ST VINCENT'S HEALTH AUSTRALIA

Serving, Seeing, Striving for something greater

St Vincent's Health Australia Group Policy

All SVHA policies must comply with the Code of Ethical Standards for Catholic Health and Aged Care Services in Australia, the Ethical Framework for Mary Aikenhead Ministries and the SVHA Ethics Policy.

Monitoring Human Research

1. Purpose:

Policy Statement

This policy provides guidance for monitoring human research projects across St Vincent's Health Australia facilities. It also provides guidance for groups for whom SVHA affiliated Human Research Ethics Committees (HRECs) provide research governance and services.

Objectives

This policy will provide an overarching policy and associated procedures including reporting requirements for monitoring human research projects.

Scope

This policy applies to all campuses of St Vincent's Health Australia, associated staff and students and groups for whom St Vincent's Health Australia provides research governance and services.

2. Definitions and Key Concepts:

Definitions

Adverse device event (ADE)

A clinical sign, symptom or condition that is causally related to the device implantation procedure, the presence of the device, or the performance of the device system.

Adverse drug reaction (ADR)

Any noxious and unintended response to an unapproved medicinal product, related to any dose. The phrase "response to an unapproved medicinal product" means that a causal relationship between the product and an adverse event is at least a reasonable possibility, i.e. the relationship cannot be ruled out. ('Unapproved medicinal product' here includes approved products used at levels or in ways that are unapproved by a Regulatory Authority).
Or
A noxious and unintended response to a drug that occurs at doses of marketed medical products

normally used in humans for prophylaxis, diagnosis or therapy of diseases or for modification of physiological function.

Adverse event

Any untoward medical occurrence/disease/injury in a clinical trial participant either administered an investigational medicinal product OR using an investigational medical device, whether or not causally related to the investigational medicinal product/investigational medical device.

Clinical trial

A form of research designed to find out the effects of an intervention, including a treatment or diagnostic procedure.

Monitoring

The process of verifying that the conduct of research approved by a Human Research Ethics Committee and local institutional governance processes conforms to the approved proposal.

Principal Researcher/Investigator

The person responsible for the conduct of the clinical trial at a trial site. In the case of a trial being conducted by a team of individuals at the site, the Principal Investigator is the responsible leader of the team.

Risk

The function of the magnitude of harm and the probability that it will occur.

Serious adverse event (SAE)

Any untoward medical occurrence that:

- results in death;
- is life-threatening (NOTE: The term "life-threatening" refers to an event/reaction in which the patient was at risk of death at the time of the event / reaction; it does not refer to an event/reaction which hypothetically might have caused death if it were more severe);
- requires inpatient hospitalisation or prolongation of existing hospitalisation;
- results in persistent or significant disability/incapacity;
- is a congenital anomaly/birth defect; or
- is a medically important event or reaction.

Serious unexpected suspected adverse reaction (SUSAR)

A serious adverse event (see definition above) for which there is some degree of probability that the event is an adverse reaction to the investigational drug and/or device, and the adverse reaction is unexpected.

Sponsor

An individual, company, institution, or organisation that takes responsibility for the initiation, management, and/or financing of research.

Unexpected adverse drug reaction

An adverse reaction, the nature or severity of which is not consistent with the applicable scientific

information (e.g. Investigator's Brochure for an unapproved investigational product or Product Information document or similar for an approved, marketed product).

Acronyms

ADE	Adverse device event
ADR	Adverse drug reaction
CPMP	Committee for Proprietary Medicinal Products now CHMP Committee for Medicinal Products for Human Use, of the European Medicines Agency (EMA);
GCP	Good Clinical Practice
HREC	Human Research Ethics Committee
ICH	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
PR	Principal Researcher
SAE	Serious Adverse Event
SUSAR	Serious unexpected suspected adverse reaction
TGA	Therapeutic goods Administration

3. Policy

3.1 Principles

Individuals conducting research involving humans, human biospecimens and/or human-derived data must comply with all aspects of the **SVHA Research Policy**.

All research must also comply with the Australian Code for the Responsible Conduct of Research (2018) NHMRC, the National Statement on Ethical Conduct in Human Research (2007, updated 2018), Ethical conduct in research with Aboriginal and Torres Strait Islander Peoples and communities: Guidelines for researchers and stakeholders (2018) and any other statutory requirements of State and Federal Legislation, and any other relevant guidelines.

In addition, as a Catholic organisation, all research undertaken at SVHA facilities must also comply with the Code of Ethical Standards (2001) CHA.

3.1.1 SVHA facilities have the ultimate responsibility for ensuring that all ethically approved research is monitored as mandated by the NHMRC via internal research governance arrangements. To achieve this, researchers must comply with the following requirements:

a) Researchers must report any unforeseen events that may occur which affect the continuing acceptability of the approved project to the local Research Governance Office

b) Researchers must submit an annual progress report to the Research Governance Office and responsible HREC

c) Researchers must submit a final report at the completion of the project to the Research Governance Office and responsible HREC

d) Researchers must submit any reports from sponsors and independent agencies (such as data and safety monitoring boards) to the Research Governance Office and responsible HREC

e) Researchers must formally report serious adverse events

f) Researchers must comply with the inspections of research sites, data and consent

documentation

3.1.2 Monitoring arrangements will be commensurate with the risk, size and complexity of the study. This may vary according to the Phase/Stage of the clinical trial.

3.1.3 For each project:

3.1.3.1 There must be appropriate mechanisms for reporting and reviewing[3];

3.1.3.2 Serious adverse drug reactions (ADRs), serious unexpected suspected adverse reactions (SUSARs), and serious adverse device events (ADE) which occur at any site for which the institution is responsible must be reported according to the research governance adverse event reporting procedure of the individual SVHA facility;

3.1.3.3 Where the project is a large multi-centre trial, a Data and Safety Monitoring Board (DSMB) should be used by the sponsor or trial group. The DSMB should also ensure a mechanism for informing the HREC/governance office of any relevant data[4];

3.1.3.4 Where the project is a local trial, there is an identified person/s or committee with suitable expertise to assist and advise the HREC/governance office about reports of serious adverse events.

3.2 Responsibilities

The responsibilities described below are specific, but not limited to, this policy and associated procedures.

3.2.1 **Principal Researcher (PR)**

Researchers have a significant responsibility to facilitate monitoring, as they are in the best position to observe any adverse events or unexpected outcomes.

They should report such events or outcomes promptly to the relevant institution/s and ethical review body/ies, and take prompt steps to deal with any unexpected risks[5]. The granting and continuation of ethical and governance approval of clinical research at SVHA sites is on the condition that researchers[6] are responsible for the following:

3.2.1.1 Ensuring processes are in place for ongoing monitoring, and for satisfying the review body that such mechanisms are appropriate to the research.

3.2.1.2 Conducting the trial in compliance with the approved protocol;

3.2.1.3 Providing reports of the progress of the trial to the HREC/governance office, at a frequency directed by the HREC/governance office in the initial approval notification (but at least annually), and related to the degree of risk to participants;

3.2.1.4 Informing the HREC/governance office, and seeking approval, of amendments to the protocol including amendments that:

a) Are proposed or undertaken in order to eliminate immediate risks to participants;

b) May increase the risks to participants; or

c) Significantly affect the conduct of the trial;

3.2.1.5 Notifying the relevant HREC/governance office of any serious adverse events at any trial sites;

3.2.1.6 Informing the HREC/governance office as soon as possible of any new safety information from other published or unpublished studies that may have an impact on the continued ethical acceptability of the trial or may indicate the need for amendments to the trial protocol;

3.2.1.7 Informing the HREC/governance office, giving reasons, if the trial is discontinued before the expected date of completion;

3.2.1.8 For trials with implantable medical devices, confirming the existence of, or establishing, a system for:

a) Tracking the participant, with consent, for the lifetime of the device; and

b) Reporting any device incidents to the TGA

3.2.1.9 Reporting serious adverse events or reactions to trial sponsors to meet the requirements of regulatory agencies, such as the TGA[7].

3.2.1.10 Meeting the monitoring responsibilities of the Principal Researcher or research team under any Research Agreement.

3.2.2 **Sponsor:** where a Sponsor is designated to a study, the sponsor is responsible for:

3.2.2.1 Monitoring responsibilities as detailed in the following documents:

a) Note Guidance on Good Clinical Practice (CPMP/ICH/135/99)

b) Note for Guidance on Clinical Safety Data Management: Definitions and Standards for Expedited Reporting (CPMP/ICH/377/95)

3.2.2.2 The ongoing safety evaluation of the investigational product(s)

3.2.2.3 Reporting serious adverse events or serious unexpected suspected adverse reactions to:

a) Regulatory agencies (such as, Therapeutic Goods Administration) to meet the conditions of approval to conduct a trial; and

b) Investigators to enable them to fulfil the conditions of ethical approval by an HREC/governance office.

c) Data and Safety Monitoring Board[1] or similar entity

3.2.3 **Human Research Ethics Committees (HRECs)**

The responsibility of Human Research Ethics Committees (HRECs), and of the institutions under which they are constituted, is to protect the safety of participants in clinical trials. In order to discharge this responsibility, HRECs need to receive sufficient reliable information about the implications of adverse events or reactions.

The individual SVHA affiliated HREC will have a standing item on each Agenda to report items related monitoring of approved research, including annual reporting, Adverse Event reports and Institutional Auditing activities. HREC members can

[1]A Data and Safety Monitoring Board (DSMB) or similar entity is established if required for the study. The DSMB is expected to review the study at predetermined intervals to review adverse event reports and to determine whether the study should continue or be suspended or terminated

request additional information or investigation at any time.

3.2.3.1 A physician with expertise associated with clinical therapeutics should be a member of HREC-D to assist with the assessment of safety, risk and adverse events. The PR must include sufficient information to facilitate the assessment of risks associated with the investigational product, and provide detailed reports of all adverse events, including causality.

3.2.3.2 A physician with expertise associated with experimental devices should be a member of HREC-D to assist with the assessment of assessment of safety, risk and adverse events. The PR must include sufficient information to facilitate the assessment of risks associated with the investigational device, and provide detailed reports of all adverse events, including causality.

3.2.3.3 Institutional research governance procedures must be in place to facilitate communication between all parties in a timely and professional manner. Governance processes must address reporting of HREC notifications as above to the executive of each SVHA facility included in any external HREC approval.

3.3 Annual Progress and Final Reporting

3.3.1 A condition of approval for studies approved by the SVHA affiliated HRECs is that a report of project progress is submitted annually. The letter of approval will identify if more frequent progress reports are required.

3.3.2 If a researcher fails to provide an annual report, approval for the study may be suspended by the HREC/governance office.

3.3.3 A final report is also due on completion of the study, or if the research is discontinued before the expected date of completion. Completion of the study means:

3.3.3.1 For commercially sponsored clinical trials, the study is considered complete once the site closeout visit has been completed

3.3.3.2 For Investigator Initiated clinical trials, the study is considered complete once the last patient has completed follow up and the data has been analysed.

3.3.3.3 For other research projects, the study is considered complete once data collection is complete and there is no further contact with patients or access to medical records or other sources of personal or health information.

3.3.4 The Annual and/or Final Report will be reviewed and acknowledged by the relevant SVHA affiliated HREC/governance office. Where concerns are raised, the matter will be referred to the Spokesperson or Chair of the relevant HREC.

3.4 Reporting Adverse Events

3.4.1 The Principal Researcher must:

a) Report all Serious Adverse Events (SAEs) occurring in patients to the HREC/governance office within 24 hours.

b) Report all Serious Unexpected Suspected Adverse Reactions (SUSARs) occurring in patients which the responsible Principal Researcher believes may

have an impact on the continued ethical acceptability of the project, or that may indicate the need for amendments to the project protocol including altered monitoring of safety or in any way impact on the patients to the HREC/governance office within

c) Comply with the terms of any Research Agreement applying to the trial.

3.4.2 Events in patients for whom the SVHA affiliated HREC/governance office is responsible:

3.4.2.1 The Principal Researcher should

a) Manage patient health and safety as required

b) Notify events to Sponsor, as required by the Sponsor, and data safety monitoring board within 24 hours (if required)

c) If the study is investigator initiated, expedite notification to TGA of a SUSAR occurring at any site within Australia.

d) Notify all events to the HREC/governance office within 24 hours of the event.

e) Notify the HREC/governance office if there are any proposed actions by the Sponsor to suspend or terminate the study

f) Obtain approval from the HREC/governance office for all amendments to the study

g) Notify the HREC/governance office of outcome of TGA review.

3.4.2.2 On receipt of the report, the Sponsor should

a) Notify TGA within 24 hours (if required)

b) Notify DSMB within 24 hours (if required)

c) Notify PR if any action is planned. For example, provide information to PR if study is suspended or terminated and provide documentation regarding amendments to Clinical Protocol, Investigator's Brochure or PICF.

3.4.2.3 On receipt of the report, the HREC/governance office should

a) Ensure the report is complete

b) Send the report to the HREC Chair/CEO or delegate as soon as possible

c) Communicate matters raised by the HREC/governance office/ CEO to the researcher in a timely manner

d) Ensure all relevant items (SAEs and other items) are included on the relevant the HREC/governance office agenda.

3.4.3 Events in patients for whom the HREC/governance office is not responsible:

3.4.3.1 The Sponsor must

a) Notify PR of events at other sites including Individual reports; Quarterly reports of SUSARs; and/or Annual reports of SAES at all sites

b) Notify PR if any action is planned. For example, provide information to PR if study is suspended or terminated and provide documentation regarding amendments to the Clinical Protocol, Investigator's Brochure or PICF.

3.4.3.2 On receipt of the report, the Principal Researcher should

a) Notify the HREC/governance office of all Serious Unexpected Suspected Adverse Reactions (SUSARs) occurring in patients which the responsible Principal Researcher believes may have an impact on the continued ethical acceptability of the project, or that may indicate the need for amendments to the project protocol including altered monitoring of safety or in any way impact on the patients for whom the SVHA site is responsible.

b) Notify the HREC/governance office if there are any proposed actions by the Sponsor to suspend or terminate the study

c) Obtain approval from the HREC/governance office for all amendments to the study

3.5 Institutional Audits

3.5.1 A random number of studies will be audited on a monthly basis

3.5.2 The audit will review:

a) Consent documentation is complete for all participants enrolled in the study.

b) Consent documentation is the version most recently approved by the HREC

c) Study documentation is stored as required.

d) The study is being undertaken in compliance with the approved protocol and study documentation approved by the HREC/governance office

3.5.3 A report of the audit will be sent to the Principal Researcher. The report will include recommendations if required.

3.5.4 The report will be tabled at each HREC meeting and included in a standing item on the HREC Agenda.

3.6 SVHA Research Reporting Requirements

3.6.1 All approved research studies undertaken at SVHA facilities will be monitored at each SVHA site as described above and in accordance with the NHMRC requirements specified in the National Statement[1].

3.6.2 All SAEs, SUSARs or other notifications that result in the discontinuation, temporary halting or cessation of participant recruitment at any SVHA site must be reported to the SVHA Group Chief Research Officer and the Group Chief Medical Officer within 24 hours.

3.6.3 All notifications to the GCRO/GCMO will be reported to the SVHA Research Council and SVHA Board Research and Education Committee under standing items on the Agendas for each meeting.

3.6.4 Reporting of Annual Report submission rates will be included in annual KPIs presented to the SVHA Research Council and SVHA Board Research and Education Committee.

Additional reports from SVHA facilities and affiliated HREC/governance office regarding monitoring of approved research will be by exception to the SVHA Research Council and SVHA Board Research and Education Committee.

4. References:

1. National Statement on Ethical Conduct in Human Research (NHMRC; 2007, updated 2018)
2. Ethical conduct in research with Aboriginal and Torres Strait Islander Peoples and communities: Guidelines for researchers and stakeholders (2018)
3. Australian Code for the Responsible Conduct of Research (2018)
4. Note for Guidance on Good Clinical Practice (CPMP/ICH/135/99)
5. Note for Guidance on Clinical Safety Data Management: Definitions and Standards for Expedited Reporting (CPMP/ICH/377/95)
6. The Australian Clinical Trials Handbook (TGA; October 2018)
7. Victorian Managed Insurance Authority Clinical Trial: Risk and Insurance Guide (2018)
8. NHMRC Guidance: Safety monitoring and reporting in clinical trials involving therapeutic goods (November 2016)
9. Risk-based management and monitoring of Clinical Trials involving Therapeutic Goods (2018)
10. Reporting of Serious Breaches of Good Clinical Practice (GCP) or the Protocol for Trials Involving Therapeutic Goods (2018)

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