GVHealth	**TITLE:**	**Clinical Trial Standard Operating Procedure 05: Communication with Human Research Ethics Committee (HREC), Research Governance Officer (RGO), Sponsor and Institution's Insurer**	
Document Type:	Procedure	**Approved by:**	CMO & EDMS
Directorate:	CMO + Medical Services	**Section:**	Research
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1. PURPOSE:

To describe the procedures relating to communication with the Human Research Ethics Committee (HREC), Research Governance Officer (RGO), Sponsor and Institution's Insurer.

2. SCOPE:

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

3. PROCEDURE:

3.1. Communication with Reviewing HREC

When communication regarding key decision points is verbal, the initiating party should follow up verbal communication with written correspondence/email and send to the call recipient. The title of the letter/email should include the term "FILE NOTE" followed by a text string which should include the decision topic. Such documentation must be filed in the Study Master File (SMF) and where applicable in the Satellite Site Study File (SSSF).

3.1.1. Prior to Study Commencement the Investigator must:

- Choose a reviewing HREC whose approval is acceptable to the Institution/s where the clinical study is being undertaken (or ensure the responsible HREC chosen by the Coordinating Principal Investigator (CPI) is likewise acceptable).
- Understand the reviewing HREC requirements, submission processes and be aware of their meeting and submission dates to better liaise with Sponsors.
- Be familiar with the relationships between HREC review and approval, governance authorisation and any other processes/approvals that need to be in place (e.g. does the HREC have Sub-Committees), before any study start-up activities can commence. This process and approval flow will be required by Sponsors, auditors, and inspectors.
- Submit an ethics application as per the reviewing HREC submission process.
- Include in the relevant section of the ethics application that the trial may be undertaken using telehealth with Satellite Sites, if applicable, and that the informed consent process and/or some or all study assessments will be undertaken using telehealth, face to face consultation or a combination of both.
- Submit any other application as per that process found on the relevant website.
- Ensure all documentation and correspondence pertaining to the submission and approval processes is filed in the SMF e.g. correspondence to and from the HREC, RGO or other body.

3.1.2. During the Study the Investigator must:

- Comply with all conditions and restrictions applied by the RGO or HREC on the conduct or continuation of the trial.
- Submit all documents/reports/summaries according to the requirements and timelines as stipulated on the respective reviewing HREC approval letter including but not limited to: Sponsor reports of accumulated safety data outcome analyses; proposed changes to the Protocol; major or Serious Breaches; annual progress reports; and unforeseen events that might affect continued ethical acceptability of the trial.
- Comply with the reporting requirements outlined in GVH_CT-SOP-12-Safety Data Monitoring and Reporting Requirements for Clinical Trials, noting that individual reports of Adverse Events (AEs), Serious Adverse Events (SAEs), Suspected Unexpected Serious Adverse Reactions (SUSARs), Unanticipated Serious Adverse Device Events (USADEs) and six-monthly line listings should NOT be submitted to the reviewing HREC unless otherwise advised.
- Although all deviations must to be reported to the trial Sponsor, only the sub-set of deviations that have a significant impact on the continued safety or rights of participants or the reliability and robustness of the data generated in the clinical trial must be reported to the HREC. These deviations (also known as 'Serious Breaches') should also be reported by the Principal Investigator (PI) to their Institution, as they may impact on medico-legal risk, the responsible conduct of research, or adherence to contractual obligations.
- Immediately notify the reviewing HREC of any notification received from a participant in a trial that they intend to initiate a claim for compensation against either the Sponsor and/or the Institution.
- File all documentation in the SMF/SSSF.

3.1.3. At the End of the Study, the Investigator must:

- Submit a trial termination/close out report according to the requirements and timelines as required by the respective reviewing HREC. This may be stipulated in the approval letter and/or on their website.
- File all documentation in the SMF/SSSF.

3.2. Communication with the Research Governance Officer (RGO):

For the purpose of this SOP, the Clinical Trial Research Agreement (CTRA), other site-specific trial-related documentation, and the Site-Specific Assessment (SSA) Form constitute a research governance application for the Primary Site. Similarly, for the Satellite Site, a SSA/research governance application consists of the Sub-Contract, the SSA form and other site-specific trial-related documentation. This application may be submitted to the RGO in parallel to the HREC submission if all governance related documentation is available and completed correctly. In the majority of cases, the final document to be provided to the RGO is the HREC approval. This has the advantage of enabling an RGO review in parallel to the HREC review and allows a more timely RGO

authorisation which may lead to expedited study start up. It is important to note, that HREC approval must be obtained and submitted to the RGO, prior to the final RGO authorisation being granted.

3.2.1. Prior to Study Commencement the Investigator must:

- Submit the CTRA, the SSA Form, and any other required documentation to the RGO.
- Ensure all documentation and correspondence pertaining to the submission and approval processes is filed in the SMF.
- Ensure each Satellite Site in the cluster (whether in a different Hospital and Health Service (HHS) to the PI or the same HHS) completes a clinical trial Sub-Contract and a SSA Form which is a subsection of the main SSA and submits to their RGO.
- Await site specific RGO authorisation before any study related activity can occur at that site.
- Ensure the Satellite Site files all documentation in the SSSF.

3.2.2. During the Trial the Investigator must:

- Submit all governance related documents/reports/summaries to the RGO according to the requirements and timelines as stipulated by the RGO including but not limited to:
  - changes to the CTRA/Sub-Contract;
  - changes to the budget;
  - any change that might affect continued financial acceptability of the trial;
  - any change that may increase Institutional risk.
- Serious Breaches (those deviations that may have a significant impact on the continued safety or rights of participants or the reliability and robustness of the data generated in the clinical trial) should be reported by the PI to their Institution, as they may impact on medico-legal risk, the responsible conduct of research, or adherence to contractual obligations.
- Immediately notify the RGO of any notification received from a participant in a trial that they intend to initiate a claim against either the Sponsor and/or the Institution.
- Ensure all training and accreditation remains current.
- Ensure the Satellite Site files all documentation in the SSSF.

3.2.3. At the End of the Trial the Investigator must:

- Notify the RGO the trial has terminated/closed.
- File all documentation in the SMF/SSSF. Poor compliance with the Protocol or Good Clinical Practice (GCP) can lead to data being rejected by regulatory authorities, can compromise participant safety, and can nullify a trials insurance/indemnity. 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)) requires that the PI (or delegate) document and explain any deviation from the

Protocol and requires that non-compliance with the Protocol, SOPs, GCP, and/or applicable regulatory requirement(s) lead to prompt action to secure compliance.

In the majority of instances, non-compliances are deviations that do not result in harm to trial participants or significantly affect the scientific value of the reported results of the trial. Some of these deviations are unavoidable (e.g. a participant misses a visit) or permitted (e.g. a deviation from the Protocol to protect a participant from an immediate hazard known as an Urgent Safety Measure). ICH GCP E6 (R2) requires all non-compliances (both minor and major) to be reported to the trial Sponsor. The National Health and Medical Research Council (NHMRC) Guideline: Reporting of Serious Breaches of GCP or the Protocol for Trials Involving Therapeutic Goods, categorises certain instances of noncompliance as a Serious Breach, defined as: A breach that is likely to affect to a significant degree: the safety or rights of the trial participant, and/or the reliability and robustness of the data generated in the clinical trial.

Deviations that may (depending on their nature) meet the definition of a Serious Breach include:

- Intentional or accidental loss of blinding of study medication.
- Failure to control Investigational Medicinal Product(s) such that participants are put at significant risk or the scientific value of the trial is compromised.
- Deviations from eligibility criteria related to the diagnosis of patients/participants.
- Non-compliance relating to evaluation of important efficacy endpoints.
- Missing Source Data which are extensive or which concern diagnosis, primary efficacy assessments, and important safety information.
- Persistent or systematic non-compliance with GCP or the Protocol that has a significant impact (e.g. systematic underreporting of serious adverse events leading to an inappropriate dose escalation in a phase I study).
- Proof of fraud relating to clinical trial records or data.

Suspected breaches occurring at the site may be identified by anyone involved in the conduct, management or monitoring of a trial. The Supervision Plan should clarify how Serious Breaches will be managed. Copies of reports (and associated documentation) will be sent to the Primary Site.

Suspected Serious Breaches should be reported to the responsible HREC as they impact on the ethical conduct of the research and to the RGO as they may have contractual implications and implications for the reputation of the Institution.

3.3. Communication with the Sponsor

- Comply with the reporting requirements outlined in GVH_CT-SOP-12 - Safety Data Monitoring and Reporting Requirements for Clinical Trials, and should consult and adhere to existing NHMRC guidance for NHMRC Guidance: Safety Monitoring and Reporting in Clinical Trials involving Therapeutic Goods.
- Notify the Sponsor within 24 hours of discovery of any Serious Adverse Events (SAE) involving trial participants under the care of the Investigator and where relevant notify the PI in parallel.

- Notify the Sponsor promptly regarding any changes significantly affecting the conduct of the trial, and/or increasing the risk to participants and where relevant notify the CPI/PI/Associate Investigator (AI). Communication must be followed up with written report/email and filed in the SMF/SSSF.
- Notify the Sponsor of any Protocol violation (which may include significant deviation from the protocol) and where relevant notify the CPI/PI/AI (see Appendix 1: Example Protocol Deviation Log).
- Be available to meet with the Sponsor to discuss study progress, issues and safety.
- Provide the Sponsor with copies of all correspondence from the reviewing HREC and/or RGO.
- Immediately notify the Sponsor of any notification received from a trial participant that they intend to initiate a claim against either the Sponsor and/or the Institution.

3.4. Communication with the Institution's Insurer:

If the Institution is notified or becomes aware that a trial participant intends to make a claim for compensation against the Institution or Sponsor for injuries arising as a result of participating in a clinical trial undertaken at the Institution or any of the Satellite Sites under supervision by the Institution, the Institution must promptly notify the Institution's insurer in writing that such an action is intended

3.4.1. Communication with Solicitor, Sponsor and CPI/PI/AI

If the Investigator is notified or becomes aware that a trial participant intends to make a claim against the Institution or Sponsor for injuries arising as a result of participating in a clinical trial undertaken at the Institution or any of the Satellite Sites under supervision by the Institution, the Investigator must promptly notify the following in writing that such an action is intended:

- the Institution's authority;
- the CPI/PI/AI as relevant; and
- the Sponsor.

The Sponsor, or the Institution acting as Sponsor, will generally be responsible for reporting to their respective solicitors.

ABBREVIATIONS AND TERMS:

Please refer to GVH_CT-SOP-Abbreviations and Terms.

KEY ALIGNED DOCUMENTS:

GV Health Procedure:

- GVH_CT-SOP-12-Safety Data Monitoring and Reporting Requirements for Clinical Trials

REFERENCES:

ICH GCP E6 (R2)

NHMRC Guideline: Reporting of Serious Breaches of GCP or the Protocol for Trials Involving Therapeutic Goods

NHMRC Guidance: Safety monitoring and reporting in clinical trials involving therapeutic goods

APPENDICES:

Appendix 1: Protocol Deviation Log

Contributors to the document

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Appendix 1: Example Protocol Deviation Log

Purpose:
To record all protocol deviations that occur at a study site (primary and satellite). It is required for both observational and interventional clinical research studies.

Definition:
A deviation is any breach, divergence or departure from the requirements of Good Clinical Practice (GCP) or the protocol that does not have a significant impact on the continued safety or rights of participants or the reliability and robustness of the data generated in the research project.

GCP requires all deviations to be reported to the trial sponsor.

Reporting Responsibilities:
The Principal Investigator is responsible for the reporting of protocol deviations. Site staff or a study monitor may prepare a Protocol deviation form, but this form should be signed by the PI. This form should be kept in the Study Master File (SMF) for the relevant site.

Protocol Deviation Codes:

A	Consent Procedures	F	Serious Adverse Event Reporting/Unanticipated Adverse Device Effect
B	Inclusion/Exclusion Criteria	G	Randomisation Procedures/Study Drug Dosing
C	Concomitant Medication/Therapy	H	Visit Schedule/Interval
D	Laboratory Assessments/Procedures	I	Efficacy Ratings
E	Study Procedures	J	Other

Protocol Deviation Tracking Log

Please use one sheet per Site. If signed by the Principal Investigator, please file and use a new form even if all 6 rows are not completed:

- Each page should be separately numbered to allow cross-referencing (e.g. deviation #3 on page 9);
- Deviation Type: (A-J) See codes on page 1 - enter the appropriate deviation code from the list.

Protocol Number:	Primary Site Name/Number:
Protocol Title (abbreviated):	Principal Investigator:
	Satellite Site Name/Number (if applicable):
	Associate Investigator (if applicable):

No.	Subject ID	Date of Deviation	Date Identified	**Deviation Description**	**Dev. Code [2]**	**Resulted in Adverse Event?**	**Did Subject Continue in Study? Date of withdrawal**	**Ethics reporting requirements (Yes/No)**	**Ethics reporting date**	**PI signature and date**
1										
2										
3										
4										
5										
6										

Investigator Signature: _____ **Date:** _____