UNIVERSITY OF LEICESTER, UNIVERSITY OF LOUGHBOROUGH
&
UNIVERSITY HOSPITALS OF LEICESTER NHS TRUST

JOINT RESEARCH SUPPORT OFFICE

STANDARD OPERATING PROCEDURES

University of Leicester (UoL) Research Governance Office SOP S-1015 UoL

Version 5, November 2016

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

OFFICE BASE

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Effective Date: April 2017

1. INTRODUCTION

This Standard Operating Procedure (SOP) describes the creation of an audit trail through the retention of essential documents in the Trial Master File (TMF) or Investigator Site file (ISF) for all research sponsored by University of Leicester.

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 trial subjects remains protected.

2. SCOPE

This SOP applies to all staff conducting research sponsored by UoL.

3. TRIAL MASTER FILE (TMF)

A TMF must be prepared prior to study initiation and must be actively maintained and updated until the trial is formally closed. When it becomes available, the final report must be filed in the TMF.

The TMF contains all the essential documents relating to a research study before the trial commences, during trial conduct and after completion of the trial. It is the responsibility of the Chief Investigator to establish a TMF for each research study they initiate. The TMF must be structured in a way that allows the reconstruction of the trial from the documentation. (Further information on site file organisation is available on the NIHR website). The documentation contained within the TMF should be sufficient to adequately reconstruct the trial activities undertaken, along with key decisions made concerning the trial. Consideration should be given to the TMF being a stand-alone set of documentation that does not require additional explanation as competent authority inspections often take place some years after trial completion when personnel involved may no longer be available.

The documentation listed in Eudralex Volume 10 should not be used as a definitive checklist for TMF content, but rather a subset of potential documentation that could be regarded as essential for reconstruction of the trial conduct as not all documents essential to reconstruct the trial are included in the above, for example, the green light document. In addition, it is recommended that an assessment of all activities is undertaken to determine whether they need to be documented to enable reconstruction of the trial conduct from the paperwork alone, for example, training provided by the investigator to site staff.

Where a risk-adapted approach is being followed, however, 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.

4. INVESTIGATOR SITE FILE (ISF)

The ISF consists of essential documents relating to the specific investigator site, before the trial commences, during trial conduct and after completion of the trial. It is the responsibility of the Principal Investigator to establish an ISF for each research study they participate in. A multi-centre study must have a TMF, and also a file for each individual site taking part in the study. It is acceptable to have individual sections rather than files for each site contained within the TMF.

For a single centre study it is acceptable for all documents to be held in one single file which acts as both the TMF and ISF.

A tabulated guide to TMF/ISF documents is contained in Appendix 1 (TMF/ISF Index for CTIMP studies) and Appendix 2 (TMF/ISF Index for Non CTIMP studies). The Index may be adapted to reflect specific study requirements.

It is expected that all TMF and ISF are 'inspection ready' at all times. Non-compliance and/or where areas of concern have been identified will be escalated in accordance with the Non compliance SOP S-1016 UoL.

It is a legal requirement that researchers retain the TMF/ISF and all other study related documentation for a minimum of 5 years following completion of the study. Research where the data are used to support a marketing authorisation have further requirements as per Directive 2003/63/EC. Hence, the documentation should be retained for at least 15 years after completion or discontinuation of the trial, or for at least 2 years after the granting of the last marketing authorisation in the European Community.

5. PROCEDURE

5.1 Responsible Personnel

The CI or PI will be responsible for establishing and maintaining the TMF / ISF and may delegate these activities to a research team member. This must be recorded on the Delegation of Authorities & Signature Log. The files must be actively maintained until the trial is formally closed

5.2 Storage of TMF / ISF

All essential documents must be appropriately stored at all times. The TMF/ISF must be stored in a secure location, preferably in a lockable cabinet, but within a secure locked area with minimal staff access, other than research staff. 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 for all documentation to be stored in one file. Where separate file/s are required, a file note must be made in the TMF/ISF which documents the location and title of the additional file/s. Where a separate pharmacy file is created for the purposes of study management, this remains part of the TMF/ISF but can remain in Pharmacy.

5.3 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 by striking through the front cover with a single line in black pen and marking as superseded by the later version. A Version Control Tracker should be utilised (Appendix 3). A file note (signed and dated by the CI/PI) must be placed in the file giving details of any missing or unavailable documents.

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5.4 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/ISF. Copies of all documentation generated by either party relating to the agreements and delegated functions must also be present.

5.5 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.

6. NON COMPLIANCE

Failure to demonstrate compliance to this SOP will result in implementation of the SOP S-1016 UoL Non Compliance SOP at a minimum of a CRITICAL Finding.

7. RESPONSIBILITIES

	Responsibility	Undertaken by	Activity
1.	Chief Investigator/Principal Investigator	Chief Investigator/Principal Investigator	Establishing the TMF/ISF at the beginning of the trial
2.	Chief Investigator/Principal Investigator	Chief Investigator/Principal Investigator	Maintaining the TMF/ISF during the life of the trial.
3.	Chief Investigator/Principal Investigator	Chief Investigator/Principal Investigator	Ensure the safe storage of the TMF/ISF at all times.
4.	Chief Investigator/Principal Investigator	Chief Investigator/Principal Investigator	Ensure the TMF/ISF is archived as per the approved protocol and the SOP S-1024 UoL Study Close-down and SOP S-1032 UoL Archiving

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

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Date Approved	10/04/2017

8. DEVELOPMENT AND APPROVAL RECORD FOR THIS DOCUMENT

9. 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.

10. DISTRIBUTION RECORD

Date	Name	Department	Received

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