STU-SOP-TM-002 – Standard Operating Procedure on Trial Master Files

1. Purpose

This Standard Operating Procedure (SOP) describes the procedure of compiling and maintaining a Trial Master File (TMF) for trials, quantitative and qualitative studies. Consideration is given to the regulatory requirements for Clinical Trials of Investigational Medical Products (CTIMPs) and device trials.

2. Background

The TMF will include all sponsor and trial-specific documents which are necessary to enable the conduct of the trial and to ensure the quality of the data meets relevant applicable standards.

The TMF evidences whether the trial is, or has been, conducted in accordance with Good Clinical Practice (GCP) or applicable regulatory requirements.

The TMF must be organised in a way that facilitates management and oversight of the trial.

In a blinded/masked trial there will be a formal documented process to control the unblinding of the research team.

3. Roles and Responsibilities

The **Sponsor** retains responsibility for the oversight of the TMF. The Sponsor usually delegates management responsibility for the TMF to the Chief Investigator (CI).

The **Chief Investigator (CI)** is responsible for the preparation and maintenance of the TMF. This role is usually delegated to the Trial Manager.

The **Trial Manager (TM)** must ensure that the TMF contains all documents essential to that trial prior to its commencement and that the research team is using the current approved versions of the documents at all times.

For blinded trials, the **unblinded trialist(s)** must ensure that an unblinded TMF contains all documents essential to that section of the TMF and that they maintain security from the wider research team until access is agreed by the Trial Steering Committee (TSC) and database lock has occurred.

The **Trial Steering Committee** (TSC) will agree which roles /people should be unblinded.

Where the TM is not based in STU, all necessary documents in accordance with STU delegated responsibilities will be held within STU files. A file note will be in place to notify where the main TMF is held.

External use of SOP: this SOP and Associated Documents (AD) may be used for research projects not adopted by STU where Swansea University (SU) staff and associated NHS organisations require guidance. In such instances, oversight responsibility for any associated tasks will not be the responsibility of STU.

4. Procedure

Every trial or study must have a TMF which holds key documentation relevant to that trial.

4.1 Preparing the TMF

The TMF must be prepared as set out in the Essential Documents Checklist (STU-AD-GDN-005). Where sections are not required this should be noted in the TMF index.

All documents filed must be attributable, legible, contemporaneous, original, accurate and complete. Duplication of documents will be avoided by placing one copy of the document in the most appropriate section and adding file notes (STU-AD-TMP-016) in any other relevant sections to indicate its location and recording these in the file note log (STU-AD-TMP-017). Alternatively, a document tracker can be used to indicate where each document is held if it is relevant to multiple sections.

At the time of trial/study initiation, the CI must have a TMF containing all documents.

Preparing the unblinded TMF (where required)

The unblinded portion of a TMF will be prepared and maintained according to sections 4.1 and 4.2.

The research team should not be unblinded without explicit need. The TSC will indicate which people or roles must never be unblinded without further approval.

An unblinding log will record who has been unblinded and reason for unblinding

The TM is not permitted to access the unblinded portion of the TMF during the trial e.g., randomisation allocations, DMC closed reports.

The unblinded trialist(s) will provide access to the unblinded TMF following database lock and agreement from the TSC..

4.2 Maintaining a paper TMF

Over the course of a trial, any version changes in documents held in the TMF must be added to the paper TMF with the most recent version appearing first in the relevant section.

Superseded versions should be marked as such, typically by writing “superseded by version [xx]” on the front page of the document and must not be removed from the TMF.

The trial Version Control document (STU-AD-TMP-003) must be updated by the TM.

It is necessary that all relevant email communications regarding decisions, queries and resolutions are printed and filed in the relevant sections when sent or received. This task must not be deferred until the end of the trial.

4.3 Electronic TMFs

STU will maintain e-TMFs in preference to complete paper TMFs.
Electronic TMFs are held in a secure environment with restricted access.
Relevant paper documentation received in a paper format (e.g. invoices) should be scanned and saved in the corresponding electronic TMF folder.

Documents with wet signatures should also be scanned and stored electronically. Scanned documents must be of sufficient quality so as to be clearly readable and have the correct number of pages.

Documentd received in a paper format will be held in a paper TMF and archived at trial end.

4.4 Storing the TMF / Unblinded Section

The paper and electronic TMF will be held in safe and secure locations by the TM/Unblinded trialist with access limited to authorised persons.

The unblinded TMF section must be stored with restricted access to unblinded trial staff only until the trial is ready for the statistician and team to be unblinded at the end.

Documents not filed in the TMF should have their location detailed on a file note stored in the TMF to allow them to be tracked (e.g. magnetic, optical, or other non-indelible media such as digital recordings of interviews). Suitable measures should be implemented to ensure that such files cannot be relocated or altered without appropriate authorisation.

Pseudo-anonymised or identifiable data will always be stored independently from the main TMF with their location detailed in a file note.

TMF storage conditions should ensure that documents are maintained in a legible condition and are available upon the request of the Sponsor, CI, STU or a regulatory authority where applicable.

4.5 Finalising the TMF at trial closure

At the end of the trial a formal process will help control the unblinding of the research team and merging of the unblinded section. The unblinded TMF folders will be merged into the main TMF by the TM.

At the close of a trial, the TMF contents must be checked by the TM and the STU quality assurance officer (or delegate) before archiving. Once checked and approved as complete, the TMF can be prepared for archiving.

5. References

- Health Research Authority website (HRA) - http://www.hra.nhs.uk/
- Medicine and Healthcare products Regulatory Agency website (MHRA) - https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency/services-information
- UK policy framework for health and social care research (2017) - https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/
- UK Medicine for Human Use (Clinical Trials) Regulations 2004 - http://www.legislation.gov.uk/uksi/2004/1031/contents/made
- GCP link

It is assumed that by referencing the principal regulations that all subsequent amendments are included in this citation.

6. Associated Documents

Number	Title	Location
STU-AD-GDN-005	Essential documents checklist for TMF, ISF & PSF	Q-Pulse
STU-AD-TMP-003	Version Control Log	Q-Pulse
STU-AD-TMP-016	File Note Template	Q-Pulse
STU-AD-TMP-017	File Note Log	Q-Pulse

7. Abbreviations

List of Abbreviations	
AE	Adverse Event
APR	Annual Progress Reports
CI	Chief Investigator
CRF	Case Report Forms
CTIMP	Clinical Trial of an Investigational Medicinal Product
DRG	Document Review Group
GCP	Good Clinical Practice
ISF	Investigator Site File
MHRA	Medicines and Healthcare products Regulatory Agency
PSF	Pharmacy Site File
SOP	Standard Operating Procedure
STU	Swansea Trials Unit
TM	Trial Manager
TMF	Trial Master File

8. Appendices

Appendix 1: Document History

Version No:	3	**Effective Date:**	22-Apr-2024
Description of changes:	Update to SOP template v5 Additional of unblinded information		