SOP 04 Protocol and Investigational Brochure Requirements

1.1 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 ICH GCP E6 (R2).

1.2 Scope

This Standard Operating Procedure (SOP) applies to all relevant employees including, but not limited to, visiting health professionals, contractors, consultants 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.

1.3 Procedure

4.1 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.

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, e.g. will the Investigational Product 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 Investigational Product?
- 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-IMP 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.

4.2 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.

4.3 Amendment/s to the Protocol and Investigational Brochure

The Investigator must inform the HREC:

- 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 HREC is HREC specific and the Investigator should be familiar with the terms of reference of their ethics committee. Refer to SOP 05 Communication with HREC, 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.

The Investigator must provide to the RGO:

- The HREC approval letter for the amendment(s).
- A copy (if required by the RGO) 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:

- 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.
- 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 their 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.

Glossary

TERM	DESCRIPTION
ADE	Adverse Device Effect
ADR	Adverse Drug Reaction
AE	Adverse Event
AHPRA	Australian Health Practitioner Regulation Agency
AI	Associate Investigator
ARPANSA	Australian Radiation Protection and Nuclear Safety Agency
ARPANSA Code of Practice	ARPANSA Code of Practice for the Exposure of Humans to Ionizing Radiation for Research
CAPA	Corrective and Preventative Actions
CASA	Civil Aviation Safety Authority
CIOMS	Council for International Organizations of Medical Sciences
CPI	Coordinating Principal Investigator
CRA	Clinical Research Associate
CRC	Clinical Research Coordinator
CRF	Case Report Form
CRO	Contract Research Organisation
CTA	Clinical Trial Approval scheme (previously Clinical Trials Exemption (CTX) scheme)
CTN	Clinical Trial Notification scheme
CTPRG	Clinical Trials Project Reference Group
CTRA	Clinical Trial Research Agreement
CV	Curriculum Vitae
DSMB	Data and Safety Monitoring Board
EMR	Electronic Medical Record
GCP	Good Clinical Practice
HHS	Hospital and Health Service
HREC	Human Research Ethics Committee

IATA	International Air Transport Association
ICH	International Council for Harmonisation of Technical Requirements of Pharmaceuticals for Human Use
IP	Investigational Product
IMD	Investigational Medicinal Device
IMP	Investigational Medicinal Product
IVRS	Interactive Voice Response System
IWRS	Interactive Web Response System
National Statement	National Statement on Ethical Conduct in Human Research (NHMRC)
NHMRC	National Health and Medical Research Council
NMA	National Mutual Acceptance
PI	Principal Investigator
PICF	Participant Information and Consent Form
PMS	Post Registration or Marketing Surveillance Study
RGO	Research Governance Officer
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SMF	Study Master File
SSA Form	Site Specific Assessment Form
SSI	Significant Safety Issue
SSSF	Satellite Site Study File
SUSAR	Suspected Unexpected Serious Adverse Reaction
TGA	Therapeutic Goods Administration
UR	Unit Record
USADE	Unanticipated Serious Adverse Device Event
USM	Urgent Safety Measure

○ Revision Chronology

Document History			
Version	**Effective Date**	**Summary of Changes**	**Author**
1.0	*13/11/2025*	Initial Version	Katie Ozdowska