STANDARD OPERATING PROCEDURE 11

Essential Documentation: Creation and Maintenance of Trial/Study Master and Investigator Site Files

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Revision Chronology:	Effective date:	Reason for change:
Version 4.0	8 Nov 2023	Minor amendments to reflect a holistic approach to the Trial/Study Master File and the importance of mapping all repositories. Addition of potential audit trigger.
Version 3.0	21 October 2021	Biennial review: Update to new SOP format. Addition of naming convention guidance. Update to template references.
Version 2.6	10 April 2019	Biennial review: Minor updates to SOP text and file indexes. Change to new format.
Version 2.5	13 July 2016	Biennial review: Minor updates to SOP text and indexes. Change to new format.
Version 2.4	2 December 2013	Biennial review: Addition of template Pharmacy File Index. Web links updated.
Version 2.3	1 August 2011	Index templates updated. No amendments to SOP text.
Version 2.2	30 January 2011	Biennial review: Updated web links. Index templates amended.
Version 2.1	30 January 2009	Biennial review. Minor changes to text, no significant change to context. Index templates amended.
Version 2.0	21st December 2006	Provide indexes listing the essential documents which should be maintained and whether they should be filed in the Trial Master File and/or Investigator Site File.
Version 1.0	January 2006	

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1. Purpose and Scope

The purpose of this Standard Operating Procedure (SOP) is to detail the essential documentation that should be maintained within a Trial/Study Master File (T/SMF), Investigator Site Files (ISF) and Pharmacy Files as required under section 8 of the International Conference on Harmonisation Good Clinical Practice guidelines (ICH GCP). This SOP applies to all staff that are responsible for, or involved in, handling research study documents.

2. Definitions

Essential Documents	Documents which individually and collectively permit evaluation of the conduct of a study and the quality of the data produced.
Trial/Study Master File (T/SMF)	Collection of essential documents for a clinical trial that may be subject to regulatory agency oversight and held at the coordinating centre. Documents may be held in a combination of paper or electronic formats and may be present in several different repositories.
Investigator Site File (ISF)	Collection of relevant essential documents necessary for the recruiting site to conduct the study.
Pharmacy File	Collection of relevant essential documents to allow pharmacies to conduct the study.

3. Background

Essential Documents serve to demonstrate the compliance of all research staff with the standards of Good Clinical Practice and with all applicable regulatory requirements.

With the large volume of documentation required for each study, a standard filing system is necessary. Filing essential documents in an orderly and timely manner assists the successful management of a study. The T/SMF, ISF and Pharmacy File (as applicable) should be established at the beginning of a study to allow the effective storage and location of essential documents.

Essential documents may be audited by study sponsors and inspected by the regulatory authorities (as appropriate) as part of the process to confirm the validity of the study conduct and the integrity of the data collected during the study.

Essential documents must be retained after the study end for sufficient periods to allow for audit and inspection by regulatory authorities and should be readily available upon request (see SOP 23 ‘Archiving’).

The sponsor and investigator(s) should know the location(s) of their respective essential documents including source documents. The storage system used during the study and for archiving (irrespective of the type of media used) should provide for document identification, version history and retrieval.

Essential documents should be supplemented or may be reduced where justified based on the importance and relevance of the specific documents to the study.

4. Procedure

4.1 Responsibilities

Chief Investigator (CI) or their delegate	• Creation, maintenance, and update of the repositories containing essential documents necessary to conduct the research.
Study coordinating centre	• Supplying each site with an ISF and Pharmacy File (if required). • Ensuring relevant revised documents are supplied to site teams.
Principal Investigator (PI) or their delegate	• Maintaining and updating their ISF/Pharmacy File as appropriate.

4.2 When?

A T/SMF should be prepared when confirmation has been received that a study will go ahead and must be updated as appropriate. The T/SMF should be checked for completeness at regular intervals.

An ISF and Pharmacy File (if required) should be provided to each site when their participation in the study is confirmed. It should be updated as appropriate throughout the study and checked for completeness at regular intervals.

4.3 How?

TMF structure

Study teams should use the template T/SMF index and map template (T26) to help with the content and structure the of essential documents in the T/SMF. The specific documents will differ according to the nature of the study so the template should be amended accordingly. The index and map template should also be used to record the location of essential documents, particularly if they are contained within different repositories. Duplication of documents should be avoided.

Templates T08 and T14 provide an index for the ISF and Pharmacy File respectively. The indexes should be reviewed at the start of each study and amended as required to make study specific.

Maintenance

The T/SMF should be regularly maintained to ensure it is up to date, its status should be reviewed regularly and documented. Failure to do this may trigger an internal audit of the T/SMF.

If a required T/SMF, ISF or Pharmacy File document is missing, all reasonable efforts must be made to acquire the document. If the document cannot be located, a note should be placed in the file identifying the document, explaining why it is missing and the efforts made to locate it.

Version Control

Appropriate document names and version control are essential to ensure that study teams are working to the correct document. For WCTU managed studies that are developing documentation please refer to SOP 45: Document Management.

Mapping

The T/SMF does not have to be one file in one location, essential documents can be present in different locations or formats. If this approach will be taken the T/SMF index and map should detail the location of each document. Considerations for the format and whether documentation needs to be printed as a hard copy to support possible inspection activity should be discussed on a study-by-study basis. Any decisions and justifications can be recorded in the risk assessment or somewhere else appropriate e.g., TMG minutes. Audit trail requirements and the security and integrity of the records should be considered when choosing the appropriate repository.

Email correspondence

Correspondence should only be filed if it contains key study related information i.e., if it documents any agreement or significant discussions regarding the study, study administration, protocol violations, study conduct or Serious Adverse Event reporting. It is best to retain email correspondence in its original format to retain all metadata. Emails can be saved in an outlook format into a master file repository or retained in the study inbox. Organisation of any email inbox where key correspondence will be retained should mirror the master file index or be clearly locatable via the T/SMF index and map.

List of abbreviations

CI	Chief Investigator
GCP	Good Clinical Practice
ICH	International Conference on Harmonisation
ISF	Investigator Site File
PI	Principal Investigator
QA	Quality Assurance
R&IS	Research & Impact Services
SOP	Standard Operating Procedure
T/SMF	Trial/Study Master File
WCTU	Warwick Clinical Trials Unit

Template Documents

Template T26 Trial Master File Index and Map
Template T08 Investigator Site File Index
Template T14 Pharmacy File Index

Associated Documents

SOP 45: Document Management