should be unlikely to become obsolete during the archiving period. Archived data should be transferred to a newer or more appropriate media if necessary. Consideration must also be given to the software/hardware requirements in order to maintain readability of the data for the archive period.

Where electronic data is produced by a Clinical Trials Unit (CTU), the responsibility for archiving this data is delegated to the CTU.

### 5.2 Off Site Archiving

For all research including CTIMPs archived off site and not using the Sponsor approved facility (Stor-a-File), the proposed archiving area will be assessed by the Sponsor to ensure it is suitable unless the facilities and storage conditions are already known and approved by the Sponsor.

This assessment must be documented using the UHL Archiving Assessment Checklist (Appendix 1). It is possible that at the start of a study facilities may not be 100% ready to be used for Archiving, but there must be a plan of action to ensure that by the time the study is ready for Archiving the facilities are fit for purpose. Each iteration of the Archiving Assessment Checklist must be saved to show progress and will form part of the TMF and audit trail.

Before the TMF is archived, it is recommended that it is checked to ensure that it is complete and that all necessary documentation has been filed. This check should be comprehensive as described in SOP S-1024 UHL.

A flow chart detailing the process is available at Appendix 3.

### 5.3 Preparation for archiving

A Checklist to aid the archiving process can be found at Appendix 2. This final check will usually be undertaken by the trial manager but may also be undertaken by other appropriate personnel. Preparation for archive is expected to be completed by the study personnel.

Before archiving, the contents of the TMF should also be assessed for any records that could be disposed of (for example, duplicates) and those that may be subject to rapid deterioration and will therefore require transferring to a more robust media prior to archiving.

Patient medical records will be subject to arrangements within the NHS Organisation that owns them, but clear identification that the patient has been involved in a Clinical Trial must be evident, e.g. a sticker on the front of the records. In addition, it must be clear if the record must be retained and not destroyed before a specified date.

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The ultimate responsibility for the documents to be retained by the investigator or institution resides with the investigator or institution. If the investigator becomes unable to be responsible for their essential documents (for example due to retirement) the Sponsor should be notified in writing and informed to whom the responsibility has been transferred.

### 5.4 Arranging for archiving

Storage is available at Stor-a-File, Wenlock Way. Leicester. LE4 9HU (part of Leicester Micro Bureau Limited (LMB)) who have NHS relationships throughout England and Wales. They offer a fully comprehensive security system together with every possible retrieval and storage requirement, both now and in the future. Bar coding at the point of collection, together with full tracking facilities exist to ensure knowledge of wherever a particular set of data is at a particular time.

In order to request boxes for storage at the facility please complete FORM A.

All related costs in relation to the archiving process are at the Chief Investigator's expense e.g.:

- Boxes – minimum of 10
- Archiving to Stor-a-File
- Storage
- Retrieval

Relevant invoices will be sent to the billing address given on the attached form(s) and must be paid promptly.

### 5.5 Sending files to storage

A designated individual within the research team must take responsibility for the process for a specific trial. The Research & Innovation (R&I) Office must be contacted at the outset for details of current costings. Boxes and Barcodes may then be ordered on the attached 'Form A-Request for Boxes & LMB Barcodes for Archiving'

The R&I Office will contact Stor-a-file to place the order and arrange delivery of printed Barcodes and boxes to a specified location. A minimum of 10 boxes and Bar Codes will be provided at each request.

Following receipt of the boxes and LMB barcodes and archive completion, the boxes must be filled in accordance with Appendix 2. Once the boxes have been checked by the Research Manager, a FORM B must be completed and forwarded to the R&I office.

A copy of all 3 sections of the form - numbered FORM B (1), (2) & (3) should be retained for your records and a copy of the sheet noting the LMB barcodes and contents of the boxes should be placed with the boxes to be archived.

The R&I Office will then contact Stor-a-file who in turn will arrange the date and time of collection with the contact person named on the form.

### 5.6 Change of ownership/responsibility

There may be occasions where change of ownership may be required e.g. Investigators may retire; CTU/external vendors may close or be acquired by other organisations such that the responsibility for the TMF is transferred. The Sponsor must be informed of any transfer of ownership. This is to ensure that the TMF remains available for inspection for the required retention time.

### 5.7 Retrieval of Archived documents

The R&I Office will facilitate all requests for retrieval of Archived documentation. Only authorised personnel from the R&I Office are permitted to request retrieval. A test of the system is made annually.

In order to request retrieval of archived documents, FORM C must be completed and sent to the R&I Office using RIAdmin@uhl-tr.nhs.uk. On receipt the request will be sent to Stor-a-File with details of delivery point and responsible person.

Once a request has been made, Stor-a-File will scan the stated LMB Barcode permitting 'exit from store'. The box can be tracked en route to stated location and on reaching its destination the same mechanism is used to identify that the box is now at that location. This ensures that the LMB database identifies retrieval from store and the date and time the box arrived at the requested location.

On arrival of the box, the receiver must notify the R&I Office of arrival. The R&I Office will then return Form C to the requester. The box(s) can be logged out for a period of one month only for Investigator File/Case Notes and therefore must be returned within a maximum of one month unless express arrangements have been made with the Head of Research Operations, in advance for the documentation to be retained out of storage for longer periods.

For return, Part 2 of the original FORM C must be completed and forwarded to the R&I office who in turn contact Stor-a-file regarding collection. It is essential that the documents retrieved are returned in full and R&I are informed of completed collection.

A flow map detailing the process is available at Appendix 4.

### 5.8 Destruction

It is the responsibility of the Sponsor to alert investigators when the archiving period has expired for their study. (Appendix 6)

It is the responsibility of the investigator/ research team to complete the destruction of study data, as per UHL Waste Management Policy and Guidance Where the investigator/ research team is no longer employed by the trust, the relevant CMG or research group will be contacted to complete the destruction process.

For multicentre studies, It is the responsibility of the CI/PI/Delegated individual to ensure that all sites receive and complete Form D Part 2 and Part 3(where applicable). Each site should retain a copy of the form and file in the Investigator Site File with a copy being provided for the Trial Master File.

Upon expiry of the archiving period, the Sponsor will email the investigator with a copy of Form D and instructions on the destruction process. The Sponsor will require confirmation of receipt of the email within 10 working days.

Where electronic documents have been used, the Investigator will ensure that all copies of archived study data held in any format i.e. Individual devices, hard drives, CD, USB sticks and computer servers are permanently deleted as soon as the study has been reported and the participants notified of the results.

If study data has been archived with Stor-a-File, Form D Part 1 will outline the details of the team completing destruction, and to whom the archived data will be sent. This needs to be returned to the R&I Admin team, who will contact Stor-a-File to retrieve the data. If study data was not archived with Stor-a-File (e.g. if onsite local research storage is available) then this must be communicated to the Sponsor via email, and Form D Part 1 does not need to be completed.

Completion of Form D Part 2 is mandatory for all UHL sponsored studies, and is not dependent on the location of archiving. Form D Part 2 and Part 3 (where applicable) confirms destruction of the study data; this must be sent back to the Sponsor once the destruction has been completed. The Sponsor will only consider the Archiving-Destruction process complete upon receipt of Form D Part 2/3.

## 6. Responsibilities

| | Responsibility | Undertaken by | Activity |
|---|---|---|---|
| 1 | UHL Head of Research Operations & CI | UHL Head of Research Operations & CI | Agree the provisional arrangements for archiving and the costings (if any) during the Sponsor review process. |
| 2 | UHL Head of Research Operations | UHL Head of Research Operations or delegate | Perform and document an assessment of proposed on-site archiving area if it is not already known to be suitable. |
| 3 | UHL Head of Research Operations | UHL Head of Research Operations or delegate | Responsible for Archiving TMFs. |
| 4 | CI | CI | Responsible for costs of archiving using an external archive facility where required |
| 5 | CI | CI or delegate | Responsible for the contents of the TMF. |

| | Responsibility | Undertaken by | Activity |
|---|---|---|---|
| 6 | CI | CI | Appoint another person responsible for the TMF and inform the Sponsor if they are no longer able to be responsible. |
| 7 | CI | Monitor or other appropriate individual | Perform a TMF Archiving Readiness check prior to archiving. |
| 8 | UHL Research & Innovation | UHL Research & Innovation Admin | Inform investigator of expiration of archiving period, advise that destruction needs to be completed. |
| 9 | CI | CI or delegate | Complete destruction per SOP S-1029 & Form D |

## 7. Supporting Documents and Key References

SOP S-1029 Appendices 1, 2, 3, 4, 5, 6 & 7

SOP S-1029 Appendix Forms A, B, C & D

SOP S-1015

SOP S-1024

## 8. Key Words

Research, Innovation, Volunteers, Participants, Trials, Archiving, Destruction, Stor-a-file, TMF, ISF, CTU, Storage, Retrieval, CTIMP, Non-CTIMP

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This table is used to track the development and approval and dissemination of the document and any changes made on revised / reviewed versions

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