Office for Research	
SOP-RTM-02	
INVESTIGATOR SITE FILE AND ESSENTIAL DOCUMENTS	

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1. PURPOSE:

This SOP describes procedures to maintain the Investigator Site File (ISF) and associated essential documents for clinical research at Epworth HealthCare (Epworth).

2. BACKGROUND

Essential documents support the credibility of the study and maybe audited and/or inspected by the OFR, reviewing HREC, sponsor or regulatory authorities as part of the process to assess that the conduct of the study/trial complies with the protocol, approvals, applicable regulations and guidelines, and the integrity of the data generated.

Filing essential documents in a timely manner is crucial in effective management of research by investigators and study teams. ICH Good Clinical Practice (GCP)[1] provides guidance on the types of documentation required at all stages of a trial and can be used as a guide for non-clinical trial research.

3. SCOPE:

This SOP is applicable to all clinical research conducted at Epworth.

4. APPLICABILITY:

Applies to all Epworth employees, non-employed staff and Visiting Medical Officers (VMOs) and to all relevant external persons or parties engaged in at Epworth.

5. RESPONSIBILITIES.

The Principal Investigator (PI) is responsible for ensuring maintenance of the ISF and associated essential documents in accordance with this SOP. The PI may delegate at his/her discretion certain study duties to suitably qualified individuals. Delegation of study activities must be recorded on the delegation log. The PI remains responsible for any delegated activity.

All Epworth employees, non-employed staff and VMOs involved in the conduct of clinical studies at or under the auspices of Epworth should be aware of and comply with this procedure.

6. DEFINITIONS:

Essential Documents – documents which individually and collectively permit evaluation of the conduct of a trial and the quality of the data produced[1].

Trial Master File (TMF) – a collection of essential documents for a trial managed by the sponsor that provide evidence that the clinical trial has been conducted following regulatory requirements (including Good Clinical Practice). The documents included in the TMF should confirm the compliance with the clinical trial protocol, Good Clinical Practice, and the integrity of the data collected without any additional explanation from the Sponsor, Investigator, and Institution[1].

Investigator Site Files (ISF) –This is part of a TMF and is maintained by the investigator and the team at a site. They also contain essential documents required for the development of clinical trial and shows that the clinical trial site and investigator comply with regulatory requirements[1].

For non-clinical trial research, these files may be called the research folders. For the purpose of this SOP the term ISF will be used to describe the ISF and research folders hereafter.

7. PROCEDURE:

7.1 Documentation of Investigational Site Qualifications and Training Records

The PI and all members of the clinical study team must:

a. Maintain an up-to-date *Curriculum vitae* (CV) (as per SOP-QA-01: Documentation of Qualifications and Training Records) and ensure this is filed in the ISF prior to the commencement of the study.

b. File evidence of required training, including training in the protocol and related techniques as required, in ISF. This should be evidenced in the CV and other training documents and certificates (see also SOP-RG-04: Researcher Credentialing, SOP-QA-01 Documentation of Qualifications and Training Records) meet all the qualifications required for the type of research to be undertaken and as specified by Epworth, applicable regulatory requirement(s) or sponsor (as applicable).

c. For clinical trials, the PI must maintain a list of appropriately qualified persons to whom they have delegated significant trial-related duties. The list is in the form of a Delegation Log. Delegated duties should be captured and signed and dated by the PI on a per person basis before they start any trial-related activities.

d. Completion of a delegation log is recommended for non-clinical trial research studies.

   A delegation log template is usually provided by the Sponsor for Commercially Sponsored clinical trials. Where Epworth is the study sponsor, or an external sponsor has not provided a delegation log template, use the Epworth delegation log template (see also SOP-TM-14 Delegation of Duties).

7.2 The Investigator Site File and Essential Documents (Research documents)

Where Epworth is the study sponsor, the file may be called a Trial Master File.

The PI and/or delegate should:

7.2.1 Establish an ISF for each study

The PI and/or delegate should:

a. Establish an ISF for each study. The ISF should be maintained electronically in SiteDocs or as a hard copy version.

b. Ensure essential documents are filed in the ISF in a timely manner.

c. Keep a minimum list of applicable essential documents (as applicable to the research project) from the following stages of the study (as per ICH GCP R2 Section 8[1]) :

- Before the clinical phase of the trial (or study start-up)
- During the clinical conduct of the trial (or study)
- After completion or termination of the trial (or study)

d. Document if any essential documents are stored outside of the ISF i.e. agreements (collaborative, funding, loan equipment, Clinical Trial Research Agreement etc.) and financial information (budgets, invoicing etc.).

e. Allow access to essential documents for review/inspection by the OFR, reviewing HREC or regulatory authority(ies) and the sponsor's representatives for all sponsored trials or other bodies as required.

f. For sponsored studies, structure the ISF, in compliance with the sponsors requirements

For commercially sponsored studies, sponsoring companies will normally provide the ISF complete with tab separators for ease and consistency of filing.

g. For Epworth sponsored trials, or externally sponsored trials including investigator-initiated trials where no ISF structure has been provided, the ISF should be structured in accordance with applicable elements of ICH GCP R2 Section 8[1]. Refer to Appendix 1 for suggested TMF and ISF Table of contents.

7.2.2 Maintenance of the ISF

The PI and/or delegate should:

a. Ensure that the ISF is stored securely and accessed only by delegated persons or nominated auditors, inspectors, or other permitted person AND in a manner that maintains confidentiality irrespective of format (electronic or paper).

b. Ensure documents are filed in the ISF in a timely manner.

c. Conduct and document periodic reviews of the Investigator Site Files (ISF) for their designated studies, and at a minimum at the following time points:

- At the start of study (site initiation)
- During study (quarterly review)
- Prior to study close-out.

h. Ensure study documentation is completed and maintained in accordance with this SOP and:

- The protocol and approvals
- SOP-QA-01 Documentation of Qualifications and Training Records
- SOP-TM-07 Source Document Management
- SOP-RTM-08 Data Entry and Query Resolution
- SOP-RTM-13 Off-site Archiving
- SOP-RTM-14 Delegation of duties
- And any other applicable requirements.

d. Document where investigational products or other medicines information is located.

i.e. for trials involving investigational products or other medicines, the site pharmacy will usually keep investigational product shipping, receipt and accountability documents in the Pharmacy Site File (PSF).

- The records must be made available to Sponsors, monitors and auditors.
- Researchers at the site itself do not have to replicate these documents but must have a record of storage location/file path of ISF

e. For studies in maintenance phase, where activities/trial visits have moved to six monthly or longer visit intervals, reviews ISF should at six monthly intervals.

7.1.3 Archiving the ISF

The PI and/or delegate should:

a. Document all archiving activities including archive content, storage location and role of person authorised to arrange access to archived files so that the ISF can be retrieved and accessed when required.

b. Ensure off-site archiving is undertaken and documented in accordance with SOP-RTM-13 Off-site Archiving.

c. Be aware that all information including archived trial ISF, remains the property of Epworth and must be available on request by the OFR/Epworth and for audit/inspection.

8. DISSEMINATION AND IMPLEMENTATION

This SOP will be disseminated by the OFR. Updates will be made available with details of planned dates of implementation.

9. MONITORING COMPLIANCE AND EFFECTIVENESS

Compliance with this SOP will be monitored as part of OFR monitoring processes. Any problems or potential problems concerning the effectiveness of this SOP may be identified during OFR monitoring process or through users informing the OFR.

10. REVIEW AND UPDATING:

This SOP will be reviewed every three years, or whenever there are changes to legislation or working practices that impact upon the content of this document. This SOP may be merged with another SOP if appropriate or removed entirely if it becomes redundant.

11. REFERENCES:

1. Integrated Addendum to ICH E6 (R1): Guideline for Good Clinical Practice E6 (R2) https://www.tga.gov.au/publication/note-guidance-good-clinical-practice

12. RELATED DOCUMENTS:

12.1 Related Forms and Templates

N/A

12.2 Related SOPs

- SOP-QA-01 Documentation of Qualifications and Training Records
- SOP-RG-04 Researcher Credentialing
- SOP-RTM-07 Source Document Management
- SOP-RTM-08 Data Entry and Query Resolution
- SOP-RTM-13 Off-site Archiving
- SOP-RTM-14 Delegation of duties

13. VERSION CONTROL

Document History			
Version	**Date**	**Summary of Changes**	**Author**
1.0	26/4/2019	N/A - First Issue	Helen Christensen
2.0	21/6/2024	Update header, formatting throughout and version control table. Insert section 2. Background, 5. Responsibilities and 6. Definitions. Move responsibilities from Section 7 to Section 5: Responsibilities. Insert sponsor, PI and study staff responsibilities Broaden scope to all research and clarify differences in requirements for clinical trials and research studies. Define that for this SOP, the term ISF refers to document storage systems for clinical trials and research folders for non-clinical trials. Remove duplications. Restructure Section 7 Procedure into new subsections and reorder information accordingly. Section 7.2.2 Maintenance of the ISF Insert, 'Ensure study documentation are completed and maintained in accordance with this SOP and: • The protocol and approvals • SOP-QA-01 Documentation of Qualifications and Training Records • SOP-TM-07 Source Document Management • SOP-RTM-08 Data Entry and Query Resolution • SOP-RTM-13 Off-site Archiving • SOP-RTM-14 Delegation of duties • And any other applicable requirements.' Reduce information in Section 7.1.3 Archiving the ISF by reference to SOP-RTM-13 Off-site Archiving and insert: a. 'Document all archiving activities including archive content, storage location and role of person authorised to arrange access to archived files so that the ISF can be retrieved and accessed when required.' b. 'Ensure off-site archiving is undertaken and documented in accordance with SOP-RTM-13 Off-site Archiving.' Insert references for • SOP-TM-07 Source Document Management • SOP-RTM-08 Data Entry and Query Resolution • SOP-RTM-14 Delegation of duties	Jane Loke Sarah Rickard

		Updated reference to SOP-RTM-13 from Trial Archiving to Off-site Archiving Insert Appendix 1.	

14. APPENDIX

Appendix 1: TMF and ISF Table of contents

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TMF	ISF
1.0 Staff training and CV 1.1 Investigator Contact details 1.2 Delegation and Responsibilities log 1.3 Coordinating site 1.3.1 Principal Investigator 1.3.2 Associate Investigator #1 1.3.3 Research Coordinator 1.4 Participating site name (if multiple-sites) 1.4.1 Site Principal Investigator name 1.4.2 Site Associate Investigator #1 1.4.3 Site Research Coordinator/Nurse	1.0 Staff training and CV 1.1 Investigator Contact details 1.2 Delegation and Responsibilities log 1.3 Site Principal Investigator name 1.4 Site Associate Investigator name #1 1.5 Site Associate Investigator name #2 1.6 Site Research Coordinator/Nurse
2.0 Investigational Product/Device 2.1 Investigator's brochure 2.1.1 Current approved 2.1.2 Superseded 2.2 Sample labelling 2.3 Shipping Records	2.0 Investigational Product/Device 2.1 Investigator's brochure 2.1.1 Current approved 2.1.2 Superseded 2.2 Sample labelling 2.3 Shipping Records
3.0 Protocol 3.1 Master protocol 3.1.1 Current approved 3.1.2 Superseded 3.2 Master Randomisation	3.0 Protocol 3.1 Master Protocol 3.1.1 Current approved 3.1.2 Superseded 3.2 Unblinding procedure
4.0 Ethics and Governance 4.1 Reviewing HREC 4.1.1 Submission Documentation 4.1.2 Initial Approval 4.1.3 Subsequent Approvals 4.2 Governance 4.2.1 Participating Institute #1 4.2.1.1 Submission documentation 4.2.1.2 Site initiation 4.2.1.3 Initial Authorisation 4.2.1.4 Amendment and Acknowledgements 4.2.1.5 Annual Reports 4.2.1.6 Final Report	4.0 Ethics and Governance 4.1 Reviewing HREC 4.1.1 Submission Documentation 4.1.2 Initial Approval 4.1.3 Subsequent Approvals 4.2 Governance 4.2.1 Submission documentation 4.2.2 Site Initiation 4.2.3 Initial Authorisation 4.2.4 Amendment and Acknowledgements 4.2.5 Annual Reports 4.2.6 Final Report
5.0 Patient documentation 5.1 Master patient facing documents 5.1.1 Informed consent form 5.1.1.1 Current Approved 5.1.1.2 Superseded 5.1.2 Brochure (if any) 5.1.2.1Current Approved 5.1.2.2 Superseded 5.1.3 Advertisement of study (if any) 5.1.3.1 Current Approved 5.1.3.2 Superseded	5.0 Patient documentation 5.1 Master patient facing documents 5.1.1 Informed consent form 5.1.1.1 Current Approved 5.1.1.2 Superseded 5.1.2 Brochure (if any) 5.1.2.1Current Approved 5.1.2.2 Superseded 5.1.3 Advertisement of study (if any) 5.1.3.1 Current Approved

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5.1.4 Case Report Forms 5.2 Site patient facing documents 5.2.1 Participating Institute #1 5.2.1.1 Informed Consent Form template 5.2.1.2 Brochure 5.2.2 Participating Institute #2 5.2.2.1 Informed Consent Form template 5.2.2.2 Brochure 5.3 Patient Screening log template 5.4 Case Report Form template	5.1.3.2 Superseded 5.1.4 Case Report Forms 5.2 Site patient facing documents 5.2.1 Informed Consent Form template 5.2.2 Brochure 5.2.3 Advertising materials 5.3 Patient Screening and enrolment log template 5.4 Case Report Forms template 5.5 Patient Identification code list template
6.0 Agreements 6.1 Agreement type #1 6.2 Agreement type #2	6.0 Agreements 6.1 Agreement type #1 6.2 Agreement type #1
7.0 Insurance and Indemnity 7.1 Certificate of Currency	7.0 Insurance and Indemnity 7.1 Certificate of Currency
8.0 Budget and invoices 8.1 Quotes 8.2 Invoices	8.0 Budget and invoices 8.1 Quotes 8.2 Invoices
9.0 Regulatory authorisation 9.1 CTN 9.2 TGA 9.3 OGTR (if any) 9.4 Department of Health (if any)	9.0 Regulatory authorisation 9.1 CTN 9.2 TGA 9.3 OGTR (if any) 9.4 Department of Health (If any)
10.0Equipment 10.1Name of equipment 10.1.1 Certification 10.1.2 Normal Value range log	10.0Equipment 10.1Name of equipment 10.1.1 Certification 10.1.2 Normal Value range log
11.0Monitoring 11.1Pre-Trial 11.2During Trial 11.3Close out	11.0Monitoring 11.1Pre-Trial 11.2During Trial 11.3Close Out
12.0Incident Management 12.1Incident log 12.2Form Templates 12.2.1 SAE 12.2.2 SUSAR 12.2.3 SSI 12.2.4 Serious Breach 12.2.5 Significant deviations	12.0Incident Management 12.1Incident log 12.2Form Templates 12.2.1 SAE 12.2.2 SUSAR 12.2.3 SSI 12.2.4 Serious Breach 12.2.5 Significant deviations
13.0Audit and Inspection 13.1Reports and Certificates	13.0Audit and Inspection 13.1Reports and Certificates
14.0Clinical Study Report	14.0Clinical Study Report

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