DO NOT USE THIS SOP IN PRINTED FORM WITHOUT FIRST CHECKING IT IS THE LATEST VERSION

Managing Investigational Product

SOP No.:	SOP_CTSU_015
Version No.:	2.0
Effective Date:	1 May 2023
Supersedes:	SOP_CTSU_015 Managing Investigational Product V1.0 Dated 1st July 2020
Review Date:	30 April 2026

	Written by	Approved by	Approved by
Name	Erfan Jaberiyanfar	Megan Ford	Les Bokey
Job Title	SWSLHD Clinical Trials Manager	Executive Director Clinical Trials, Ingham Institute & SWSLHD	Director of Research, Ingham Institute & SWSLHD
Date	April 2023	April 2023	April 2023
Signature	Signature on file	Signature on file	Signature on file

1.0 Introduction / Background

An Investigational Medicinal Product (IMP/IP) is any pharmaceutical form of an active ingredient or placebo being tested in a clinical trial. Conducting a clinical trial using an unapproved investigational medicinal product that has not been evaluated by the Therapeutics Goods Administration (TGA) for quality, safety and efficacy is required to be formally reviewed. The TGA mandates using the Clinical Trial Notification (CTN) or Clinical Trial Application (CTA) schemes.

The trial sponsor is responsible for the initiation, management and financing (or arranging the financing) of the trial and carries the medico-legal responsibility associated with its conduct. The Australian trial sponsor is also the entity that is responsible for submitting a CTN or CTA to the TGA. The trial sponsor takes the overall responsibility for trials conducted under the CTN and CTA schemes.

Management of the IMP/IP on site is the responsibility of the Principal Investigator who delegates responsibility to a Clinical Trial Pharmacist or as appropriate. The IMP/IP is managed from site initiation to close out by the delegated staff member in accordance with the approved protocol and ICH GCP. Local Policy and guidelines are also adhered to ensure storage and destruction of IMP/IP are managed appropriately.

Investigational Medicinal Products (IMP) that are unused, expired or returned by the patients and no longer required for the study must be reconciled and disposed of appropriately, they should be either returned to the Sponsor of the relevant clinical trial or destroyed on-site. Destruction or return must only be undertaken with approval from the Sponsor and must be fully documented.

Local Policy and guidelines are also adhered to ensuring receipt, storage and destruction of IMP/IP are managed appropriately.

2.0 Objective

To describe the process and requirements for the receipt, storage, dispensing, and return or destruction of Investigational Product (IMP/IP) at the clinical trial site.

3.0 Scope

This SOP applies to all staff involved in clinical trials at SWSLHD and the Ingham Institute.

4.0 Ownership and Responsibility

This SOP applies to those members of the study team involved in the process receipt, storage, dispensing, and return or destruction of Investigational Product (IP). These include the following:

- Principal Investigator (PI)
- Clinical Trial Coordinator (CTC)
- Clinical Trial Pharmacist
- Research Nurse
- Support Staff

5.0 Associate Documents

SOP_CTSU_02 Investigator Responsibilities

FM_19 Participant Investigational Product Accountability Log

FM_20 Batch Investigational Product Accountability Log

FM_21 Investigational Product Returns Form

FM_22 Investigational Product Destruction Form

6.0 Procedure

6.1 Prior to receipt of Investigational Product (IMP/IP)

The Principal Investigator (PI) must identify appropriately qualified staff member(s) and ensure that the management of the IMP/IP will be managed in accordance with the Clinical trial protocol and that an area with restricted access, appropriate temperature control for IMP/IP storage is available. Ideally, these discussions take place during feasibility where the Pharmacy staff or appropriate delegate, are provided with the clinical trial protocol and Investigational Brochure to review and provide comments. Discussion will also encompass budget requirements and review of the Clinical Trial Research Agreement (CTRA) or as appropriate.

Following this discussion, the Pharmacy Head of Department (HOD) at the site will indicate their support via the Site Specific Application (SSA) in REGIS. Once SSA approval and appropriate training is provided by the Sponsor/PI, a Delegation and Training log will be completed. The clinical trial pharmacist will commonly be assigned the responsibility for IP receipt, storage, dispensing, destruction and accountability.

6.2 Receipt of Investigational Product (IP)/ Study Drug

Upon receipt of the IMP/IP shipment at the site, the Pharmacist or delegated member will unpack the IP and check the IP inventory against the provided shipping form.

Checking the inventory is dependent on current site Pharmacy processes such as an approved interdepartmental dispensing program that incorporates the following:

- Allocation for checking and verifying unique kit numbers
- Documenting the number of IPs in the container (s) as appropriate
- Checking IP expiry date

Any discrepancies (e.g. tampering/ breakage of the IP kit, mismatch in the number of kits, temperature excursions etc.) identified must be documented and the CRA/Monitor contacted immediately to provide further advice.

Local interdepartmental processes for temperature monitoring for clinical trial drugs are as follows;

6.3 Site management of the IMP/IP requiring refrigeration

Refrigerated clinical trial stock is unpacked and placed in the clinical trials fridge by the clinical trials pharmacist or pharmacy stores person. The paperwork is marked with the date and time of unpacking and placed on the Clinical Trials desk. If a temperature monitoring device is provided with the transport then it is stopped and placed with the paperwork. If it is unable to be stopped it will be placed with the stock in the fridge.

A certified calibrated data logger in the clinical trials fridge is set to read temperatures every 30 minutes. Data will be downloaded on a monthly basis on the first Tuesday of every month. A soft copy of the data logger download is saved and a hard copy is also maintained and filed by the delegated pharmacist.

In addition, a thermometer with a visual display is set to record maximum, minimum and current temperature and is checked and reset on a weekly basis (every Tuesday).

The clinical trials fridge is connected to red power points (i.e. priority power supply) and has visual temperature displays and alarms. If the temperature falls below 2.5°C or rises above 7.5°C, then an audible alarm will sound in Pharmacy. In the event of an alarm, hospital security will receive an automated page. Engineering (BMCS) and senior pharmacy staff will receive an automated email alerting them of the incident. During working hours, the Pharmacy will be contacted to investigate and engineering must monitor and adjust the temperature if necessary. The pharmacist will continue to monitor and/or relocate stock if required. Out of hours, security will contact the Assistant Director of Nursing (ADON) who will contact the on-call pharmacist for instructions. Normally the ADON will enter the pharmacy and relocate the affected stock to appropriate storage. The clinical trials pharmacist will be notified of the incident during normal working hours.

In the event of a temperature excursion, all affected stock will be marked by a coloured dot sticker with the date of excursion and quarantined. Data from the logger will be downloaded and read by Pharmacy. The appropriate CRA/Monitor and the study coordinator will be contacted and trial-specific forms completed if required. If the stock can be released from quarantine a different coloured dot sticker marked with OK will be placed overlapping the quarantined date sticker.

6.4 Site management of the IMP/IP stored at room temperature

A certified calibrated data logger is set to read temperatures every 30 minutes.

Data will be downloaded on a monthly basis on the first Tuesday of every month. A soft copy of the data logger download is saved and a hard copy is also maintained and filed by the delegated pharmacist.

In addition, a thermometer with a visual display is set to record maximum, minimum and current temperature and is recorded and reset on a weekly basis.

Room temperature is controlled by air-conditioning and kept under 25°C. This is monitored and maintained by the hospital engineering department via a back to base monitoring.

The hospital has backup generators that will maintain power in the event of power failure. All the room temperature drugs are held at approximately 22°C by the air-conditioning system. At 21°C the system will begin heating. At 23°C the system will begin cooling. If the temperature goes above 24°C or below 20°C then engineering is alerted by alarm and adjusts the air-conditioning.

If an alarm sounds during working hours, a pharmacist will investigate and contact engineering to adjust the air-conditioning as necessary. Out of hours, the alarms will sound remotely to alert hospital security and engineering. Security will contact the after-hours manager who will contact the hospital engineering department to adjust the air-conditioning as appropriate. The on-call pharmacist will be notified after hours, and the clinical trials pharmacist will be notified during work hours.

In the event of a temperature excursion data from the logger will be downloaded and read by Pharmacy. The appropriate CRA/Monitor and study coordinator will be contacted and trial-specific documentation completed as required.

6.5 Investigational Product Dispensing

The IP must be dispensed by the Pharmacist or delegated study team member for the recruited participant. The Pharmacist or delegated study team member will maintain a record of drugs dispensed to and retrieved for each participant.

The Pharmacist or delegated study team member may be required to document the following using the FM_19 Participant Investigational Product Accountability Log or as per

local processes by using the SWSLHD accredited Pharmacy Dispending program. Both systems have the ability to document the following key items;

- Trial/Study ID number
- Initial of the participant
- Date of IP dispensing
- Batch number and quantity of IP dispensed
- Expiry date

The delegated study team member will explain to each participant during the clinic visit or as appropriate the drug accountability needs for the study (e.g., the need for the participant to return unused, partially used, and empty packages unless otherwise instructed).

Requests for IMP/IP resupply are attended by the delegated study team member in communication with the Sponsor/CRO. This may be attended via an online platform provided to the site or using an automated resupply procedure. Confirmation of this procedure should be discussed during the clinical trial start-up process and/or Site initiation Visit.

6.5 Participant Study Drug Return process

The study participant will return all drug and study-related supplies to CTC/delegated study team members at each study visit or as otherwise instructed.

The CTC/delegated study team member will count the returned drug and compare this with the amount of drug expected to have been used since the previous study visit.

CTC/delegated study team members must document the IP returned by the participant in their source/medical notes. The IP returns are then provided to the delegated trial pharmacist or as appropriate who will verify the IP returns and complete the drug accountability log FM_19 Participant Investigational Product Accountability Log. The accountability log will be filed within the appropriate section of the ISF/eISF.

In case of missing IP or extra IP, the CTC/delegated study team member must obtain the information from the Participant and document the clarification in the source notes and CRF. Provide this information to the delegated pharmacist on return of the IP to ensure appropriate documentation in the Participant Investigational Product Accountability Log or equivalent.

Returns (both used and unused) will be returned to Pharmacy where possible. Closed oral drug bottles and empty boxes will be stored in Pharmacy until the trial monitor is able to reconcile IMP/IP returns.

Whether the drug is to be returned to the sponsor or destroyed on-site will be determined by the instructions in the protocol or as discussed during the initial feasibility and/or start-up process of the trial.

Used vials/syringes/infusion bags etc. will **NOT** be accepted by Pharmacy due to potential Work Health & Safety issues guidance from NSW Health.

Where requested, Pharmacy will retain empty boxes for monitors to reconcile (kit details, batch numbers, expiry date etc. are usually also on this outer box) and can keep perforated tear-off / peel-off labels of each dispensed kit in the allocated pharmacy folder.

If initially agreed upon by the research team during feasibility, used vials/syringes/infusion bags, may be stored with the study coordinator until CRA/Monitor reconciliation.

6.6 Return of IP to Sponsor

As specified in the protocol and or initial start-up visit, the IP will be returned to the sponsor at intervals or at the end of the study, or when quantity exceeds allocated space.

The FM_21_Investigational Product Returns Form is completed by the pharmacist and couriered to the sponsor with the IMP/IP, which is suitably packaged for the excursion.

The Sponsor should be asked to acknowledge receipt of the IMP/IP by signature/date and return of the form.

Retention samples, if required for regulatory testing are kept in the pharmacy department and clearly labelled and stored as per protocol requirements.

6.7 Destruction of IP

All returned, expired, and unused IMP/IP that is no longer required are either destroyed on-site or sent to the Sponsor for destruction. Each pharmacy site file will contain information detailing the agreement with the Sponsor on where destruction will occur for the clinical trials IMP/IP for that study.

Before any clinical trials, IMP/IPs are returned or sent for destruction, quantities of IMP/IP must be recorded, accounted for and reconciled for using the SWSLHD accredited iPharmacy program or as appropriate. A destruction log FM_22 Investigational Product destruction Log has been provided if required as a form of documentation.

If the IMP/IP Destruction is required at the site the clinical trials pharmacist and witnessed by CRA or a second pharmacy staff member. This process is documented via the iPharmacy program or via the FM_22 Investigational Product Destruction Log.

Drugs are to be placed in the designated yellow biohazard bin or purple cytotoxic waste as appropriate.

When full, the container is sealed and sent for destruction by high temperature incineration by the certified hazardous waste management company currently contracted by SWSLHD.

6.8 IMP/IP Management at study completion

At study completion, post final IP returns and or destructions the Clinical trials Pharmacist will provide the Clinical Trials Coordinator (CTC) with the trial-specific Pharmacy Folder. This folder will be combined with the Investigator Site File (ISF/eISF) and archived as per the record retention process outlined in SOP-CTSU_17 Data Recording - source data, case report forms, record keeping and archiving.

7.0 References

Medication Handling in NSW Public Health Facilities

ICH GCP (E6 R2): Good Clinical Practice Guidelines - Annotated by TGA

National Statement on Ethical Conduct in Human Research (2018)

Australian Code for the Responsible Conduct of Research (2018)

Therapeutic Goods Administration

8.0 Amendment History

Version	Date	Amended by	Details of Amendment
2.0	April 2023	Erfan Jaberiyanfar	• General update of the procedures • Specifying Assistant Director of Nursing (ADON) • Using degree celsius symbol (°C) • Indicating ISF/eISF • Indicating that at study completion, the final IP returns and or destructions should have occurred • Superceded links have been updated

END OF DOCUMENT