STANDARD OPERATING PROCEDURE

TRIAL MASTER SITE FILE

LinCTU SOP 12

Version Final 2.0 Date 01 May 2022

Effective Date: 01 August 2022

Next review: 2 years

Author:	Sam Lewis Research Governance Manager
Approved by:	Recoverable Signature X Graham Law co-Director LinCTU Signed by: 2c8f737e-1e53-4b91-90f7-a001dc32b085

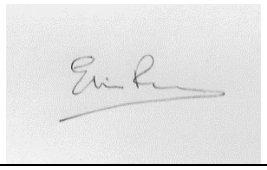
Version History	Reason for change
1.0	First Clinical Governance version
2.0	First LinCTU version

NOTE: All SOPs are subject to regular review.

Please ensure that the version of this SOP is the most up-to-date.

OUT OF DATE DOCUMENTS MUST NOT BE USED AND HARD COPIES SHOULD BE DESTROYED

The following have read, reviewed and advised on the SOP

Reviewer name	**Role**	**Date**	**Signature**
Graham Law	Statistician and reviewer	11/04/2022	
Elise Rowan	Data Manager	26/05/2022	
LinCTU Steering Committee		23/06/2022	

1. PURPOSE

To outline the process for the set-up of Trial Master / Investigator Site Files for clinical trials sponsored by the University of Lincoln or supported by the Lincoln Clinical Trials Unit (LinCTU).

2. SCOPE

This SOP applies to clinical research where LinCTU are providing support in Trial Management unless specified by the Sponsor or funder.

3. BACKGROUND

3.1 The Chief Investigator (CI) has overall responsibility for Trial Master Files. However, set-up and maintenance may be delegated to a person with the relevant knowledge, skills and experience as recorded on the RF CG08-RF01 Study Delegation Log. Where LinCTU trial management support is provided, this is likely to be the assigned LinCTU Trial manager.

3.2 The local Principal Investigator (PI) for multi-site trial has overall responsibility for Investigator Site File (ISF) at their local site. However, set-up and maintenance may be delegated to a person with the relevant knowledge, skills and experience and experience as recorded on the RF CG08-RF01 Study Delegation Log.

3.3 Trial Master File (TMF) and Investigator Site File (ISF) may be either hard copy or electronic.

- Where hard copy records are kept, files should be stored securely i.e. locked storage / restricted access.
- Where electronic records are kept, access should be password protected and restricted to trial staff.

3.4 Regulation 31 a of SI 2004/1031 requires that a readily available TMF is kept, which contains the essential documents (see appendix 1) relating to that clinical trial, whilst demonstrating compliance with the principles of GCP.

3.5 Essential documents relating to a clinical trial are those which enable both the conduct of the clinical trial and the quality of the data produced to be evaluated; and show whether the trial is, or been, conducted in accordance with the applicable requirements of the Regulations.

3.6 The filing of essential documents in an orderly and timely manner allows the reconstruction of trial activities and also greatly assists the smooth running of the trial. TMF and ISF should be made available for any future audit or inspection as requested by authorised individuals.

Clinical trials with an external Sponsor (LinCTU managed trials)

3.7 Where there is an external Sponsor, the sponsoring organisation may provide an Investigator Site File (ISF). If the Sponsor does not provide the participating site with an ISF, LinCTU may follow this SOP.

4. CROSS REFERENCES

GCP information can be sourced at:

https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/good-clinical-practice/

SI 2004/1031 The Medicines for Human Use (Clinical Trials) Regulations 2004 and any subsequent amendments

CG-QMS SOP CG13 Monitoring and Audit

CG-QMS SOP CG15 Archiving (Clinical data)

CG-QMS CG09-RF01 Screening and Enrolment Log

Study File Index and Essential Documents (Appendix one)

5. PROCEDURE

Trial Master File (TMF) / Investigator Site File (ISF) Set-up

The Chief Investigator / Principal Investigator or designated nominee shall:

5.1 Ensure that a TMF/ISF is established as soon as possible after an outline protocol is available and/or first contact is made with the trial Sponsor.

5.2 For multi-site trials, the CI will keep site-specific sections within their TMF for the essential documents relating to each of the other centres taking part.

5.3 Local PI will keep site-specific sections within their ISF for the essential document relating to their centre.

5.4 The CI and/or delegated trial manager must ensure that access to the TMF is restricted to relevant trial team members only.

5.5 Local PIs must ensure that access to ISFs is restricted to relevant local trial team members only.

5.6 A TSF/ISF may consist of more than one folder and should be labelled in accordance with Appendix One Study File Index and Essential Documents.

5.7 Hard Copy Files

- Documents should be filed in chronological order within the relevant section.

5.8 Electronic Files

- Documents should be filed with a document specific file name, including version number and date and retained in the relevant section of the electronic folder.

Trial Master File (TMF) / Investigator Site File (ISF) Maintenance

5.9 The TSF / ISF must be actively maintained from its establishment until the trial is formally closed.

5.10 While certain documents, such as the protocol or participant information sheets, may need to be amended during a project, all superseded version of documents must be retained in the TMF / ISF.

5.11 Hard Copy Files

- Documents should be filed in chronological order within the relevant section. Previous / out of date copies of trial documents should retained but marked as superseded.

5.12 Electronic Files

- Documents should be filed with a document specific file name, including version number and date and retained in the relevant section of the electronic folder. Previous / out of date copies of trial documents should retained but marked as superseded / moved to archive folder. Original versions of each document should be available in a read only format (to prevent un-approved changes).

Trial Master File (TMF) / Investigator Site File (ISF) Archiving

5.13 TSF / ISF are considered essential documents and must be archived at the end of the trial in accordance with SOP CG15 Archiving (Clinical data).

6. FLOW CHART

Not required.

Appendix One Study File Index and Essential Documents

1. STUDY DOCUMENTS

Protocol, information sheet(s), consent form(s) and investigator brochure (where applicable) final version

Case Report Forms and any other data collection documents, final versions.

Superseded versions (marked accordingly)

2. APPROVAL AND AGREEMENTS

Ethical approval

Competent Authority

Health Research Authority (HRA) and Local R&D Capacity and Capability

Statement of Activities

Schedule of Events (SoECAT)

Financial and Legal Documentation

3. STAFF PARTICIPATION

Delegation Log

Curriculum Vitae and Training Records

SOP Compliance records of trial team staff

4. MEDICAL TESTING AND PHARMACY (WHERE APPLICABLE)

Accreditation / certification of supporting Laboratories and pharmacies

'Normal ranges' issued by local laboratories

Investigational product handling (where applicable) – local procedures where not in the study protocol

Investigational product control (where applicable) – local procedures where not in the study protocol

Investigational medicinal product records – certificate of analyses, shipping records, labelling to be use

5. RANDOMIZATION AND BLINDING

Randomization, blinding and un-blinding procedures where not in the study protocol.

6. STUDY AMENDMENTS AND APPROVALS

Notification of minor/substantial amendment(s) and any revised/additional documents

HRA/Ethics committee approvals and confirmation of local R&D capacity and capability

7. INFORMED CONSENT

Participant Screening and Enrolment Log

Signed consent forms of all study participants*

*where appropriate this may be stored in a separate secure file and the location of this should be documented in the study site file as a file note.

8. CASE REPORT FORMS (CRF) AND SOURCE DOCUMENTS

Completed CRFs (or file note regarding location of completed CRFs) and amended CRFs

Source documents related to the study

9. SERIOUS ADVERSE EVENTS / PHARMACOVIGILANCE

SAE reporting forms

CIOMs form (IMP trials only)

SAE reporting forms to the ethics committee

Annual safety reports to ethics committee and competent authority (where applicable) inc Development Safety Update Report (DSUR)

Evidence of notification of actions to be taken and their implementation following a SUSAR (where applicable).

10. BIOLOGICAL MATERIALS (IF RELEVANT TO THE STUDY)

List and location of retained samples

Human Tissue / Material Transfer Agreements

Transfer documents

11. MONITORING, AUDIT AND REPORTING

Annual progress report(s) to host institution and the ethics committee.

Copies of any regular reports to the trial funder or trial steering committee.

Monitoring reports.

Sponsor audit reports and corrective action forms.

Data Monitoring Committee reports (only applicable if this does not compromise unblinding).

Correspondence from the Data Monitoring Committee

Trial Steering Committee meeting minutes and correspondence

Minutes of Trial Management Group Meetings/team meetings and any associated consort/progress charts

Statistical analysis reports

Copies of protocol violations

12. CORRESPONDENCE

Correspondence letters, relevant emails etc

13. CLOSURE

Notification of study closure to the ethics committee / competent authority

Notification of study closure to the host organisation

Notification of study closure to the Sponsor

14. AUDIT

Final study report

Final close-out audit report (as applicable)