CLINICAL TRIAL SOP 10: Protocol and Investigational Brochure Requirements

Purpose

To describe the procedures related to the development of a research Protocol, an Investigational Brochure (IB), and amendments to these documents ensuring compliance to ICH GCP E6 (R2).

Scope

This SOP applies to all Investigators (Principal and Sub-Investigator), Study Coordinators, visiting medical officers (VMO), and other Research staff and volunteers who propose to undertake, administrate, review and/or govern human research involving patients/participants and staff. All study personnel involved in the clinical study must operate within their scope of practice.

Cabrini Health policies and regulatory requirements

This SOP should be read in conjunction with policies and other documents provided by the Cabrini Research Governance Office (CRGO) relevant to the conduct of clinical research at Cabrini Health including but not limited to:

- Aboriginal and Torres Strait Islander Health – asking for Aboriginal and Torres Strait Islander identity
- Monitoring of Research Policy
- Research Integrity and Misconduct Policy
- Safety Monitoring and Reporting in Research Policy
- Cabrini Research Data Management, Access and Sharing Policy
- Data Classification and Labelling Standard
- Cabrini Authorship and Publications for Research Policy
- Research Participants Complaints and Compliments Procedures Policy
- Cabrini Research Governance Handbook

Researchers at Cabrini must foster quality research and abide by the following directives:

- The National Clinical Trials Governance Framework (NCTGF)
- National Statement on Ethical Conduct in Human Research (2023)
- Catholic Health Australia Code of Ethical Standards
- Act in accordance with Cabrini Research policies in order to protect the rights, safety and welfare of research participants
- Support patient and family carer involvement in their own research participation through abidance with the Australian open disclosure policy, and Charter of healthcare rights.
- Agree to comply with all reasonable directions and policies by Cabrini Research for Cabrini to meet or exceed the requirements of the NCTGF. To the extent that the NCTGF applies to the position, compliance with the specified roles and functions of the workforce, as set out by the NCTGF.

Cabrini Health specifically acting as a sponsor or lead site

All investigators should be aware that Cabrini does not currently support trials as a sponsor or act as a lead site in multisite trials. This position is currently under review. Please contact the Cabrini Research Governance Office (CRGO) for further information or queries in how this may impact your project.

Procedure

10.1 Protocol Content and Development

Specific content of a Protocol will vary depending on the subject of the research, the level of risk to participants, the phase of the research and study design, and whether a medicinal product or a device or a therapeutic intervention is being researched. Consequently, the terminology will be different and should be adapted appropriately.

A range of guidance material may inform and be referred to in development of the Protocol, including but not limited to Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) and the Consolidated Standards of Reporting Trials (CONSORT).

However, where the Investigator is responsible for the Protocol development they must ensure the Protocol follows the outline as per ICH GCP E6 (R2) Section 6 Clinical Trial Protocol and Protocol Amendment(s). This Protocol table of contents is not mandated but it is recommended a trial Protocol should generally include the topics detailed in the section. However, site specific information may be provided on separate Protocol page(s), or addressed in a separate agreement, and some of the information listed may be contained in other Protocol referenced documents, such as an IB.

The following considerations are to be addressed such that Protocol deviations are not created.

- The process by which participants will be informed about the risks and benefits of participation and their agreement (or otherwise) to participate will be clearly described and documented, including what evidence will be recorded for auditing purposes (i.e. face-to-face, videoconference, via telehealth, skype, phone etc).
- Description of how study procedures will be undertaken, e.g. how visits, assessments, collection of data and medical consultations will be conducted i.e. face-to-face or via telehealth or a combination of both.
- Description of storage and handling of Investigational Product, e.g. will the Investigational Product be stored at Cabrini Malvern Pharmacy and shipped to Cabrini Brighton via appropriate handling and shipping method when a participant is deemed eligible?
- Description of the handling of other study related non-IMP materials.
- Description of the roles and responsibilities of Investigators and other staff who will be involved in the study.
- Inclusion of a Data Management Plan (DMP) either as a named section of the protocol, or as a separately developed document.

10.2 Investigational Brochure Content and Development

Where the Investigator contributes to the content and development of the IB they must ensure the Investigational Brochure follows the outline as per ICH GCP E6 (R2) Section 7 Investigator's Brochure.

An example of an IB Table of Contents is found in Section 7.5 Appendix 2 section in the above link. While it is not mandated, its use is recommended as it ensures adherence to ICH GCP E6

(R2). The IB should remain up-to-date via annual revision at a minimum, depending on the type of product and its stage of development.
In some situations, for Investigational Medicinal Products, where a product is registered, and has a well-understood pharmacology, a Product Information document may be substituted for an IB, provided that current and comprehensive information about the product under study is available to the Investigators. If a product is registered, but is being trialled for a new indication, or in a different population to the approved indication, an IB must be collated with reference to this new indication/population.

10.3 Amendment/s to the Protocol and Investigational Brochure

The Investigator must inform the approving HREC and Cabrini Research Governance Office (CRGO):

- and obtain acknowledgement of receipt of the updated IB.
- and obtain approval of all amendments to the Protocol including amendments that:
  - are proposed or undertaken without prior HREC approval in order to eliminate immediate risks to participants;
  - may increase the risks to participants;
  - may alter the ethical acceptability of the trial;
  - may affect the viability of the trial;
  - may impact on the scientific validity of the trial; or
  - significantly affect the conduct of the trial (including changes to the Inclusion/Exclusion criteria).
- as soon as possible after any new safety information from other published or unpublished studies is identified that may have an impact on the continued ethical acceptability of the project or may indicate the need for amendments to the research Protocol.

Notification to the approving HREC is HREC specific and the Investigator should be familiar with the terms of reference of their ethics committee. Refer to SOP 08 Communication with HREC, CRGO, Sponsor and Institution's Insurer, regarding communication with the HREC.
The Investigator must comply with any additional conditions placed on the project by the HREC as a result of the Protocol variation.

The Investigator must provide to the CRGO:

- The HREC approval letter for the amendment(s).
- A copy of all HREC approved amended documents.

A CRGO Governance Application Form (Site Specific Form) and CRGO Project Costing Template will need to be completed.

Where there is an amendment to the Protocol, authorisation from the CRGO to continue the project must be obtained, including Protocol amendments that:

- are proposed or undertaken without prior HREC approval in order to eliminate immediate risks to participants however that amendment will be implemented prior to governance authorisation.
- may increase the risks to participants.

- significantly affect the conduct of the trial (including changes to the Inclusion/Exclusion criteria).
- pose a risk to the Institution.
- require contract variations or impose additional contractual requirements or obligations by the relevant Institution.

Notification to the CRGO is site specific and the Investigator should be familiar with their processes.

Current Version

DOCUMENT ID:	CLINICAL TRIAL SOP 10: Protocol and Investigational Brochure Requirements
VERSION:	1.0
EFFECTIVE DATE:	01 October 2024
REVIEW DATE:	01 October 2026

Document Approval

NAME	POSITION	SIGNATURE	DATE
Professor Gary Richardson	Group Director, Cabrini Research		18 September 2024

Document History

VERSION NUMBER	EFFECTIVE DATE	DETAILS OF AMENDMENTS /EDITIONS