# University of Leicester and University Hospitals of Leicester NHS Trust joint Research Support Office Standard Operating Procedures

## University of Leicester (UoL) Research Governance Office

## SOP S-1015 UoL

## Management of Essential Documents and Trial Filing for Research Sponsored by the University of Leicester


Office Base

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**Version 6.0 September 2023**

**Effective Date: September 2023**


This SOP will be implemented in line with this document's effective date for all UoL Sponsored research still in set up. For active clinical research that is already in the recruitment phase (or further) at the time of implementation, this SOP must be implemented within 3 months of the effective date.

Please note the appendices associated with this SOP may be subject to interim changes. Please ensure that appendices are downloaded from the RGO webpages prior to use to ensure the latest version of the document is being used. For active studies there is no requirement to update appendices to the latest version.

## 1.0 Introduction & Scope

This Standard Operating Procedure (SOP) describes the requirements for the retention of essential documents in the Trial Master File (TMF) or Investigator Site File (ISF) for all staff conducting research sponsored by the University of Leicester (UoL).

The essential documents relating to a research study are those documents which individually and collectively enable both the conduct of the research study and the quality of the data produced to be evaluated. These documents serve to demonstrate compliance with the standards of Good Clinical Practice (GCP) and with all regulatory requirements.

All clinical information must be recorded, handled and stored in such a way that it can be accurately reported, interpreted and verified, while the confidentiality of the study subjects remains protected.

## 2.0 Trial Master File (TMF)

There should be one TMF per study and this should be stored and maintained at the lead research site or lead coordinating centre (i.e., at a Clinical Trials Unit). The TMF must be prepared prior to study initiation and be actively maintained and updated until the study is formally closed. When it becomes available, the final report must be filed in the TMF. A well-kept TMF can help with efficient study management and can facilitate the reconstruction of the conduct of the study during the audit/inspection process.

Consideration should be given to the TMF being a stand-alone set of documentation that does not require additional explanation as regulatory and/or competent authority inspections often take place some years after study completion when personnel involved may no longer be available.

Where a risk-adapted approach is being followed, some documents listed in the guidance may not be in the TMF-for example-IMP temperature storage records. If this is the case the rationale for this must be documented in the trial risk assessment.

There are a variety of TMF Contents List to choose from depending on whether the study is a Clinical Trial of an Investigational Medicinal Product (CTIMP), whether the trial does not involve investigational medicinal products (non-CTIMPs), whether it is single or multi-site and whether or not it is management by an external coordinating centre e.g. a Clinical Trials Unit (CTU). These contents lists provide guidance on the essential documentation which must be included within a TMF and have regard for EudraLex Volume 10 (and for clinical investigations of medical devices for human subjects, ISO 14155:2020). The documentation referred to in the contents lists will form part of the TMF but not necessarily form the entire TMF. Where documents are not available within the TMF, a note to file documenting the location and access requirements for the documents must be in place. At the end of a study you must ensure that any documentation that were stored outside of the main TMF (i.e., temperature logs, sample tracking logs), are archived within the TMF or will remain accessible for the duration of the archiving period.

For multi-site studies, copies of relevant documents should be kept at each participating site in an **Investigator Site File** (ISF), for further details refer to section 3.0 below.

### 3.1 Maintaining an electronic TMF (eTMF)/eISF

At the point of publishing this SOP the UoL does not have an approved IT solution for the maintenance of an eTMF/eISF. If a site plans to maintain an eTMF/eISF, consideration

needs to be made as to security and access arrangements as well as archiving arrangements at the end of the study. The eTMF/eISF should be stored in a complete state, and crucially, should be stored in such as a way that it is possible to fully rebuild if required, and in a form which will not deteriorate (e.g. using technology that may become outdated during the archiving period). Consideration also needs to be made in relation to appropriate safeguards in the event of document corruption, preventing unauthorised access and maintaining retention schedules.

Where possible the filing structure should reflect the TMF/ISF contents lists (Appendix 4-11) and documents should ideally be named appropriately to fall in sequential order and allow ease of identification.

Example naming structure:

- 2023-01-01_STUDY ID_REC VA
- 2023-01-02_STUDY ID_REC FO
- 2023-01-03_STUDY ID_RESEARCH AGREEMENT v1.0
- 2023-01-04_ STUDY ID_SA01

In the event of a monitoring visit or inspection, the team must be prepared to provide the TMF/ISF in paper format at the request of the Sponsor/inspector.

## 3.0 Investigator Site File (ISF)

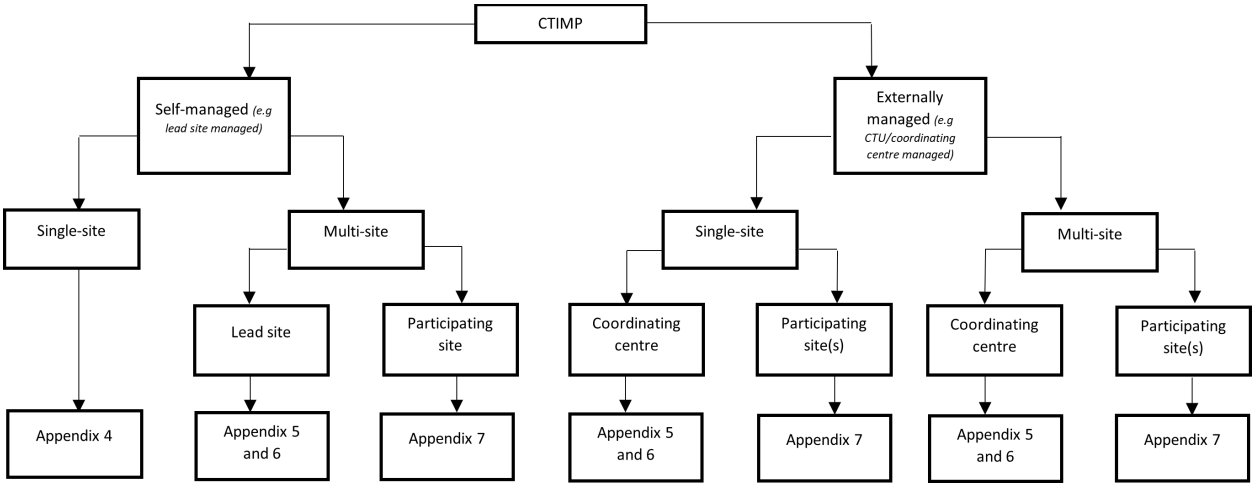
The ISF contains essential documents relating to a specific investigator site. An ISF contents list is available for both CTIMPs and non-CTIMPs.

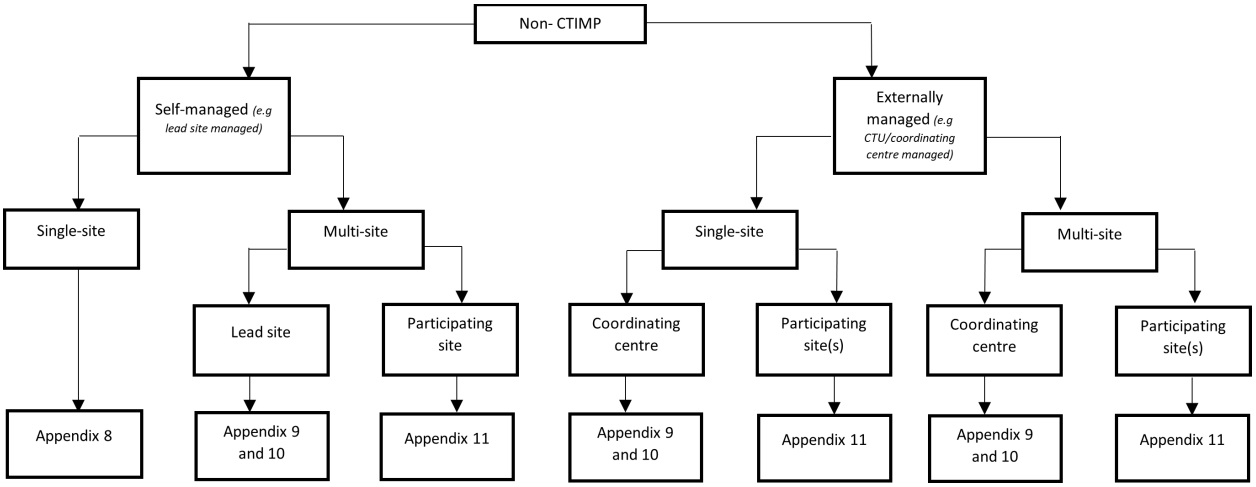
## 4.0 TMF/ISF Maintenance

The TMF and ISF must be ‘inspection ready’ at all times.

It is a legal requirement that researchers retain the TMF/ISF and all other study-related documentation (e.g. case report forms (CRFs) and source data) for a minimum of 6 years following completion of a non-CTIMP. For CTIMPs, or research where the data are used to support a marketing authorisation, the TMF/ISF and other study related documentation should be retained for at least 25 years after completion or discontinuation of the study, or for at least 2 years after the granting of the last marketing authorisation in the European Community. Please ensure that you are aware of the appropriate retention period.

If you are unsure which contents list you require, please refer to the decision tree(s) below:




## 5.0 Single site studies

For a single site study, where the lead site is also the coordinating centre it is acceptable for the TMF and ISF to come together as one.

Where for example a CTU is acting as the coordinating centre, A TMF will be maintained by the coordinating centre and the ISF should be maintained by the site.

## 6.0 Multi-site studies

In the case of multi-site studies, the lead site/coordinating centre must maintain the TMF in addition to a separate site-specific file(s) (SSF), or section(s), containing local-level documents relating to each of the participating sites. A separate Site Specific contents list is available within the Appendices of this SOP and should be duplicated and maintained per each participating site. Each participating site must maintain its own ISF using the ISF contents list.

## 7.0 Procedure

### 7.1 Responsible Personnel

The Chief Investigator (CI) and/or Principal Investigator (PI) are responsible for establishing and maintaining a TMF/ISF (respectively) for every study but may delegate these activities to a research team member. This must be recorded on the Delegation of Authority & Signature Log.

### 7.2 Storage of the TMF/ISF

The TMF/ISF must be stored in a secure location, preferably in a lockable cabinet, with access limited to relevant members of the research team/coordinating centre. The Investigator must be able to demonstrate that all reasonable measures have been taken to ensure its security and to protect confidentiality and data integrity. It may not be possible or practical for all documentation to be stored in one file or location. e.g. where a separate pharmacy file is created for the purposes of study management, this remains part of the TMF/ISF but can be stored in Pharmacy. This can either be amalgamated into the TMF/ISF or archived separately at the end of the study. Where documents are stored separately, a file note should be created detailing their location. Where the TMF/ISF comprises of more than one file, we recommend that the spines of the files are clearly labelled (e.g Study name/ID, PI name, File X of Y, archiving duration and Sponsor contact details).

### 7.3 Version Control

All documents must be version controlled, signed and dated where appropriate. All previous versions of documents must be retained, but marked as superseded. To superseded a document you should;

- Strike a single line diagonally across the front page of the document
- Write 'superseded by…' and add the version and date of the updated document i.e. Superseded by v2.3 01/01/2023
- Initial or sign and date next to the annotation

### 7.4 Document Trackers

#### 7.4.1 Version Control Tracker

A Version Control Tracker should be utilised (Appendix 3 (a or b)) which details all the approved study documents, their different versions and dates (where applicable) and dates of approval and/or implementation.

#### 7.4.2 Participant Identification Centre (PIC) Site Tracker

Where relevant, we recommend the use of a PIC Site tracker (Appendix 12) to maintain a list of all the PIC sites involved in a study and the dates agreements were signed and approvals granted.

#### 7.4.3 Personnel Tracking Log

We recommend the use of an investigator tracker (Appendix 13) to maintain a list of all the individuals involved in a study, dates of relevant training e.g. GCP/CV/consent/SOP read logs and dates of document expiry.

### 7.5 Vendors/Third Party Contractors

Copies of fully executed contracts and any formal technical agreements/plans detailing delegated functions between the Vendor and Sponsor must be maintained within the TMF. Copies of all documentation generated by either party relating to the agreements and delegated functions must also be present.

### 7.6 Archiving

Archiving of the TMF/ISF and all associated essential documents must be undertaken as per SOP S-1024 UoL Process for Study Close Down for Research Sponsored by UoL and SOP S-1032 UoL Archiving of Essential Documents for Research Sponsored by UoL.

## 8.0 Non compliance

Where non-compliance and/or areas of concern are identified, this may be escalated in accordance with the Non-compliance SOP (S-1016) or may result in the issue of a Correction Action/Preventative Action (CAPA) Plan.

## 9.0 Responsibilities

| Responsibility | Undertaken by | Activity |
|---|---|---|
| Chief Investigator/Principal Investigator | Chief Investigator/Principal Investigator | Establishing the TMF/ISF at the beginning of the study |
| Chief Investigator/Principal Investigator | Chief Investigator/Principal Investigator | Maintaining the TMF/ISF during the life of the study. |
| Chief Investigator/Principal Investigator | Chief Investigator/Principal Investigator | Ensuring the safe storage of the TMF/ISF at all times. |
| Chief Investigator/Principal Investigator | Chief Investigator/Principal Investigator | Ensuring the TMF/ISF is archived as per the approved protocol and per SOP S-1024 and S-1032. |

## 10.0 Development and approval Record for this document

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

| Author | Job title | Reviewed by | Approved by | Date approved |
|---|---|---|---|---|
| Cat Taylor | Head of Research Governance | UoL Research Sponsorship Management and Operation Group (RSMOG) | Professor Nigel Brunskill  | 31 August 2023 |

## 11.0 Review Record

| Date | Issue Number | Reviewed By | Description Of Changes (If Any) |
|---|---|---|---|
| Oct 2013 | 2 | Wendy Gamble | Version 1 amended following review of Sponsor processes. Now version 2 |
| Feb 2014 | 3 | Wendy Gamble | Version 2 amended to include essential documents, document renamed accordingly (was previously Creating and maintaining a trial master file or investigator site file for research sponsored by UoL). Now version 3 |
| June 2015 | 4 | Wendy Gamble | V 2 updated on front page and reformatted. Now v4 |
| Nov 2016 | 5 | Diane Delahooke | Logo changed. Appendices updated for HRA. ISF Contents updated for HRA and brought in line with UHL. |
| Sept 2021 | 5.1 | Cat Taylor | Administrative changes |
| September | 6.0 | Cat Taylor | Administrative changes |

| Date | Issue Number | Reviewed By | Description Of Changes (If Any) |
|---|---|---|---|
| 2023 | | | Information about eTMF maintenance.<br>Addition of TMF/ISF index decision tree<br>Streamlining of wording to reduce repetition<br>Removal of original CTIMP and non CTIMP TMF/ISF Index Appendices (Appendix 1&2)<br>Addition of the following new appendices and guidance on where they should be used;<br>• Appendix 4 & 7 CTIMP and non CTIMP Single Site TMF Contents List<br>• Appendix 5 & 9 CTIMP and non CTIMP Multi-Site TMF Contents List<br>• Appendix 6 & 10 CTIMP and non CTIMP Site Specific File Contents List<br>• Appendix 7 & 11 CTIMP and non CTIMP Investigator Site File Contents List<br>• Appendix 12 PIC site tracker<br>• Appendix 13 - Personnel training tracking log<br>• Appendix 3b - Version control tracker excel spreadsheet |