GVHealth	**TITLE:**	**Clinical Trial Standard Operating Procedure 07: The Study Master File**	
Document Type:	Procedure	**Approved by:**	CMO & EDMS
Directorate:	CMO & Medical Services	**Section:**	Research
Author/Prepared by:	Dr Ainsley Robinson	**Position:**	Clinical Trials Coordinator

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Document Details

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1. PURPOSE:

To describe the procedures related to the maintenance of the Study Master File (SMF) held at all clinical research sites/units, according to International Council for Harmonisation of Technical requirements for Registration of Pharmaceuticals for Human Use Good Clinical Practice (and requirements of the Integrated Addendum to this Guideline published by the Therapeutics Goods Administration (TGA)) (ICH GCP E6 (R2)) Section 8 to ensure it is current at all times for the duration of the clinical study.

2. SCOPE:

This Standard Operating Procedure (SOP) applies to all Goulburn Valley Health (GVH) employees, visiting health professionals, contractors, any external researchers, consultants, and volunteers who propose to undertake, administrate, review and/or govern human research involving GVH patients/participants, facilities and/or staff. All study personnel involved in the clinical study must operate within their scope of practice.

ICH GCP E6 (R2) defines Essential Documents as, 'documents which individually and collectively permit evaluation of the conduct of the trial and the quality of the data produced'.

A **Study Master File (SMF)** (otherwise referred to as the **Investigator Site File (ISF)** in some jurisdictions) should be established at the beginning of the trial so that Essential Documents can be filed in an organised way that will facilitate the conduct of the trial, audit, and inspection. Contents should enable the adequate reconstruction of trial conduct at the site along with any key trial decisions.

The SMF/ISF contains identifiable data and proprietary information and should be stored securely with restricted access to authorised staff. It should be actively maintained as the trial progresses. All documentation filed should be complete, accurate and legible. If Essential Documents are stored separately from the SMF/ISF, (e.g. staff training records, maintenance/calibration records for key equipment used in the trial) a file note in the SMF/ISF should indicate their location. Superseded documents should be retained but scored through to indicate that the document is no longer in use. Direct access to all trial related records stored in the SMF/ISF should be provided when requested by monitors, auditors, ethics committees or regulatory authorities. Essentials Documents stored in the SMF/ISF should be originals or certified copies of original documents. Essential Documents include the correspondence generated during a trial. These documents (e.g. emails, telephone call reports, meeting minutes) are an important component in reconstructing the trial as they contain key decisions and discussions relating to the care of participants and the management of the trial.

For Satellite Sites, key trial documents (for example study Protocol/IB), as well as clear evidence of the manner and frequency of supervision of the Satellite Site by the Primary Site (e.g. minutes of calls with Satellite Site staff to review patients/participants and study progress) should be maintained in both the SMF/ISF and the **Satellite Site Study File (SSSF)**.

3. PROCEDURE:

3.1. The Study Master File – Principal Investigator Responsibilities:

3.1.1. The Principal Investigator must:

- Ensure an Study Master File (SMF) is created, if not provided by the Sponsor, prior to study commencement and that it must contain at a minimum the Essential Documents listed in Appendix 1: Example of Study Master File Index. The SMF is stored at the Primary Site (Satellite Site Study File (SSSF) in the case of the Principal Investigator (PI) initiating a Satellite Site).
- Where the Teletrial Model is implemented, have control of all Essential Documents and records generated by the Investigator/Institution/Satellite Site before, during, and after the trial.
- Establish the maintenance rules of the SMF and relationship between Primary Site SMF and SSSF. For example, the contents of the SSSF, how and which documents generated at the Satellite Site will be sent to the Primary Site and filed in the SMF and archiving of SSSF after study close out. When establishing the maintenance rules, it will be important to ensure that key documents from the SSSF are present in the SMF and vice-versa after the close out of the study but prior to archiving, so that a full record of all study activities under the control of the PI is contained in the SMF.
- Establish prior to the commencement of the trial and maintain a current record of the location of all Essential Documents including Source Documents and where relevant, study related Essential Documents from Satellite Site. The storage system used during the study and for archiving (irrespective of the type of media used) should provide for document identification and location, version history, search ability and retrieval for the length of the archiving retention time.
- File Essential Documents in a timely manner.
- Ensure Satellite Sites also maintain SSSF and file study related essential documents in a timely manner, with focus on version control.
- Maintain a current contact list of all Study Personnel including staff at all Satellite Site/s within the Cluster involved in the clinical trial, clearly identifying the Primary Site, the Satellite Site, and any External Service Provider.
- Ensure study documentation is kept and archived as specified in GVH_CT-SOP-013-Site Close Out and Archiving.

3.2. The Study Master File - Documentation

- Study related Essential and Source Documents generated for/by the Primary Site, as per Appendix 1: Example of Study Master File Index at a minimum, will be filed in the SMF.
- The SMF should be prefaced with an index of contents as well as indicate the location(s) of all Essential/Source Documents.
- Certified copies of study related Essential and Source Documents generated for/by the Satellite Site, the identity of which will be established prior to the

commencement of the trial, will be sent to the Primary Site and filed in the SMF, on request by either, the Sponsor, monitor or Primary Site staff as per rules established prior to the commencement of the trial and documented in the Supervision Plan.

- Where financial documentation, such as the Clinical Trial Research Agreement (CTRA) and Sub-Contract, invoicing and remittances etc., may be filed in a separate location to the SMF, the location is to be recorded on the SMF index. See Appendix 1: Example of Study Master File Index. A copy may be filed in the SMF if requested by the Sponsor.
- Investigational Product (IP) handling documentation e.g. shipping, receipt, Interactive Voice Response System (IVRS), Interactive Web Response System (IWRS), codes, randomisation list and accountability and destruction documents etc. may be kept in a separate file e.g. at the site pharmacy. In this case the location to be recorded on the SMF index. However, the records must be made available to Sponsors, monitors, auditors and regulatory agencies at any time. The IP documentation will be archived with the SMF after completion of the study.
- Sample handling procedures are to be clearly documented if performed e.g. in a laboratory manual. Sample management records at both Primary and Satellite Site/s including the storage, processing and transportation of samples between Satellite and Primary Sites are filed in the SMF/SSSF as agreed.
- Other study related materials handling documentation are filed in the SMF/SSSF as agreed.

3.3. The Satellite Site Study File – Contents

The content of the SSSF can be decided with the study team and the Sponsor. The SSSF may be a sub-set of the SMF and should be prefaced with an index of contents as well as indicate the location(s) of all Essential/Source Documents.

3.3.1. The Satellite Site Study File should contain:

- All the relevant site specific Essential Documentation pertinent to the activities that have been and that are to be performed at the Satellite Site, similar to Appendix 1: Example of Study Master File Index.
- All Source Documents generated at the Satellite Site (or indicate the location of all Source Documents for example the electronic medical record (EMR) at the Satellite Site).
- Relevant HREC approval and governance authorisation documentation.
- Sub-contract with the CTRA in annexure.
- Study specific Supervision Plan.
- Satellite Site Delegation Log.
- Satellite Site Training Records.
- Satellite Site, Site Specific Assessment form.
- IP shipping, receipt, and accountability documents.
- Details of the processing, storage of samples at both Sites and transportation between Satellite and Primary Sites and related documentation (if performed).

- Files notes indicating if the original document is found in another location e.g., pharmacy folder with the pharmacy, a document will be found in the SMF.

ABBREVIATIONS AND TERMS:
Please refer to GVH_CT-SOP-Abbreviations and Terms.

KEY ALIGNED DOCUMENTS:
GV Health Procedure:
- GVH_CT-SOP-013-Site Close Out and Archiving

REFERENCES:
ICH GCP E6 (R2)

APPENDICES:
Appendix 1: Example of Study Master File Index

Contributors to the document

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Appendix 1: Example of Study Master File Index

1. These examples are guides when paper SMF/SSSF are in use. eSMF/eSSSF will follow the software guidelines.

2. Ensure the Supervision Plan outlines which, how and when relevant Satellite Site document is to be sent to the Primary Site for filing in the SMF.

File Section	Documentation	Location	Primary Responsible	Satellite Responsible
Contact List	Contact list for study related personnel at both Primary and Satellite Sites.		Holds for all sites	Satellite Site only. Copy to Primary Site as indicated on Supervision Plan. Request full list if needed.
Correspondence (Not HREC or Governance)	General correspondence with sponsor, CRO, teleconference and meeting notes.		All Satellite Sites	Copy from Primary
Agreements	CTRA location, site indemnities, confidentiality agreement(s) location, letters of intent, Health Service Directive for clinical trial regulatory process for Satellite Sites.		Held at Primary Site	Copy from Primary
Finance	Financial disclosure Forms as appropriate.		Held at Primary Site	Copy from Primary
Ethics Committee • **Approvals** • **Acknowledgements** • **Composition** • **Correspondence**	All ethics correspondence and documentation including all versions of the informed consent form, ethics committee composition, statement of committee compliance to the National Statement, approval letters, reports to ethics committee, correspondence as applicable to commercial sponsorship, submission package(s), sample informed consent form, approved advertising materials/wording, other information provided to study participants and approved by ethics, tracked changes to protocol and summary tables, insurance certificate.		Held at Primary Site	Copy from Primary

File Section	Documentation	Location	Primary Responsible	Satellite Responsible
Investigator Brochure and safety updates	All versions as provided to ethics, safety updates from Sponsor.		Held at Primary Site	Copy from Primary
Protocol	All versions as provided to and as approved by ethics, signed Protocol signatory page should also be in this.		Signed by Primary Site	Copy from Primary
Regulatory documents	Australian CTA or CTN form (fully executed), other regulatory agency forms, all correspondence to the regulatory agencies.		Held at Primary site	Copy from Primary
Sample CRF	Approved version of sample CRF (a blank set that can be duplicated).		Held at Primary Site	Copy from Primary
Serious Adverse Events	Documentation tracking the incidence and reporting of SAEs, reports to ethics, reports to the applicable agency (interim and final).		Site specific Primary notified of any SAEs at the same time as sponsor	Site specific Primary notified of any SAEs at same time as sponsor
Monitoring	All general monitoring correspondence unless specifically belonging in another file section, pre-trial monitoring report, feasibility assessments, monitoring visit reports and follow-up letters, monitor-site correspondence, close-out visit reports.		Sponsor visit face-to-face or via digital platform	Via telehealth or face-to-face
Audit	Auditor correspondence, audit reports (if available) and auditor follow-up letters.		Held at Primary Site	Only if requested
Laboratory	Clinical laboratory certification (NATA, CLIA), laboratory normal values for medical/ laboratory/ technical procedures and/or tests included in the Protocol, all provided.		From Primary Site	Only if used
Curriculum Vitae	Signed and dated copies of CVs for all medical staff, (Principal Investigator, Associate Investigators) and other staff delegated significant duties as listed on the delegation log for the duration of the research project.		All Investigators and staff with significant duties from all sites	Site specific staff and key Primary

File Section	Documentation	Location	Primary Responsible	Satellite Responsible
Signature Log	Site personnel signature sheet with a list of signatures and initials of all persons authorised to make entries and/or corrections on the CRFs and e-CRFs and certain delegated tasks.		All staff from all sites	Site only
Shipping records for IMP and other study related materials	Shipment records, date of shipment, batch numbers, method, shipment receipt records, certificate of analysis for IP, storage conditions.		Site specific and on ward to Satellite. Stored in Pharmacy	Site specific receipt, use and return
Accountability and destruction records	IP accountability and destruction correspondence and records.		Site specific and on ward to Satellite. Stored in Pharmacy	Site specific receipt, use and return
Decoding and Unblinding	Any correspondence relating to decoding and unbinding. Documents how identity of blinded IP can be revealed in case of emergency.		Site specific and Satellite information stored	Site specific
Participant Screening Logs	Screening logs including participant identification logs (site only for identification in case of emergency), participant registration/screening logs containing a chronological listing of screening/enrolment of participants.		Site specific (Primary has copy of Satellite Site for emergency)	Site specific
Participant identification code list	A confidential list of names of all participants allocated to trial numbers upon enrolment in the trial. Allows investigator/institution to reveal participant identity in the case of emergency or for reasons of safety.		Primary has all details	Site specific only
Participant enrolment logs	Chronological enrolment of participants by participant number		Site specific only	Site specific only
Visit log	Records for all site visits, monitoring visits, sponsor visits, auditor visits, agency audits.		Sponsor visit	Only if sponsor visits

File Section	Documentation	Location	Primary Responsible	Satellite Responsible
Data query tracking	Data query tracking, monitors site queries and correspondence.		Sponsor visit	Remotely accessed
Clinical study report	Final clinical study report (signed copy) if provided.		Sent to Primary	Copy from Primary
Signed Informed Consent Forms	Informed Consent forms should be fully signed with all signatories dating their own signature. In addition, time of consent should be recorded in order to establish that consent was obtained prior to any trial procedures. Where informed consent is placed in the medical record, a file note stating this must be added to this section of the file.		All sites	Held at site, witnessed and processed by telehealth if required
Other-study specific	Other documents not included in the previous sections.		All	Copy from Primary where relevant
Supervision Plan	A plan recording the oversight for the project and staff involved in the study and the role of the Primary Site overseeing the Satellite sites and reporting structure for the study.		Held at site	Explained to all site staff
Monitoring Plan			At Primary Site	Copy from Primary
Safety Monitoring Plan			At Primary Site	Copy from Primary