Clinical Research Facility investigational product management and administration

PURPOSE

This work instruction describes processes relating to Investigational Product (IP) management and IP administration in the Clinical Research Facility (CRF), located at the Princess Alexandra Hospital (PAH) and operated by Metro South Health (MSH) on behalf of the Translational Research Institute (TRI).

OUTCOME

This work instruction outlines:

- a consistent approach in IP management and IP administration in the CRF to ensure participant safety and compliance with relevant PAH, CRF, MSH and TRI requirements.
    - Note: management of investigation product must be conducted in compliance with Good Clinical Practice (GCP) and Good Manufacturing Practice (GMP) guidelines as well as the clinical trial protocol, Investigator Brochure (IB), IP Manual and any other relevant documents provided by the study sponsor and regulatory authorities.
- the process which ensures that Genetically Modified Organism (GMO) IP management is 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.

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 CRF and PAH Pharmacy and Cancer Services Pharmacy employees, eligible users of the CRF and all employees involved in clinical research conducted at the CRF.

WORK INSTRUCTION

1. STEP 1: RECEIPT OF INVESTIGATIONAL PRODUCT

- The following process will be used for receipt of IP which is to be stored in the CRF.

1.1 Receipt and storage

- Receipt and storage of IP will be immediately completed on delivery of IP by staff trained (i.e. CRF and PAH Pharmacy employees) and delegated for IP management on the clinical trial.

1.2 Inspection of outer packaging

- Staff will inspect the outer packaging to ensure the IP has been delivered intact. The Principal Investigator/lead researcher and sponsor will be notified immediately if there is evidence of tampering.
- The outer packaging will be opened only in the final storage location and the IP will be immediately transferred to the appropriate storage conditions defined by the research protocol/IP manual.

1.3 Temperature recording

- Temperature recording devices included in the shipment will be inspected to ensure a temperature excursion did not occur.
- In the event of a temperature excursion, the sponsor will be notified immediately using the temperature excursion forms provided by the sponsor.
- All IPs will be placed in quarantine until written confirmation has been provided by the sponsor that the IP can be used.

1.4 IP delivery documents

- The IP delivery documents will be inspected to ensure that the delivery contents are correct including quantity and IP name, strength, dose, batch number(s) and expiry date.
- Each batch delivered to the CRF must have a certificate of analysis provided by the sponsor.
- Any discrepancy will be notified to the sponsor.

1.5 IP accountability log/Interactive Web/Voice Response Systems (IW/VRS)

- The IP accountability log provided by the sponsor will be updated and IP delivery documents will be filed in the Investigator Site file.
- Any additional processes required by the sponsor (e.g., receipt of IP in an IW/VRS) will be completed if applicable.

2. STEP 2: IP PRESCRIPTIONS

- Principal Investigators/lead researchers are encouraged to create electronic prescriptions where the IP 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 Metro South Health (MSH) guidelines.

2.1 Prescription template development

- Where electronic prescriptions are not used, the CRF Manager will create a prescription template to be printed on PAH in-patient medication charts using the clinical trial protocol, IP manual and any other relevant documentation provided by the sponsor. A different prescription template is required for each treatment detailed in the clinical trial protocol (e.g. each possible treatment allocation or cohort).
- The prescription template must clearly contain the following information (at a minimum):

- Clinical Trial Protocol Number
- Treatment Arm, Cohort, Dose Level details (if applicable)
- Complete IP prescription: IP name, dose, and route
- Comment: ‘Prescription Template Approved by: __’ with principal investigator signature line and date
    - Each template must have a wet ink Principal Investigator signature to be valid.
- Comment: ‘Prescription based on protocol version __’
    - New prescription templates must be implemented at each protocol amendment and previous prescription templates marked as superseded.
- Comment: ‘The prescription must contain the prescriber’s name, signature and date prescribed to be valid prescription.
    - This is in addition to the principal investigator wet ink signature which approves the template only. A patient specific prescription requires a valid prescribers name, signature and date following patient review.

2.2 Prescription templates and PAH Clinical Trials Pharmacist review

- The prescription template(s) is forwarded to the PAH Clinical Trials Pharmacist for review.
- The PAH Clinical Trials Pharmacist will review the template and approve their use pending Principal Investigator/lead written researcher review and approval.
- Correspondence confirming review and approval will be filed in the Investigator Site File by the CRF Manager.

2.3 Principal Investigator/lead researcher review

- The prescription template(s) is sent to the principal investigator/lead researcher for review. The principal investigator/lead researcher will review the template and once satisfied approve their use.
- Correspondence confirming review and approval will be filed in the Investigator Site File by the CRF Manager.

2.4 Prescription templates approval

- Once approved, the CRF Manager will print the prescription templates on the required number of PAH in-patient medication charts and provide them to the principal investigator/lead researcher for wet ink signature.
- A PDF version of each prescription template will be stored in the protocol specific folder on the CRF electronic drive.

2.5 Prescribing IP on the prescription template

- The Principal Investigator/lead researcher or delegated doctor can prescribe IP on the prescription template following participant review by signing their name, signature, and date on the appropriate section of the prescription.
- The prescribing doctor is responsible for ensuring that the correct prescription template has been used for the patient visit and that the principal investigator/lead researcher wet ink signature is present to validate the template.
- Staff administering IP in the CRF can only proceed with IP administration when all required elements are completed to provide a valid prescription.

3. STEP 3: IP DISPENSING

3.1 Review

- The Principal Investigator/lead researcher or delegated medical professional is responsible to ensure that the participant is suitable to proceed with treatment and complete an approved prescription.

3.2 Confirm appropriate storage

- The staff member dispensing the IP must ensure that the IP has been stored correctly.
- If no restrictions are applied to the IP, the required quantity of IP can be retrieved from the IP storage location.

3.3 Dispensing as per the prescription

- Two staff trained and delegated to complete IP management on the clinical trial will check the IP to ensure that the correct IP is being dispensed as per the prescription.
- The study specific protocol identifier, IP name, strength, dose, batch number(s), medication number(s) (if assigned by sponsor/IVRS/IWRS) and expiry date will be checked, and the IP accountability logs provided by the sponsor will be completed.
- Instructions provided by the sponsor for IP dispensing, including blinding procedures if applicable, will be strictly adhered to by IP management staff.

3.4 Labelling

- CRF staff will label the IP (and/or packaging if appropriate) with the patient's unique subject ID, visit identifier and date dispensed.
- The IP is dispensed to the Principal Investigator/leader researcher or delegate for administration to the participant.
- The Principal Investigator/lead researcher or delegate is responsible for IP administration and providing adequate education to the participant.

4. STEP 4: IP ADMINISTRATION.

- For clinical trials where IP administration is coordinated by the CRF the following process will be applied.

4.1 Admission and medical approval

- The participant is admitted to CRF for administration of IP clinical trial visit.
- Medical approval to proceed with IP dosing must be documented by the Principal Investigator/lead researcher or delegate in the participant's electronic medical record (ieMR).
    - The principal investigator/lead researcher or delegate must provide evidence of cohort or dose level allocation from the sponsor if appliable.

4.2 Participant Information and Consent Form (PICF)

- The participant's signed PICF must be visualised by the person administering the IP.
- Signed informed consent forms are available to view in ieMR and CHARM (if applicable).
- Verbal consent will be obtained from each participant prior to each IP administration.

4.3 Education

- The Principal Investigator/lead researcher or delegate (including CRF staff if applicable) is responsible for providing adequate education to the participant prior to IP administration.

4.4 Clinical staff coverage

- Staff administering IP must ensure that required staff are present in the CRF for IP administration (including additional medical cover for first dose IP if applicable).
- The participant and IP will be checked by a minimum of two clinical staff (doctor or nurse) using the 'seven rights' as per the MSH procedure PR2022-304 Medicines management.
- In addition, the prescription will be checked against the research protocol and IP administration guidelines by two clinical staff immediately prior to IP administration to ensure that the prescription matches the expected treatment allocation (e.g. treatment and dose as per randomisation and cohort).

4.5 IP administration

- IP must be administered as per the clinical trial research protocol, IP administration guidelines provided by the sponsor and as per the MSH procedure PR2022-304 Medicines management and relevant supporting documents.
- Participant monitoring and investigations will be completed as per the clinical trial protocol. IP administration will be documented in ieMR and CHARM (if applicable).
- Source data sheets designed by the sponsor or provided by the clinical trial coordinator will be completed if applicable.

5. STEP 5: IP RETURN AND DESTRUCTION

5.1 Non-injectable/oral IP (non-GMO)

- Clinical trials where IP management is conducted by the CRF will follow the following procedure for non-injectable/oral IP.

5.1.1 Unused IP

- Staff administering IP must collect unused IP (and used packaging if required) from the subject at each study visit if applicable.
- Unused IP (and used packaging if required) will be returned to the relevant PAH Pharmacy where IP management (reconciliation) is external to the CRF.

5.1.2 IP accountability logs

- The returns are documented in the IP accountability logs provided by the sponsor.

5.1.3 Oral IP storage

- Oral IP returns can be securely stored in the CRF in the allocated storage space until destruction. Oral IP destruction will only occur once IP accountability has been performed; all discrepancies have been investigated, satisfactorily explained and reconciliation accepted; and written approval has been provided by the sponsor/monitor.

5.1.4 IP destruction

- IP destruction is to be documented on the IP return and destruction forms provided by the sponsor.
- Once approved by the sponsor, IP can be disposed of in a yellow clinical waste sharps bin or waste bin.

5.2 Injectable IP (non-GMO)

- Clinical trials where IP management is conducted by the CRF will follow the following procedure for injectable IP.

5.2.1 Discarding injectable vials

- All used vials of injectable medicine are discarded immediately after they have been prepared for safety reasons to avoid the potential for hazardous materials to leak and break in the appropriate receptacle.
- This is PAH policy and is adhered to for all clinical trials.
- Empty packaging that contained the vials or vial labels can be retained for accountability purposes.

5.2.2 Investigational product return and destruction forms

- IP destruction is to be documented on the IP return and destruction forms provided by the sponsor as required.

5.2.3 Disposal of IP

- Non-cytotoxic IP must be disposed of in a yellow clinical waste sharps bin and Cytotoxic IP must be disposed of in approved cytotoxic waste sharps bins as per PAH procedure Waste Management (80016) and PAH procedure Cytotoxic and Related Waste Management (01533).

6. STEP 6: GENETICALLY MODIFIED ORGANISMS (GMOS)

- GMOs will be handled, prepared, disposed in accordance with CRF Standard Operating Procedure SOP2024-001 Genetically modified organisms.

RESPONSIBILITIES

Position	Responsibility	Audit criteria
CRF Manager	CRF Manager is responsible to ensure adequate resources are in place to provide safe, high-quality research in the CRF, including the necessary resources to ensure safe IP management and administration.	N/A
PAH Pharmacy and Cancer Services Pharmacy	The PAH Pharmacy Department and Cancer Services Pharmacy are responsible for IP management of clinical trials at PAH. PAH Pharmacy Department or PAH Cancer Services Pharmacy (as appropriate) review and approval is required if IP management responsibilities are assumed by the CRF.	N/A
Principal Investigator (PI)/lead researcher(s)	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. Review IP management and administration requirements with the Manager, CRF during feasibility review. Provide all applicable sponsor documents relating to investigational management and administration to the Manager, CRF to ensure protocol compliance. Provide all IP management and administration procedures to PAH Pharmacy for review and approval.	N/A
Researchers/CRF Users	Share responsibility and accountability for research being conducted according to	N/A

	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. Ensure IP management and administration in the CRF is compliant with processes outlined in this procedure, sponsor requirements, MSH policies and procedures and all applicable national and international regulations relating to IP management and administration.	

DEFINITIONS

Term	Definition
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.
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 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 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.
IP Management	• Receipt, storage, labelling, dispensing and destruction of IP.
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.

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)*

	Regulations • Gene Technology Regulations 2001 (Cth) • Therapeutic Good (Medical Devices) Regulations 2002 (Cth) • Therapeutic Goods Regulations 1990 (Cth) **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)

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	**Procedures** • PR2023-411 Research excellence • PR2023-412 Research support and management • PR2023-413 Research administration and compliance • PR2022-304 Medicines management • PR2018-97 Risk management • PAH 80016 Waste management • PAH 01533 Cytotoxic and related waste management **Work instructions** • WI2024-335 CRF application and use • WI2024-336 CRF participant admission, supervision and clinical management • WI2024-338 CRF adverse event and clinical incident reporting • WI2024-339 CRF laboratory alarm response • WI2024-340 CRF archiving of clinical trial documents • TRI-600-050 Human Blood Tissue Fluids **SOPs** • SOP2024-001 Genetically modified organisms

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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