STANDARD OPERATING PROCEDURE FOR ESTABLISHING AND MAINTAINING A TRIAL MASTER FILE, INVESTIGATOR SITE FILE AND PHARMACY SITE FILE FOR USE IN CLINICAL RESEARCH

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1. PURPOSE

This document describes the procedure for establishing and maintaining a Trial Master File (TMF), an Investigator Site File (ISF) and a Pharmacy Site File (PSF) for Clinical Trials of Investigational Medicinal Products (CTIMPs) and non-CTIMPs.

2. SCOPE

This document applies to all clinical research studies sponsored or co-sponsored by the University of Dundee and/or NHS Tayside.
The document applies to all individuals responsible for establishing and maintaining a TMF, ISF and PSF.

3. RESPONSIBILITIES

Chief Investigator (CI) or delegate:

- Establishing and maintaining the TMF.
- Keeping the TMF in a secure location.
- Providing ISF/PSF index to sites where appropriate.
- For multicentre trials, ensuring that ISFs and PSFs are in place at individual sites.
- Ensuring TMF is complete at end of trial.
- Archiving TMF.

Principal Investigator (PI) or delegate:

- Establishing and maintaining the ISF and PSF.
- Keeping the ISF and PSF in a secure location.
- Ensuring ISF and PSF are complete at end of trial.
- Archiving ISF and PSF.

4. PROCEDURE

Sections 4.1-4.4 assume a paper based TMF, ISF and PSF. Documents that are stored as electronic files prior to printing should follow the same index, index numbering and structure as the paper documents. Where a hybrid of paper and electronic files is used,

there should be written guidance on the format (e.g. Word, pdf) and naming (versions and dates) of the electronic files for consistency across the study team.

4.1 ESTABLISHING A TMF

4.1.1 The TMF must be established at the beginning of the trial and prior to participant recruitment.

4.1.2 The TMF must contain all the essential documents relating to the clinical trial. Essential documents are defined as "those documents which individually and collectively permit evaluation of the conduct of the trial and the quality of the data produced. These documents serve to demonstrate the compliance of the investigator, Sponsor, and monitor with the standards of Good Clinical Practice (GCP) and with all applicable regulatory requirements (ICH GCP section 8.1).

4.1.3 All essential documents must be legible, accurate and complete.

4.1.4 A TMF index (Doc Ref 018) must be kept at the front of the file to show which documents are stored in the TMF.

4.1.5 If an essential document is not considered applicable, this should be documented on the TMF index.

4.1.6 Where a document is considered applicable but is located out with the TMF, this should be documented on the TMF index or a note to file documenting the location should be added to the relevant TMF section.

4.1.7 For non-CTIMP studies, sections which are not applicable to the study (e.g. IMP section) should be deleted from the index and the index re-numbered accordingly. Additional sections and sub-sections of existing sections should be added if necessary, for non-CTIMP studies.

4.2 MAINTAINING A TMF

4.2.1 The TMF should be updated as the trial progresses and filing (paper and/or electronic as appropriate) should be done as soon as possible.

4.2.2 The TMF must be stored securely (physically, electronically, or both) and made available for the purposes of monitoring or audit by the sponsor and for regulatory inspection. In addition, items held outside of the TMF but documented as part of the TMF must also be made available.

4.2.3 The TMF must be securely archived after the completion of the trial for a minimum of 25 years for CTIMP studies and 5 years for non-CTIMP studies. The appropriate archiving period will be determined by the sponsor based on the type of trial and the current regulations/guidance.

4.2.4 Archived TMFs must be retrievable by the CI or delegate in the event of a sponsor audit or regulatory inspection. The programmes/media used to store any electronic files must be updated as required throughout the archiving period, so that electronic files remain accessible.

4.3 ESTABLISHING AN ISF AND A PSF

4.3.1 Each participating site should have an ISF and CTIMP studies should have a PSF.

4.3.2 For multicentre trials a TMF is required at the lead site. All essential documents will be filed in this TMF, therefore a separate ISF is not essential at the lead site.

4.3.3 The ISF and PSF should be established at the beginning of the trial, prior to participant recruitment.

4.3.4 All essential documents should be legible, accurate and complete.

4.3.5 An ISF index (Doc Ref 019) and PSF index (Doc Ref 118) must be kept at the front of their respective files.

4.3.6 For non-CTIMP studies, sections which are not applicable to the study (e.g. IMP section) should be deleted from the index and the index re-numbered accordingly. Additional sections and sub-sections of existing sections should be added if necessary, for non-CTIMP studies.

4.3.7 If a document is not considered applicable, a reason for this decision should be documented on the ISF and/or PSF index.

4.3.8 Where a document is considered applicable but is located out with the ISF and/or PSF, this should be documented on the ISF and/or PSF index or a note to file documenting the location should be added to the relevant ISF and/or PSF section.

4.3.9 The ISF and PSF must be stored securely and made available for the purposes of monitoring or audit by the sponsor and for regulatory inspection. In addition, items held outside of the ISF and/or PSF but documented as part of the ISF and/or PSF must also be made available.

4.4 MAINTAINING AN ISF AND A PSF

4.4.1 ISF and PSF should be updated as the trial progresses and filing should be done as soon as possible.

4.4.2 The ISF and PSF must be made available for the purposes of monitoring or audit by the sponsor and for regulatory inspection.

4.4.3 The ISF and PSF must be securely archived after the completion of the trial for a minimum of 25 years for CTIMP studies and 5 years for non-CTIMP studies. The appropriate archiving period will be determined by the sponsor based on the type of trial and the current regulations/guidance and must be agreed with the site prior to the start of the trial. ISFs/PSFs will be archived at sites unless otherwise agreed with sponsor.

4.4.4 Archived ISFs/PSFs must be retrievable by the PI or delegate in the event of a sponsor audit or regulatory inspection. The programmes/media used to store any electronic files must be updated as required throughout the archiving period, so that electronic files remain accessible.

5. ABBREVIATIONS & DEFINITIONS

CI	Chief Investigator
CTIMP	Clinical Trial of Investigational Medicinal Product
GCP	Good Clinical Practice
ISF	Investigator Site File
PI	Principal Investigator

PSF	Pharmacy Site File
SOP	Standard Operating Procedure
TASC	Tayside Medical Science Centre
TMF	Trial Master File

6. ASSOCIATED DOCUMENTS & REFERENCES

Doc Ref 018 TMF Index
Doc Ref 019 ISF Index
Doc Ref 118 PSF Index

7. DOCUMENT HISTORY

History prior to 2021 is in the archived SOPs available from TASC Quality Assurance Dept.

Version Number:	Reviewed By (Job Title):	Effective Date:	Details of editions made:
7	Tracy Petrie (Quality Assurance Support Officer)	18/01/2021	Uploaded to new TASC SOP template which shows the new TASC website in the footer. Physical scan converted to electronic pdf as a requirement for upload to new TASC website.
8	Margaret Band (Senior Trial Manager) Wendy Saywood (Clinical Research Project Manager, MEMO)	09/06/2021	Scheduled review, SOP now covers both CTIMPs and non-CTIMPs. Title change.
9	Margaret Band (Senior Trial Manager)	09/06/2023	Scheduled review, no changes required.

8. APPROVALS

Approved by:	Date:
Dr Valerie Godfrey, TASC Quality Assurance Manager, on behalf of TASC Clinical Research Guidelines Committee	07 June 2023