Study Master File

Table of Contents and Section Detail Guide

This Filing system is for Investigator Files and:

- Can be used for all study types (drug/device and non-drug/device research)
    - Grey sections = drug/device trials only
- Contains material relating to the conduct of the study
- Original documents should be securely located in the Principal Investigator's office or departmental office. The study staff in each department across the Institution where study procedures are performed should also have access to copies of relevant essential trial documentation.
- Must be kept in accordance with these guidelines (contain standard dividers)
    - A copy of this filing guideline is placed in each investigator file
- May be reviewed by HREC/Governance personnel at any time
- Must NOT contain detailed participant identifying documentation (except for screening/enrolment logs and consent forms)
- Has been formulated to meet the guidelines of the National Statement on Ethical Conduct of Research in Humans and Notes for Guidance on Good Clinical Practice (with TGA's annotated comments).

Archiving

- While the study is open study documents are stored at the site where the study is conducted
- Once the study is closed documents are archived in accordance with the appropriate Institutional Record Keeping Policy Document and MHMRC guidelines (may include off-site document storage and electronic archiving)

File Notes: Must be placed in the section that they are relevant to.

Other files

Pharmacy Documentation

- The pharmacy department may maintain their own files and records of study drugs. Although the responsibility for the investigational medicinal product (IMP) rests with the PI; duties in relation to the IMP may be delegated to an appropriately qualified person. It is strongly recommended that the delegation be to PCH pharmacy as clinical trials pharmacists have the knowledge and experience to manage all aspects to the required regulatory and good clinical practice standards.

    - Product delivery to the trial site
    - Product inventory including dispensing to participants and managing returned, product expiry and product disposal
    - Managing product storage requirements

This pharmacy documentation should be returned to the PI at the completion of the study and archived with the main site files as per the checklist.

Case Report Forms (CRF) and Participant/Parent Information and Consent Forms (and other participant documentation)

- CRFs and copies of signed PICFs as well as any other participant documents (e.g. completed questionnaires) are stored separately by study staff in individual participant files

Templates:

The following templates are available for your adaptation and use:

- Check list for study start
- Signature log and delegation of duties
- Participant screening log
- Participant enrolment log
- Eligibility checklist
- Training Log
- Meeting Minutes Template
- Self-audit checklist
- Note to File
- Non-compliance log
- DSMB Charter template
- WA Health PGICF & PICF Guidelines and Templates are available via RGS

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DEFINITION AND REQUIREMENTS OF EACH SECTION

1. Contact list

Contact list (usually a table) listing all study related personnel and services that the study staff may need to contact during the course of the study.

Include any of the following that apply:

- All members of study staff
- Pharmacy personnel
- Collaborators, such as statisticians
- Laboratory services
- Address for shipping of any samples
- Companies for ordering any supplies
- Randomisation services
- Any emergency contact details

Suggested detail:

- Email addresses
- Phone, Pager, Mobile and Fax numbers
- Mailing addresses
- Notes on availability

2. Study Start Up Checklist

Certain steps must be taken before a research team is ready to start recruiting participants into a new study. It is recommended that a checklist is completed and filed to document that all the necessary steps were fulfilled prior to initiating the study.

Other documentation related to the commencement of the study should be filed in this section, such as minutes from a study team initiation meeting, if one is conducted, to confirm the preparedness of the all the research staff and formalise the start of the study.

3. Protocol

All versions as provided to and as approved by ethics, including signed protocol signatory page, should also be in this section

3.1. Current HREC approved study protocol

A copy of the most updated, currently approved protocol must be on file and easy to find for all study staff that may need to refer to it.

3.2. Superseded study protocol

To document revisions of the protocol that takes effect during the trial.

3.3 Peer Review

Evidence of Peer Review. Note, this may not be applicable if the trial underwent CAHS Sponsorship approval process.

4. Participant Information

Master documents that can be copied and provided to potential participants (and/or their parents) should be kept in here.

4.1. Current HREC approved Information and Consent Forms (PICF) and Assent forms

A blank copy of the currently approved information statement and consent form(s).

4.2. Current HREC approved other information for participants (diaries, questionnaires etc.)

A blank copy of all currently approved documents in this category

4.3. Superseded PICF and Assent forms

Blank copies of all previously approved PICFs and Assent forms must be included here, include tracked versions.

4.4 Superseded other information

5. Ethics and Governance

The purpose of this section is to document that the trial, and any amendments and/or revisions have been subject to HREC review and given approval plus to identify the current version number and date of the study document(s).

5.1. HREC approvals and Site Approvals

Ensure that this section contains letter/s documenting the ethics committee's approval of the following documents:

- Approval of the current protocol
- Approval of the current informed consent form
- Approval of the current version of any participant materials (such as recruitment advertising materials, participant letters, participant questionnaires or diary cards, if applicable)
- Approval of the prior versions of all of the above documents, if applicable
- Approval of the Annual Report submitted for Annual Review
- Site or Governance approvals should also be filed in this section

Ethics approval letters must document the version number and version date of the document being approved, as well as the date the approval is granted.

5.2. Ethics submission documentation (initial and amendments)

The complete signed ethics/governance applications that were submitted for review should be filed in this section, along with any pertinent correspondence between the study staff and

the ethics office, such as requests for changes to documents or responses to questions raised by the committee.

The ethics conditions of approval states that*: "The CPI is responsible for submitting and amendments to the approved documents listed on the approval letter, or any new documentation to be used in the project. Any new or amended documentation should be submitted in a timely manner and cannot be implemented at any participating site until they have received HREC approval".*

Therefore, you must file all submissions made subsequent to the initial ethics application, such as a copy of each complete Amendment Request Form documenting submission by the study staff of each protocol amendment, revised PICF or recruitment advertisement or questionnaire to the ethics committee for approval.

Note: An RGS automated email will be generated when you make a submission, this will list all forms and documents submitted and the date of submission.
Related Link: Ethics submission resources and information

5.3. HREC membership statement

To document that the HREC is constituted in agreement with Good Clinical Practice.

5.4. Annual and final study reports

Ethics approval is conditional on annual review of each ongoing project by the ethics committee.

It is an NHMRC requirement that all investigators undertaking research approved by an Institutional Ethics Committee submit a Final Report once the research has ceased.
A copy of the submitted Final Research Report must be filed in this section, prior to archiving the contents of the study binder.

5.5. Safety Reports

A copy of all safety reports submitted via RGS along with any correspondence and HREC acknowledgements to be filed in this section.

5.6. Other Correspondence

Include in this section any other documents submitted to the ethics committee for approval including requests for ethics approval extension (CAHS HREC provides initial ethics approval for up to 3 years). If additional time is required, an ethics renewal application must be made and must be accompanied by the annual progress report.

Also include is this section any letters to and from the ethics committee that do not fall into one of the categories above. This will include (but is not limited to) protocol deviations and violations, change of investigator letters and data safety and monitoring board letters.

6. Participant Screening and Enrolment logs

The purpose of a **screening log** is to keep a record of all potential participants who were screened for inclusion in the trial, tracking the outcome of the screening.

The log includes data on those that are screened but found to be ineligible, and those that refuse consent. The reason for screened patients being excluded from enrolment is recorded. This information can be valuable as it builds up over time to identify any selection bias. For studies with difficult recruitment, the screening log may also provide patterns of ineligibility which may be helpful to investigators.

The participant **enrolment log** is a list of all participants enrolled into the study, in chronological order of enrolment. The log documents the status of each enrolled participant; current study participants, number enrolled, number that have completed the study, and number of early withdrawals.

A Participant ID log which links the participant to their study ID# to be filed in this section. If this is to be stored electronically, please add a note to file in this section stating where the log is stored and who has access.

7. Study Procedures

A Study Procedures Manual (sometimes called a Manual of Operations or a Study Coordinator's Manual) is a reference document that clearly outlines the details of how to carry out the procedures detailed in protocol.

The following are examples of some sections that are commonly included in a study manual:

- *Diagram of procedures to be conducted at each visit*
    - A quick reference flow chart describing the procedures that are required at each participant visit, based on the protocol. This ensures no procedures are omitted and is a more practical reference than the protocol.
- *Sample Handling Procedures*
    - A reference or flow diagram of steps to follow when collecting blood, tissue or urine samples for the study, to ensure that they are processed, packaged, labelled, stored and transported correctly.
- *Annotated Forms*
    - Examples of correctly completed forms can be filed as useful references for study staff, such as a pathology request form completed for a 'dummy participant'.
- *AE Grading Reference*
    - If the criteria for grading the severity of adverse events are not detailed in the protocol, file an appropriate grading scheme in the Study Procedures Manual, such as Common Terminology Criteria for Adverse Events version 5

This section also contains the current, approved version of any materials to be viewed by participants and/or their legally acceptable representatives (such as recruitment advertising materials, participant letters, updates, participant questionnaires or diary cards).

Superseded versions of previously approved participant materials should be filed behind the current version and clearly marked as 'superseded'.

8. Data Forms and Procedures

Case Report forms are the official data-recording documents used in a study. Relevant data is transcribed from the patient record (and other sources) onto the CRF pages in a specific format, in accordance with the protocol. This allows for efficient and complete data processing, analysis and reporting. The CRF is designed according to the protocol: all data specified in the protocol *must* be collected on the CRF, and data that will not be analysed **should not** appear on the CRF.

A blank copy of all other data collection tools, such as surveys, eligibility forms, templates for the patient study visit data, should also be filed in this section.

8.1. Blank Sample CRF

Approved version of sample CRF (a blank set that can be duplicated)

8.2. Superseded CRF

Any versions of the CRF that have been superseded (clearly marked as so) so that this section forms a complete record of any changes in data collection throughout the study.

8.3. CRF completion guidelines

It is advisable to create a document describing the rules for completing CRFs to ensure consistency in the data. For example, the guidelines may specify how to complete fields if some data was not collected or unknown, how to correct errors made on the CRF, etc.

8.4 Data Queries

Include details in this section regarding how queries will be generated from completed CRF's and the resolution processes and timelines.

8.5 Decoding and Unblinding

Include information regarding how, in case of an emergency, the identity of blinded investigational product can be revealed for a participant if required.

9. Adverse Events, Serious Breaches and Non-Compliance Log

Internal SAEs and SUSARs (Suspected Unexpected serious Adverse Reactions)

A condition of ethics committee approval for each study is that certain Serious Adverse Events (SAEs) are reported to the ethics committee, for ongoing review of the ethical acceptability of the study. The participant should be referred to in the report by their study ID, not their name, so that this documentation does not compromise patient confidentiality. Any supporting documentation submitted to the ethics committee (such as blood results or death certificates) should be de-identified.

A copy of the submitted documentation for every SAE reported to the ethics office can be filed in this section, or in the specific patient's study file. If they will be filed in the participant file then a file note should be completed indicating their location.

The Checklist for Onsite Management of Adverse Events should also be filed here.

9.1 External SAEs and SUSARs

Any SAEs that occur at other sites and SUSAR Periodic line listings that require submission to the ethics committee should be filed here.

9.2 Sponsor-level Serious Breaches and CAPAs

Sponsor-level Corrective and Preventive Action Plan – to be completed, signed by Sponsor-Investigator and submitted to CAHS HREC and CAHS RGO via a safety report on RGS for review. This report should detail any corrective and preventative action to be taken in addressing the serious breach encountered at sponsor level.

9.3 Non-Compliance Log

A complete list of non-compliance events/protocol deviations must be included in a Non-Compliance log and filed here.

Related links/resources: CAHS SOP Procedure-304 on Safety and Adverse Event Reporting
Risk Assessment Table available on the CAHS intranet

10. Data safety and Monitoring

If a Data and Safety Monitoring Board (DSMB) has been established to oversee the study, this section should contain the DSMB terms of reference and membership, correspondence between the study staff and DSMB and the DSMB letters or reports.

Related links: NHMRC DSMB Guidance document
DSMB Charter template available on CAHS intranet

11. Monitoring/Audit

If your study is audited by a member of the Ethics Office or an external monitor, letters and reports documenting the auditor's visit and findings should be filed here.
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 should be included here.

Related Links: CAHS SOP Procedure-310 on monitoring visit activities
CAHS self-audit checklist available on the CAHS intranet

12. Site Documentation

This section must include details of any supporting departments to be used during the study to document competence of the facilities to perform the required test(s) and support the reliability of test results. For example laboratory certification (NATA, CLIA), laboratory normal values for medical/laboratory/technical procedures and/or tests included in the protocol; refrigerator and or freezer temperature logs.

13. Study Team Documentation

13.1 Delegation and signature log

The delegation logs are to document signatures and initials of all persons authorised to make entries and/or corrections on CRFs, sign consent forms and undertake procedures as detailed in the protocol.

The delegation log is a record of the study tasks that have been delegated to each staff member by the Principal Investigator (PI). The delegation log provides a quick reference of who is authorised to do what on the study; staff must only perform tasks for which they have been delegated.
The delegation log also captures the signature and initials of all staff members prior to start on the study which helps authenticate study documentation.

13.2 Qualifications (CV) and Training

The Principal Investigator is responsible for ensuring that all research staff are qualified by education, training and experience to adequately perform their delegated study tasks and, if applicable, to provide medical supervision of research participants.

In this section file documentation evidencing the appropriate qualification of all study staff listed on the delegation log as appropriate for your project. Such documentation may include copies of signed and dated CVs, training certificates (e.g. ICH-GCP, hazardous substances, IATA) or licences (e.g. a licence to give injections, a medical license).

Include GCP training certificates from all key research team personnel from the Central Trial Coordinating Team. GCP Training is required for all staff listed on the delegation log. Please contact CAHS Research Office for further information. GCP training must be completed every three years to remain current. Evidence of current GCP certification can also be uploaded under each RGS users profile on RGS.

Related Link: An online GCP training course is available via the WA Health Translation Network (WAHTN) Research Education & Training Program (RETP) - https://www.retprogram.org/training Alternatively, any training that meets the minimum criteria for ICH GCP Investigator Site Personnel Training identified by TransCelerate BioPharma can be completed.

Any study specific training materials generated for the study staff and training logs related to protocol, amendments, and study procedures should also be filed in this section.

14. Supplies / Shipping records

In this section file documentation in relation to study supplies apart from IMP (such as blood collection tubes/ documentation

15. Legal Documentation

Any agreements that are made in relation to the study should be filed in this section, such as the agreement of a collaborating statistician to provide a certain number of hours of support, a publication agreement made with collaborators, a clinical trial agreement or an agreement with the pharmacy that clarifies their role in the study.
If agreements are revised during the course of the study, revised documents should be filed in the section, marking the prior versions 'superseded'.

The following documents should also be filed in this section:

- Indemnity
- Insurance Certificate
- Copy of Financial Agreement/Budget Details (including grant application and conditions of award)
- Confidentiality agreements
- Correspondence with hospital insurers or lawyers

Related links: WA Health Agreement templates available via RGS

16. Finance (Financial disclosure forms)

File a copy of the Study Budget and revisions, clearly indicating the most recent version.

Any records related to participant reimbursements, if these will be made in your study and have been approved by the ethics committee, should be maintained in this section.

Any financial disclosure forms required for your study or conflict of interest forms can also be filed here.

Related links:
RGS budget guidance
WA Health Research Budget Template v5.0 Nov 2021
WA Health Research Budget Template v4.0 Nov 2016 – Example

17. Correspondence

Keep pertinent correspondences detailing any agreements or significant decisions or discussions regarding study conduct. The correspondence may take the form of emails, letters, meeting notes/minutes and/or notes of telephone calls.

17.1 Sponsor/Funding body

Any pertinent correspondence between the study team and the sponsor or the funding body of the study including grant applications should be filed.

17.2 Study team meetings – agenda and minutes

Any meeting minutes where the study was discussed should be filed here. Regular meeting between the PI and study team should be held and documented to ensure evidence of appropriate PI oversight.

17.3 Newsletters

Any newsletters from the sponsor of the trial regarding the project, or any newsletters generated by the study team for distribution

17.4 General

Any correspondence that doesn't fall in the above sections, include three-way communications.

18. Study reports/publications

This section can be used to file the publications related to the study and the study interim report, if applicable.

19. Other

Include here any documents that do not fall into any of the above sections.

***** Drug/ Device trials only *****

20. Regulatory documents

This section must include a printed copy of the Australian CTA or CTN application form (fully executed) and the acknowledgment notification. All correspondence to the regulatory agencies (e.g. TGA) should also be filed here including safety reporting to the TGA.

Related links: Information required for submitting CTN form

21. Investigator brochures (IB)

The IB documents that relevant and current scientific information about the investigational product has been provided to the investigator. Include the current HREC approved IB here.

Superseded IB

This can be the front page of the document only (to conserve space)

If your trial uses a product already registered in Australia please keep on file the Product Information Document.

22. Investigational Product

The purpose of this section is to document shipment dates, batch numbers and method of shipment of investigational product(s) and trial-related materials. This allows tracking of product batch, review of shipping conditions and accountability. Include information such as:

- date of shipment
- batch numbers
- method
- shipment receipt records,
- certificate of analysis for investigational product
- storage conditions
- dispensing details and returns from study participants

This may be kept in the pharmacy files during the conduct of the study but should be returned to the investigator files prior to archiving.