MELBOURNE HEALTH	OFFICE FOR RESEARCH		
	STANDARD OPERATING PROCEDURE: SOP002		
	The Study Site Master File and Essential Documents		
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1. AIM

To describe the procedures related to the maintenance of the study site master file and associated essential documents.

2. SCOPE

Applicable to all clinical research projects undertaken at Melbourne Health, including investigator initiated research, collaborative research and all phases of clinical investigation of medicinal products, devices and diagnostics.

3. APPLICABILITY

Principal Investigator/ Investigator, Sub-Investigator(s) research coordinators and other staff involved in research/ trial-related duties.

4 PROCEDURE

4.1 The Study Site Master File (also called Site Investigator file (SIF)) and Essential Documents

The SIV may be as electronic files, paper files or a combination of both for these formats.

This SOP should be read together with the following documents:

- Research Policy MH18
- Data Management in Research Guideline
- Data Storage and Security Guideline including Appendix A: the structure for an electronic study file
- Archiving, retention, and disposal of data Guideline
- SOP 001 - Documentation of investigational site qualifications, adequacy of resources & training records
- SOP 007 - Case report forms, source documents, record keeping & archiving
- MH OFR SOP Data Sharing and Access Plan

The investigator(s) should:

4.1.1 File essential documents at the site in a timely manner. All site-related materials should be made available for review, by auditors or regulatory authority(ies) and the sponsor's representatives for sponsored studies for ALL studies.

4.1.2 Keep a minimum list of essential documents (as applicable to the research project) from the following stages of the trial (see Appendix 1):

- Before the clinical phase of the study (if applicable).
- During the clinical conduct of the study.
- After completion or termination of the study.

4.1.3 Refer to SOP 007 - Case report forms, source documents, record keeping & archiving for information on the minimum periods that study records should be maintained, noting that these are minimum periods.

- Retention of records should be in accordance with approvals
- For legal reasons, sites may consider indefinite archiving periods
- An appropriate custodian should be nominated to curate the study records. This is generally the study PI at the organisation (or Head of Department where the study PI leaves the organisation and the study is closed)

4.2 Documentation of Investigational Site Qualifications and Training Records

The investigator(s) should:

4.2.1 Be qualified by education, training, and experience to assume responsibility for the proper conduct of the research.

- This should be evidenced in a current CV, other training documents, certificates and registrations.

4.2.2 Meet all the qualifications required for the type of research to be undertaken and as specified by the applicable regulatory requirement(s) or sponsors for sponsored clinical trials (as applicable). Evidence of training i.e. current medical practitioner registration details and any other documentation should be referenced in the CV.

4.2.3 Maintain a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties.

- The Delegation Log may be combined with a signature log
- Delegated duties should be captured and signed and dated by the investigator on a per person basis.
- Refer to SOP001: Appendix 2 for the template Signature and Delegation of Duties log.
- A delegation log is usually provided by the Sponsor Company for Sponsored clinical trials.

4.2.4 Ensure that the *Curriculum vitae* (CV) of each research staff on the project are current and are signed and dated by the researcher at the start of a study.

- Refer to the Office for Research website for an example of a CV template.
- CVs should be updated when there is a change that is relevant to the research project such as updated training information.

4.3 The Site File

The site file should contain all the applicable essential documentation referred to in Appendix 2.

- For Investigator Initiated research projects departments may reorganise these site files to comply with their specific requirements as necessary
- For commercially sponsored studies, sponsoring companies will normally provide site file complete with tab separators for ease and consistency of filing.
- For studies conducted on behalf of smaller companies which may not provide the site file structure, the site file should be structured in accordance with the template provided in Appendix 3.
- Agreements (collaborative, funding, loan equipment CTRA etc.) and financial information (budgets, invoicing etc.) may be filed in a separate location to the Site File.
- For studies involving investigational products or other medicines, the site pharmacy will usually keep investigational product shipping, receipt and accountability documents. Researchers at the site itself do not have to replicate these documents. However, the records must be made available to sponsors monitors and auditors.

5 GLOSSARY

Essential Documents

Documents which individually and collectively permit evaluation of the conduct of a study and the quality of the data produced

Good Clinical Practice (GCP)

A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial participants are protected.

International Conference on Harmonisation (ICH)

International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use is a joint initiative involving both regulators and research-based industry focusing on the technical requirements for medicinal products containing new drugs.

Investigator

An individual responsible for the conduct of a research projects including clinical trials at a research/trial site and ensures that it complies with GCP guidelines. If a research/trial is conducted by a team of individuals at a research/trial site, the investigator is the responsible leader of the team and may be called the Principal Investigator. In this instance they may delegate tasks to other team members.

Site File

A file that contains all the applicable essential documentation for the research project / clinical trial. This may also be called the Investigator file.

Sub Investigator

Any individual member of the research/clinical trial team designated and supervised by the investigator at a research/trial site to perform critical trial-related procedures and/or to make important research/trial-related decisions (e.g., associates, residents, research fellows).

6 REFERENCES

1. MH Research Policy MH18
2. Documentation and Records Management Policy MH05
3. Clinical Documentation MH05.01
4. Privacy and Confidentiality of Patient Information MH03.08
5. Note for guidance on Good Clinical Practice (CPMP/ICH/135/96) annotated with TGA comments DSEB, July 2000
6. VMIA CTN Guidelines (2006)
7. Data Management in Research Guideline
8. Data Storage and Security Guideline including Appendix A: the structure for an electronic study file
9. Archiving, retention, and disposal of data Guideline
10. SOP 001 - Documentation of investigational site qualifications, adequacy of resources & training records
11. SOP 007 - Case report forms, source documents, record keeping & archiving
12. MH OFR SOP Data Sharing and Access Plan

7. APPENDICES

Appendix 1: SOP Change Log
Appendix 2: List of documents to be generated during the conduct of a clinical trial from initiation to close-out
Appendix 3: Master Site File index and contents template

APPENDIX 1: SOP CHANGE LOG

Version No.	*Author, date, reason for Issue*
1	Sarah Rickard, Manager Research Governance and Audit • First issue
2	Sarah Rickard, Manager Research Governance and Audit 26/9/2013 • Documents use of departmental site file systems
3	Sarah Rickard, Manager Research Governance and Audit 8/2/2017 • Review of document and minor updates
4	Sarah Rickard, Manager Research Governance and Audit 16/9/2020 • Insert related documents in 4.1 • Insert numbering for subclauses • Reorder section 4.2 • Reformat SOP Change Log • Add related documents to Reference section4.1 • Minor formatting changes throughout the document

DOCUMENT END

APPENDIX 2: LIST OF DOCUMENTS TO BE GENERATED BEFORE AND KEPT DURING AND AFTER COMPLETION/TERMINATION OF THE TRIAL (ADAPTED FROM ICH-GCP)

Before the Research Phase Commences

During this planning stage the following documents should be generated and should be on file before the trial formally starts. Specific studies may require some or all the following documents depending on the type of research being conducted.

Title of Document	Purpose
Investigator's Brochure (or Product Information document for a marketed product- see SOP004 section 4.4)	To document that relevant and current scientific information about the investigational product has been provided to the investigator.
Protocol **Signed protocol (If sponsored clinical trial)** **Protocol amendments, if any (i.e. where your site is added to a study)** **Case Report Form (CRF)**	To document study procedures To document investigator and sponsor agreement to the protocol/amendment(s) and CRF. To ensure PI has all approved documents required to undertake the research. To ensure the PI/research staff record required information appropriately.
Information given to trial participants: • **Informed Consent Form** (including all applicable translations) • **Any other written information** (if used) • **Advertising for participant recruitment** (if used)	To document the informed consent. To document that the participant will be given appropriate written information (content and wording) to support their ability to give fully informed consent. To document that recruitment measures are appropriate and not coercive.
Financial aspects of the trial (if funding involved)	To document the financial agreement between the investigator/institution and the funder/sponsor or other organisation as applicable.
Insurance statement (where required)	To document that compensation to participant(s) for trial-related injury will be available.
Signed agreement between involved parties (as applicable) **e.g.:** • Investigator/institution and another institution • Investigator/institution and sponsor • Investigator/institution and CRO • Sponsor and CRO • Investigator/institution and authority(ies) (where required)	To document relationships and responsibilities of organisations involved in the study.

Title of Document	Purpose
HREC approval (Dated), of the study and documents including (as applicable)**:** • Protocol and any amendments • CRF (if applicable) • Informed consent form(s) • Any other written information to be provided to the participant(s) • Advertisement for participant recruitment (if used) • Participant compensation (if any) • Any other documents given approval/favourable opinion	To document that the trial has been participant to HREC review and given approval/favourable opinion. To identify the version number and date of the approved document(s).
HREC Composition	For sponsored clinical trials: to document that the HREC is constituted in agreement with GCP.
Regulatory authority(ies) authorisation/ approval/notification of protocol (where required)	To document appropriate authorisation/approval/ notification by the regulatory authority(ies) has been obtained prior to initiation of the trial in compliance with the applicable regulatory requirement(s).
CV and/or other relevant documents evidencing qualifications of investigator(s) and sub-investigator(s)	To document qualifications and eligibility of a researcher to undertake their role/s in the research (or trial and/or provide medical supervision of participants in a clinical trial) as appropriate.
Normal value(s)/range(s) for medical/laboratory/ technical procedure(s) and/or test(s) included in the protocol	To document normal values and/or ranges of the tests.
Medical/laboratory/technical procedures/tests: • Certification; or • Accreditation; or • Established quality control and/or external quality assessment; or • Other validation (where required)	To document competence of facility to perform required test(s) and support reliability of results.
Instructions for handling of investigational product(s) and trial-related materials (if not included in protocol or Investigator's Brochure)	To document instructions needed to ensure proper storage, packaging, dispensing and disposition of investigational products and trial-related materials.
Shipping records for investigational product9s) and trial-related materials	To document shipment dates, batch numbers and method of shipment of investigational product(s) and trial-related materials. Allows tracking of product batch, review of shipping conditions and accountability.
Title of Document	**Purpose**
Decoding procedures for blinded trials	To document how, in case of an emergency, identity of blinded investigational product can be revealed without breaking the blind for the remaining participant' treatment.
Trial initiation monitoring report (for monitored	To document that trial procedures were reviewed with

trials. Maybe sponsored, collaborative group etc.)	the investigator and the investigator's trial staff.

During the Conduct of the Research Study

In addition to having on file the above documents, the following should be added to the study files during the conduct of the research as evidence that all new relevant information is documented as it becomes available:

Title of Document	Purpose
Investigator's Brochure Updates	To document that investigator is informed in a timely manner of relevant information as it becomes available.
Any revision to: • Protocol/amendment(s) and CRF • Informed consent form • Any other written information provided to participants • Advertisement for participant recruitment (if used)	To document revisions of these trial related documents that take effect during the trial.

HREC approval (Dated) of the following:
• Protocol amendment(s)
• Revision(s) of:
  ○ Informed consent form
  ○ Any other written information to be provided to the participant
  ○ Advertisement for participant recruitment (if used)
• Any other documents given approval/favourable opinion
• Continuing review of trial (where required
	To document that the amendment(s) and/or revision(s) have been participant to HREC review and were given approval/favourable opinion.
	To identify the version number and date of the document(s).

Regulatory authority(ies) authorisations/ approvals/notifications where required for: • Protocol amendment(s) and other documents	To document compliance with applicable regulatory requirements.
Curriculum vitae for new investigator(s) and/or sub-investigator(s)	To maintain up to date information of research team.
Updates to normal value(s)/range(s) for medical/laboratory/technical procedure(s)/ test(s) included in the protocol	To document normal values and ranges that are revised during the trial.
Updates of medical/laboratory/technical procedures/tests: • Certification; or • Accreditation; or • Established quality control and/or external quality assessment; or • Other validation (where required)	To document that tests remain adequate throughout the trial period.
Documentation of investigational product(s) and trial-related materials shipment	

Title of Document	Purpose
Relevant communications other than site visits: • Letters • Meeting notes • Notes of telephone calls	To document any agreements or significant discussions regarding trial administration, protocol violations, trial conduct, adverse event (AE) reporting.
Signed informed consent forms (Copy only – original to be stored in the participant's medical record)	To document that consent is obtained in accordance with GCP and protocol and dated prior to participation of each participant in trial. Also to document direct access permission.
Source documents	To document the existence of the participant and substantiate integrity of trial data collected. To include original documents related to the trial, to medical treatment, and history of participant.
Signed, dated and completed case report forms (CRF)	To document that the investigator or authorised member of the investigator's staff confirms the observations recorded.
Documentation of CRF corrections	To document all changes/additions or corrections made to CRF after initial data were recorded.
Notification by originating investigator to sponsor of serious adverse events and related reports	Notification by originating investigator to sponsor of serious adverse events and related reports.
Notification by sponsor and/or investigator, where applicable to regulatory authority(ies) and HREC of unexpected serious adverse drug reactions and of other safety information	Notification by sponsor and/or investigator, where applicable, to regulatory authorities and HREC of unexpected serious adverse drug reactions and other safety information.
Notification by sponsor to investigator of safety information	Notification by sponsor to investigators of safety information.
Interim or annual reports to HREC and authority(ies)	Interim or annual reports provided to HREC and to authority(ies).
Participant screening log	To document identification of participants who entered pre-trial screening.
Participant identification code list	To document that investigator/institution keeps a confidential list of names of all participants allocated to trial numbers on enrolling in the trial. Allows investigator/institution to reveal identity of any participant and to make future contact if required.
Participant enrolment log	To document chronological enrolment of participants by trial number.
Investigational products accountability at the site	To document that investigational product(s) have been used according to the protocol.
Signature sheet	To document signatures and initials of all persons authorised to make entries and/or corrections on CRFs.
Record of retained body fluids/tissue samples (if any)	To document location and identification of retained samples if assays need to be repeated.

APPENDIX 3: SITE MASTER FILE CONTENTS TEMPLATE

File Section	Documentation	Done
Signature and delegation 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 certain delegated tasks	☐
Contact List	Contact list table for study related personnel (can be included in the Signature and delegation log)	☐
Correspondence	General correspondence with sponsor, CRO, teleconference and meeting notes	☐
Agreements	Clinical trial agreement location, site indemnities, confidentiality agreement(s) location, letters of intent	☐
Finance	Financial disclosure forms for any person listed on the FDA Form 1572 (IND study only) – only if requested by sponsor	☐
Ethics committee 5.1. Ethics Committee Approvals/ Acknowledgements 5.2. Ethics Committee Composition 5.3. Ethics Committee Correspondence	All ethics correspondence and documentation including all versions of the informed consent form, ethics committee composition, statement of committee compliance to NH&MRC 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	☐
Investigator's Brochure and safety updates	All versions as provided to ethics, safety updates from sponsor	☐
Protocol	All versions as provided to and as approved by ethics, signed protocol signatory page should also be in this section	☐
Regulatory documents	Australian CTX or CTN form (fully executed), IND form 1572 (US FDA form – only if requested by sponsor), other regulatory agency forms, all correspondence to the regulatory agencies	☐
Sample CRF	Approved version of sample CRF (a blank set that can be duplicated)	☐
Serious Adverse Events	Documentation tracking the incidence and reporting of SAEs, reports to ethics, reports to the applicable agency (interim and final)	☐
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	☐
Audit	Auditor correspondence, audit reports (if available) and auditor follow-up letters	☐
Laboratory	Clinical laboratory certification (NATA, CLIA), laboratory normal values for medical/laboratory/technical procedures and/or tests included in the protocol, all laboratory related correspondence	☐
Curriculum vita	Signed and dated copies of *curriculum vita* for all medical staff, principal investigator, sub-investigators updated to include current positions. CVs should be present for all those listed on the delegation's log	☐

File Section	Documentation	Done
CRF completion guidelines	Any correspondence, presentations and/or CRF completion guidelines provided by the Sponsor	☐
Shipping records	Shipment records, date of shipment, batch numbers, method, shipment receipt records, certificate of analysis for investigational product, storage conditions. Shipping details of other study related documentation or materials should also be recorded.	☐
Accountability records	Investigational product accountability correspondence and/or records	☐
Decoding and unblinding	Any correspondence relating to decoding and unblinding. Documents how identity of blinded investigational product can be revealed in case of emergency.	☐
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	☐
Participant identification code list	A confidential list of names of all participants allocated to trial numbers on enrolment in the trial. Allows investigator/institution to reveal participant identity	☐
Participant enrolment logs	Chronological enrolment of participants by participant number	☐
Visit log	Records for all site visits, monitoring visits, sponsor visits, auditor visits, agency audits	☐
Data query tracking	Data query tracking, monitors site queries and correspondence	☐
Clinical study report	Final clinical study report (signed copy) if provided	☐
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 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	☐
Other-study specific	Other documents not included in the previous sections	☐