CLINICAL RESEARCH – INVESTIGATIONAL MEDICINAL PRODUCT (IMP)

PROCEDURE ©

KEY POINTS

- This document has been created to consolidate all previous individual Investigational Medicinal Product (IMP) documents. It contains under separate sections all aspects relating to IMP procedures.
- The purpose of this procedure is to ensure that IMP for clinical research is prepared and dispensed in accordance with NSW Health, Sydney Children's Hospitals Network (SCHN), National Clinical Trials Governance Framework (NCTGF), International Council for on Harmonisation (ICH) Good Clinical Practice (GCP), The Poisons Standard, regulatory and protocol requirements and best practice recommendations.
- The procedure must be followed by all personnel involved in the preparation and dispensing of IMP used in clinical research.
- This document reflects what is currently regarded as safe practice. However, as in any clinical situation, there may be factors which cannot be covered by a single set of guidelines. This document does not replace the need for the application of clinical judgement to each individual presentation.

CHANGE SUMMARY

- Combined several documents into this single Procedure, including local work procedures.
- **25/2/25** – minor review to update links to NSW Health Policies.

READ ACKNOWLEDGEMENT

- Personnel performing IMP preparation, dispensing, handling, destruction, accountability tasks, receipt, processing and storage for clinical research should read and acknowledge (sign-off) having read and understood this document.
- Clinical research personnel involved in the creation, approval, completion and authorisation of prescriptions for IMP used in clinical research should read and acknowledge (sign-off) having read and understood this document.

TABLE OF CONTENTS

1 IMP Accountability

1.1 Purpose/Scope

The purpose of this procedure is to ensure consistency in the performance of accountability tasks for IMP for clinical research, in compliance with NSW Health, SCHN, NCTGF, ICH-GCP, regulatory and protocol requirements and best practice recommendations.

Adherence to this procedure will ensure that:

- Detailed records of all occasions of the receipt, dispensing and return of IMP for clinical research are maintained.
- IMP for clinical research is managed in accordance with the protocol-specific instructions of the Sponsor (or Delegate); and
- IMP for clinical research is only used in accordance with, and for the purposes of, the approved clinical research for which it has been provided.

The procedure must be followed by all personnel involved in performing accountability tasks for IMP used in clinical research.

1.2 Background

In accordance with ICH-GCP Section 4.6.1 and 4.6.2, responsibility for IMP at the Site is retained by the Investigator/Institution.

The Investigator (or Delegate) is responsible for ensuring that detailed records of the receipt, dispensing and return of IMP for clinical research are maintained, and that IMP is only used in accordance with the approved protocol.

The records will serve as evidence that clinical research participants were dispensed the appropriate IMP, at the appropriate dose(s) and intervals, as defined by the protocol.

1.3 Procedure

- The Senior Clinical Trials Pharmacist (Lead) (or Delegate) is responsible for maintaining accountability records detailing the receipt, dispensing and return of IMP for clinical research, as per the protocol-specific instructions of the Sponsor (or Delegate). The Lead Pharmacist will be listed on the primary clinical trial and will keep an internal log of relevant pharmacists and pharmacy technicians associated with the trial within the Pharmacy folder.
- All accountability records will be maintained in accordance with any SCHN Clinical Research Policies and Procedures found on the Intranet.
- Accountability records will include the specific details of the IMP (name, strength, form), date(s), quantities, batch/lot number(s), expiry/test-retest date(s), and/or kit number(s) (as applicable); The logs utilised will be provided by Sponsor. If unavailable, SCHN templates are available for use (Appendix 1a & Appendix 1b).

- A blank copy of the IMP Accountability Logs (or equivalent), will be filed in the Investigator Site File (ISF) at initiation of the clinical research to allow additional pages to be used for contemporaneous record keeping, as required.
- Any discrepancies identified though the performance of accountability tasks must be promptly reported according to the protocol-specific instructions of the Sponsor (or Delegate);
- All discrepancies must be investigated until their resolution, and the outcome(s) and/or resolutions, agreed with the Sponsor (or Delegate), clearly documented and filed in the ISF.
- Accountability tasks will continue until the Sponsor (or Delegate) has reviewed and authorised the final reconciliation of IMP for clinical research at the time of the close-out visit or equivalent.
- The original accountability records, and any corresponding documentation, must be retained in the ISF and a copy returned to the Sponsor (or Delegate), where required.
- Please see the SCH Pharmacy - Delegation, Training and Document Storage LWP (Appendix 9) for relevant site-specific procedures

2 IMP Destruction

2.1 Purpose/Scope

The purpose of this procedure is to ensure that unused or unfit IMP, authorised for disposal by the Sponsor (or Delegate), is disposed of in compliance with NSW Health, SCHN, NCTGF, ICH-GCP, regulatory and protocol requirements and best practice recommendations.

This procedure must be followed by all personnel involved in the disposal of IMP for clinical research.

2.2 Background

In accordance with ICH-GCP, the Sponsor is responsible for maintaining a system for retrieving IMP and documenting the retrieval (e.g. for deficient product recall, reclaim after trial completion, expired product reclaim) (Section 5.1.14.4c).

The Sponsor may elect for unused or unfit IMP for clinical research to be either returned to the Sponsor (or Delegate) for destruction or sent for secure destruction by the Investigator or Delegate, as per the protocol-specific arrangements made prior to initiation of the clinical research.

2.3 Procedure

- The Senior Clinical Trials Pharmacist (or Delegate) is responsible for ensuring that written authorisation is provided by the Sponsor (or Delegate) for the disposal of IMP for clinical research by the Site.
- Tasks related to the disposal of IMP for clinical research by the Site must only be performed after the IMP has been fully accounted for and reconciled as per Section 1 – IMP Accountability.
- A full audit trail for all actions taken must be maintained in accordance with any SCHN Clinical Research Policies and Procedures found on the Intranet;
- On receipt of written authorisation, the Senior Clinical Trials Pharmacist (or Delegate) must update the destruction-related documentation provided by the Sponsor or Delegate.
- The IMP Destruction Certificate (Appendix 2) is recommended for adaptation in the absence of protocol-specific documentation being provided by the Sponsor or Delegate.
- Documentation must identify the:
  - IMP description (name, strength, form)
  - Batch/lot or kit number(s)
  - Expiry/re-test date(s)
  - Quantity

- Date of action
- Name and initials of the Senior Clinical Trials Pharmacist or Delegate(s) performing the action; and
- Name and initials of a witness

- The Senior Clinical Trials Pharmacist (or Delegate) must ensure that all labels or markings containing participant or prescriber identifying information, including dispensing labels, are removed in full as appropriate; For IMPs destroyed on site they are disposed of directly into incinerated clinical waste bin as per the normal pharmacy practice, de-identifying may not be necessary.
- Unused IMPs returned from a patients' home, must be sealed in clear plastic bags, by the principal investigator (PI) (or Delegate) or clinical trials pharmacist, within their labelled secondary containers before returning to the pharmacy service for disposal. For accountability, unused IMPs, for example tablets, must be returned to the pharmacy services for disposal. Pharmacy will generally only do a medication return accountability, and not an accountability based on the patient dosing diary.
- Sharps, used syringes or other IMP that may pose a hazard to staff unless enclosed in a sharps container will not be accepted for returns. Used vials or containers that are destroyed immediately after preparation will be documented on the accountability log; a separate Certificate of Destruction will not be completed.
- The disposal of IMP for clinical research by the Site will comply with the requirements of the SCHN Policy 2015-9070 – Waste Management and NSW Health PD2020_049 Clinical and Related Waste Management for Health Services;
- Additional requirements as per the NSW Health PD2022_032 Medication Handling must be complied with for the disposal of IMP for clinical research classified as S8 medications; Disposal must also be done in accordance with NSW Health PD2023_021 Preparation of pharmaceutical and advanced therapeutic products.
- The details of the licensed external waste disposal service provider contracted by SCHN for the management of pharmaceutical waste can be provided to the Sponsor (or Delegate), on request.
- The original of the IMP Destruction Certificate, as well as any corresponding documentation, must be filed in the ISF, with a copy provided to the Sponsor (or Delegate), if required.

3 IMP Preparation and Dispensing

3.1 Purpose/Scope

The purpose of this procedure is to ensure that IMP for clinical research is prepared and dispensed in accordance with NSW Health, SCHN, NCTGF, ICH-GCP, regulatory and protocol requirements and best practice recommendations.

Adherence to this procedure will ensure that IMP is accurately and safely prepared, dispensed (including packaged and labelled) and released to clinical research participants in a timely manner, as per the protocol.

The procedure must be followed by all personnel involved in the dispensing (including packaging and labelling) of IMP used in clinical research, as applicable.

3.2 Background

In accordance with ICH-GCP Section 4.6.1 and 4.6.2, responsibility for IMP at the Site is retained by the Investigator/Institution.

Preparation and dispensing practices for IMP for clinical research requires additional safeguards from standard clinical care practices due to the:

- Range and complexity of dosing regimens.
- Absence of full knowledge of adverse events /or anticipated outcomes from use in a given population; and
- The need to maintain the integrity of randomisation and/or blinding practices (as applicable).

3.3 Procedure

Preparation

- Prior to dispensing, the Senior Clinical Trials Pharmacist (or Delegate) will ensure that a record of the IMP for clinical research has been generated within the SCHN dispensing system, iPharmacy and in the electronic Medical Record (eMR) if it will be administered as an inpatient.
- The Investigator (or Delegate) must notify the Senior Clinical Trials Pharmacist (or Delegate) in the event that a potential clinical research participant is identified for screening and the outcome from screening, as soon as possible once known.
- The Investigator (or Delegate) will prepare and provide a prescription (electronic or paper) for dispensing IMP in accordance with Section 4 IMP Prescriptions.
- If IMP is to be administered by SCHN personnel, the Investigator (or Delegate) will prepare a Medication Administration Record (MAR).
- The provision of the MAR and prescription is to be completed in advance of the proposed protocol-specific visit, where feasible. In such cases, the Investigator (or Delegate) must inform the Senior Clinical Trials Pharmacist of any cancellations and/or changes to the proposed visit date.

Review

- The Senior Clinical Trials Pharmacist (or Delegate) is responsible for thorough review of the prescription (electronic or paper) to ensure the entries are complete, legible, consistent and appropriately authorised.
- Special attention will be given to ensure consistency with the requirements of the current protocol and/or existing records relating to the clinical research participant, including Interactive Voice/Web Response System (IXRS (if applicable);
- Incomplete, unclear, inconsistent or incorrect prescriptions (electronic or paper) will be promptly returned to the Investigator (or Delegate) for correction.
- Any anomalies identified will be promptly communicated, discussed and clarified with the Investigator (or Delegate), prior to the Senior Clinical Trials Pharmacist proceeding to dispensing.

Dispensing

- The Senior Clinical Trials Pharmacist (or Delegate) will perform dispensing in accordance with the protocol-specific instructions provided by the Sponsor (or Delegate) and all NSW Health, SCHN and regulatory requirements.
- The tasks performed will include, but are not limited to:
    - Collection of the IMP for clinical research required from its storage location.
    - Confirmation that the IMP is viable through visual inspection and cross-checking of the expiry or test-retest date
    - Preparation of the IMP under appropriate conditions as per protocol requirements (e.g. sterile products must be produced in the aseptic suite);
    - Packaging and labelling the IMP according to all applicable regulations and/or protocol requirements, ensuring the integrity of the blind (if applicable);
    - Entering the details of the dispensing into the dispensing system, iPharmacy;
    - Requesting that the dispensed IMP is checked against the prescription and all applicable regulations and/or protocol requirements by a second Pharmacist; and
    - Updating all accountability records and/or systems, as per Section 1 IMP Accountability and any SCHN Clinical Research Policies and Procedures found on the Intranet.
- Standard of care medications supplied by the site will be dispensed as per standard pharmacy processes and will not have accountability performed.
- Once the IMP is ready for release, the Senior Clinical Trials Pharmacist (or Delegate) will notify the Investigator (or Delegate);
- The Investigator (or Delegate) will ensure that counselling and/or education regarding the safe and appropriate use of the IMP, in accordance with the protocol, is provided.

- Supplementary counselling and/or education may be delivered verbally by the Senior Clinical Trials Pharmacist (or Delegate), if responsible for the release of IMP to the clinical research participant.
- Any supplementary counselling and/or education will not replace nor negate the provision of any protocol-specific participant-facing information that has been approved for use by the responsible HREC and RGO.
- The Investigator will check, at intervals appropriate to the protocol and/or as outlined by the Sponsor and/or Delegate, that clinical research participants are following the instructions correctly and taking any action(s) required to remediate issues.
- Please see the SCH Pharmacy - Clinical Trials Production LWP (Appendix 8) for relevant site-specific procedures.

4 IMP Prescriptions

4.1 Purpose/Scope

The purpose of this procedure is to ensure that prescriptions for IMP used in clinical research are created, approved, completed and authorised, in compliance with NSW Health, SCHN, NCTGF, ICH-GCP, regulatory and protocol requirements and best practice recommendations.

The procedure must be followed by all personnel involved in the creation, approval, completion and authorisation of prescriptions for IMP used in clinical research.

4.2 Procedure

Creation

- All prescriptions used in clinical research must meet the requirements of the NSW Health PD2022_032 Medication Handling;
- The creation of protocol-specific prescription template(s) may be required in circumstances where:
  - The Sponsor has not provided a prescription template(s) for use; or
  - The Sponsor (or Delegate) has provided prescription template(s) that do not comply with local regulatory or other operational requirements; or
  - The standard Hospital prescription does not clearly delineate the prescription as being for clinical research purposes and/or allow all necessary aspects of the protocol to be adequately captured.
- If the creation of protocol-specific prescription template(s) is required, the Senior Clinical Trials Pharmacist (or Delegate) will prepare a draft, in consultation with the Investigator and Sponsor (or Delegate);

- Adaptation of the IMP Prescription template (Appendix 3) is recommended to ensure consistency in capturing all pertinent information for clinical research prescribing, including, but not limited to:
  - Protocol details (number, full title)
  - Site number
  - Principal Investigator's name
  - Participant ID number/code
  - Participant height/weight and BSA (if applicable)
  - Arm/group allocation (if applicable/appropriate to disclose)
  - Protocol visits and/or time point (e.g. Visit 1 – Month 1 - Day 28)
  - IXRS pack or kit reference code(s) (if applicable)
  - Clinical Research Coordinator/Nurse name and contact details

Approval

- The protocol-specific prescription template(s) created must be reviewed and approved by the Investigator as well as the Sponsor or Delegate, prior to finalisation.
- A full audit trail, including appropriate version control, must be maintained in accordance with any SCHN Clinical Research Policies and Procedures found on the Intranet;
- The protocol-specific prescription template(s) approved, as well as any corresponding documentation such as approvals, must be filed in the ISF.
- In the event of amendments to the protocol and/or systems that materially affect the validity of protocol-specific prescription template(s), a modified version of the protocol-specific prescription template(s) must be created, according to the procedure outlined above.

Completion & Authorisation

- All prescriptions used in clinical research must be completed and authorised (including signed and dated) by the Investigator (or Delegate);
- The Investigator (or Delegate) must ensure that prescriptions used in clinical research are clear, legible and not open to misinterpretation.

5 IMP Quarantine

5.1 Purpose/Scope

The purpose of this procedure is to ensure that unused or unfit IMP identified by clinical research personnel, the Sponsor (or Delegate) or the manufacturer as requiring quarantine is managed in compliance with NSW Health, SCHN, NCTGF, ICH-GCP, regulatory and protocol requirements and best practice recommendations.

The procedure must be followed by all personnel involved in the handling of IMP for clinical research.

5.2 Background

IMP for clinical research may be deemed to be unfit for a variety of reasons, including, but not limited to:

- Deviations to required storage conditions including temperature excursions;
- Expiry;
- Recall; and/or
- Breakage, spoilage or any other damage.

Supplies of unused or unfit IMP for clinical research may require quarantine to protect against unintended use prior to their return to the Sponsor (or Delegate) or secure destruction by the Investigator (or Delegate).

All records related to the quarantine of IMP will be maintained in accordance with any SCHN Clinical Research Policies and Procedures found on the Intranet.

5.3 Procedure

Placing IMP into Quarantine

- The Senior Clinical Trials Pharmacist (or Delegate) is responsible for recording the details of any unused or unfit IMP identified on the IMP Quarantine Notice (Appendix 4).
- The IMP Quarantine Notice will reference the IMP (name, strength, form), date placed into quarantine, quantity, batch/lot number(s), kits number(s) (if applicable); and the reason for quarantine;
- Unused or unfit IMP and//or Sponsor provided therapies/supplies will be stored under the required storage conditions, in its original packaging, and an additional sealable container or bag, in dedicated quarantine storage areas within Pharmacy;
- The quarantine storage area(s) will be clearly marked and segregated from any storage areas used for any IMP suitable for use and/or any clinical research participant returns;
- The IMP Quarantine Notice (Appendix 4) will be placed with the unused or unfit IMP being placed into quarantine, in such a way that the details are clearly visible within the sealed container or bag;

- The Senior Clinical Trials Pharmacist (or Delegate) is responsible for promptly reporting any quarantine actions to the Sponsor (or Delegate), as per the protocol-specific instructions of the Sponsor (or Delegate);
- The IMP Quarantine Notice, as well as any other documentation or correspondence, is to be retained in the ISF and a copy returned to the Sponsor or Delegate(s), as required.

Releasing IMP from Quarantine

- The Senior Clinical Trials Pharmacist (or Delegate) is responsible for ensuring that written authorisation is provided by the Sponsor (or Delegate) for the release of IMP from quarantine;
- On receipt of written authorisation, the Senior Clinical Trials Pharmacist (or Delegate) will update the IMP Quarantine Notice noting the resolution and date of removal from quarantine;
- The IMP Quarantine Notice, as well as any other documentation or correspondence from the Sponsor (or Delegate) approving or disapproving use of IMP, is to be retained in the ISF and a copy returned to the Sponsor (or Delegate(s)), as required.

6 IMP Receipt and Storage

6.1 Purpose/Scope

The purpose of this procedure is to ensure that deliveries of IMP for clinical research are received, processed and stored in compliance with NSW Health, SCHN, NCTGF, ICH-GCP, regulatory and protocol requirements and best practice recommendations.

It is acknowledged that there may be some variations in the procedure for the receipt and storage of IMP depending upon the protocol-specific requirements dictated by the Sponsor (or Delegate), and in accordance with risk-assessments made by Pharmacy, as applicable.

Adherence to this procedure will ensure that:

- Pharmacy personnel receiving deliveries promptly identify that the delivery contains IMP for clinical research purposes; and
- Deliveries of IMP are appropriately processed and stored by the Senior Clinical Trials Pharmacist (or Delegate).

The procedure must be followed by all personnel involved in the receipt processing and storage of IMP for clinical research.

6.2 Background

In accordance with ICH-GCP Section 4.6.1 and 4.6.2, responsibility for IMP at the Site is retained by the Investigator/Institution.

IMP may be provided to the Institution or Investigator by or on behalf of the Sponsor (or Delegate) for the purposes of conducting approved clinical research. The items supplies will be:

- Stored under the conditions specified by the Sponsor (or Delegate), in accordance with all applicable NSW Health, SCHN, regulatory and Protocol requirements;
- Only to be used in accordance with, and for the purposes of, the approved clinical research for which it has been provided; and
- Handled in compliance with all requirements of NSW Health PD2022_032 Medication Handling.

IMP for clinical research must not be shipped to the Site until all required regulatory approvals are in place.

The Sponsor (or Delegate) is responsible for notifying the Investigator (or Delegate) of the intention to ship a delivery of IMP, prior to its release, so the availability of local storage space can be assessed by the Senior Clinical Trials Pharmacist.

Receipt and storage must also be done in accordance with NSW Health PD2023_021 Preparation of pharmaceutical and advanced therapeutic products.

6.3 Procedure

Receipt

IMP for clinical research must be delivered via a courier or equivalent service, with tracking details, to the Pharmacy shipping address nominated by the Senior Clinical Trials Pharmacist (or Delegate) within standard operating hours, unless prior arrangements have been made.

On receipt, the receiver will acknowledge receipt of the delivery by SCHN through completion and/or signing of any shipping documentation required.

Deliveries of IMP for clinical research received by personnel other than the responsible Senior Clinical Trials Pharmacist (or Delegate) must be immediately transferred to the nominated shipping address and the responsible Senior Clinical Trials Pharmacist alerted. The package(s) must not be opened prior to transfer.

Processing

On receipt of the delivery, the IMP for clinical research will be thoroughly inspected by the Senior Clinical Trials Pharmacist (or Delegate) to confirm the:

- Use of the correct shipping address details and contact person(s);
- Protocol details to which the delivery relates;
- Integrity of the inner and outer packaging;
- Integrity of the required storage conditions during transit, with reference to the Investigators Brochure (IB) or equivalent, and any temperature monitoring devices (E.g. Temp-Tale) where provided;
- Integrity of the contents as free of breakages, spoilage or any other damage;
- Validity with reference to the delivery documentation including batch/lot and/or kit number(s), expiry/test-retest date(s) and the quantity supplied, as applicable; and

- Accuracy of any enclosed documentation (e.g. certificates of analysis/release and/or statements of compliance (as applicable).
- The processing of IMP that requires refrigerated, frozen or other special storage conditions, as specified on shipment documentation and/or IB, will be prioritised.
- The Senior Clinical Trials Pharmacist (or Delegate) is responsible for acknowledging receipt of the shipment, and reporting any issues identified, according to the protocol-specific instructions provided by the Sponsor (or Delegate).
- The IMP Acknowledgement of Receipt Log (Appendix 5) is recommended for adaptation in the absence of protocol-specific instructions and/or systems being provided by the Sponsor (or Delegate).
- Whilst awaiting the advice of the Sponsor (or Delegate) in the event of any issues being identified at inspection, the IMP must be quarantined under appropriate storage conditions, in accordance with the Section 5 – IMP Quarantine.
- The Senior Clinical Trials Pharmacist (or Delegate) is responsible for taking action to rectify any issue(s) identified, in accordance with the instructions of the Sponsor (or Delegate), as applicable.
- The original of the IMP Acknowledgement of Receipt Log, as well as any corresponding documentation, must be filed in the ISF.

Storage

- Full IMP accountability records for any IMP received must be maintained as Section 1 IMP Accountability.
- Dedicated storage areas for IMP with temperature monitoring, maintained as per Section 7 IMP Temperature Monitoring. Storage areas for IMP will be labelled with the protocol reference number or equivalent. Separate, segregated storage areas will be maintained for quarantined IMP until approved for use or destruction by the Sponsor (or Delegate).
- IMP will be stored in compliance with NSW Health PD2022_032 Medication Handling and under the conditions specified by the Sponsor (or Delegate).
- All IMP must be stored within the correct temperature range and environmental conditions as specified in the study protocol, IB, Pharmacy Manual or other approved product information and in compliance with NSW Health PD2022_032 Medication Handling.
- Storage conditions must be continuously monitored (24 hours a day, 7 days a week).
- IMP must be stored in secure facilities with restricted access to authorised staff only. SCHN facilities are connected to the hospital electricity backup generator. In the event of storage equipment power failure and/or breakdown, IMP will be transferred to alternative storage facilities within the pharmacy or hospital.
- IMP requiring refrigerated storage (2ºC to 8ºC) will be unpacked (with any gel packs and/or blue ice removed) prior to storage in the refrigerator.
- IMP requiring frozen storage that is delivered in packages containing dry ice must be unpacked with reference to the precautions in any SCHN Clinical Research Policies and Procedures found on the Intranet and promptly stored in the allocated freezer.

Re-labelling

If required by the Sponsor, short-dated IMP maybe re-labelled if appropriate testing and documentation has been provided by the Sponsor, charges for stock re-labelling are as per the Pharmacy budget.

Exemptions

In some instances, the Sponsor, Investigator or their Delegates may recommend the storage of IMP for clinical research in an alternate secure location (e.g. outside of Pharmacy). This may be required if the IMP needs to be accessed in an emergency or outside of standard operating hours. In these cases, the above provisions for appropriate storage still apply.

The Senior Clinical Trials Pharmacist (or Delegate) will retain responsibility for completing the IMP Storage Location Assessment Form (Appendix 6) if relevant to assess the suitability of the proposed storage location.

The Senior Clinical Trials Pharmacist will be responsible for communicating the outcome of the assessment to the Investigator and Sponsor (or Delegate), prior to the IMP being stored.

A copy of the IMP Storage Location Assessment Form as well as any corresponding documentation must be filed in the ISF.

Transit and Transfer

Transfer of IMP between sites may be required if the receiving site is responsible for distributing IMP once all site approvals have been obtained. The IMP risk assessment must include risks associated with IMP transfer and document all appropriate mitigations. Pharmacy oversees this process, and the transfer process must be fully documented as per Sponsor documentation.

Prior to moving any IMP, personnel transferring IMP must be delegated to the specific trial and familiar with the correct storage conditions for the IMP being transferred.

An IMP onsite Transfer document must accompany any IMP being transferred internally, this is provided by the Sponsor or the IMP Transfer Form (Appendix 12) can be utilised if not available from Sponsor. Each individual trial will have an individual form completed.

Consideration should be made early on in protocol development as to the need for IMP to be posted or couriered to patients. Any process for IMP supply must be fully risk assessed and documented for each study.

When transferring IMP, it should be packaged appropriately according to storage conditions and temperature requirements – this may include the need for temperature monitors and use of Esky’s

7 IMP Temperature Monitoring

7.1 Purpose/Scope

The purpose of this procedure is to ensure that the quality and integrity of IMP is maintained through consistent temperature monitoring practices of IMP storage locations, in compliance with NSW Health, SCHN, NCTGF, ICH-GCP, regulatory and protocol requirements and best practice recommendations.

Adherence to this procedure will ensure that:

- A valid, continuous record of temperature is available for all locations used for the storage of IMP for clinical research; and
- Temperature deviations are promptly identified, escalated and acted upon, as appropriate, in consultation with the Sponsor or Delegate.

The procedure must be followed by all personnel involved in the handling of IMP for clinical research.

7.2 Background

In accordance with ICH-GCP Section 4.6.1 and 4.6.2, responsibility for IMP at the Site is retained by the Investigator/Institution.

IMP for clinical research must be stored under suitable storage conditions at all times, as per Section 6 IMP Receipt and Storage. Continuous temperature monitoring of the locations used for IMP storage is vital to assuring the integrity and quality of IMP.

The Investigator (or Delegate) is responsible for ensuring that any deviations from this procedure, due to the approved storage of IMP in locations outside of Pharmacy, are appropriate documented and filed in the ISF.

7.3 Procedure

Systems

- Continuous temperature monitoring of refrigerators and freezers used for the storage of IMP for clinical research is provided via a commercial monitoring system (e.g. Matos Monitoring or Schneider EMS) ;
- Continuous temperature monitoring of ambient storage areas used for the storage of IMP for clinical research is provided via an approved management system (e.g. Building Management System (BMS));Preventative maintenance and/or calibration will be performed on all items of temperature monitoring equipment annually, or more frequently if required by the Sponsor, to ensure all equipment remains in good working order.
- Fridges, freezers, and associated monitoring systems are maintained in accordance with any SCHN Clinical Research Policies and Procedures found on the Intranet ;
- The acceptable temperatures for IMP storage locations are as follows: Ambient: 15ºC to 25ºC, Refrigerated: 2ºC to 8ºC, Frozen: -15°C and -25°C or as otherwise defined;

- Notifications are issued by the commercial monitoring system via SMS in the event of temperature breaches, power failures and/or network failure for action by designated personnel;
- The use of separate temperature loggers (e.g. temp-tales) for protocol-specific temperature monitoring of IMP in shared Pharmacy storage locations is not permitted.

Monitoring

- The Senior Clinical Trials Pharmacist (or Delegate) will access and review temperature monitoring records for designated IMP storage locations on a daily basis (with the exception of weekends and public holidays);
- The minimum and maximum temperature for each IMP storage location will be recorded on the IMP Temperature Monitoring Log (Appendix 7) or electronic monitoring system and a cumulative graph(s) of temperature generated at the end of each month if required;
- Where continuous temperature monitoring occurs, a regular electronic download of the graphs will be filed in a central secured pharmacy folder;
- The IMP Temperature Monitoring Log via electronic temperature logs and cumulative graph(s) will be stored in an electronic master file accessible to the Pharmacy personnel responsible for the designated IMP storage location(s);
- Complete electronic temperature records will be made available via email or secure OneDrive SharePoint link for inspection by Sponsors or Delegates on request to the Senior Clinical Trials Pharmacist or Delegate, or at routine monitoring visits;
- Please see the SCH IMP Storage and Temperature Monitoring LWP (Appendix 11) for relevant site-specific procedures

Excursions

- In the event of a true temperature excursion, the Senior Clinical Trials Pharmacist is responsible for:
  - Determining the cause of the excursion and instigating corrective action, if feasible;
  - Promptly reporting the excursion according to the protocol-specific instructions of the Sponsor or Delegate, and providing a copy of the IMP Temperature Monitoring Log and/or cumulative graph; Reporting will usually occur within ONE business day unless otherwise stated in the Pharmacy Manual
  - Placing the IMP into quarantine in accordance with Section 5 IMP Quarantine until such time that further instruction is received from the Sponsor or Delegate; and
  - If the IMP is deemed to be unfit for use, advising the Investigator (or Delegate) of the temperature excursion so that alternative arrangements can be made for any imminent visits requiring dispensing (if applicable);
- False temperature excursions, displaying as sharp peaks on the cumulative graph(s), may occur due to opening or closing the fridge and/or freezer during re-stocking. Such excursions will only be reported if substantiated by the receipt of an alert from the commercial monitoring system;

- If no alert is received, the Senior Clinical Trials Pharmacist will initial and date the corresponding graph(s) noting the occurrence as a 'False Temperature Excursion';
- The original of the electronic IMP Temperature Monitoring Log data, graphs and any corresponding documentation, must be filed in the ISF, and a copy provided to the Sponsor or Delegate, as required.
- Please see the SCH IMP Storage and Temperature Monitoring LWP (Appendix 11) for relevant site-specific procedures

Faults

- In the event of a suspected fault to the temperature monitoring system(s), the Senior Clinical Trials Pharmacist is responsible for:
  - Notifying designated personnel to request that checks of the power, air conditioning, and/or associated systems are undertaken (as appropriate); and
  - Placing the IMP into quarantine in accordance with Section 5 IMP Quarantine until such time that further instruction is received.
- Please see the SCH Internal Monitoring Activities LWP (Appendix 10) for additional relevant site-specific procedures.

Appendices

Appendix 1a – IMP Accountability Log (Master)

- https://webapps.schn.health.nsw.gov.au/epolicy/policy/6681/attachments/13224/download

Appendix 1b – IMP Accountability Log (Participant Specific)

- https://webapps.schn.health.nsw.gov.au/epolicy/policy/6681/attachments/13226/download

Appendix 2 – IMP Destruction Certificate

- https://webapps.schn.health.nsw.gov.au/epolicy/policy/6681/attachments/13228/download

Appendix 3 – IMP Prescription

- https://webapps.schn.health.nsw.gov.au/epolicy/policy/6681/attachments/13230/download

Appendix 4 – IMP Quarantine Notice

- https://webapps.schn.health.nsw.gov.au/epolicy/policy/6681/attachments/13232/download

Appendix 5 – IMP Acknowledgement of Receipt Log

- https://webapps.schn.health.nsw.gov.au/epolicy/policy/6681/attachments/13234/download

Appendix 6 – IMP Storage Location Assessment Form

- https://webapps.schn.health.nsw.gov.au/epolicy/policy/6681/attachments/13236/download

Appendix 7 – IMP Temperature Monitoring Log

- https://webapps.schn.health.nsw.gov.au/epolicy/policy/6681/attachments/13238/download

Appendix 8 – SCH Pharmacy - Clinical Trials Production Local Work Procedure

- https://webapps.schn.health.nsw.gov.au/epolicy/policy/6681/attachments/13240/download

Appendix 9 – SCH Pharmacy - Delegation, Training and Document Storage Local Work Procedure

- https://webapps.schn.health.nsw.gov.au/epolicy/policy/6681/attachments/13242/download

Appendix 10 – SCH Pharmacy - Internal Monitoring Activities Local Work Procedure

- https://webapps.schn.health.nsw.gov.au/epolicy/policy/6681/attachments/13244/download

Appendix 11 – SCH Pharmacy - IMP Storage and Temperature Monitoring Local Work Procedure

- https://webapps.schn.health.nsw.gov.au/epolicy/policy/6681/attachments/13246/download

Appendix 12 – IMP Transfer Form

- https://webapps.schn.health.nsw.gov.au/epolicy/policy/6681/attachments/13248/download

Abbreviations

BMS	Building Management System	MAR	Medication Administration Record
BSA	Body Surface Area	NCTGF	National Clinical Trials Governance Framework
C	Celsius	NSW	New South Wales
GCP	Good Clinical Practice	PSF	Pharmacy Site File
HREC	Human Research Ethics Committee	PD	Policy Directive
IB	Investigators Brochure	RGO	Research Governance Office
ICH	International Conference on Harmonisation	S8	Schedule 8
ID	Identification	SCH	Sydney Children's Hospital - Randwick
ISF	Investigator Site File	SCHN	Sydney Children's Hospitals Network
IMP	Investigational Medicinal Product	SMS	Short Message Service
IXRS	Interactive Voice/Web Response System	TGA	Therapeutic Goods Administration

Related Documents

- ACSQHC (2022) - **National Clinical Trials Governance Framework and user guide for health service organisations conducting clinical trials**, February 2022: https://www.safetyandquality.gov.au/publications-and-resources/resource-library/national-clinical-trials-governance-framework-and-user-guide
- NSW Health PD2023_021 **Preparation of pharmaceutical and advanced therapeutic products:** https://www1.health.nsw.gov.au/pds/Pages/doc.aspx?dn=PD2023_021
- NSW Health PD2022_032 **Medication Handling:** https://www1.health.nsw.gov.au/pds/Pages/doc.aspx?dn=PD2022_032
- NSW Health PD2020_049 - **Clinical and Related Waste Management for Health Services**: https://www1.health.nsw.gov.au/pds/Pages/doc.aspx?dn=PD2020_049
- **SCHN Clinical Research Policies and Procedures**: https://webapps.schn.health.nsw.gov.au/epolicy/search?query=clinical+research
- **Pharmacy Department - Preparing Advanced Therapeutic Medicinal Products for Administration – CHW**: https://webapps.schn.health.nsw.gov.au/epolicy/policy/5827
- **SCHN Waste Management** Policy: https://webapps.schn.health.nsw.gov.au/epolicy/policy/6038
- TGA - PE009-13 - **The PIC/S guide to GMP for medicinal products - TGA interpretation and expectations for demonstrating compliance** - Version 2.1, September 2020: https://www.tga.gov.au/sites/default/files/pe009-pics-guide-gmp-medicinal-products.pdf

- TGA - **Pharmaceutical Inspection Convention, Pharmaceutical Inspection Co-Operation Scheme – Guide to Good Manufacturing Practice for Medicinal Products** Annexes: https://www.tga.gov.au/sites/default/files/manuf-pics-gmp-medicines-annexes.pdf
- TGA - **Standard for the Uniform Scheduling of Medicines and Poisons:** https://www.legislation.gov.au/F2024L01228/asmade/textC
- TGA - **ICH Guideline for Good Clinical Practice**: https://www.tga.gov.au/resources/publication/publications/ich-guideline-good-clinical-practice