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HEALTH+MEDICAL RESEARCH

# Investigational medicinal product management and emergency unblinding

Standard Operating Procedure



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## 1. Purpose

This procedure describes the clinical trial site requirements for the management and handling of investigational medicinal products (IMP) used in clinical trials. To ensure that sites conducting clinical trials take appropriate account of the Guidelines for Good Clinical Practice based on sponsor requirements<sup>1</sup>.

## 2. Scope

All clinical trials (except Teletrials)<sup>2</sup> conducted at NSW Public Health Organisations that involve IMP (including biologicals regulated as medicinal products).

## 3. Applicable to

The principal investigator (PI) and all staff involved in any aspect of the IMP management or chain of custody including its receipt, handling, storage, prescribing, dispensing and return or destruction.

All staff involved in trials where an IMP emergency unblinding process is in place.

## 4. Definitions

Refer to SOP-G-01: Glossary of terms.

## 5. Background

Records supporting the provision of IMP should permit the reconstruction of IMP accountability so that it is possible to demonstrate that trial participants received the correct IMP(s), at the correct dose, at the correct time.

The responsibility for IMP accountability at a trial site lies with the PI. The task of maintaining IMP accountability may be delegated to a pharmacist and/or other appropriately qualified staff in accordance with legislation and medication handling policies.

IMP should be transported and stored according to specified conditions and local policy. The majority of IMP will be received, stored and managed within a pharmacy\*. However, exceptionally, it may be necessary for IMP to be stored in a ward or facility (e.g. for trials where IMP is administered in the emergency setting or outside of pharmacy opening hours). In public health organisations, arrangements for IMP storage outside of the pharmacy should only occur following consultation with local pharmacy service\*. Where organisational policy allows delivery directly to storage areas outside pharmacy, these

should be assessed by staff (e.g. pharmacy) to ensure storage conditions are adequate, temperature monitoring is in place and accountability (including an area for returns) meets protocol/pharmacy manual requirements.

*\*All medications must be stored in accordance with the NSW Poisons and Therapeutic Goods Act and Regulations, and for public health facilities, in line with NSW Policy: Medication Handling in NSW Public Health Facilities and other applicable policies.*

When IMP is self-administered, the PI or designee (pharmacist or other qualified individual) is responsible for explaining the correct use of the IMP to each participant and should check at intervals appropriate for the trial, that each participant is following the instructions provided.

Where IMP is logged out of pharmacy and transferred to a department/facility/area (or other location) for administration to the patient (e.g. IV infusion in a ward or administration of a vaccination at a participant's home), 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 be able to demonstrate that it was transported and administered within the specified timeframe.

IMP should not be destroyed without prior written authorisation by the sponsor. IMP that is unused, expired or returned by patients should be stored in an appropriately controlled area, until ready for return to the sponsor (usually at intervals) or disposal at site. Returned IMP should be stored separately to unused IMP. Where IMP is to be returned to the sponsor, all patient-identifiers must be removed beforehand.

### Unblinding for safety reasons

The PI or delegate should assess the need for emergency unblinding and only unblind if it is essential for the ongoing medical management of the participant. Wherever feasible, the PI or delegate should discuss the case with the sponsor/coordinating PI. Where a participant is withdrawn from a trial, the withdrawal should be recorded.

## 6. Procedure

### Principal Investigator (PI)

<sup>1</sup> All trials must comply with the principles of GCP (Section 2 of ICH GCP (E6 R2) or Clause 4 of ISO 14155) however sponsors submitting data to regulatory authorities will normally require full compliance with ICH GCP (E6 R2) or ISO 14155 GCP Guidelines.

<sup>2</sup> NSW Health have published an annotated version of these SOPs for sites utilising a Teletrials model.

Ensure all staff delegated duties for IMP handling and management are appropriately qualified and trained:

- the task of prescribing IMP is only delegated to as appropriate, to medical practitioners, dentists or nurse practitioners.
- the task of administering IMP is only delegated to medical or clinical staff (e.g. registered nurses).

In most cases, a lead pharmacist is delegated the task of IMP management. This person then delegates all specific tasks to pharmacy department staff and ensures all IMP activities are conducted in accordance with the protocol/pharmacy manual.

Maintain oversight to be satisfied that IMP is managed/used in accordance with the trial protocol/pharmacy manual.

### PI or delegate

Contact the pharmacy as early as possible in the trial set up process to discuss requirements for the study.

Provide (or ensure the sponsor provides) the key documents needed for the pharmacy to undertake a feasibility review of the study and an assessment of capacity, capability, and costs to fulfil all protocol requirements.

Ensure pharmacy are provided with all relevant information as the trial progresses (e.g. protocol amendments).

### Pharmacy delegate

Confirm IMP certification and all relevant trial approvals/notifications are in place before releasing IMP for dispensing to participants (i.e. ethics and governance approval, CTN/CTX, drug committee approvals and product compliance with guidance documents and legislation).

Ensure that individuals within pharmacy handling or dispensing IMP have received training and/or instruction commensurate to their role.

Ensure that the IMP supplies are managed in accordance with the protocol/ pharmacy manual\*. This includes ensuring that:

- IMP is received in an appropriate condition and appropriately labelled.
- IMP is stored in a secure location with restricted access to approved staff.
- Storage conditions are monitored and recorded such that the stability of the IMP is protected.
- A process is in place to identify and manage IMP temperature excursions whilst stored on-site.

- IMP is only dispensed to participants in accordance with any randomisation lists/IWRS confirmations on receipt of a prescription or medication chart.
- Accountability records are kept for all aspects of IMP handling and any unused or expired IMP is returned to pharmacy.
- If required by the sponsor, returned/used IMP is destroyed and documents relating to the destruction are retained as defined by the protocol and by any organisational policy.

*\* NHMRC Guidance: Risk-Based Monitoring and Management of Clinical Trials Involving Therapeutic Goods permits a risk-adapted approach to IMP management. For some trials, lower levels of accountability may be approved (e.g. the use of general pharmacy stock and local prescribing practice).*

When the site is responsible for IMP destruction, ensure this is carried out in accordance with Organisation's waste management policy. Proof of destruction should be documented (e.g. a certificate of destruction).

Develop and maintain standard operating procedures (SOPs) for the handling and management of IMP; referencing all appropriate guidelines/legislation.

### PI

Ensure all staff follow the randomisation procedures detailed in the protocol and that all randomisation codes have been received to before the first patient is recruited.

Ensure that all relevant staff are aware of, and understand the emergency unblinding procedure and that the code is broken only in accordance with the protocol and any premature unblinding of the IMP is explained and documented.

## 7. References

[ICH GCP \(E6 R2\): Good Clinical Practice Guidelines – Annotated by the TGA](#)

[NSW Poisons and Therapeutic Goods Act 1966](#) and [NSW Poisons and Therapeutic Goods Regulation 2008](#)

[NSW Policy: Medicines Handling in NSW Public Health Facilities \(PD2013\\_043\)](#)

[PIC/S Guide to Good Manufacturing Practice for Medicinal Products \(Annex 13\)](#)

## 8. Associated documents

Accountability log templates – available in the Standard Operating Procedures templates [zip file](#)