Metro South Health

Quality healthcare every day

Clinical Research Facility

Handbook

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ICARE² values

INTEGRITY COMPASSION ACCOUNTABILITY RESPECT ENGAGEMENT EXCELLENCE

Queensland Government

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Purpose

Metro South Health (MSH) uses policies and procedures to mandate and direct specific business activity across the Hospital and Health Service (HHS). The MSH Policy Framework ensures appropriate governance and consistency for policy development and supports the management of policy through the policy life cycle.

The Research Policy Framework forms part of the MSH Policy Framework and the processes outlined in this document comply with the MSH Policy Framework. PL2023-92 Research Policy encompasses more than just the management of research in MSH. The Research Policy aims to embed MSH's commitment to conducting research that advances knowledge and innovation and enhances our ability to serve our community. MSH believes in conducting research with integrity, respect for participants, and in compliance with ethical and legislative standards.

MSH procedure PR2024-453 Clinical Research Facility (CRF) aims to provide a consistent, clear and detailed framework, including work instructions and supporting documentation, to inform and guide users of the Clinical Research Facility (CRF). This Handbook, which is attached to MSH procedure PR2024-453 Clinical Research Facility (CRF), aims to outline the standards and principles which MSH and users of the CRF must comply with to ensure:

- All research being undertaken in the CRF is conducted in a manner consistent with nationally recognised ethical clearance and research governance guidelines and Legislation, including but not limited to:
    - National Health and Medical Research Council (NHMRC) National Statement on Ethical Conduct in Human Research 2023 ('National Statement')
    - NHMRC Australian Code for Responsible Conduct of Research 2018 ('the Code')
    - Integrated Addendum to ICH E6 (R1): Guideline for Good Clinical Practice ICH E6(R2).
- All research projects undertaken in the CRF involving MSH employees, participants and/or resources are submitted to a NHMRC Certified Human Research Ethics Committee (HREC) for ethical clearance and the Metro South Research Governance Office (MSRGO) for Site Specific Assessment (SSA) authorisation.
- Any research involving non-MSH participants with minimal MSH resource impact requires ethical clearance from a NHMRC accredited HREC and a MSH SSA waiver.
- When undertaking research, researchers uphold the principles of the:
    - MSH Research Strategy
    - TRI Strategic Plan
    - MSH policy PL2023-92 Research Policy
    - relevant MSH, Translational Research Institute (TRI) and Princess Alexandra Hospital (PAH) policies and procedures.

1.0 Governance, Oversight and Management

The TRI is a unique, Australian-first initiative of 'bench to bedside' medical research. The TRI combines clinical and translational research to advance progress from laboratory discovery to application in the community.

The CRF is a multi-use research facility which provides specialist facilities and resources required by clinical researchers to conduct high quality translational research. The CRF is the interface where TRI and MSH work collaboratively to deliver translational research for the benefit of research participants and the wider community.

MSH operates the CRF on behalf of and in collaboration with the TRI in accordance with the Clinical Research Facility (R-Wing) Services Agreement and is committed to:

- undertaking world-class research that enhances patient care, challenges clinical practice and promotes innovative health service delivery.
- improving health care outcomes for our patients and the wider community.
- expanding and enhancing the clinical research capability and delivery of translational trials on the PAH/TRI campus.

1.1 TRI CRF Committees

1.1.1 TRI CRF Committee

The TRI CRF Committee is responsible for overseeing the administration and governance of the CRF. It also monitors financial and operational performance and manages identified risks. Committee membership is drawn from the participating partner institutions. Key responsibilities include:

- Undertake risk management assessments of TRI Clinical Research Facilities including the risk matrix used for study approvals, on an annual basis.
- Provide recommendations for the TRI Clinical Research Facilities budgets, including appropriate employee resourcing.
- Recommend annual equipment and infrastructure equipment for TRI Clinical Research Facilities.
- Provide guidance on the performance of TRI Clinical Research Facilities.
- Provide guidance on potential future development of TRI Clinical Research Facilities.
- Review reports on utilisation of TRI Clinical Research Facilities and the Translational Trials team and provide advice on strategies to enhance user outputs.
- Engagement with the clinical research support services to enable clinical trial related translational activities.
- Review reports on TRI Clinical Research Facility user experience and requirements
- Review incident reports from TRI Clinical Facilities and if required recommend alterations to policies and procedures.

1.1.2 CRF User Committee

The CRF User Committee allows individual researchers and user groups to have a voice in how the facility operates on a day-to-day basis. Members of the CRF User Committee are sought by approaching new users of the CRF when inducted, by expression of interest within the TRI research community, or nomination by TRI shareholder senior management. New users may apply to become a member of the CRF User Committee by contacting the CRF Manager.

1.2 Compliance

1.2.1 Policy and procedures

The CRF Manager is responsible for maintenance and review of established CRF procedures and work instructions. Policies and procedures which are applicable to the CRF can be accessed from the following sites:

- MSH Policy Index
- Metro South Research website - Policies and procedures
- TRI policies and procedures / PAH policies and procedures

CRF procedures and work instructions are available via the internet and intranet. CRF users, including those who are not MSH employees, can access relevant PAH policies and procedures by request from the CRF Manager as required.

Researchers must comply with legislation and other mandatory requirements outlined within the MSH Research Policy Framework and CRF procedures and work instructions.

A requirement for a new CRF procedure or work instruction can be identified by any user of the CRF and discussed with the CRF Manager. In consultation with the Director, Research Development, Metro South Research, the CRF Manager will initiate the development of any new procedures and work instructions if appropriate.

New MSH or PAH policies and procedures, relating to the CRF, require review and approval by the TRI CRF Committee. New and existing MSH CRF procedures require review and approval as per MSH procedure PR2013-01 Policy Document Management and MSH Policy PL2023-92 Research.

MSH CRF procedures take precedence over TRI Standard Operating Procedures (SOPs) if covering the same topic.

All PAH policies and procedures relating to patient care and management must be complied with and supersede any other TRI or CRF policies or procedure relating to patient care.

MSH must comply with all work health and safety polices of TRI as notified by TRI from time to time (to the extent they comply with applicable laws and regulations and are not less onerous than any policy of MSH).

1.2.2 CRF employee employment records

Employment records will be maintained for all CRF employees by MSH Human Resources and the CRF Manager. Records must include evidence of relevant qualifications applicable to an employee's assigned role.

1.2.3 Training for CRF employees

All clinical CRF employees are required to maintain a personal training record which will include a current Curriculum Vitae (CV) containing details of clinical experience and relevant training. Evidence of other training relevant to an employee's role or continuing professional development is to be retained in their personal training record. All applicable training records will be made available on request to trial sponsors and regulatory bodies.

All clinical CRF employees who support research projects must undertake GCP training and evidence of training and certification will be retained in their personal training record. GCP training is to be renewed every three years. Refer to MSH procedure PR2023-411 Research excellence for more information.

1.2.4 Protocol specific training and delegation logs

Prior to CRF employees being able to provide specific support for a clinical research study the Principal Investigator must ensure they are provided with relevant training and delegate authority appropriately.

Principal Investigators/research groups conducting research in the CRF are responsible for ensuring that documentation of protocol specific training and delegation of duties is compliant with sponsor requirements. Evidence of protocol specific training and delegation for CRF clinical staff will be documented in line with the process approved by the research group coordinating the relevant study.

1.2.5 Personal training records management

Personal training records will be maintained and updated by all active clinical CRF employees and will be stored in a secure location in the CRF. Electronic training records will also be stored as applicable on the CRF electronic shared drive.

1.2.6 Storage and archiving of personal training records

Personal training records will be retained in the CRF for a minimum of seven years after the end of an employee's employment in accordance with the Queensland Government General Retention and Disposal Schedule (2023).

Personal training records will be confidentially and securely stored in the CRF.

If archiving outside of the CRF is required for any reason the PAH Central Document Management Service can arrange external archiving as per the PAH Work Instruction: Archiving non-clinical or administrative records (PAH60029).

Disposal within the CRF will be via the PAH confidential document bins (when required).

2.0 Application and use

Please refer to MSH work instruction WI2024-335 CRF application and use for further information.

2.1 CRF credentialing of research staff

Appropriate credentialing of CRF staff and users is required to ensure the safe conduct of research. All medical practitioners and other health professionals (nurses, allied health practitioners) employed within MSH are required to provide evidence of tertiary and other qualifications in addition to their relevant professional registration before commencing employment.

Where a TRI staff member requires credentialling in order to perform their role, MSH will facilitate credentialling for this staff member where feasible.

2.2 User charges and invoicing

User charges for commercial and non-commercial trials are available on request from the CRF Manager.

The CRF Manager (or delegate) will provide a quote for all commercial trials during the feasibility assessment process. The quote will be based on expected costs following review of the research protocol and associated documentation. A completed costing template will be provided to the Principal Investigator/lead researcher for submission to the sponsor and inclusion in the MSH Site Specific Assessment (SSA) application. The cumulative total visit cost will be charged to the Principal Investigator/lead researcher at the completion of the participant visit.

Non-commercial trials can request a quote during feasibility from the CRF Manager for invoicing based on a total visit cost or can be charged for individual resources calculated following each participant visit.

Research protocol amendments or altered research activity may necessitate an updated quote. The Principal Investigator/lead researcher is responsible to ensure that the CRF Manager is notified of all research amendments so a review can be completed for any potential impact on study conduct and financial implications.

During the application process the Principal Investigator/lead researcher is required to nominate a cost centre and internal order number, chart string or alternative approved payment method which will be charged for CRF use.

Costs associated with each participant visit or use of CRF resource is managed through the centralised TRI CRF booking system: PPMS. The TRI will raise an invoice for payment by the Principal Investigator/lead researcher for each month that research activity has been conducted in the CRF. Principal Investigators/lead researchers are expected to ensure prompt payment on receipt.

2.3 Feasibility and risk assessment

The CRF manager can approve or decline a CRF application based on the feasibility and risk assessment matrix agreed by the TRI CRF Committee. Any concerns regarding the suitability of a CRF application will be escalated by the CRF Manager to the TRI CRF Committee for final decision.

If a Principal Investigator/lead researcher wishes to dispute a decision made by the CRF Manager regarding an application to the CRF, they can escalate their concerns to the TRI CRF Committee who will determine the CRF application outcome.

2.4 CRF induction and swipe card access

Staff requiring access to the CRF must complete a CRF induction with the CRF Manager (or delegate) before they can be issued access clearance. The induction will cover information relating to CRF facilities, including safety and emergency procedures. CRF induction will also comply with First Response Evacuation Instructions (FREI) and General Evacuation Instructions (GEI) as required by MSH.

An online induction may also be suitable for certain applicants requiring limited access to the CRF (e.g. short visits during business hours without primary care responsibilities for participants).

Access levels, which restrict access to certain areas in the CRF based on the applicant’s role and requirements, are determined by the CRF Manager for each applicant.

Swipe access can be linked to a TRI, PAH or UQ ID badge as preferred by the CRF user. If a new TRI badge is required, the inductee is advised to coordinate an appropriate time with the TRI Security staff located on Level 2 of the TRI Building by contacting them on 3443 7733.

2.5 CRF bookings

2.5.1 Participant visits

CRF applications must be approved prior to any bookings taking place. Enough time must be allocated when booking a clinical space to allow set-up and clearing of the room, before and after use.

The CRF Manager reserves the right to amend bookings in consultation with the requesting Principal Investigator/lead researcher/research team, to ensure the most effective use of available resources.

In the event of conflicting appointments for CRF resources the CRF Manager will work with the two parties to facilitate a solution.

Out-of-hours access may be facilitated if all requirements are met by the Principal Investigator/lead researcher.

2.5.2 CRF meeting rooms

The CRF Presentation Room and CRF Conference Room are located on Level 5 of the CRF and can be booked by CRF users. Bookings are on a first-come, first-served basis and can be requested by contacting the CRF Administration Officer.

2.5.3 CRF office/desk space

Level 5 of the CRF has dedicated free TRI partner desks and rentable desk space. The TRI Facilities Management team manage applications for use of rentable desk and office space.

TRI partner organisations manage access to TRI partner desks and allocation of free partner desk space is approved by the nominated TRI partner representatives. The CRF Manager can provide contact details and further information.

2.5.4 CRF out-of-hours access

The standard office hours for the CRF are 8am – 4pm weekdays (excluding public holidays), however if required the CRF can provide nursing clinical support between 7am - 7pm with CRF Manager approval. The CRF Manager will consider all requests for clinical support outside of standard hours and endeavour to provide the necessary staffing and resources to accommodate the request (additional charges may apply). A minimum of two clinical staff competent in PAH emergency response procedures must be available in the CRF at all times that a participant is present.

Out-of-hours access to conduct participant visits without CRF staff present will only be considered for minimal or low risk research projects following an application for out-of-hours access by the Principal Investigator/lead researcher. The Principal Investigator/lead researcher would be required to authorise nominated staff to conduct the visits and the research staff must be suitably qualified and adhere to all relevant policies and procedures.

At least one individual must be clinically qualified (e.g. medical practitioner, nurse or allied health professional) and delegated to carry out the required procedures. Both individuals must be competent in Basic Life Support (BLS) and PAH emergency response procedures. Research staff who have external BLS qualifications are required to complete a practical assessment by a MSH BLS Assessor to ensure compliance with MSH procedures.

The researcher must highlight the need for an out-of-hours participant visit and resource requirements when requesting a CRF booking. If CRF nursing support is required:

- The CRF Manager will consider the request to ensure that adequate staffing and resource is available if approved to proceed.
- The CRF Manager will confirm with the investigator if the participant visit is approved to proceed. If the participant visit cannot be accommodated at the requested time the Principal Investigator/lead researcher is responsible to find a suitable alternative time.

2.6 CRF and investigator equipment

The CRF provides shared clinical and laboratory equipment to facilitate the conduct of clinical research. Shared equipment (e.g. vital signs monitors, phlebotomy trolleys, centrifuge) is available for use during participant visits on a first-come first-served basis. The CRF Manager will assist in providing additional shared equipment when required. The CRF Manager is responsible for ensuring CRF owned equipment is maintained in accordance with manufacturing guidelines and PAH and TRI policies and procedures, including electrical safety testing on all electrical items. Calibration and maintenance certificates can be provided to sponsors or regulatory bodies on request.

Clinical equipment (including but not limited to infusion pumps, observation machines, Electrocardiograms) provided by the PAH Central Clinical Resource Unit (CCRU) is maintained in accordance with manufacturing guidelines and PAH policies and procedures. Individual calibration certificates will not be provided to sponsors for equipment provided by CCRU, however clinical trial monitors can inspect equipment present in the CRF at any time to confirm appropriate calibration as documented by a sticker applied by the relevant PAH department to confirm compliance.

Principal Investigators/lead researchers can apply to the CRF Manager to use and store investigator owned or project specific equipment in the CRF. The Principal Investigator/lead researcher retains responsibility for the maintenance of this equipment. All electrical equipment requires electrical safety testing before use in the CRF and annually as required by PAH policies and procedures. The CRF Manager can assist researchers to ensure compliance.

An equipment register for CRF and investigator owned equipment is maintained by the CRF Manager. The Principal Investigator/lead researcher is required to provide specific details (equipment type, model, serial number etc) as requested by the CRF Manager. All investigator equipment is to be clearly labelled with the research project details, contact details and stored as agreed with the CRF Manager.

2.7 CRF storage

In accordance with TRI procedures related to operation of their facilities, users are required to pay a fee for each key that is issued for specific use. This fee is reimbursed when the key is returned, however if the key is lost/misplaced this fee will not be reimbursed. A new fee will be charged for any key that must be re-issued.

Allocation of space will be on a first-come, first-served basis and subject to CRF Manager's approval. Researchers are encouraged to highlight storage requirements during the CRF application and feasibility process. Storage requests will be documented on the CRF feasibility form.

The CRF Manager will review storage allocation and use periodically. If it is noted at review that allocated space is not being used as per the original application, and requests are made from other research groups for the space, the researchers will be required to justify their continued occupancy. Researchers can be asked to vacate the space and it may be re-allocated to other research groups if the justification is not accepted by the CRF Manager. Decisions can be escalated to the TRI CRF Committee if requested by the researcher.

The CRF has a purpose-built document storage room and several lockable filing cabinets that can be used for the storage of sensitive documentation. This room is known as the Records Storeroom. Users of the CRF will only be granted ID access to this room for storage of their research related documents by approval of the CRF Manager. Users who are granted access to this Records Storeroom are bound by the agreed TRI CRF schedules and consequently must not access or attempt to access documentation that is not related to their research/clinical trial.

The CRF has a large room for the storage of project specific research equipment which is known as the Equipment Store. This room is a shared space in the facility and can be accessed by multiple users to store their equipment between use. No charge applies to the use of space in this equipment room.

The CRF has several lockable cupboards throughout the facility (e.g. each investigation room, the clinical hallways, short stay rooms). Some of these cupboards are specified for use by the CRF employees only but the remainder of these cupboards can be made available to researchers for storage of the equipment and/or clinical supplies that are specific to a research project. A charge applies to the use of these storage cupboards.

2.8 Completion of research projects in the CRF

Principal Investigators/lead researchers are required to notify the CRF Manager when a research project completes recruiting. All research related documents, files, clinical supplies, equipment and/or biological samples related to a research study must be removed from the CRF at the completion of the study unless specific arrangements for storage of these items have been formally agreed and approved by the CRF Manager.

The CRF Manager (or delegate) will notify TRI Security to disable access to the CRF for any CRF users who no longer require access to the CRF at the completion of their research project.

3.0 Participant admission, supervision and clinical management

Please refer to MSH work instruction WI2024-336 CRF participant admission, supervision and clinical management for further information.

3.1 Participant supervision

The Principal Investigator/lead researcher (or delegate) is responsible for ensuring adequate supervision of the participant while in the CRF. CRF staff can assist with participant visits and supervision as required. A minimum of two clinical staff competent in PAH emergency response procedures must be available in the CRF when a participant is present.

3.2 Clinical management

Clinical management of research participants, including clinical management of unwell participants in the CRF and medical emergencies will be according to the clinical trial protocol and PAH procedures relevant to participant management.

4.0 Investigational product management and administration

Investigational product administration must be conducted in accordance with the clinical trial protocol, investigational product administration instructions and PAH procedures relevant to medication administration to ensure participant safety and research protocol compliance.

Adequate safety measures must be in place to ensure the correct procedures are followed relating to each stage of the investigational product administration process.

Investigational product management and administration must only be completed by appropriately qualified staff who have adequate protocol specific training and are delegated by the Principal Investigator to perform each task.

The overall responsibility for investigational product management and administration relating to a clinical trial remains the responsibility of the Principal Investigator.

Investigational product management is routinely provided by the PAH Pharmacy department or PAH Cancer Services Pharmacy as appropriate for clinical trials conducted in the CRF.

IP management responsibilities can be assumed by the CRF only following review and approval by the appropriate PAH Pharmacy department during study set-up. Investigational product management must be conducted in compliance with GCP and Good Manufacturing Process (GMP) guidelines as well as the clinical trial protocol, Investigator Brochure (IB), investigational product manual and any other relevant documents provided by the study sponsor.

Refer to MSH work instruction WI2024-337 CRF investigational product management and administration for more information.

4.1 Investigational product security

Where appropriate the CRF Medication Room and CRF Freezer Room can store investigational product for clinical trials according to the conditions outlined in the investigational product manual provided by the clinical trial sponsor. The CRF Medication Room is also used to store non-trial medications required to support clinical research.

Access to the CRF Medication Room and CRF Freezer Room is strictly controlled, and additional security measures are in place to ensure compliance with GCP guidelines and PAH policies and procedures related to medicines management and storage.

The CRF Medication Room is not an approved dispensing pharmacy and therefore is not under the direct control of a registered pharmacist.

Only researchers/CRF users who have a clinical research project or trial approved to be conducted in the CRF and who require access to the CRF Medication Room and CRF Freezer Room will be granted individual ID access to these secure rooms.

Access is restricted by access levels assigned to staff following CRF Induction. The appropriate access level is approved by the CRF Manager and implemented by TRI Security. Refer to MSH work instruction WI2024-335 CRF application and use for further information.

A record of persons authorised to access the medication room and freezer room is maintained by TRI Security. The CRF Manager will liaise with TRI Security to arrange or disable an individual's ID and security code access when required.

Security measures in place to prevent unauthorised access and to protect against any loss, misuse or theft of investigational product includes individual ID Swipe access controls throughout the CRF, with additional individual keypad code access and a closed-circuit surveillance system that is monitored by TRI Security 24 hours a day in the CRF Medication Room.

If any ID Access Door and/or the CRF Medication Room security keypad alarm triggers, the TRI Security team will respond immediately in the first instance and PAH Security will be notified to help if required.

The CRF Manager (or delegate) and the TRI Building Services Manager will also be notified immediately and will investigate and document the alarm incident and decide on what further action is deemed necessary.

In the event of a security concern affecting investigational product in the CRF, the sponsor of any affected clinical trial will be notified immediately, and appropriate action taken as required.

Refer to MSH work instruction WI2024-339 CRF laboratory and alarm management for more information.

4.2 Storage of investigational product

Researchers/CRF users should discuss any requirement for investigational product storage with the CRF Manager during the project feasibility process so that appropriate allocation of storage can be arranged. Refer to MSH work instruction WI2024-335 CRF application and use for further information.

Storage conditions will be defined by the clinical trial investigational product manual and/or research protocol as provided by the sponsor. Investigational product that can be stored at room temperature will be allocated space in one of the lockable cupboards in the CRF Medication Room.

Investigational product that must be stored at fridge temperature will be allocated space on one of the shelves in the lockable fridges located in the CRF Medication Room. Investigational product that must be

stored in the secure drug cabinet (S4 and S8 drugs) will be allocated space on one of the shelves in the secure lockable cabinet located in the CRF Medication Room. Investigational product that must be stored in the freezer will be allocated space in the appropriate freezer (e.g. -20 degrees or -80 degrees) located in the CRF freezer Room.

The allocated shelf will be clearly labelled with a clinical trial identifier and only investigational product relevant to a specific study must be stored on the assigned shelf. The key to each lockable space will be available from the CRF Manager.

All areas where investigational product may be stored in the CRF have 24-hour monitoring for temperature excursions with alarm management by TRI and PAH. If the fridge, freezer or room temperature detected is out of the set range an alarm will be triggered which will notify TRI Security, the CRF Manager and TRI Building Services Manager or TRI Senior Scientific Services Manager (as appropriate) of the temperature excursion. An immediate response will be instigated to investigate the temperature excursion and investigational product can be moved to an alternative storage location if required.

In the event of a temperature excursion the sponsor will be notified immediately using the temperature excursion forms provided by the sponsor. All investigational products will be placed in quarantine until written confirmation has been provided by the sponsor that the investigational product can be used.

An EasyLog CFR21 Compliant USB Temperature Data Logger is available to monitor the Medication Room, fridge and freezer (excluding -80) temperatures if required. The data logger software allows users to store data in compliance with the United States Food and Drug Administration (FDA) requirements which provides an audit trail of activities and actions taken. Data is downloaded and stored monthly and can be provided to sponsors on request.

Temperature data for the -80 freezers is recorded by the freezer. Temperature logs are downloaded and stored monthly and can be provided to sponsors on request. All investigational products brought into or stored in the CRF must be recorded in the CRF Hazardous Chemical and Drug Register in accordance with TRI requirements.

4.3 Investigational product prescriptions

Investigational product must be prescribed as per the MSH Prescribing Guidelines. Oncology and Haematology trial investigational product must be prescribed using CHARM which is managed by the PAH Cancer Services Pharmacy. For clinical trials where investigational product management is coordinated by PAH Pharmacy, electronic or paper prescriptions will be designed and approved by the PAH pharmacy for use in the CRF.

Principal Investigators/lead researchers will be encouraged to create electronic prescriptions where the investigational product can be prescribed using the Medication Administration Record (MAR) function in the participants integrated electronic Medical Record (ieMR). MAR prescriptions will be developed and approved as per Queensland Health and MSH guidelines.

Refer to MSH work instruction WI2024-337 CRF investigational product management and administration for more information where investigational product prescriptions are coordinated by the CRF.

4.4 Investigational product labelling

All investigational product that is brought into the CRF must be clearly labelled by the sponsor in accordance with Australian pharmaceutical regulations, GMP/OGTR guidelines and GCP guidelines.

Re-labelling for investigational product stored in the CRF will be completed as per instructions provided by the clinical trial sponsor when required (e.g. new expiry date following stability analysis).

4.5 Investigational product dispensing

Investigational product dispensing will be conducted by the PAH Pharmacy and PAH Cancer Services Pharmacy for clinical trials conducted in the CRF in the first instance. Where appropriate and approved by the PAH Pharmacy, investigational product management including dispensing may be conducted by CRF staff trained and delegated for investigational product management on the clinical trial.

4.6 Investigational product administration

Investigational product administration must be conducted in accordance with the clinical trial protocol, investigational product administration instructions and PAH procedures relevant to medication administration to ensure patient safety and research protocol compliance.

Adequate medical and nursing cover is required for patient safety during investigational product administration. The Principal Investigator/lead researcher or delegated doctor must be on the PAH campus and contactable by phone to attend immediately if requested by the staff administering the investigational product for all participant visits.

A minimum of two clinical staff competent in PAH emergency response procedures must always be available in the CRF when a participant is present. Investigational product administration requires two clinical staff to complete the investigational product and participant checks prior to administration.

Investigational product administration will be reviewed during the feasibility assessment conducted by the CRF Manager. The CRF Manager will liaise with the Principal Investigator/lead researcher to confirm if additional safety precautions are requested due to the safety profile of the investigational product. Additional safety precautions will be implemented by the CRF Manager in collaboration with the relevant staff and departments. Investigational product administration cannot proceed in the CRF if provisions for additional precautions cannot be met.

Adverse event and clinical incident reporting procedures are outlined in MSH work instruction WI2024-338 CRF adverse event and clinical incident reporting.

4.6.1 Phase 1 trials (First in Human)

Where the CRF is administering a Phase 1 (first in human) Investigational Product which has not been administered in human subjects before, the Principal Investigator/lead researcher or delegate must be present in the CRF for the administration of a participant’s first dose of investigational product and for any additional doses as determined during the feasibility process due to the safety profile of the investigational product. The timing and duration that the Principal Investigator/lead researcher or delegate must be present in the CRF will be determined by the Principal Investigator/lead researcher based on the safety profile of the investigational product. The same safety requirement will be applied to all clinical trials where the investigational product safety profile requires additional precautions as determined by the Principal Investigator/lead researcher or CRF Manager. Investigational product administration cannot proceed in the CRF if these conditions are not met.

For Phase 1 (first in human) Investigational Products which have not been administered in human subjects before, the Principal Investigator/lead researcher is required to notify the PAH ICU Medical team of the first investigational product administration time and provide available information regarding the investigational product safety profile and mechanism of action. The CRF Manager will notify the PAH Emergency Response teams of the first dose investigational product administration time.

4.7 Genetically Modified Organisms (GMOs)

Genetically Modified Organism (GMO) IP management must be conducted in accordance with Office of the Gene Technology Regulator (OTGR) regulations, policies and procedures including the Dealings Not Involving Intentional Release (DNIR) relevant to the GMO. Refer to MSH work instruction WI2024-337 CRF investigational product management and administration for more information.

5.0 Adverse Event and Clinical Incident Reporting

Refer to MSH work instruction WI2024-338 CRF adverse event and clinical incident reporting for more information.

Safety reporting and clinical incident reporting processes are required to ensure the safe conduct of clinical research in compliance with relevant legislation, sponsor and regulatory requirements and the principles of Good Clinical Practice (GCP).

All clinical incident management and AE reporting must be as per:

- MSH: Clinical Incident Management and Reporting Procedure (PR2022-255)
- Patient Safety Health Service Directive (QH-HSD-032:2014)
- Guideline for Clinical Incident Management Health Service Directive (QH-HSDGDL-032-2)
- *Hospital and Health Boards Act 2011 (Qld).*

It is the responsibility of all CRF employees, researchers and partners to ensure that activities related to the CRF are carried out in accordance with prevailing norms and ethical principles.

6.0 Laboratory and Alarm Management

Refer to MSH work instruction WI2024-339 CRF laboratory and alarm management for more information.

Robust laboratory and alarm management processes are required to ensure safe work practices and equipment compliance, and appropriate processing, storage and monitoring for clinical trial samples and Investigational Product (IP) managed in the CRF.

7.0 Archiving of clinical trial documents

7.1 Archiving and destruction of administrative records

Refer to MSH work instruction WI2024-340 CRF archiving of clinical trial documents for more information.

It is the responsibility of the CRF Manager to ensure that the archiving and destruction of CRF administrative records is managed in accordance with relevant MSH policies and procedures. CRF administrative records will be confidentially and securely stored within the Record Storage (4.RS.40) room on Level 4 of the CRF until disposal in the first instance. Disposal will be via the PAH confidential document bins.

If archiving outside of the CRF is required for any reason the PAH Central Document Management Service can arrange external archiving as per the PAH Work Instruction: Archiving non-clinical or administrative records (PAH60029).

7.2 Storage and archiving of clinical trial records

It is the responsibility of the Principal Investigator (PI) to ensure appropriate archiving of clinical trial records in accordance with GCP and sponsor requirements.

Any documentation that is used to support the conduct of clinical research and clinical drug trials is required to be retained for a minimum period of seven (7) to fifteen (15) years, respectively. A longer retention period may be required in certain circumstances, including clinical drug trials in children or involving genetically modified organisms. It will be the responsibility of the CRF Manager to maintain and manage clinical trial documents and archiving in compliance with legislative and sponsor requirements and the principles of ICH-GCP.

Clinical trial records can be archived in the CRF on request from the PI.

8.0 Definitions

Term	Definition
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/participant.
Clinical Trial (National Clinical Trials Governance Framework definition)	• A clinical trial is 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. Clinical trials include but are not limited to: • Surgical and medical treatments and procedures • Experimental drugs • Biological products • Medical devices • Health-related service changes • Health-related preventative strategies • Health-related educational interventions.
Credentialing	• The formal process used to verify and review the qualifications, experience, professional standing and other relevant professional attributes of health professionals for the purpose of forming a view about their competence, performance and professional suitability to provide a safe, high quality healthcare service within specific environments.
Dealings Not Involving Intentional Release (DNIR)	• Dealings Not Involving Intentional Release (DNIR) refers to activities or transactions that do not intentionally release or expose substances, organisms, or materials into the environment.
Genetically Modified Organism (GMO)	• Genetically modified organism means: (a) an organism that has been modified by gene technology; or (b) an organism that has inherited particular traits from an organism (the initial organism), being traits that occurred in the initial organism because of gene technology; or

	(c) anything declared by the regulations to be a genetically modified organism, or that belongs to a class of things declared by the regulations to be genetically modified organisms. but does not include: (d) a human being, if the human being is covered by paragraph (a) only because the human being has undergone somatic cell gene therapy; or (e) an organism declared by the regulations not to be a genetically modified organism, or that belongs to a class of organisms declared by the regulations not to be genetically modified organisms (Gene Technology Act, 2000).
Good Clinical Practice (GCP)	• A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial participants are protected.
Good Manufacturing Practice (GMP)	• Good Manufacturing Practice (GMP) is a set of quality assurance guidelines and practices implemented in the manufacturing, packaging, testing, and storage of pharmaceuticals, food, medical devices, and other products.
ieMR	• Integrated Electronic Medical Record (PAH Patient electronic Medical Record)
Investigational Product (IP)	• A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including 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, or when used to gain further information about an approved use (ICH-GCP E6 (R2)).
IP Administration	• A route of administration in pharmacology and toxicology is the path by which a drug, fluid, poison, or other substance is taken into the body. • Routes of administration are generally classified by the location at which the substance is applied. • Common examples include oral and intravenous administration.
IP Brochure	• An Investigational Product Brochure is a comprehensive document that provides detailed information about an investigational product being studied in a clinical trial. • It serves as a critical resource for investigators, study coordinators, and participants involved in the trial, as well as regulatory authorities and ethics committees.
IP Management	• Receipt, storage, labelling, dispensing and destruction of IP.

IP Manual	• An Investigational Product Manual is a comprehensive document that provides detailed instructions and guidelines for the handling, storage, administration, and management of an investigational product in a clinical trial.
Policy framework documents	• Policy documents include policies, procedures, work instructions and guidelines – PR2013-01 Policy Document Management.
Research	• Clinical research - A type of scientific research that is conducted with human participants to understand, diagnose, prevent, or treat medical conditions or diseases. It involves the study of human biology, physiology, pharmacology, and psychology, among other disciplines, in order to improve our understanding of health and disease. Clinical research can take many forms, including observational studies, randomised controlled trials, and retrospective analyses of patient data. In some cases, clinical research involves testing new drugs, medical devices, or other interventions in human subjects to evaluate their safety and efficacy. Clinical research is typically conducted in a controlled environment, such as a hospital, and is overseen by a team of researchers, including physicians, nurses, and other healthcare professionals. The goal of clinical research is to generate new knowledge that can improve patient outcomes, inform clinical practice, and advance medical science. • Non-clinical research - The concept of research is broad and includes the creation of new knowledge and/or the use of existing knowledge in a new and creative way so as to generate new concepts, methodologies, inventions and understandings. This could include synthesis and analysis of previous research to the extent that it is new and creative.
Research Policy Framework	• A framework inclusive of policy, procedures, work instructions, guidelines and supporting documents, aligned to MSH research practices.
RiskMan	• Electronic information system to collect, integrate, manage and report clinical incidents, workplace incidents, consumer feedback and risk.
Scope of clinical practice (SoCP)	• The extent of an individual health professional's approved clinical practice within an organisation based on the individual's credentials, competence, performance and professional suitability and the needs and capability of the organisation to support the health professional's SoCP.