Research Governance Office Sponsorship Standard Operating Procedures

Management of Essential Records

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1.0 Introduction and Scope

This Standard Operating Procedure (SOP) outlines the procedures for the compilation, organisation, maintenance, and archiving of essential records generated throughout the lifecycle of a research project (referred to as 'trial' hereafter) sponsored by the University of Leicester (UoL).

Essential records are the documents and data (and relevant metadata), in any format, associated with a trial that facilitate its ongoing management and collectively allow the evaluation of the methods used, the factors affecting a trial and the actions taken during the trial conduct to determine the reliability of the results produced, and the verification that the trial was conducted in accordance with GCP and applicable regulatory requirements.

1.1 Trial Master File (TMF)

As per the CI Roles and responsibilities document, the CI is delegated the task of creating and maintaining the TMF. The CI may further delegate this via the Delegation of Activities log (See SOP S-1010). The TMF provides a record of a trial as a whole and includes data sets, statistical analysis and records of activities carried out by third party vendors. It must clearly demonstrate regulatory compliance, data integrity, decision-making, issue management, and trial related activities.

1.2 Investigator Site File (ISF)

The ISF is a set of essential records relating to each individual trial location. The PI is delegated the task of creating and maintaining the ISF. It contains location-specific records that show how the trial was conducted at that location, and demonstrates compliance with trial, regulatory and local requirements.

2.0 TMF and ISF Indexes

TMF and ISF Indexes are available for download from the Sponsor SOP webpages (SOP S-1015). The CI/PI is responsible for ensuring the correct version is used.

The TMF Index is mandated for UoL Sponsored and managed trials. For trial locations, the use of the ISF Index is preferred, however, it is acknowledged that host locations may require use of their own Index. In such cases, the CI/PI must ensure both indexes are compared, and that all essential records required by the Sponsor's Index are included within the location ISF.

The UoL Indexes comply with Appendix C of ICH GCP E6 (R3), which provides further guidance on what records should be considered essential and therefore require retention.

3.0 Creation and Maintenance of the TMF and ISF(s)

The TMF and ISF(s) should be in place prior to the start of the trial, they must be accurately and contemporaneously maintained, and readily available for inspection throughout the entire lifecycle of a trial and its retention period.

Essential records may originate in paper or electronic formats. Some essential records will always be electronic (i.e., Electronic Data Capture, will always generate electronic outputs which form part of the essential records set and even if printed, their source (and metadata) remains electronic).

A full eTMF/eISF may be used, provided it is a validated system that meets all regulatory requirements for document control, contemporaneous filing, accessibility, and audit readiness (e.g., a cloud-based solution such as Florence).

As the UoL does not have a validated system for maintaining a full eTMF, a hybrid TMF is recommended. A hybrid TMF utilises both paper-based and electronic formats to manage study records. Simple electronic storage locations (e.g., shared drives such as the R Drive) do not constitute an eTMF but may form part of a hybrid TMF record storage. The electronic filing structure of a hybrid TMF should mirror the TMF index and documents must be named in a clear sequential manner to support ease of identification and retrieval. An eTMF index has been created by the RGO and is available upon email request (rgosponsor@le.ac.uk).

Guidance of the preferred style of naming electronic documents is available here (UoL log in required).

To maintain a complete and reliable TMF, the location and format of each essential record must be clearly documented either within the relevant 'location' column of the TMF index, a 'Note to File' or in the TMF plan.

Research locations may use a hybrid ISF if they comply with the above, otherwise paper is recommended.

In the event of a monitoring visit or inspection, the investigator must ensure that appropriate access to the eTMF or eISF is available to the monitor or inspector. If electronic access cannot be provided, the investigator must be prepared to provide the TMF or ISF in paper format upon request of the Sponsor or Inspector.

For CTIMPs, it is expected that investigators, and any individual or organisation that the sponsor delegates trial related activities to, have due regard to the expectations contained in the MHRA GXP data integrity guidance.

3.1 Managing electronic records

Electronic records must be stored in a state and format that allows for full reconstruction. Systems must maintain audit trails, metadata, and ensure long-term readability. Migration to new formats must be validated and documented. Where certified true copies are created, scanning processes must be verified to ensure authenticity and completeness, including relevant metadata, where applicable.

Records should not rely upon outdated or unsupported technologies. Appropriate safeguards must be in place to prevent document corruption and unauthorised access. Compliance with retention schedules is required.

3.2 Version Control

All documents must be version controlled. Previous versions must be retained and clearly marked as superseded.

Guidance of the preferred style of superseding is available here (UoL log in required).

Guidance on the preferred style of version control is available here (UoL log in required).

3.3 Tracking Logs

Throughout the TMF and ISF indexes, references are made to various trackers that support regulatory compliance, data integrity, and operational efficiency.

The table below provides an overview of some of the available trackers and their intended use:

Tracker	Use
Document Version Control Tracker	Tracks changes to documents, including version numbers, dates of updates, approvals, and implementation.
Participant Identification Centre (PIC) Tracker	Tracks all PICs contributing to trial location, including dates of signed agreements and approvals.
Investigator Training Tracker	Records all study staff at each trial location, including training completion dates (e.g., GCP, CV, consent, SOP read logs) and expiry dates.
CRF Tracker	Tracks updates to Case Report Forms (CRFs), including version history, approval dates, and implementation dates

3.4 Verifiable Signatures

A verifiable signature is a handwritten or electronic signature that can be independently confirmed as authentic, providing clear evidence of who signed, when they signed, and assurance that the document has not been altered since the signature was applied.

For electronic signatures this requires the signature to be supported by secure user authentication, audit trails, and associated metadata that allow the confirmation of its validity and integrity. Electronic signatures can be applied to essential records provided they are obtained via a validated and regulatory compliant platform (i.e., Adobe Acrobat Sign, DocuSign). A scanned handwritten signature may be applied only if it is accompanied by an email from the signer confirming its authenticity. However, this method should be considered as a last resort and an exception rather than standard practice.

4.0 Storage of the TMF and ISF

Regardless of the format, all essential records must be must be stored in a secure location, with access limited to appropriate and delegated members of the research team.

The TMF should be managed and stored at the CI's institution and coordinating centre (i.e. UoL) unless TMF management has been formally delegated to a third-party (e.g. a Clinical Trials Unit). Elements of the TMF may be stored with other delegated third-parties during the conduct of a trial, this must be documented within the location column of the TMF Index or detailed in the TMF plan.

The ISF(s) should be maintained and stored at the trial location(s). A ISF contains participant identifiable information and should not be moved from the trial location.

5.0 TMF Plan

During the conduct of a study, certain components of the TMF may be maintained and stored by third party vendors such as database providers, laboratories, or other delegated organisations. The location and format of all such records must be clearly documented.

A TMF Plan can be used to describe the location, format, access arrangements and responsibilities for all essential records held within the TMF and ISF(s) for the entire lifecycle of the study to ensure full oversight, traceability, and inspection readiness. Where used, it should be regularly reviewed (at least annually) and updated whenever changes occur to ensure a complete and accurate record is maintained.

The implementation of a TMF plan is mandated for all CTIMP and Medical Device studies, and is recommended for non-CTIMPs. A TMF Plan template is available for download from the Sponsor SOP webpages (SOP S-1015).

6.0 Archiving

Non-CTIMPs essential records must be retained for a minimum of 6 years as per UoL policy.

CTIMP retention periods are defined by the Clinical Trial Regulations. Generally, records should be kept for at least 25 years after the trial ends, but this may be longer if data is required to support a marketing authorisation or the research involves children. Some funders may also specify their own archiving requirements. It is the responsibility of the trial team to ensure they are aware of, and comply with, the applicable retention period.

During trial setup, it is important to carefully assess the archiving requirements for all TMF components and, for electronic records, determine how access will be managed throughout the archive retention period.

Key considerations include:

- Ensuring access is removed for all individuals except the designated owners of the archived records

- Maintaining clear ownership of the files for the full archive duration so information remains accessible for audits and inspections
- Protecting records from being altered or unintentionally deleted during the retention period

At the end of the trial, essential records held by third-parties should be collated into the TMF ensuring completeness and long-term accessibility. Any transfer of records must preserve their integrity and electronic records should meet standards for authenticity and reliability. Where transfer is not practicable/possible assurances must be provided that records will be retained and accessible for the full duration of the required archiving period. The TMF plan/TMF Index should be updated to provide an accurate record.

The TMF must be securely stored, with controlled access, and protection against unauthorised alteration or destruction of archived records.

Archiving of the TMF must be agreed with the Sponsor and carried out in accordance with the Sponsor Archiving SOP (S-1032).

Essential records held in the ISF should remain at the trial location. Archiving of the ISF must be agreed by the Sponsor but is the responsibility of the host location and must follow local SOPs.

7.0 Non compliance

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

8.0 Development Record

The table below summarises the revisions introduced in this version. Full historical change records are available within archived SOP versions.

Date	Version Number	Description Of Changes (If Any)
April 2026	7.0	• Removal of Office Address • Major revisions to clarify; • The differences between a TMF and ISF and who is responsible for each. • The requirements for the creation, maintenance, storage and archiving of the TMF and ISF • Clarification of the content of the TMF and ISF with particular attention paid to electronic data capture and statistical analysis • Introduction of a TMF Plan to specify the location of all essential records throughout the active and archive phases of the study.

Date	Version Number	Description Of Changes (If Any)

		• Removal of responsibilities table as responsibilities are laid out within the body of the SOP.
		• Removal of full historical SOP review record; only the latest approved revision is now displayed, with prior versions retained in the document archive.
		• Revisions to the following appendices to clarify the essential records required within the TMF and ISF.
		  ○ Appendix 5
		  ○ Appendix 7
		• Removal of the following appendices as these are replaced by appendix 5 and 7; Note: there are no longer separate CTIMP and non CTIMP or single and multi-site indexes.
		  ○ Appendix 4 CTIMP single site TMF Contents list
		  ○ Appendix 6 CTIMP Site Specific file contents lists
		  ○ Appendix 8 non CTIMP single site TMF Contents list
		  ○ Appendix 9 non CTIMP TMF contents list.
		  ○ Appendix 10 CTIMP Site Specific file contents lists
		  ○ Appendix 11 non CTIMP ISF contents list.
		• Appendix 13 – Personnel Tracking Log. This has been revised and added as an appendix to SOP S-1020.