Clinical Research Facility adverse event and clinical incident reporting

PURPOSE

This work instruction describes the processes for Adverse Event (AE) and clinical incident reporting in the Clinical Research Facility (CRF), which is operated by Metro South Health (MSH) on behalf of the Translational Research Institute (TRI).

OUTCOME

This work instruction outlines processes to ensure that responsible personnel abide by Legislative requirements and principles of Good Clinical Practice (GCP), Princess Alexandra Hospital (PAH), TRI and MSH policies and procedures and sponsor and regulatory requirements for Adverse Event (AE) and clinical incident reporting.

This work instruction outlines processes described in MSH procedure PR2024-453 Clinical Research Facility (CRF) and upholds principles outlined within the Clinical Research Facility Handbook.

SCOPE

This work instruction applies to all eligible users of the CRF, and all employees involved in clinical research conducted at the CRF.

WORK INSTRUCTION

1. STEP 1: ADVERSE EVENT REPORTING

1.1 Identification

- An AE or Adverse Reaction (AR) may be identified from participant assessment, verbal communication or from source documents (e.g., pathology reports, discharge summary).
- When an AE or AR is identified by researchers/CRF users it must be documented in the source notes (e.g., integrated electronic Medical Record (ieMR).

1.2 Source documentation and Case Report Form

- All source documentation must be complete and include all required information for the completion of the Case Report Form. For example, source documentation should include:
- Common Terminology Criteria for Adverse Events (CTCAE) term and grade (if required by the clinical trial protocol).
    - start and stop date
    - causality assessment.

- Causality assessments are only to be conducted by the principal investigator/lead researcher or co-Investigator and documented in the source data.

1.3 Assessment

- All AEs and ARs should be assessed to determine if they meet the criteria of a Serious Adverse Event (SAE) or Suspected Unexpected Serious Adverse Reaction (SUSAR) and reported as required (please see the SAE and SUSAR reporting process below).

1.4 Case Report Form

- AEs and ARs are to be recorded in the Case Report Form, as specified in the trial protocol, and any other trial specific documentation relating to the recording of AEs and ARs (e.g., Case Report Form completion guidelines).

2. STEP 2: SAE AND SUSAR REPORTING

2.1 Assessment of 'expectedness'

- The Principal Investigator/lead researcher or co-Investigator must complete an assessment of 'expectedness' to determine if the AE/AR is an SAE or SUSAR and report as appropriate.
- An unexpected AE/AR is an adverse reaction, the nature or severity of which is not consistent with the applicable product information (e.g., Investigator's Brochure for an unapproved investigational medicinal product).

2.2 Reporting

- AEs and ARs which are assessed at the time of notification to meet the criteria for an SAE or SUSAR must be immediately reported in accordance with ICH-GCP which states:
    - 'All SAEs should be reported immediately to the sponsor except for those SAEs that the protocol or other document (e.g. Investigator's Brochure) identifies as not needing immediate reporting. The immediate reports should be followed promptly by detailed, written reports.
    - The immediate and follow-up reports should identify subjects by unique code numbers assigned to the trial participant rather than by the participants names, personal identification numbers, and/or addresses.
    - The investigator should also comply with the applicable regulatory requirement(s) related to the reporting of unexpected serious adverse drug reactions to the regulatory authority(ies) and the Institutional Review Board (IRB)/Institutional Ethics Committee (IEC)'.
- SAEs and SUSARs are to be reported to the sponsor using the communication method specified in the clinical trial research protocol and any other trial specific documentation relating to the reporting of SAEs and SUSARs.
- 'Immediate' reporting timelines for SAEs and SUSARs are outlined in each clinical trial research protocol. NHMRC guidance requires the sponsor to be notified within 24 hours of clinical trial staff becoming aware of the event.

2.3 ieMR update

- The participant's medical record must be updated to reflect that an SAE or SUSAR has occurred and has been submitted to the sponsor.

2.4 MSH Ethics and/or Research Governance reporting

- The NHMRC does not require sites to notify Human Research Ethics Committees (HRECs) of individual AE/AR/SAE/SUSARs or sponsor provided safety reports, unless the Principal Investigator deems that the event poses consideration of the ongoing ethical clearance or site-specific acceptability of the study.
- The sponsor is required to provide the applicable HRECs, Investigators and TGA with notifications as per the NHMRC guidance.

3. STEP 3: URGENT SAFETY MEASURES AND SIGNIFICANT SAFETY ISSUES

3.1 Eliminate an immediate hazard

- Any actions required to eliminate an immediate hazard to the participant's health or safety must be done without delay.

3.2 Notification

- All SSI and USMs are to be notified to the sponsor within 24 hours.
- The sponsor is required to provide the applicable HRECs, Investigators and TGA with notifications as per the NHMRC guidance.

4. STEP 4: CLINICAL INCIDENT MANAGEMENT AND REPORTING

4.1 Immediate action

- All clinical incident or near misses are to be reported as outlined in this procedure and in compliance with MSH policies and procedures.
- Researchers/CRF users who witness an incident or near miss must take immediate action to ensure the safety of participants and staff.

4.2 Notify CRF Manager,

- Researchers/CRF users must notify the CRF Manager who will assist as required.

4.3 RiskMan

- All clinical incidents (actual or near miss) are to be electronically reported into the electronic reporting system, Metro South RiskMan. Incidents should be reported as soon as practical and preferably before the completion of the shift or within 24 hours.

- All clinical incidents reported on MSH RiskMan will be managed as per the MSH procedure PR2022-255 Clinical Incident Management and Reporting Procedure, MSH Procedure PR2022-290 Documentation of Clinical Incidents in RiskMan and Queensland Health Clinical Incident Management guideline (QH-HSDGDL-032-2).

4.4 TRI Health and Safety

- Where permissible under contractual obligations with the sponsor, the CRF Manager will notify TRI Health and Safety as soon as it is practicably possible (within 72 hours), of any clinical incidents or near misses that may occur, and subsequently provide complete details of any such incident or near miss including results of investigations into its cause and any recommendations or strategies for future prevention, as soon as practicable after.
- Where it is relevant to TRI's obligations under State or Federal work health and safety laws, MSHHS must notify TRI of any Serious Breach of a trial protocol or procedure within 72 hours of becoming aware of it.

RESPONSIBILITIES

Position	Responsibility	Audit criteria
CRF Manager	Provide direction to researchers to ensure all AEs and clinical incidents are managed in accordance with CRF procedures and work instructions.	N/A
Principal Investigator (PIs)/lead researchers	Retains overall responsibility for the conduct of their research at the CRF in accordance with the principles of GCP. Ensures that the research project complies with appropriate legal, regulatory and guidance requirements applicable to their research project. Ensures the safety and rights of participants is paramount in all research activities.	N/A
Researchers/CRF users	Researchers/CRF users who become aware of an AE must determine the appropriate reporting mechanism required for the AE depending on its classification as an AE, Adverse Reaction (AR), Serious Adverse Event (SAE), Suspected Unexpected Serious Adverse Reaction (SUSAR), Significant Safety Issue (SSI), Urgent Safety Measure (USM) and	N/A

	comply with all relevant regulations and standards. Share responsibility and accountability for research being conducted according to appropriate regulatory, ethical and scientific standards. Comply with applicable TRI, MSH and PAH policies and procedures. Work in accordance with their scope of practice and comply with their relevant professional standards	

DEFINITIONS

Term	Definition
Adverse Event (AE)	• Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. • An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product.
Adverse Reaction (AR)	• An AR is a noxious and unintended response to a medicinal product related to any dose. The phrase 'response to a medicine' means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility, i.e., the relationship cannot be ruled out. A reaction, in contrast to an event, is characterised by the fact that a sponsor, investigator or reporter suspect there is a causal relationship between the medicine and the occurrence: • **Expected adverse reaction:** An expected adverse reaction is an adverse reaction known to be associated with the use of the medicine, as reflected in the product information document or label warning statement. • **Unexpected adverse reaction:** An unexpected adverse reaction is an adverse reaction in which its nature (that is, its specificity or outcome), severity or frequency is either not identified, or not consistent with the term or description used, in the product information document or label warning statement.
Case Report Form	• A printed, optical, or electronic document designed to record all the protocol required information to be reported to the sponsor on each trial subject.

Clinical Incident	• Any event or circumstance which has actually or could potentially lead to unintended and/or unnecessary mental or physical harm to a patient.
ieMR	• Patient electronic medical record.
Incident (patient safety incident)	• An event or circumstance which could have resulted, or did result, in unintended harm to a patient.
RiskMan	• Electronic information system to collect, integrate, manage and report clinical incidents, workplace incidents, consumer feedback and risk.
Serious Adverse Event (SAE) or Serious Adverse Drug Reaction (Serious ADR)	• Any untoward medical occurrence that at any dose: o results in death o is life-threatening o results in inpatient hospitalisation or prolonged hospitalisation o results in persistent or significant disability or incapacity o is associated with a congenital anomaly or birth defect o is a medically important event or reaction
Serious Breach	• A breach of Good Clinical Practice (GCP) or the protocol that is likely to affect to a significant degree: o The safety or rights of a trial participant, or o The reliability and robustness of the data generated in the clinical trial.
Significant Safety Issue (SSI)	• A safety issue that could adversely affect the safety of participants or impact on the continued ethical acceptability or conduct of the trial.
Suspected Unexpected Serious Adverse Reaction (SUSAR)	• An adverse reaction that is both serious and unexpected.
Urgent Safety Measure (USM)	• A measure required to be taken to eliminate an immediate hazard to a participant's health or safety.

RELATED AND SUPPORTING DOCUMENTS

Legislation and other Authority	**Legislation (as updated and replaced from time to time)** • *Hospital and Health Boards Act 2011 (Qld)* • *Human Rights Act 2019 (Qld)* • *Information Privacy Act 2009 (Qld)* • *Gene Technology Act 2011 (Cth)* • *Public Health Act 2005 (Qld)*

	• *Therapeutic Goods Act 1989 (Cth)* • *Work Health and Safety Act 2011 (Qld)* **Regulations** • Gene Technology Regulations 2001 (Cth) • Therapeutic Good (Medical Devices) Regulations 2002 (Cth) • Therapeutic Goods Regulations 1990 (Cth) • Work Health and Safety Regulation 2011 (Qld) **Other authority** • National Statement on Ethical Conduct in Human Research 2023 • Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice ICH E6(R2) • Queensland Health Clinical Incident Management guideline (QH-HSDGDL-032-2)

Standards	• National Clinical Trials Governance Framework
	• National Safety and Quality Health Service (NSQHS) Standards 2nd Ed.
	  ○ Standard 1 – Clinical Governance
	  ○ Standard 2 – Partnering with Consumers

Supporting documents	**MSH Procedures** • PR2022-255 Clinical Incident Management and Reporting • PR2022-290 Documentation of Clinical Incidents in RiskMan • PR2023-411 Research excellence • PR2023-412 Research support and management • PR2023-413 Research administration and compliance **MSH Work instructions** • WI2024-335 CRF application and use • WI2024-336 CRF participant admission, supervision and clinical management • WI2024-337 CRF investigational product management and administration • WI2024-339 CRF laboratory alarm response • WI2024-340 CRF archiving of clinical trial documents **TRI Policy and Procedure** • TRI-600-002 Health, Safety and Wellness (HSW) Policy • TRI-700-032 TRI Privacy Policy • TRI-600-064 TRI Accident and Incident Reporting and Management

HUMAN RIGHTS ACT 2019

Metro South Hospital and Health Service is committed to respecting, protecting, and promoting human rights. Under the Human Rights Act 2019, Metro South Research has an obligation to act and make decisions in a way that is compatible with human rights and, when making a decision, to give proper consideration to human rights. When making a decision about the Clinical Research Facility, decision-makers must comply with that obligation. Further information about the Human Rights Act 2019 is available at: https://www.forgov.qld.gov.au/humanrights.

WORK INSTRUCTION DETAILS

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1.0	28/06/2024	3/07/2024	Executive Director, Metro South Research	• New MSH work instruction adapted from rescinded PR2021-242.