Standard Operating Procedure

Title: Management of Investigational Product

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CONTENTS

1. PURPOSE

To document the procedures for the management of Investigational Medicinal Product (IMP) used in research involving human participants, following dispensing from Clinical Trials Pharmacy.

1.1 Quality Improvement

Compliance with this SOP ensures/facilitates:

- trial participants receive the IMP per the Medication Management Procedure
- storage of the IMP at the correct temperature at all times following dispensing from Clinical Trials Pharmacy
- demonstration of the chain of custody from receipt of IMP at RCH/MCRI until administration or handover to the participant/family

1.2 Participant Safety

Compliance with this SOP ensures the IMP is stored and administered to participants as per protocol and the Medication Management Procedure, ensuring:

- the right IMP is administered
- to the right participant
- at the right dose and for the right indication
- through the right route
- at the right time
- and participants have the right to refuse at any time.

2. SCOPE

This Standard Operating Procedure (SOP) covers the management of IMP in research involving human participants, including the chain of custody from dispensing of IMP by RCH Clinical Trials Pharmacy, through to:

- handover to the research team member for administration to the participant, or
- to the participant/family for administration at home.

It also includes storage, shipment, and return of IMP.

Processes undertaken by Clinical Trials Pharmacy including IMP ordering, receipt, dispensing, accountability, and authorised destruction of IMP, are not covered within this SOP.

Management of Investigational Medical Devices (IMDs) is not covered in this SOP. A separate SOP is to be developed that provides the procedures for receipt, storage, accountability, use, shipment and destruction of IMDs. Until this SOP is available, the Principal Investigator of any

clinical trial using an IMD should seek guidance from both the Sponsor and Clinical Research Development Office on how to comply with the relevant regulations for managing IMDs.

In some clinical trials, the IMP may be stored outside the clinical trial pharmacy and dispensing will be the delegated to trained staff within the research team. These procedures are outside the scope of this SOP. In these cases, the Clinical Trial Protocol and associated trial SOPs must provide the storage conditions, temperature monitoring and dispensing procedures.

3. RESPONSIBILITY

This SOP applies to staff involved in clinical trials of IMP at Melbourne Children's at the site level and who have any of the following roles:

- PI
- All members of the research team who have been delegated responsibility for the handling of IMP in clinical trials (eg: Sub-Investigator, Clinical Trial Coordinator, Research Nurses, Clinical Trial Pharmacists).

All study personnel involved in the clinical study must operate within their scope of practice.

The PI is responsible for the management of IMP at the trial site but may delegate responsibility. This delegation must be recorded on the study delegation log. The PI remains responsible for delegated duties.

4. PROCEDURE

4.1 Training and Delegation

Train staff on the Clinical Trial Protocol and current Reference Safety Information, i.e. Investigator's Brochure (IB), approved Australian Product Information, or other country's equivalent. Document all training on the trial-specific Training Log or using MCTC017 Template | Study Staff Training Log template .

Where applicable, train clinical trial participants and parent/guardians to handle and administer IMP. This training must be done by delegated clinical trial staff and documented and filed in site files (source document/participant file).

Document delegation of staff on the trial-specific Delegation Log using either the log provided by the Sponsor or MCTC025 Guidance | Signature and Delegation Logs template. All delegated staff must be signed on/off by the PI.

4.2 IMP movement/chain of custody

The site must document evidence of chain of custody of IMP, from Clinical Trial Pharmacy, to the trial participant, transport to participant's home, return of IMP to Clinical Trial Pharmacy, storage, and destruction. This is to ensure that the integrity of IMP has been maintained, through evidence of appropriate storage and transit conditions. IMP must be traceable from receipt to dispensing/administration to participant.

Where the IMP is dispensed from Clinical Trial Pharmacy and transferred to a department/facility/area for administration to the participant, appropriate chain of custody records should be maintained. Where IMP (compounded or reconstituted in pharmacy or for immediate use by nursing or other qualified staff) has limited stability/short half-life, records should demonstrate that it was transported and administered within the specified timeframe.

When transport between the Clinical Trial Pharmacy and treatment areas is required, the Clinical Trial Pharmacist or appropriately delegated trial staff must transport the IMP after it has been dispensed.

4.3 Administration of IMP

- IMP must be administered according to the prescription, administration guidelines within the Clinical Trial Protocol, participant facing IMP instructions, other IMP guidance documents provided by Sponsor, and the Medication Management Procedure.
- IMP must only be administered to clinical trial participants by qualified and professionally registered individuals authorised to do so under Australian law (eg: medical practitioners and registered nurses who are appropriately trained and delegated).
- Where clinical trial participants/parents/guardians are expected to administer IMP, they must be trained to administer the IMP as per trial protocol by clinical trial staff. This training must be documented in the source document. Trial staff should check at regular intervals that study participants/parents/guardians are administering IMP per study protocol.
- Ethics approved patient facing resources illustrating/documenting administration instructions must be provided to the parent/guardian +/- participant if relevant to the protocol. This must be recorded, and the individuals must be able to demonstrate their ability to safely and adequately administer IMP.
- Depending on the specific protocol, relevant paperwork/electronic data entry on approved devices/Apps may be used to record administration (location, dose, date, time, etc.). For IMP administered by participants/parents/guardians at home, the Principal Investigator/Sub-Investigator should document review of the completed

diaries at regular intervals throughout the trial to ensure it is being completed accurately and in a timely manner.

4.4 Storage of IMP

IMP must be stored at the correct temperature (eg: ambient/refrigerated/frozen) according to the Clinical Trial Protocol, Investigator's Brochure, and participant facing IMP instructions/guidance documents provided by Sponsor.

Please refer to RCH SOP on Storage of Clinical Trial Drugs for further information on storage of IMP within Clinical Trial Pharmacy. The clinical trial participants and parent/guardians must be trained on storage of IMP by trial staff. This training must be documented and filed in source document/participant file.

4.5 Direct to Patient (DTP) Shipment of IMP

Trials that have Direct to Patient (DTP) shipment of IMP included in their protocols, or where sponsor approved DTP has been consented to by participants/families for either ad hoc usage (COVID-19) or as a scheduled event, will follow all sections of this SOP.

Delegated clinical trial staff will collect the IMP from Clinical Trials pharmacy and deliver the IMP to an authorised courier who will deliver to a destination as agreed with the Parent/Guardian(s) of the Participant. Communication with the courier should be filed.

Protocol specific documentation of this process (including contents being shipped, date and time of collection and delivery, plus relevant temperature control tracking device data) will be adhered to by the Research Nurse/ Trial Coordinator. A record of items shipped will be documented and filed in participant folder.

As per the trial protocol, all relevant documentation will be completed and filed in the participant folder.

4.6 Return of IMP

All IMP (used and unused) may be required to be returned to site in accordance with the Clinical Trial Protocol. Parents/guardians +/- participants must complete training on return of IMP, including expired and empty containers/blister packs.

5. CORRECTIVE ACTIONS

Any deviation to the required storage conditions, administration or documentation of chain of custody of the IMP must be notified to the Sponsor in a timely manner and in accordance with the Clinical Trial Protocol.

Where trial participants/guardians have demonstrated poor medication compliance, additional counselling by the Principal Investigator/Sub-Investigator may be required.

If the IMP needs to be quarantined, contact RCH Clinical Trials Pharmacy for advice on the process to follow.

6. GLOSSARY

Clinical Trial

The World Health Organization (WHO) definition for 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'.

Electronic Medical Record (EMR)

An electronic medical record includes information about a patient's health history, such as diagnoses, medicines, tests, allergies, immunisations, and treatment plans.

Guardian

A person who has the legal right and responsibility of taking care of someone who cannot take care of himself or herself.

Investigator

A person responsible for the conduct of the clinical trial at a trial site. There are four types of Investigator roles used to describe Investigators with different levels of responsibility for the conduct of clinical trials. These are described below.

Sub-Investigator

Any individual member of the clinical trial team designated and supervised by the Principal investigator at a trial site to perform critical trial-related procedures and/or to make important trial-related decisions (e.g., associates, residents, research fellows). May also be referred to as Associate Investigator.

Principal Investigator

The PI is the person responsible, individually or as a leader of the clinical trial team at a site, for the conduct of a clinical trial at that site. As such, the PI supports a culture of responsible clinical trial conduct in their health service organisation in their field of practice and, is responsible for adequately supervising his or her clinical trial team.

The PI must conduct the clinical trial in accordance with the approved clinical trial protocol and ensure adequate clinical cover is provided for the trial and ensure compliance with the trial protocol.

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.

Investigator's Brochure (IB)
The document containing a summary of the clinical and non-clinical data relating to an investigational medicinal product that are relevant to the study of the product in humans.

Melbourne Children's Campus
The campus encompassing all staff from The Royal Children's Hospital, Murdoch Children's Research Institute and Department of Paediatrics University of Melbourne who initiate or carry out research under one or more of these institutional affiliations.

Melbourne Children's Trials Centre (MCTC)
Melbourne Children's Trials Centre (MCTC) is a collaboration between the Royal Children's Hospital, The Murdoch Children's Research Institute, The Royal Children's Hospital Foundation and The University of Melbourne. This Centre brings together expertise in research, clinical practice, and education and incorporates anyone who initiates or carries out research under one or more of these institutional affiliations.

Murdoch Children's Research Institute (MCRI)
An Australian paediatric medical research institute located in Melbourne, Victoria, affiliated with the Royal Children's Hospital and the University of Melbourne. The institute has six research themes: cellular biology, clinical sciences, genetics, infection and immunity, population health, and data science.

Participant
A participant is a person that is the subject of the research.

Protocol
A document that describes the objective(s), design, methodology, statistical considerations, and organization of a trial.

Reference Safety Information
The information contained in either an Investigator's Brochure (IB) or an approved Australian Product Information (or another country's equivalent). This information is used to determine what adverse reactions are considered expected and the frequency and nature of those adverse reactions.

Sponsor
An individual, organisation or group taking on responsibility for securing the arrangements to initiate, manage and finance a study. For investigator-initiated trials, MCRI or RCH will act as the Sponsor but delegate many sponsor responsibilities to the Coordinating Principal Investigator. In this case the CPI has the role of both Sponsor and Investigator and hence the MCTC has adopted the term Sponsor-Investigator to reflect the dual role of the CPI in investigator-initiated trials.

Standard Operating Procedure (SOP)

Detailed, written instructions to achieve uniformity of the performance of a specific function.

Clinical Trial Coordinator

A research worker who works at a clinical research site under the immediate direction of a Principal Investigator, whose research activities are conducted under Good Clinical Practice guidelines. May also be called a research coordinator, study coordinator or (for clinical trials research) a clinical trial coordinator.

7. REFERENCES

Australian Commission on Safety and Quality in Health Care. The National Clinical Trials Governance Framework and user guide for health service organisations conducting clinical trials. Sydney: ACSQHC; 2022 available at https://www.safetyandquality.gov.au/sites/default/files/2022-05/final_design_-_national_clinical_trials_governance_framework_and_user_guide_-_30_may_2022.pdf

Integrated Addendum to ICH E6 (R1): Guideline for Good Clinical Practice ICH E6 (2) 2016 – Annotated with TGA comments available at https://www.tga.gov.au/publication/note-guidance-good-clinical-practice

National Statement on Ethical conduct in human research (2007, updated 2018) , available from https://www.nhmrc.gov.au/about-us/publications/national-statement-ethical-conduct-human-research-2007-updated-2018

The National Standard Operating Procedures for Clinical Trials, including Teletrials, in Australia. SOP 11 Management of Investigational Product. Available from: https://www.health.gov.au/resources/publications/national-standard-operating-procedures-for-clinical-trials?language=en#:~:text=National%20Standard%20Operating%20Procedures%20for%20Clinical%20Trials%20This,have%20been%20agreed%20by%20all%20states%20and%20territories.

Therapeutic Goods Act 1989

8. COLLABORATORS

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9. RELATED DOCUMENTS

RCH SOP Destruction of Clinical Trial Materials

RCH SOP Dispensing of Clinical Trial Materials

RCH SOP Receipt of Clinical Trial Materials Non GMO or Ultra Cold Storage

RCH SOP Storage of Clinical Trial Drugs

RCH Medication Management Procedure

https://www.rch.org.au/policy/policies/Medication_Management/

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