GV Health	**TITLE:**	**Clinical Trial Standard Operating Procedure 04: Protocol and Investigational Brochure (IB) Requirements**	
Document Type:	Procedure	**Approved by:**	Research Management and Governance Committee
Directorate:	CMO + Medical Services	**Section:**	Research
Author/Prepared by:	Dr Ainsley Robinson	**Position:**	Clinical Trials Coordinator

DO NOT USE THIS STANDARD OPERATING PROCEDURE IN PRINTED FORM WITHOUT FIRST CHECKING IT IS THE LATEST VERSION.

The definitive versions of all Goulburn Valley Health (GV Health) Clinical Trial Standard Operating Procedures (SOPs) appear online, not in printed form, to ensure that up to date versions are used. If you are reading this in printed form check that the version number and date below is the most recent one as shown on the GV Health website or Prompt.

Document Details

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Name:	Research Management and Governance (RM&G) Committee
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Amendment History

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1.0	12 Nov 2020	16 June 2023	Dr Ainsley Robinson Research and Ethics	Reviewed and updated to v2.0
2.0	16 June 2023	22 March 2024	Usman Tahir, Research and Ethics	Reviewed and updated to v3.0

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1. 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 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)).

2. SCOPE:

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

3. PROCEDURE:

3.1. 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 research and study design, 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).

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). The 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.

Where Satellite Sites will be involved in the study, no specific wording will be required in the Protocol, as the following considerations will be addressed in other study-specific documents which may be annexed to the Protocol e.g., the site selection report, ethics application, Supervision Plan, the monitoring manual, laboratory manual, pharmacy manual, safety monitoring manual or a trial specific working guideline. Nevertheless, 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 (IP), e.g. will the IP be stored at the Primary Site and shipped to the Satellite Site via appropriate handling and shipping method when a participant is deemed eligible or will Satellite Sites with appropriate facilities store the IP?
- Description of storage and handling of laboratory samples at Satellite Sites if involved and if relevant e.g. frequency of and timelines between transport of samples to Primary Site or direct to a Central or Local laboratory.
- Description of the handling of other study related non-IP materials.
- Description of the roles and responsibilities of Investigators and other staff who will be involved in the study at both the Primary and Satellite Sites.

3.2. Investigational Brochure (IB) Content and Development

Where the investigator contributes to the content and development of the IB, they must ensure the IB 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 (IMPs), 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.

3.3. Amendment/s to the Protocol and IB

3.3.1. The Investigator must inform the Human Research Ethics Committee (HREC):

- and obtain acknowledgement of receipt of the updated IB; and
- obtain approval of all amendments to the Protocol including amendments that:
  - a) are proposed or undertaken without prior HREC approval in order to eliminate immediate risks to participants;
  - b) may increase the risks to participants;
  - c) may alter the ethical acceptability of the trial;
  - d) may affect the viability of the trial;
  - e) may impact on the scientific validity of the trial; or

f) 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 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 HREC is HREC specific and the Investigator should be familiar with the terms of reference of their ethics committee. Refer to GVH_CT-SOP-05-Communication with Human Research Ethics Committee (HREC), Research Governance Officer (RGO), Sponsor and Institution's Insurer, regarding communication with the HREC.

The Investigator must comply with any additional conditions place on the project by the HREC as a result of the Protocol variation.

3.3.2. The Investigator must provide to the RGO:

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

A Site-Specific Assessment (SSA) Form will need to be completed for both the Satellite Site and the Primary Site.

Where there is an amendment to the Protocol, authorisation from the RGO to continue the project must be obtained from both the Primary and Satellite Sites where a governance aspect has been affected (if required) including Protocol amendments that:

a) are proposed or undertaken without prior HREC approval in order to eliminate immediate risks to participants;
b) may increase the risks to participants;
c) significantly affect the conduct of the trial (including changes to the Inclusion/Exclusion criteria); or
d) pose a risk to the Institution.
e) require Clinical Trial Research Agreement (CTRA) variations or impose additional contractual requirements or obligations by the relevant Institution.
f) For a teletrial, if a variation to the Sub-Contract is required, this will need to be negotiated between the Primary and Satellite Sites.

Notification to the RGO is site specific and the Investigator should be familiar with the processes of the GV Health RGO.

For the avoidance of doubt, where there is an amendment to the Protocol, a variation to the Clinical Trial Sub-Contract between the Primary and Satellite Sites will be needed if the contract variation impacts on the Satellite Site, as determined by the Primary Site.

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

KEY LEGISLATION, ACTS & STANDARDS:
National Safety and Quality Health Service (NSQHS) Standards:

- Standard 1 Clinical Governance

KEY ALIGNED DOCUMENTS:
GV Health procedure:

- GVH_CT-SOP-05-Communication with Human Research Ethics Committee (HREC), Research Governance Officer (RGO), Sponsor and Institution's Insurer

REFERENCES:
ICHGCP.NET, Good Clinical Practice. (2019). Ichgcp.net. https://ichgcp.net/

National Clinical Trials Governance Framework and User Guide, Australian Commission on Safety and Quality in Health Care. (2022). Safetyandquality.gov.au. https://www.safetyandquality.gov.au/publications-and-resources/resource-library/national-clinical-trials-governance-framework-and-user-guide

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