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**STUDY BINDERS - Guidelines, table of contents and section detail**

**The Study Binder:**

* Can be used for all study types - public health studies, clinical research studies including clinical trials (drug/device trials and non-drug/device research)
* Contains material relating to the conduct of the study
* Should be maintained centrally within Western Health (if multiple departments within WH sites are participating, each department should maintain core sections for staff reference).
* 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 audited by the Office for Research or delegates
* Must NOT contain participant identifying documentation (except for screening logs [initials])
* 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)

**File Notes**

* Place these in the section that they are relevant to.

**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 institutional, ICH, FDA, Department of Human Services guidelines (may include off-site document storage and electronic archiving). (Refer to Data Management Research Guideline OG-GC7 Section 7.10)

**Other files**

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

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

**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 contact details for those of the following (where applicable):

* All members of study staff
* Sponsor contacts
* 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

**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 the start-up 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 all study staff and to formalise the start of the study.

**3. Protocol**

All versions as provided to and as approved by ethics, including signed protocol signatory (‘acknowledgement’) 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 study.

**4. Participant information**

Master documents that can be copied and provided to potential participants should be kept in here.

**4.1. Participant Information & Consent Forms – Current HREC Approved versions**

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

**4.2. Participant Information & Consent Forms – Current Governance Authorised versions**

A blank copy of the current site governance authorised information statement and consent form(s).

**4.3. Other participant information/materials – Current HREC approved (e.g. advertisements, diaries, letters)**

A blank copy of the currently approved.

**4.4. Other participant information/materials – Current Governance Authorised (e.g. advertisements, diaries, letters)**

A blank copy of the current site governance authorised documents.

**4.5. Superseded Participant Information & Consent Forms**

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

**4.6. Superseded Other participant information/materials**

Blank copies of all previously approved other documents must be included here, include tracked versions.

**4.7. Translated documents**

Retain forward-translations and back-translations and certification by translators.

**5. Ethics & Governance**

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

**5.1. HREC approval and RGO authorisation letters**

Ensure that this section contains letter/s documenting the Human Research Ethics Committee (HREC) approval and site governance authorisation from Research Governance Office (RGO) of the following documents:

* Approval of the current protocol
* Approval of the current informed consent form
* Approval of the current version of any materials viewed by participants (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

All 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. Submission documentation (initial)**

The complete signed applications that were submitted to the ethics/governance office should be filed in this section, along with any pertinent correspondence between the study staff and the ethics/governance office, such as requests for changes to documents or responses to questions raised by the committee. Ensure all signatures and Statement of Approvals form heads /supporting head of department/s are kept.

**5.3. Submission documentation (amendments)**

All subsequent complete submissions to HREC and RGO needs to be filed. This includes (but is not limited to) protocol amendments, revised PICF or recruitment advertisements.

**5.4. Annual and final study reports**

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

Final report – At the end of the study, a final report must be submitted and a copy filed in this section, prior to archiving.

**5.5. Other Correspondence**

Include in this section any letters to and from the ethics/governance office 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 date safety and monitoring board letters.

**6. Participant recruitment: Pre-screening log and Consent, screening & enrolment log**

For the purposes of this document:

* **Pre-screening** refers to the evaluation of generalised characteristics prior to consent and screening to initially determine eligibility (following ethical and governance approval of the study). The characteristics may be determined from the medical record, a referring clinician or other sources as appropriate to the study (including self-referrals by potential participants), but not via any procedures undertaken specifically for the study.
* **Screening** refers to the collection of information that is in addition to clinical care, it is collected for the reason of assessing eligibility for the study. Some examples of this are: testing cognition, assessing level of physical function, taking blood samples, and requesting medication history. As such this information is always collected after consent has been obtained.
* **Enrolment** refers to participants who have provided informed consent, have been screened for study eligibility and have been deemed eligible. **Note that for clinical trials, enrolled refers to participants who have been assigned to the trial intervention.**

Initial eligibility can be determined from the medical record (e.g. Epic), a clinician’s referral to the study, telephone contact, website registration or other sources as appropriate to the study. During pre-screening, the person may be excluded due to one or more of a range of factors such as demographic information (e.g. age, sex), medical history, current or previous treatments. Note that the study should be introduced to the potential participant by an individual who, by virtue of his/her position, would normally have access to the potential participant’s confidential information.

**6.1. Pre-Screening Log**

Good Clinical Practice guidance\* requires that the principal investigator document all pre-study recruitment activities. A Pre-screening Log should be maintained to record limited details of those who were pre-screened, tracking the outcome of the screening (e.g. ineligible, potentially eligible but declined further study involvement, potentially eligible and attended a Screening Visit). This allows study personnel to track reasons and trends for non-inclusion in a study (which may prompt a protocol amendment) and check whether potentially eligible participants are being missed. Completion of a pre-screening log is also useful to ensure that those already excluded or who declined participation are not re-contacted.

**6.2. Consent, Screening & Enrolment Log**

Good Clinical Practice guidance\* requires that the principal investigator document, in chronological order, all participants screened and enrolled in a study. This document also acts as a master record providing the link between a participant’s personal identifiers and their assigned study code.

\* Integrated Addendum to ICH E6 (R1): Guideline for Good Clinical Practice ICH E6 (R2) – Annotated with TGA comments

**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’.
* Adverse event 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 the NCI’s Common Terminology Criteria for Adverse Events (CTCAE) available at: https://ctep.cancer.gov/protocolDevelopment/adverse\_effects.htm

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 management – procedures**

Please also refer to the Western Health Data Management in Research Guideline OG-GC7 for more guidance.

**8.1. Data Management Plan**

A Data Management Plan should be prepared for all studies and filed in this section. This should include aspects such as:

* Roles and responsibilities
* Types of data
* Data collection, coding and entry
* Quality assurance and control activities
* Data storage
* Data access and security
* Data preservation and retention.

**8.2. Case Report Forms (CRFs)**

CRFs are the official data-recording documents used in a study. Relevant data is transcribed from the patient record (and/or 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** be collected and thus not appear on the CRF.

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

**8.2.1. Blank Sample CRF**

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

**8.2.2. 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 (this is relevant only if your site is responsible for CRF design).

**8.2.3. 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.

**8.2.4. Data queries**

Include details in this section regarding how queries will be generated from completed CRFs and the resolution process and timelines. Include Data query tracking, monitors site queries and correspondence.

**9. Safety monitoring and reporting**

**9.1. Safety event reporting**

Reports to, and correspondence with, the approving HREC, the site’s Research Governance Office (RGO) or government regulatory bodies regarding safety events should be filed in this section. This includes Suspected Unexpected Serious Adverse Reactions (SUSAR), Urgent Safety Measures (USM), Significant Safety Issues (SSI) and Serious and non-serious Breaches.

**9.2. Annual safety report (clinical trials only)**

For clinical trials, an annual safety report, prepared by the study Sponsor, is also required to be submitted to the approving HREC and site Research Governance Offices (RGO).The report and associated correspondence should be filed in this section.

For further details on safety reporting requirements and procedures, refer WH website: https://www.westernhealth.org.au/EducationandResearch/Research/Research%20Governance/Pages/Safety-and-Adverse-Event-Reports.aspx

**9.3. Data Safety Monitoring groups (clinical trials only)**

For intervention studies, a plan for monitoring safety should be developed and adhered to. All safety monitoring plans should be filed in this section.

Where separate groups (e.g. data monitoring group or an independent Data and Safety Monitoring Board [DSMB]) are utilised to oversee the study, all reports and correspondence should be filed in this section.

DSMB (if applicable) terms of reference and membership should also be filed in this section (that is if your site is undertaking overall conduct of the study).

**10. Study quality assurance, monitoring & audits**

For all studies, a quality assurance/self-audit program should be established to ensure that:

* The study is being conducted in accordance with the protocol and, where applicable, Good Clinical Practice (GCP) guidelines and applicable regulatory requirements
* The participant’s safety, rights and well-being are protected
* Data recorded on the case report forms are accurate, complete and verifiable from source documentation.

Quality control/self-audit activities can be undertaken by a member of the study team, except in the case of clinical trials where these activities should be undertaken by a person / persons appointed as the Study Monitor.

The Monitor should follow a study-specific Clinical Monitoring Plan (CMP) based on the level of risk involved in the trial.

All documentation regarding the quality assurance, quality control checks, monitoring and auditing should be filed in this section.

**11. 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
* log of tissue samples retained at site
* refrigerator and/or freezer temperature logs.

**12. Study team documentation**

**12.1. 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, for example, helps to authenticate CRF entries and prescriptions.

**12.2. 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. Such documentation may include:

* copies of signed and dated CVs (check CV is current and lists current institution
* and role)
* training certificates (e.g. ICH-GCP, hazardous substances, IATA)
* licences (e.g. a licence to give injections, a medical license).
* Study-specific training (protocol, protocol amendments etc)

Any study specific training materials generated for training study staff should also be filed in this section.

**13. Supplies/Shipping records**

For accountability, in this section file documentation relating to study supply provision (excluding investigational drugs/devices – see section 22).

**14. Financial agreements and legal documentation**

In this section file:

* Original Financial Agreement/Budget Details (including grant application and conditions of
* award) – original and any revisions (if applicable) - clearly indicate the most recent version.
* Any other 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 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:

* Confidentiality agreements
* Correspondence with hospital insurers or lawyers
* Indemnity (if applicable)
* Insurance Certificate (if applicable)

**15. Other finance documentation**

In this section file:

* Any records related to participant reimbursements (if applicable and approved by the ethics committee).
* All other finance documentation.

**16. 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.

**16.1. Sponsor/Funding body**

Any pertinent correspondence between the study team and the sponsor or the funding body of the study.

**16.2. General**

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

**16.3. Newsletters**

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

**16.4. General**

Include in this section any other correspondence.

**17. Study reports/publications**

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

applicable.

**18. Clinical trial (and observational study) registration**

In 2004 the International Committee of Medical Journals Editors (ICMJE, including editors of the

Medical Journal of Australia, Lancet, New England Journal of Medicine and others) declared that

they would not consider a trial for publication without evidence that it had been registered in a

publicly accessible trials registry prior to enrolment of the first participant.

Some journals, including the Lancet and BMJ, encourage prospective registration of observational studies in order to consider manuscripts of observational studies for publication. BMJ also supports the posting of results in publically accessible registries. It is for this reason that MCTC recommends prospective registration of observational studies in a primary register of the WHO international clinical trials registry platform (ICTRP), clinical.trials.gov or anzctr.gov.au.

**19. Other**

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

**FOR CLINICAL TRIALS**

**20. Regulatory documents**

*(for trials of investigational drugs/devices)*

For clinical trials of drugs and devices being conducted under the Clinical Trials Notification (CTN) scheme, this section must include evidence of acknowledgement by TGA of the clinical trial (i.e. initial notification and any variations to the initial notification).

For clinical trials conducted under the Clinical Trial Exemption [CTX] scheme), detailed documentation of submission to and approval from the TGA should be retained here.

**21. Investigational product information – Investigator Brochure (IB)**

*(for trials of investigational drugs/devices)*

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

Note that information on investigational products that are already registered in Australia can be found on the TGA website http://www.tga.gov.au/about/ebs-picmi.htm#.UwWYl63xuUk in the form of:

* Consumer Medicine Information (CMI) – this is a plain language leaflet about the safe and effective use of a medicine.
* A Product Information document (PI) provides health professionals with a summary of the scientific information relevant to the safe and effective use of a prescription or pharmacist only medicine. The information has been written by the pharmaceutical company responsible for the medicine and has been approved by the TGA.

**21.1. Superseded IB/PI/CMI**

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

**22. Investigational product accountability**

*(for trials of investigational drugs/devices)*

Responsibility for investigational product accountability rests with the Principal Investigator; it is usually delegated by the Principal Investigator to an appropriately qualified person. It is strongly recommended that this be delegated to RCH Pharmacy as clinical trials pharmacists have the knowledge and experience to manage all aspects to the required regulatory and good clinical practice standards. The requirements cover areas such as detailed recording of:

* Product delivery to the trial site
* Product inventory including dispensing to and returns by participants, product expiry, product disposal
* Adherence to product storage requirements

**23. Unblinding procedure**

The protocol should provide details of how, in case of an emergency, the identity of blinded investigational product can be revealed for a specific participant. More detailed site specific information may be stored here, where indicated.