Safety Monitoring and Reporting for Clinical Trials Conducted in NSW Public Health Organisations

Summary NSW Health sets a standard framework for safety monitoring and reporting in clinical trials, outlining roles and responsibilities to ensure consistent practice and protect participant wellbeing across all Public Health Organisations.

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NSW Health
Policy Statement

Safety Monitoring and Reporting for Clinical Trials Conducted in NSW Public Health Organisations

Policy Statement

NSW Health provides a standard framework for safety monitoring and reporting for clinical trials conducted within NSW Public Health Organisations, to ensure a consistent approach and safeguard participant wellbeing.

This Policy Directive outlines the regulatory and good clinical practice requirements for safety monitoring and reporting in clinical trials conducted within NSW Public Health Organisations (PHOs). It defines the roles and responsibilities of PHOs, Sponsors, Investigators, Human Research Ethics Committees (HRECs) and Research Governance Offices (RGOs). It provides a standard framework for all trials to ensure a consistent approach to safety monitoring and reporting across NSW PHOs.

Mandatory Requirements

NSW Health requires all trials conducted within NSW PHOs to maintain rigorous safety monitoring and reporting practices to safeguard participant wellbeing. All safety monitoring and reporting must align with nationally recognised guidelines and demonstrate compliance with International Council on Harmonisation (ICH) *Guideline for Good Clinical Practice* (GCP). Mandatory requirements for safety and monitoring reporting are below:

Unapproved Therapeutic Goods Trials

For trials involving unapproved therapeutic goods, such as trials conducted under the Clinical Trial Acceptance (CTA) or Clinical Trial Notification (CTN) schemes, sponsors and investigators are to conduct safety monitoring and reporting activities in accordance with the National Health and Medical Research Council (NHMRC) Guidance: *Safety Monitoring and Reporting in Clinical Trials Involving Therapeutic Goods* (2016) [the NHMRC Guidance].

For trials not conducted under the CTA or CTN scheme, sponsors and investigators are to also conduct safety monitoring and reporting activities in accordance with the NHMRC Guidance. However, when reporting to the Therapeutic Goods Administration (TGA), sponsors should comply with the TGA's requirements for post-marketing trials.

Non-Therapeutic Goods Trials

For trials involving interventions other than therapeutic goods, for example, surgery, radiotherapy, or psychotherapy, safety monitoring and reporting activities are to be aligned, as far as possible, with the requirements for therapeutic goods trials as set out in the NHMRC Guidance and this Policy Directive.

All Clinical Trials

Any adverse event arising from a clinical trial that meets the definition of an incident according to the NSW Health Policy Directive *Incident Management* (PD2020_047), as updated from time to time, must be managed in accordance with PD2020_047.

Implementation

The protection of participant safety in clinical trials is a shared responsibility The following outlines the key responsibilities of roles involved in clinical trials:

- Sponsors are responsible for the ongoing safety evaluation of their trials and for reporting changes in the risk-benefit ratio to all concerned parties.
- Investigators are responsible for the ongoing medical care of trial participants and for reporting safety events to the sponsor and their institution.
- Human Research Ethics Committees are responsible for oversight of the risk-benefit balance of approved clinical trials.
- Research Governance Offices are responsible for acting on any information arising from clinical trials that may impact on the institution's duty of care to trial participants.

Revision History

Version	Approved By	Amendment Notes
PD2026_002 January-2026	Deputy Secretary, Clinical Innovation and Research	Revised and updated policy. Amendments include: • Administrative refinements • Remove Attachments: Significant Safety Issue Notification Form and Local SUSAR/USADE/URSAE Notification Form • Incorporate reference to Research Ethics and Governance Information System (REGIS) for safety reporting notifications • Consolidation of Key Definitions, Roles and Responsibilities • Updates to NSW Health policy references as required, including reference to the incident management system (ims+)
PD2017_039 June-2017	Deputy Secretary, Population and Public Health & Chief Health Officer	New Policy Directive.

Contents

1. Background

1.1. About this document

This Policy Directive applies to all clinical trials conducted within NSW Public Health Organisations (PHOs). It outlines the safety monitoring and reporting requirements for trials involving investigational medicines, biologicals and medical devices (referred to as unapproved therapeutic goods trials). This Policy Directive also details the safety monitoring and reporting requirements for trials involving other types of intervention (referred to as non-therapeutic goods trials).

1.2. About the regulatory and governance environment in Australia

International Good Clinical Practice Guidelines[1] set out the responsibilities of sponsors and investigators who must have processes in place for the collection, verification, classification, reporting and management of clinical trial adverse events. In addition, Australian guidelines[2] set these responsibilities in the context of the Australian regulatory environment. As such, these guidelines outline the responsibilities of Human Research Ethics Committees (HRECs) and institutions in relation to ensuring that any changes in the risk-benefit ratio of a clinical trial are compatible with continued ethics approval and site authorisation.

The sponsor of a clinical trial is responsible for the ongoing safety evaluation of the trial. The sponsor may delegate some or all the functions to the Coordinating Principal Investigator (CPI) or other third party (such as a coordinating centre) but in doing so, must be satisfied that the individual or party has the necessary training and experience to undertake those tasks and must maintain oversight of their trials. Where safety monitoring and reporting functions have been delegated to the CPI, they will undertake both the investigator and sponsor responsibilities described in this Policy Directive.

The nature and extent of safety monitoring should be proportionate to the risks of the trial and should be determined through a risk assessment. The protocol (and/or separate document) should clearly demonstrate that the trial sponsor has implemented appropriate measures to monitor the safety of participants. The protocol should also clearly outline the responsibilities of the principal investigator so that the collection, review and reporting of safety information is undertaken appropriately.

Investigators working within NSW PHOs should also ensure that any research-related adverse events that meet the definition of an incident are reported in accordance with the

[1] *Guidelines for Good Clinical Practice (ICH E6 R2) and ISO 14155 (2020): Clinical Investigation of Medical Devices for Human Subjects: Good Clinical Practice*.

[2] *National Statement on Ethical Conduct in Human Research (2025); NHMRC Guidance: Safety Monitoring and Reporting in Clinical Trials involving Therapeutic Goods (2016)*.

NSW Health *Incident Management* (PD2020_047).

Where a clinical trial involves unapproved therapeutic goods supplied under the Clinical Trial Acceptance (CTA) or Clinical Trial Notification (CTN) schemes, all stakeholders must comply with any relevant requirements outlined within the *Therapeutic Goods Act 1989* (Cth) and associated regulations.

1.3. Key Definitions

Adverse Event (AE) [investigational medicinal product and biological trials]	Any untoward medical occurrence in a patient or clinical trial participant administered an **investigational medicinal product (IMP)**, which does not necessarily have a causal relationship with the treatment. For non-therapeutic goods trials, an adverse event is any untoward medical occurrence in a patient or clinical trial participant associated with the intervention.
Adverse Event (AE) [investigational medical device]	Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in participants, users or other persons, whether or not related to the **investigational medical device (IMD)**. This definition includes events related to the IMD or the comparator. This definition includes events related to the procedures involved. For users or other persons, this definition is restricted to events related to IMDs.
Adverse Device Effect (ADE)	An adverse event related to the use of an investigational medical device (IMD). This definition includes: • adverse events resulting from insufficient or inadequate Instructions for Use, deployment, implantation, installation, or operation • adverse events resulting from any malfunction. • any event resulting from use error • any event resulting from intentional misuse.

Adverse Reaction (AR)	Any untoward and unintended response to an investigational medicinal product related to any dose administered. All adverse events judged by either the reporting investigator or the sponsor as having a **reasonable possibility of a causal relationship** to an investigational medicinal product would qualify as an adverse reaction. In this context, the expression 'reasonable causal relationship' means that there is evidence or argument to suggest a causal relationship.
Clinical Trial	Any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes.
Coordinating Principal Investigator (CPI)	The Coordinating Principal Investigator is: • In relation to a clinical trial conducted at a single trial site, the Principal Investigator (PI) for that site • In relation to a clinical trial conducted at more than one trial site, the health professional who takes primary responsibility for the conduct of the trial, whether or not they are an investigator at a particular site.
Clinical Trial Acceptance (CTA) or Clinical Trial Notification (or CTN)	The principal schemes that provide access to unapproved therapeutic goods for clinical trials conducted in Australia (see TGA website).
Data Safety Monitoring Board (DSMB)	An independent and multidisciplinary group established by the trial sponsor to review, at intervals, accumulating trial data, in order to monitor the progress of a trial and to make recommendations on whether to continue, modify or stop the trial for safety or ethical reasons.
Decentralised Clinical Trial (DCT)	A trial where some or all the trial-related activity occur at a facility, location or institution (or group of institutions) other than the investigators primary site. This approach is an innovative method for delivery of trial activities to enable participants to access clinical trials closer to home. The investigator, who is always at the primary site, remains responsible for the oversight of any individual delegated to perform trial-related activities in accordance with the protocol, including safety monitoring or reporting duties or functions.

Device Deficiencies	Inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance. Device deficiencies include malfunctions, use errors, and inadequate labelling.
Good Clinical Practice (GCP)	An international ethical and scientific quality standard for the design, conduct, performance, monitoring, auditing, recording, analyses and reporting of clinical trials.
Incident	Refer to the NSW Health Policy Directive *Incident Management* (PD2020_047) (as updated).
ims+	NSW Health incident management system. Refer to the NSW Health Policy Directive *Incident Management* (PD2020_047) (as updated). Staff must follow local incident management requirements in a way that complies with this Policy Directive and the NSW Health Policy Directive *Incident Management* (PD2020_047).
Investigational Medical Device (IMD)	Medical device being assessed for safety or performance in a clinical investigation. This includes medical devices already on the market that are being evaluated for new intended uses, new populations, new materials or design changes.
Investigational Medicinal Product (IMP)	A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial. This includes a product with a marketing authorisation when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, a new patient group or when used to gain further information about an approved use. This definition includes biologicals used as investigational medicinal products.
Investigator's Brochure (IB)	The document containing a summary of the clinical and non-clinical data relating to the **IMP** that is relevant to the study of the product in humans. Compilation of the current clinical and non-clinical information on the **IMD** relevant to the clinical investigation.
Near Miss	Refer to the NSW Health Policy Directive *Incident Management* (PD2020_047) (as updated).
Non-Therapeutic Goods Trials	Trials other than Therapeutic Goods Trials (see TGA website).

Principal Investigator (PI)	The person responsible for the conduct of a clinical trial at a site, either individually or as the lead of the research team. In a single centre trial, the **PI** may also be the **CPI**.
Product Information (PI)	In relation to therapeutic goods, information relating to the safe and effective use of the goods, including information regarding the usefulness and limitations of the goods. In some trials, the approved **PI** may replace the **IB**.
Protocol	A document that provides the background, rationale and objectives of the research and describes its design, methodology, organisation and the conditions under which it is to be performed and managed. The term 'protocol' is generally reserved for use in clinical research.
Reference Safety Information (RSI)	The information contained in either an IB or an approved Australian PI (or another country's equivalent). This information is used to determine what adverse reactions are considered expected adverse reactions, as well as the frequency and nature of those adverse reactions.
Related Adverse Event	An adverse event that is judged as having a reasonable causal relationship with the trial intervention.
Research Ethics and Governance Information System (REGIS)	A portal to help manage ethics and site governance approvals, as well as ongoing monitoring of human research projects in NSW Public Health Organisations (PHOs), Affiliated Health Organisations (AHOs), including health services in TAS and ACT.
Safety Critical Adverse Events	Adverse events and/or laboratory abnormalities identified in the protocol as critical to safety evaluation that should be reported to the sponsor, according to the reporting requirements specified in the protocol.
Serious Adverse Device Effect (SADE)	An adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.

Serious Adverse Event/Serious Adverse Reaction (SAE/SAR) [investigational medicinal product]	Any adverse event/adverse reaction that results in death, is life-threatening, requires hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, or is a congenital anomaly or birth defect. The term 'life-threatening' in the definition of 'serious' refers to an event in which the patient was at risk of death at the time of the event. It does not refer to an event which hypothetically might have caused death if it were more severe. Medical and scientific judgement should be exercised in deciding whether expedited reporting is appropriate in other situations. This includes important medical events that may not be immediately life-threatening or result in death or hospitalisation but may jeopardise the patient or may require intervention to prevent one of the other outcomes listed above. These should also usually be considered serious.

Serious Adverse Event
[investigational medical device]
	An adverse event that:
	• results in death
	• led to serious deterioration in the health of the participant, that either resulted in:
	  ○ a life-threatening illness or injury
	  ○ a permanent impairment of a body structure or a body function
	  ○ an in-patient or prolonged hospitalisation
	  ○ a medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure of a body function
	• led to fetal distress, fetal death or a congenital abnormality or birth defect
	• for non-therapeutic trials, considered medically significant by the investigator
	Planned hospitalisation for a pre-existing condition, or a procedure required by the protocol without serious deterioration in health, is not considered a “serious adverse event."

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.
Site	A facility, location or institution (or group of institutions) that resource, conduct and manage clinical trials.

Sponsor	An individual, organisation or group taking on responsibility for securing the arrangements to initiate, manage and finance a study.
Suspected Unexpected Serious Adverse Reaction (SUSAR)	An adverse reaction that is both serious and unexpected.
Therapeutic Goods Trials	Trials investigating the safety and/or efficacy/effectiveness of medicines, biologicals or medical devices (therapeutic goods).
Unanticipated Serious Adverse Device Effect (USADE)	A serious adverse device effect which by its nature, incidence, severity or outcome has **not** been identified in the current version of the risk analysis report (and/or Investigator's Brochure/Instructions for Use). By comparison, an anticipated serious adverse device effect (ASADE) is an effect which by its nature, incidence, severity or outcome has been identified in the risk analysis report (and/or Investigator's Brochure/Instructions for Use).
Unapproved Therapeutic Goods	A product not entered on the Australian Register of Therapeutic Goods (ARTG), including: • any new formulation of an existing product • any new route of administration • in the case of an existing medical device, any new technology, new material or a new treatment modality. A product being used beyond the conditions of its marketing authorisation, including: • new indications extending the use of a medicine to a new population group • extension of doses or duration of treatments outside the approved range.
Unexpected Adverse Reaction (UAR)	An adverse reaction, the nature or severity of which is not consistent with the **RSI.** The RSI should be contained in the investigator's brochure for an unapproved medicinal product or PI (or another country's equivalent of the PI) for an approved medicinal product.

Unexpected and Related Serious Adverse Event (URSAE)	An adverse event that is: • Serious – meets the definition of a serious adverse event • Related – resulted from administration of the trial intervention • Unexpected – the event is not described in the protocol as an expected occurrence.
Urgent Safety Measure (USM)	A measure required to be taken in order to eliminate an immediate hazard to a participant's health or safety. 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.

2. Safety Reporting Assessment of adverse events in clinical trials

Each adverse event must be evaluated for seriousness, causality and expectedness.

Therapeutic Goods	Non-Therapeutic Goods
• **Seriousness:** An assessment of whether the Adverse Event (AE) meets the definition of a Serious Adverse Event (SAE) • **Causality:** A clinical assessment of whether there is a reasonable causal relationship between the AE and the Investigational Medicinal Product (IMP) or the use of the Investigational Medicinal Device (IMD) • **Expectedness:** An assessment of whether the Adverse Reaction (AR) [IMP trial] or Adverse Device Effect (ADE) [IMD trial] is consistent with information previously described in the trial's Reference Safety Information (RSI). For trials involving **Therapeutic Goods**, this Policy Directive requires sponsors and investigators to adhere to the requirements set out in the **National Health and Medical Research Council (NHMRC) Guidance**: • **Part 1, Section B - Safety Reporting Assessment Flowchart: IMP Trials**[i] • **Part 2, Section B - Safety Reporting Assessment Flowchart: IMD Trials**[ii]	• **Seriousness:** An assessment of whether the AE meets the definition of a SAE • **Causality:** A clinical assessment of whether there is a reasonable causal relationship between the AE and the trial intervention • **Expectedness:** An assessment against the SAEs listed in the protocol as expected occurrences (considering the nature and frequency of the event).

i Assessed using the trial's reference safety information (current Investigator's Brochure or Product Information).

ii Based on the current literature and experience in the risk analysis report and/or contained in the Investigator's Brochure, Instructions for Use or protocol.

3. Responsibilities

The following tables summarise the responsibilities of key parties involved in the safety monitoring and reporting of clinical trials. It distinguishes between obligations for trials involving Unapproved Therapeutic Goods and Non-Therapeutic Goods, aligning with national guidelines, including the National Health and Medical Research Council (NHMRC) Guidance *Safety Monitoring and Reporting in Clinical Trials involving Therapeutic Goods* (2016) (the NHMRC Guidance).

The tables provide clarity on role-specific responsibilities for:

- Sponsors
- Investigators
- Human Research Ethics Committees (HRECs)
- Research Governance Offices (RGOs).

3.1. Sponsors

Therapeutic Goods	Non-Therapeutic Goods
Sponsors should have documented processes to manage the ongoing safety evaluation of their clinical trials. Sponsors should ensure that the nature and extent of safety monitoring is determined through a risk assessment so that safety monitoring plans developed are proportionate to risks identified. The trial protocol (or other document) should clearly demonstrate to those reviewing safety monitoring plans, that appropriate measures to monitor the safety of participants are in place. When the sponsor is a Public Health Organisation (PHO), the PHO may delegate some or all sponsor functions to the Coordinating Principal Investigator (CPI) or other third party (for example, a coordinating centre). When CPIs are delegated sponsor functions, they are to undertake both the investigator and sponsor responsibilities referenced in this Policy Directive. For trials involving **Therapeutic Goods**, this Policy Directive requires sponsors to adhere to the requirements set out in the **NHMRC Guidance**: • **Part 1, Section C, for IMP trials** • **Part 2, Section C, for IMD trials** **For trials not conducted under the Clinical Trial Approvals (CTA) or Clinical Trials Notification (CTN) schemes,**	Sponsors should have documented processes to manage the ongoing safety evaluation of their clinical trials. Sponsors should ensure that the nature and extent of safety monitoring is determined through a risk assessment so that safety monitoring plans developed are proportionate to risk identified. The trial protocol (or other document) should clearly demonstrate to those reviewing safety monitoring plans, that appropriate measures to monitor the safety of participants are in place. When the sponsor is a PHO, the PHO may delegate some or all sponsor functions to the CPI or other third party (for example, a coordinating centre). When CPIs are delegated sponsor functions, they are to undertake both the investigator and sponsor responsibilities referenced in this Policy Directive. As part of the sponsor oversight of clinical trials for **Non-Therapeutic Goods**, proportionate levels of monitoring and audit should be implemented. Sponsors should: • Ensure all sponsor responsibilities are allocated/delegated appropriately and that any third parties (for example, the CPI) are aware of their responsibilities.

reporting to the Therapeutic Goods Administration (TGA) must comply with post-marketing trial requirements.	• Ensure the protocol (or equivalent) describes risk assessment/management and references safety reporting definitions, procedures, responsibilities and timelines.
	• Ensure the protocol lists expected Serious Adverse Reactions (SARs) and, where applicable, details of the nature and frequency of Serious Adverse Events (SAEs).
	• Maintain records of all adverse events.
	• Provide a summary of the trial's evolving safety profile in the annual progress report to the Human Research Ethics Committee (HREC), including mitigation measures.
	• Notify the HREC and investigators in writing of significant safety issues (SSIs):
	  ○ Urgent safety measures – within 72 hours
	  ○ Other SSIs – within 15 calendar days.

3.2. Investigators

Therapeutic Goods	Non-Therapeutic Goods
Investigators must have the necessary training[3] and experience to undertake Good Clinical Practice (GCP) responsibilities for safety monitoring and reporting. The investigator is responsible for supervising any individual or party to whom they have delegated safety monitoring or reporting duties or functions. Investigators must ensure that any members of the trial team are appropriately qualified and trained to undertake those activities. For trials involving **Therapeutic Goods**, this Policy Directive requires adherence to **NHMRC Guidance**: • **Part 1, Section C.1 for IMP trials** • **Part 2, Section C.1 for IMD trials** Investigators should also ensure that any events that meet the definition of an incident are managed in accordance with the NSW Health Policy Directive *Incident Management* (PD2020_047).	Investigators must have the necessary training and experience to undertake GCP responsibilities for safety monitoring and reporting. The investigator is responsible for supervising any individual or party to whom they have delegated safety monitoring or reporting duties or functions. Investigators must ensure that any members of the trial team are appropriately qualified and trained to undertake those activities. For trials involving **Non-Therapeutic Goods**, this Policy Directive requires safety monitoring and reporting to be aligned, as far as possible, with the requirements for therapeutic goods trials as set out in the NHMRC Guidance and conducted within the framework set out in this Policy Directive. Investigators should: • Capture and assess all adverse events occurring at the site, in accordance with the protocol • Report SAEs to the sponsor **within 24 hours**, except those exempted in the protocol • Report any urgent safety measure (USMs) to the sponsor **within 24 hours**

[3] NSW Health *Research Handbook* (as updated).

	• Act on all verbal or written reports of SSIs from the sponsor to ensure any implications for trial participants are managed appropriately
	• Report to the institution (Research Governance Office [RGO]) within **72 hours**:
	  ○ All SSIs
	  ○ Unexpected and Related Serious Adverse Events (URSAEs) arising from the local site.
	Investigators should also ensure that any events that meet the definition of an incident are managed in accordance with the NSW Health Policy Directive *Incident Management* (PD2020_047).

3.3. Human Research Ethics Committees (HRECs)

Therapeutic Goods	Non-Therapeutic Goods
HRECs must assess whether the sponsor's safety monitoring plans are acceptable and whether changes to the risk-benefit ratio reported during the trial are compatible with continued ethics approval. HRECs should: • Assess the safety of proposed trials, including whether the evaluation of the anticipated benefits and risks is satisfactory and ensure that the sponsor has proportionate systems in place to mitigate and manage any identified risks. • Be satisfied that the sponsor's ongoing safety monitoring arrangements are adequate, including the justification for appointing/not appointing a Data Safety Monitoring Board, any 'stopping rules' and/or criteria for withdrawing individual participants from the trial. • Keep under review the adequacy and completeness of the informed consent process and documentation in the light of new information about risks and benefits. • Assess whether changes to the risk-benefit ratio that are reported by the sponsor are compatible with continued ethics approval. • For CTA or CTN trials, advise the TGA, investigators and their institutions of any decision to withdraw approval.	HRECs must assess whether the sponsor's safety monitoring plans are acceptable and whether changes to the risk-benefit ratio reported during the trial are compatible with continued ethics approval. HRECs should: • Assess the safety of proposed trials, including whether the evaluation of the anticipated benefits and risks is satisfactory and ensure that the sponsor has proportionate systems in place to mitigate and manage any identified risks. • Be satisfied that the sponsor's ongoing safety monitoring arrangements are adequate, including the justification for appointing/not appointing a Data Safety Monitoring Board, any 'stopping rules' and/or criteria for withdrawing individual participants from the trial. • Keep under review the adequacy and completeness of the informed consent process and documentation in the light of new information about risks and benefits. • Assess whether changes to the risk-benefit ratio that are reported by the sponsor are compatible with continued ethics approval. • For CTA or CTN trials, advise the TGA, investigators and their institutions of any decision to withdraw approval.

• Acknowledge receipt of any safety-related communication.	• Acknowledge receipt of any safety-related communication.

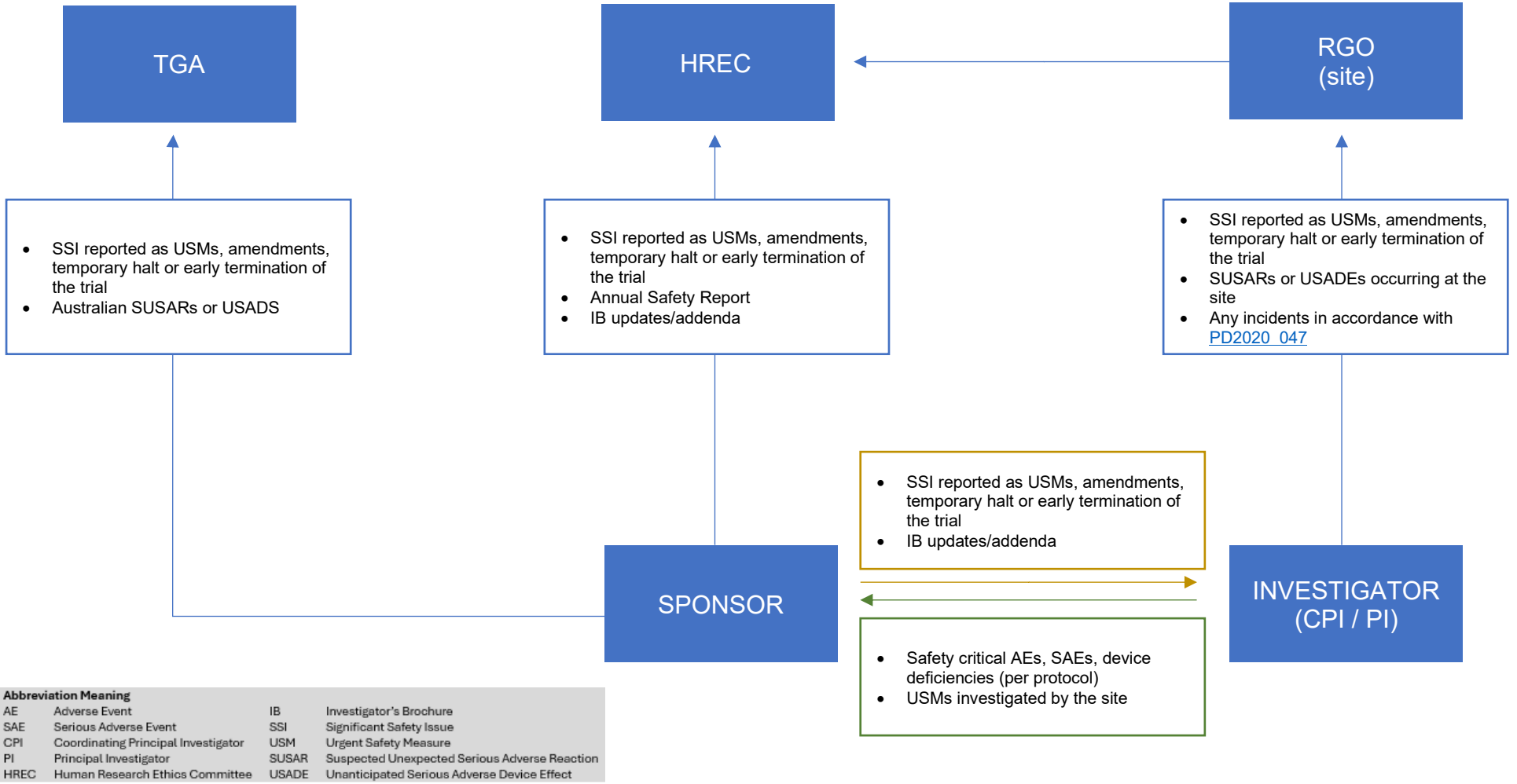
3.4. Research Governance Offices (RGOs)

Therapeutic Goods	Non-Therapeutic Goods
Research governance staff must act on any information received during a trial that may impact the institution's duty of care to patients and trial participants. Research governance staff should: • Assess whether any safety reports received impact on medico-legal risk, the responsible conduct of research, adherence to contractual obligations or the trial's continued site authorisation and, where applicable, facilitate the implementation of corrective and preventative action plans (CAPA). • Develop clear guidance for investigators detailing the requirements for safety reporting and monitoring in clinical trials. This document(s) should cover the requirements for both externally sponsored clinical trials and, if applicable, internally sponsored investigator-initiated or collaborative group trials. • Acknowledge receipt of any safety-related communication.	Research governance staff must act on any information received during a trial that may impact the institution's duty of care to patients and trial participants. Research governance staff should: • Assess whether any safety reports received impact on medico-legal risk, the responsible conduct of research, adherence to contractual obligations or the trial's continued site authorisation and, where applicable, facilitate the implementation of corrective and preventative action plans (CAPA). • Develop clear guidance for investigators detailing the requirements for safety reporting and monitoring in clinical trials. This document(s) should cover the requirements for both externally sponsored clinical trials and, if applicable, internally sponsored investigator-initiated or collaborative group trials. • Acknowledge receipt of any safety-related communication.

Table 1: Summary of Notifications to the HREC and Research Governance Office for Therapeutic Goods Trials

Type of Notification	Responsible	To Whom	When	How
Significant Safety Issue (SSI) implemented as an Urgent Safety Measure (USM)	Sponsor	Lead HREC (and all investigators participating in the study)	Within **72 hours** of the sponsor becoming aware of the SSI	SSI Notification Form **via** REGIS
Significant Safety Issue (SSI) **not** implemented as an Urgent Safety Measure (USM)	Sponsor	Lead HREC (and all investigators participating in the study)	Within **15 days** of the sponsor becoming aware of the SSI	SSI Notification Form **via** REGIS
All Significant Safety Issue (SSI)	Principal Investigator (PI)	RGO for the site where the event occurred	Within **72 hours** of the PI becoming aware of the SSI	SSI Notification Form **via** REGIS
Suspected Unexpected Serious Adverse Events (SUSARs) and Unanticipated Serious Adverse Device Effects (USADEs)	Principal Investigator (PI)	RGO for the site where the event occurred	Within **72 hours** of the PI becoming aware of the event	SUSAR/USADE/URSAE Notification Form **via** REGIS
Significant Safety Issue (SSI) implemented as an Urgent Safety Measure (USM)	Sponsor	Lead HREC (and all investigators participating in the study)	Within **72 hours** of the sponsor becoming aware of the SSI	Submitted with a cover sheet or as part of an annual progress/annual safety report **via** REGIS
IB Updates/Addenda	Sponsor	Lead HREC	As and when updates are generated	Amendment or with the annual progress/annual safety report **via** REGIS
Annual Safety Report	Coordinating Principal Investigator (CPI) or Sponsor	Lead HREC	With the annual progress report or aligned with the safety reporting cycles of global companies	Annual Progress Report **via** REGIS
Adverse Event (meeting criteria for Incident as per *Incident Management* PD2020_047)	Principal Investigator (PI)/ Trial Coordinator/ Health service staff	Sponsor and RGO for the site where the event occurred	As soon as identified	ims+

Figure 1: Reporting Pathway for Therapeutic Goods Trials



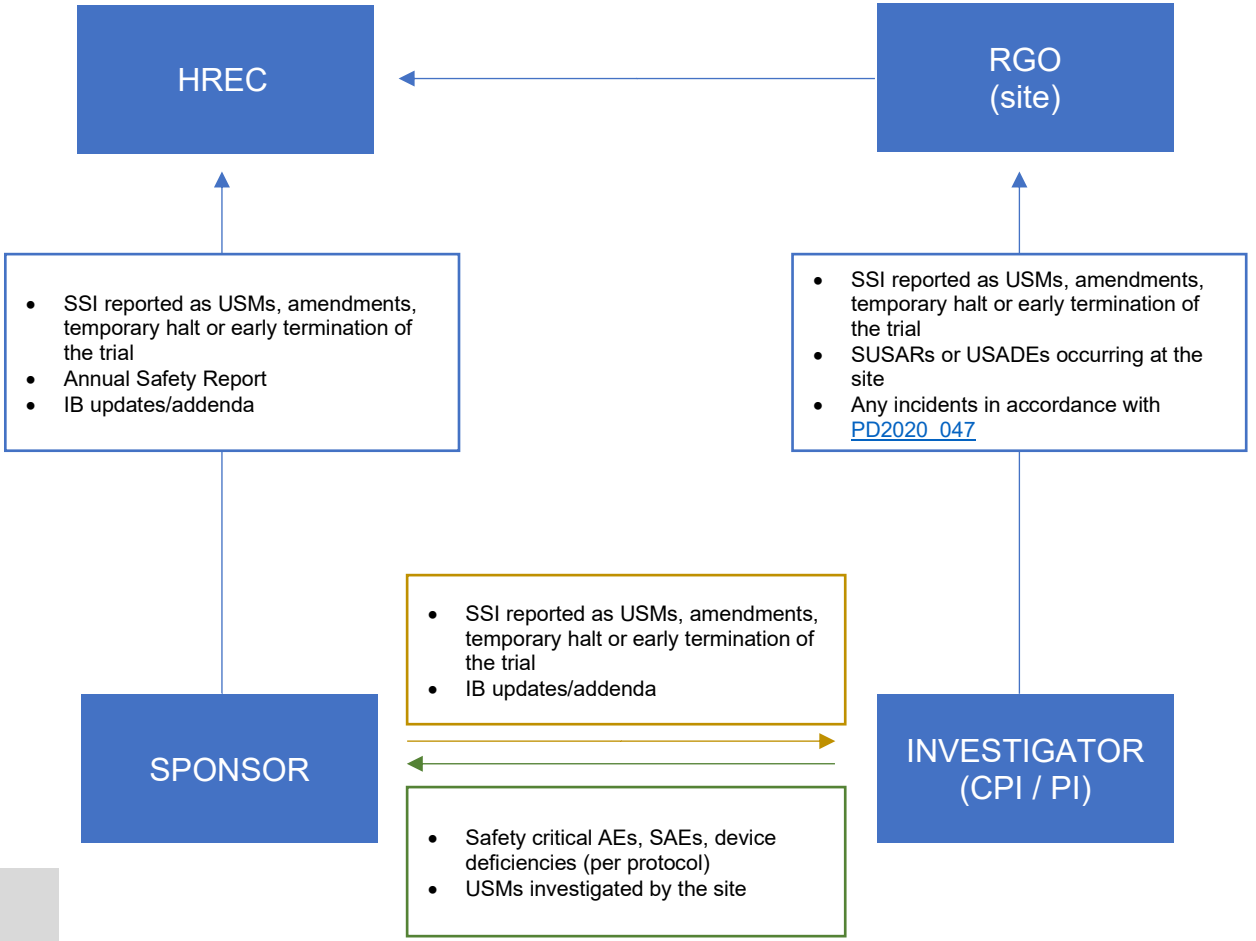
Abbreviation	Meaning	Abbreviation	Meaning
AE	Adverse Event	IB	Investigator's Brochure
SAE	Serious Adverse Event	SSI	Significant Safety Issue
CPI	Coordinating Principal Investigator	USM	Urgent Safety Measure
PI	Principal Investigator	SUSAR	Suspected Unexpected Serious Adverse Reaction
HREC	Human Research Ethics Committee	USADE	Unanticipated Serious Adverse Device Effect

Table 2: Summary of Notifications to the HREC and Research Governance Office for Non-Therapeutic Goods Trials

Type of Notification	Responsible	To Whom	When	How
Significant Safety Issue (SSI) that has been implemented as an Urgent Safety Measure (USM)	Sponsor	Lead HREC (and all investigators participating in the study)	Within **72 hours** of the sponsor becoming aware of the USM	SSI Notification Form **via** REGIS
Significant Safety Issue (SSI) **not** implemented as an Urgent Safety Measure (USM)	Sponsor	Lead HREC (and all investigators participating in the study)	Within **15 days** of the sponsor becoming aware of the SSI	SSI Notification Form **via** REGIS
All Significant Safety Issues (SSIs)	Principal Investigator (PI)	RGO for the site where the event occurred	Within **72 hours** of the PI becoming aware of the SSI	SSI Notification Form **via** REGIS
Unexpected and Related Serious Adverse Event (URSAEs) occurring at the site	Principal Investigator (PI)	RGO for the site where the event occurred	Within **72 hours** of the PI becoming aware of the event	SUSAR/USADE/URSAE Notification Form **via** REGIS
Annual Safety Report*	Sponsor/CPI	Lead HREC	With the annual progress report sent to the HREC	Annual Progress Report **via** REGIS
Adverse Event (meeting criteria for Incident as per *Incident Management* PD2020_047)	Principal Investigator (PI)/ Trial Coordinator / Health service staff	Sponsor and RGO for the site where the event occurred	As soon as identified	ims+

Note: There is no separate annual safety report for non-therapeutic good trials. The sponsor/CPI should give a brief description of the evolving safety profile of the trial in the annual progress report.

Figure 2: Reporting Pathway for Non-Therapeutic Goods Trials



Abbreviation	Meaning	Abbreviation	Meaning
AE	Adverse Event	IB	Investigator's Brochure
SAE	Serious Adverse Event	SSI	Significant Safety Issue
CPI	Coordinating Principal Investigator	USM	Urgent Safety Measure
PI	Principal Investigator	SUSAR	Suspected Unexpected Serious Adverse Reaction
HREC	Human Research Ethics Committee	USADE	Unanticipated Serious Adverse Device Effect

4. References

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