1 PURPOSE & SCOPE

The purpose of this SOP is to describe the Peter MacCallum Cancer Centre (Peter Mac) Ethics Committee process for submission and handling of safety reports arising out of research reviewed by the Peter Mac Ethics Committee as the reviewing Human Research Ethics Committee (HREC).

For safety reporting requirements for research conducted at Peter Mac that was reviewed by an Ethics Committee other than Peter Mac, refer to Guideline 001 Peter Mac Governance Review Requirements for Human Research.

This SOP is consistent with the *NHMRC National Statement on Ethical Conduct in Human Research (2007 and updates)* and the *NHMRC Safety monitoring and reporting in clinical trials involving therapeutic goods (November 2016 and updates)*.

2 TARGET AUDIENCE

The target audience is Sponsors, Contract Research Organisations, Investigators, participating Institutions and their delegates, of clinical research projects that were approved by the Peter Mac HREC.

3 RELATED POLICY

POLICY 21.1.1: Responsible Conduct of Research

Ethics Committee SOP 004: Monitoring of Ongoing Research

Ethics Committee Secretariat Guideline 001: Peter Mac Governance Review Requirements for Human Research

4 DEFINITIONS

Definitions stated in the NHMRC document *Safety monitoring and reporting in clinical trials involving therapeutic goods November 2016* are the governing definitions for Investigational Medicinal Product (IMP) Trials and Investigational Medical Device (IMD) Trials.

The Definitions provided below are broader in scope to allow inclusion of clinical research outside the scope of an IMP or IMD trial in this SOP.

For further explanation of any of the definitions consult the NHMRC document *Safety monitoring and reporting in clinical trials involving therapeutic goods November 2016*.

Investigator's Brochure (IB)	The document containing a summary of the clinical and non-clinical data relating to an investigational medicinal product or device that are relevant to the study of the product or device in humans.
Product Information (PI)	The approved Australian summary of the scientific information relevant to the safe and effective use of a prescription medicine. If the conditions of use differ from those authorised, the PI should be

	supplemented with a summary of relevant clinical and non-clinical data that supports the use of the product in the trial.
Annual Safety Report	Summary of all new available safety information relevant to a trial that is received over a 12 month period (the Executive Summary of safety information produced for international regulators, such as the Development Safety Update Report (DSUR) may serve as the Annual Safety Report).
Significant Safety Issue (SSI)	A safety issue that could adversely affect the safety of participants or materially impact on the continued ethical acceptability or conduct of the trial.
Urgent Safety Measure (USM)	A measure required to be taken in order to eliminate an immediate hazard to a participant's health or safety. Note: This type of significant safety issue can be instigated by either the investigator or sponsor and can be implemented before seeking approval from HRECs or institutions.
Reviewing HREC	The Human Research Ethics Committee (HREC) that issued the Ethical Approval for the project. Under the multisite review system a NHMRC certified HREC can review and issue ethical approval for a project at multiple sites. These multiple sites will be named in the initial Ethical Approval or be added as an amendment to the initial Ethical Approval. The "reviewing HREC" is responsible for the ongoing monitoring of the project at those sites.
Institution	An institution named as a Participating Site on an Ethical Approval issued by the Peter Mac HREC.

5 RESPONSIBILITIES

The NHMRC National Statement on Ethical Conduct in Human Research (2007 and updates) permits monitoring arrangements to be commensurate to the risk, size and complexity of the trial. The nature and extent of participant safety monitoring should be based on the assessment of the risks of the trial intervention(s) relative to standard care and the extent of knowledge about the investigational medicinal product or device being tested. The sponsor's plans for safety monitoring should be documented and continually reviewed and adapted during the trial, as real time assessments of safety data are performed.

The sponsor, through their independent safety monitoring arrangements, has the primary responsibility for monitoring the ongoing safety of the investigational medicinal product or device. The HREC should be satisfied that the sponsor's arrangements are sufficiently independent and commensurate with the risk, size and complexity of the trial.

It is the responsibility of Sponsors, Contract Research Organisations, Investigators, Institutions and their delegates, conducting clinical research projects that were approved by the Peter Mac HREC and all Ethics Committee Secretariat staff members to follow and adhere to the procedures set out in this SOP.

It is the responsibility of Sponsors, Contract Research Organisations, Investigators, Institutions and their delegates, of clinical trials involving therapeutic goods that were approved by the Peter Mac HREC to also comply with the reporting requirements in NHMRC document *Safety monitoring and reporting in clinical trials involving therapeutic goods November 2016* (Appendix 1 and Appendix 2 from this document are included in this SOP for reference).

6 PROCEDURE

When communicating safety information to the Peter Mac HREC the Sponsor or their delegate must clarify the impact of each report on patient safety, trial conduct and trial documentation. The items below required to be submitted to the Peter HREC by the Sponsor or delegate will be acknowledged by the Peter Mac HREC.

NOTE: For reporting of Serious Breaches of Good Clinical Practice or the protocol, refer to SOP004 Monitoring of Ongoing Research, Section 6.4 (Serious Breach reporting replaces Protocol Deviation/Violation reporting).

The procedure to be followed is provided in the following table.

Reporting party	Report required and timeline	Supporting information required
SPONSOR or delegate	Provide the HREC with **annual** update of the **Investigator's Brochure** or where applicable, **Product Information**. Provide the HREC with any Addenda to the **Investigator's Brochure** or where applicable, **Product Information**.	*Impact of the update/addenda on patient safety, trial conduct and trial documentation*
SPONSOR or delegate	Provide the HREC with an **Annual Safety Report** including a clear summary of the evolving safety profile of a trial. NOTE: The HREC has the discretion to request more frequent reporting for specific trials, such as early phase trials. Such a request may be stated on the initial Ethical Approval for a trial or may be instituted during the conduct of the trial.	*A brief description and analysis of new and relevant findings;* *For IMPs not on the Australian Register of Therapeutic Goods, a brief analysis of the safety profile of the IMP and implications for participants taking into account all available safety data and results of relevant clinical or non-clinical studies* *A brief discussion of the implications of the safety data to the trials risk-benefit ratio* *A description of any measures taken or proposed to minimise risks*

SPONSOR or delegate	Notify the HREC of all Significant Safety Issues that adversely affect the safety of participants or materially impact on the continued ethical acceptability or conduct of the trial. I. Significant Safety Issues that meet the definition of an **Urgent Safety Measure** should be notified **within 72 hours**. II. All other **Significant Safety Issues** should be notified **within 15 calendar days** of the sponsor instigating or being made aware of the issue. III. **Significant Safety Issues** often result in safety-related changes to trial documentation. Any resulting **amendment** should be submitted to the HREC **without undue delay**. IV. **Temporary halt of trial for safety reasons** should be notified **within 15 calendar days** of the sponsor's decision to halt the trial. V. **Early termination of a trial for safety reasons** should be notified without undue delay and **within 15 calendar days** of the sponsor's decision to terminate the trial	*I. Reason for the urgent safety measure; measures taken; further actions planned* *II. Details of the significant safety issue; further actions planned* *III. Submit amendment per Ethics Committee SOP004* *IV. Reasons for the halt; the scope of the halt (e.g. suspension of recruitment or cessation/interruption of trial treatment); measures taken; further actions planned.* *V. Reasons for the early termination; measures taken; further actions planned*
HREC	Advise the TGA, investigators and their institutions of any decision to withdraw approval.	*Reasons for the withdrawal of approval and date of withdrawal of approval*

7 KEY PERFORMANCE INDICATORS

At least 90% of all notifications required by this SOP to be received within the specified timeframe.

If a notification is not received within the notified time frame the submitting project and/or sponsor will be notified that the correct timeframe was not met, what the correct timeframe for the item is and will be provided with a copy or link to this SOP.

8 RELATED MATERIALS

Consult the Peter MacCallum Cancer Centre website for any forms required for submission: https://www.petermac.org/research/doing-research-us/ethics-governance

9 REFERENCES

INTERNAL DOCUMENTS

- POLICY 21.1.1: Responsible Conduct of Research
- Ethics Committee SOP 004: Monitoring of Ongoing Research
- Ethics Committee Secretariat Guideline 001: Peter Mac Governance Review Requirements for Human Research

EXTERNAL DOCUMENTS

- National Statement on Ethical Conduct in Human Research (2007, and updates)
- NHMRC Safety monitoring and reporting in clinical trials involving therapeutic goods (November 2016 and updates)
- NHMRC Reporting of Serious Breaches of Good Clinical Practice (GCP) or the Protocol for Trials Involving Therapeutic Goods (2018)

10 FURTHER INFORMATION

For enquiries related to this Procedure please email ethics@petermac.org

11 VERSION AND APPROVAL HISTORY

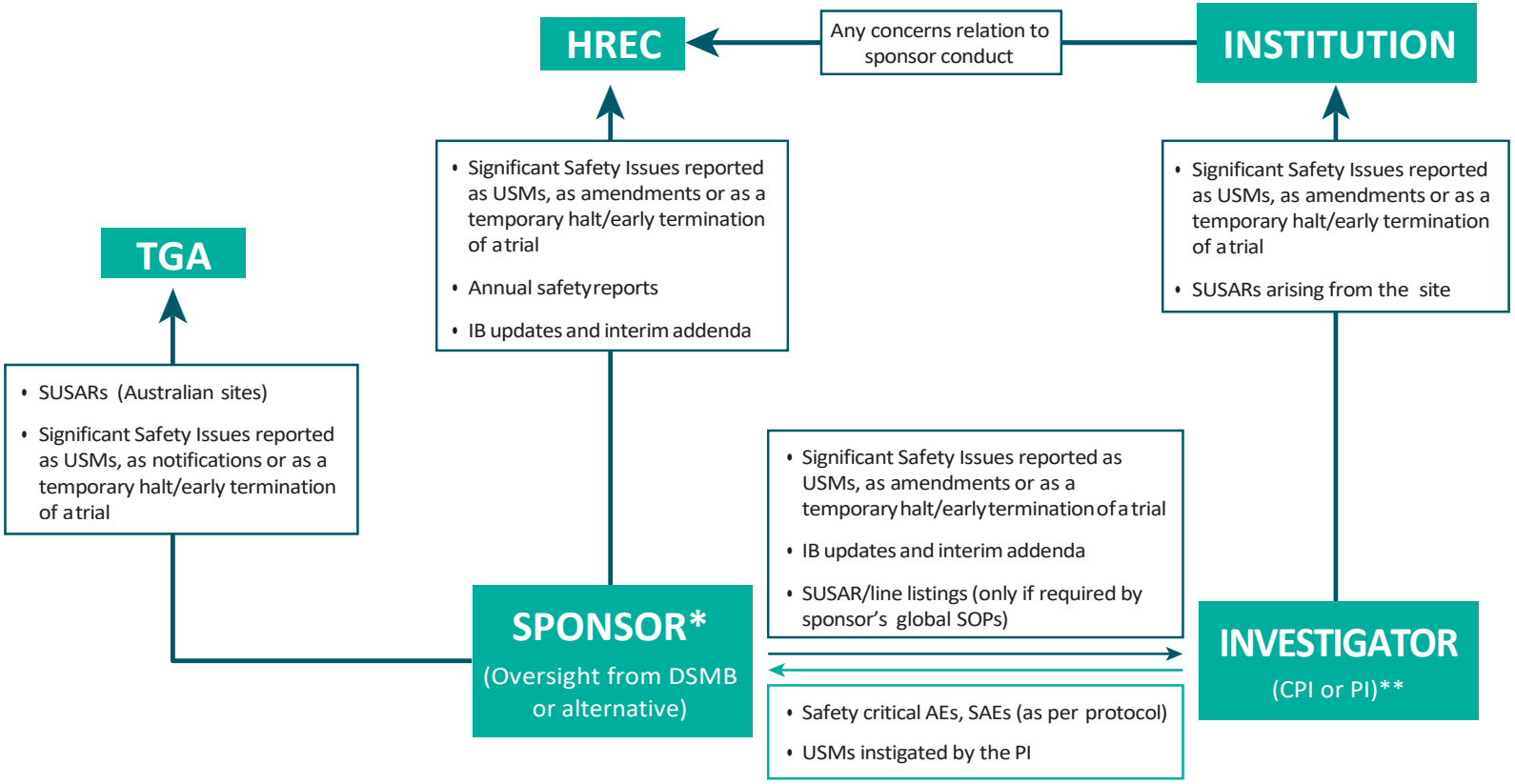
Date	Version #	Author; Owner and Authoriser Changes
August 2011	1.0	Author: Dianne Snowden, Ethics Coordinator; Owner: Ethics Committee; Authorised by: Chair, Clinical Research Governance Summary of Changes: Additional reporting requirements removed and SOP streamlined to be consistent with the NHMRC Australian Health Ethics Committee (AHEC) Position Statement on Monitoring and Reporting of Safety for Clinical Trials Involving Therapeutic Products (May 2009) Stakeholders involved in the review process: Clinical Research Committee; Ethics Committee Clinical Research Governance Committee.
August 2014	2.0	Author: Dianne Snowden, Ethics Coordinator; Owner: Ethics Committee; Authorised by: Chair, Research Governance Committee Summary of Changes: SOP updated to reflect the multisite ethical review process Stakeholders involved in the review process: Clinical Research Committee; Ethics Committee; Research Governance Committee
January 2017	3.0	Author: Dianne Snowden, Manager Human Research Ethics; Owner: Ethics Committee; Authorised by: Associate Director, Clinical Research

		Summary of Changes: SOP reporting requirements updated based on *NHMRC Safety monitoring and reporting in clinical trials involving therapeutic goods (November 2016)*. Stakeholders involved in the review process: Clinical Research Committee; Ethics Committee; Parkville Cancer Clinical Trials Unit.
June 2018		Author: Dianne Snowden, Manager Human Research Ethics; Owner: Ethics Committee; Authorised by: Associate Director, Clinical Research Summary of Changes: Refer to SOP004 regarding Serious Breach reporting based on revised *NHMRC Reporting of Serious Breaches of Good Clinical Practice (GCP) or the Protocol for Trials Involving Therapeutic Goods 2018*.

NHMRC document

Safety monitoring and reporting in clinical trials involving therapeutic goods November 2016

Appendix 1: Report Flowchart for Investigational Medicinal Product Trials



KEY

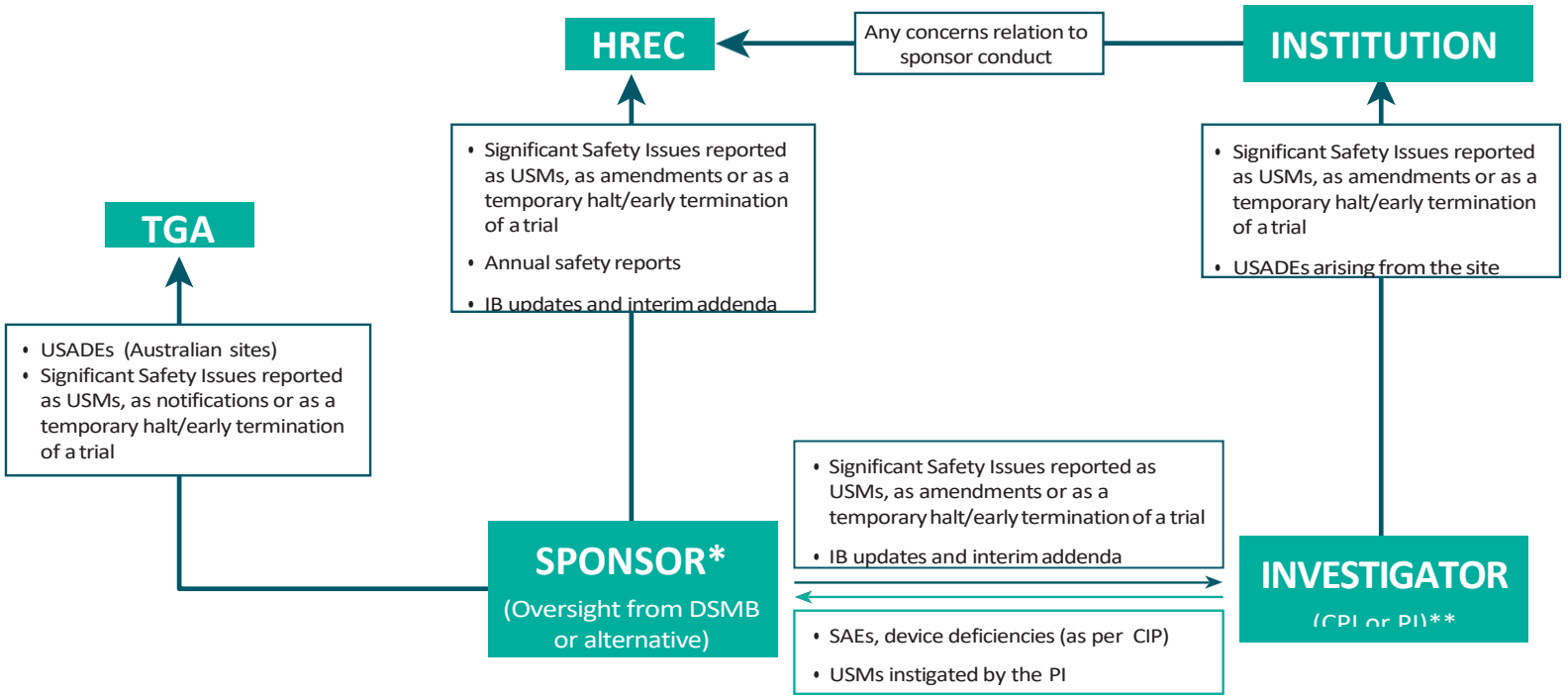
AE – Adverse Event
SAE – Serious Adverse Event
SUSAR – Suspected Unexpected Serious Adverse Reaction
USM – Urgent Safety Measure
SOP – Standard Operating Procedure
IB – Investigator's Brochure
PI – Product Information
DSMB – Data Safety Monitoring Board
CPI – Co-ordinating Principal Investigator
PI – Principal Investigator

* The sponsor (or their delegate) should report to all parties in accordance with the timelines indicated within this document.
**The CPI should be provided with all correspondence sent by the sponsor to PIs and/or the HREC.

NHMRC document

Safety monitoring and reporting in clinical trials involving therapeutic goods November 2016

Appendix 2: Reporting Flowchart for Investigational Medical Device Trials



KEY

AE – Adverse Event
SAE – Serious Adverse Event
USADE – Unanticipated Serious Adverse Device Effect
USM – Urgent Safety Measure
SOP – Standard Operating Procedure
CIP – Clinical Investigation Plan
IB – Investigator's Brochure
IFU – Instructions for Use
DSMB – Data Safety Monitoring Board
CPI – Co-ordinating Principal Investigator
PI – Principal Investigator

* The sponsor (or their delegate) should report to all parties in accordance with the timelines indicated within this document.
**The CPI should be provided with all correspondence sent by the sponsor to PIs and/or the HREC.