Document Title: Supply of Clinical Trials Investigational Medicinal Products (IMP): Dispensing, Returns and Accountability

Document Number: PTUC SOP072

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Department:	Research and Development
For use by:	NHS Staff Trust-Wide
Review due:	November 2023

Summary of Amendments:

Version Number	Modification:
Version 3.0	Updated SOP cross referencing and general clarification

Key Points of this Document

- This document sets out the procedures to be followed by staff when dispensing or returning clinical trials medication according to the individual clinical trial protocol to ensure that all medication is dispensed in a safe a correct manner and that accountability is maintained throughout.

1 Purpose and contents of this document

a. All clinical trials medicine that is stored and supplied through Royal Papworth Hospital should be routinely dispensed through the pharmacy clinical trials department.

b. On occasion it may be necessary for this to take place outside of the pharmacy - this document outlines the steps to be followed when proposing that an IMP (Investigational Medicinal Product) is dispensed and managed outside of the pharmacy.

c. This document defines the procedure for all staff who are involved in preparing, dispensing and checking clinical trial products prior to handing to a patient or using within the hospital for clinical trials purposes.

d. This document also outlines the necessary requirements regarding IMP accountability and management of returns.

e. To define the procedure for handling errors in dispensing and accountability.

2 Roles and responsibilities

a. Only members of staff who have been named on the delegation log for the task of IMP management should dispense, or receive returns for that clinical trial.

   1. When no member of the pharmacy trials team is available to dispense an appropriately trained member of pharmacy will dispense and will be named on the pharmacy signature log.

b. It is the investigator's responsibility to ensure that all members of staff who are delegated such tasks are suitably trained in IMP management.

c. Handling of returned medication should also be only undertaken by delegated members of staff. Returned trial material should be stored separately from unused material and appropriate accountability performed as per the trial protocol. Pharmacy should handle

returns. For all procedures relating to return of IMP please refer to SOP082: Returns of IMP to Pharmacy.

d. Any clinical trial medication that is not stored or dispensed from the pharmacy must be done so with the sponsor's authorisation and should have a separate local procedure for the safe and appropriate management of the medicine which should be written and approved by Pharmacy.

3 Policy

a. The sponsor is responsible for ensuring that records that document the dispensing, return and destruction of IMPs are maintained as they are listed as essential documents in UK Clinical Trial Regulations. These records should be filed in the Pharmacy File. The Chief Investigator (CI) and Sponsor have responsibility for IMP accountability which may be delegated to an appropriate pharmacist or individual who is under the supervision of the CI or delegate (e.g., Pharmacy Monitor).

b. All research staff should be aware of this SOP at local induction. Failure to follow this SOP may result in disciplinary procedures.

4 Set up Procedure

a. The PI (Principal Investigator), CI or delegate should have an initial meeting with pharmacy clinical trials team to discuss the dispensing, accountability and return requirements for the study.

b. In all circumstances clinical trial investigational material must be received by the pharmacy (See SOP076 Transport, Storage and Environmental Monitoring of IMP's (Investigational Medicinal Products)) before it is sent out for use elsewhere in the hospital. Pharmacy should be used for all aspects of IMP management.

c. For Royal Papworth sponsored trials: If the trial is multicentre the CI or delegate must ensure that the IMP is received by a pharmacy at each individual site.

d. A Clinical Trials Pharmacist or Technician should review the trial protocol and develop specific IMP Handling Guidelines and appropriate Royal Papworth dispensing labels prior to the start of the study. This should be approved by the sponsor.

1. In the case of Royal Papworth sponsored studies it may be necessary to develop specific clinical trial labelling (Annex 13 compliant) depending on the requirements set out by

the MHRA Risk adaptive approach to IMP trials. This label will form part of the Clinical Trial Authorisation submission and will require MHRA approval. See Pharmacy SOP CT22.

2. In addition to any clinical trial labelling the Royal Papworth dispensing label must detail the Pharmacy departments address, contact numbers and the words "Keep out of reach of Children".

e. Where required the pharmacy will ensure that a trial specific prescription is prepared. A blank copy of this form will be filed in the Pharmacy File.

f. Pharmacy will ensure that IMP handling guidelines are prepared as a separate document following the template (Appendix 1). The IMP handling guidelines should include the following:

1. Details on receipt and handling of drug
2. Details on storage of drug and temperature monitoring
3. Details on dispensing and accountability
4. Details on handling of returns and destruction
5. Code break requests (if applicable)

g. Drug accountability logs should be prepared for each IMP. These forms should allow for the documentation of full drug accountability from arrival of the IMP, to dispensing and return of IMP or packaging.

h. When pharmacy is not suitable for storage and dispensing of IMP then the CI and Lead Pharmacist or Technician for clinical trials must identify a suitable site and staff member to manage the IMP handling. **NB:** Pharmacy will retain responsibility for receiving the IMP and delivering it to the identified storage site. IMP handling guidelines and accountability logs will still be required and the Investigator or delegate will take responsibility for oversight of all subsequent tasks including dispensing, accountability, returns and 24 hour code break access (if applicable).

i. The Pharmacy clinical trials team will ensure the site is suitable as per pharmacy SOP CT015 (Authorisation of IMP (Investigational Medicinal Product) storage areas outside of the Pharmacy Clinical Trials Department). Pharmacy will perform regular checks to ensure the site continues to be suitable for storage and supply of the IMP for the duration of the study, as well as an annual audit (please refer to SOP076: Transport, Storage and Environmental Monitoring of IMPs).

5 Dispensing Procedure

a. Dispensing of IMP should not occur until the following have been received:

1. Staff have been trained on trial specific dispensing procedures
2. Regulatory and local approvals in place
3. Code break access i.e. appropriate Interactive Voice/Web Response System (IVRS/IWRS) access is set up and tested or physical envelopes are delivered to the appropriate site.
4. A copy of the delegation log is filed in the pharmacy file
5. A copy of the IMP handling guidelines along with blank copies of relevant paperwork files is filed in the Pharmacy File
6. Training log completed

b. The prescription should be written on dedicated clinical trial paperwork and signed by a delegated prescriber.

c. A prescription form will be issued for each trial subject when dispensing is required and a copy filed in EMR, the Site File and the trial specific case notes as appropriate.

d. If randomisation is required at this point the authorised research team member with access to the randomisation service should follow the procedure to obtain the randomisation allocation.

e. Before dispensing or checking a trial prescription the IMP handling guidelines must be read. This will be located in the Pharmacy File.

f. The trial medicine should be dispensed and labelled according to the IMP handling guidelines.

g. A Royal Papworth Pharmacy dispensing label will be applied to identify the origin of the trial medication.

h. All clinical trial medicine dispensed must be recorded in the trial drug accountability logs found in the pharmacy trial file.

1. **NB** some trials will keep patient specific logs as well as master drug accountability logs
2. Some studies may use electronic accountability via the online IWRS systems

i. A second check must be completed on any medicine before use or handing to a patient. Within the pharmacy this task can be undertaken by the clinical trials pharmacist, another trained pharmacist or accuracy checking pharmacy technician (ACPT) who has passed the clinical trials checking competency. Any pharmacist or ACPT who checks a clinical trial dispensing should read the IMP handling guidelines and sign the pharmacy signature log as a record of their involvement in the trial.

NB. Locum pharmacists are not authorised to check clinical trial medicines.

j. Where dispensing and accountability takes place outside of the pharmacy a second delegated staff member named on the delegation log should be available to provide a

second check. This person should also be suitably trained and be familiar with the IMP handling guidelines and trial protocol.

k. The prescription should be appropriately endorsed by the dispenser and the checker to establish quantities given and the date dispensed. Accountability logs must be completed and checked.

l. Once dispensed clinical trial medication should be stored in the designated storage area until an appropriate member of the research team is able to collect. All collections of trials medication from pharmacy should be signed for on the prescription to acknowledge receipt of the IMP. Whoever collects must be listed on the clinical trials delegation log.

m. Where specific training is required for a patient to self-administer the trial medication this role should be clearly defined on the delegation log and the relevant staff member be suitably trained in the clinical trial in question. It is the responsibility of the PI (or delegated staff member) to ensure that appropriate training is given to the patient before they begin to self-administer. Please see p 226 of the Good Clinical Practice Guide, MHRA, 2012, section 6.15.5 outlined below:

> *Subjects or, in the case of vulnerable patients, their carers may need to be trained to administer the IMP themselves. The trial team will need to ensure that subjects and/or carers are trained according to the requirements of the protocol in terms of storage, reconstitution, method of administration, record keeping (diary card), and retention of used vials and the use of any equipment provided by the sponsor. This is usually performed at the start of the trial, when site personnel will demonstrate and advise the subjects/carers on drug administration. However, site personnel will need to assess the subject's understanding before allowing self-administration. It is recommended that subjects have regular checks to reaffirm their understanding and assess their compliance with the protocol. This must be documented to demonstrate it has been undertaken.*

n. If the patient is to collect the clinical trial medication direct from the Pharmacy then this must be communicated to the pharmacy team. Pharmacy staff handing out clinical trials medication must make the identification checks to ascertain that the patient is the correct patient (per pharmacy protocol). Pharmacy staff should also make appropriate checks to ensure the patient has been told how to take the medication correctly. Where the patient is not aware of how to self-administer the PI (or delegated staff member) should be contacted.

6 Handling of returns and destruction of IMP

a. Expired IMP, or IMP returned by patients should be returned to the site it was dispensed from so that accountability logs can be updated with the return.

b. Returned IMP must be stored separately from IMP not yet dispensed.

c. Once accountability logs have been updated the IMP may be stored until the next monitor visit or sent for destruction according to the IMP handling guidelines. **NB** destruction should not occur until the sponsor has given written authorisation.

7 Dispensing errors

a. Dispensing errors are defined as a patient receiving the wrong medication, incorrectly labelled medication, the wrong quantity of medication or expired stock. These do not include prescribing errors where the prescription is incorrect or administration errors where correctly dispensed medication is not given according to protocol.

b. Where a dispensing error is identified prior to the medication leaving the pharmacy or dispensing area it is defined as a "near miss".

c. Dispensing errors that have left the pharmacy or dispensing area, once identified, should be reported immediately (within 24 hours), to the relevant members of trials staff; the chief investigator and sponsor should also be informed.

d. Deviations of the dispensing procedure (i.e., IMP Handling Guidelines), leading to a dispensing error should be reported to the sponsor immediately, within 24 hours knowledge of the event if it is likely to cause a protocol violation. The deviation must be documented in a file note in the Pharmacy File, including any corrective and preventative actions. This should be available for the Study Monitor to review at the next visit. The dispensing procedure should be amended accordingly to reflect a safer way of working and sent to the sponsor for approval. Staff should receive training in the updated dispensing procedure and this should be documented on the study training log. A Datix will be

completed and subsequent investigations made to identify actions that will prevent further re-occurrence.

e. Immediate action should be taken to avoid and/or minimise harm to the patient. If possible the incorrect medication should be retrieved and the correct medication dispensed.

f. The pharmacy internal procedure for the dispensing of medications includes steps to be taken on the discovery of a dispensing error. These should be followed. For errors that occurred outside of pharmacy the same process should be used and pharmacy should be involved in the investigation.

8 Risk Management / Liability / Monitoring & Audit

8.1 Staffing

a. Whenever possible GCP trained members of the pharmacy clinical trials team will dispense all trial related medication. When this is not possible due to restrictions in staffing then an appropriately qualified member of pharmacy will be identified in advance to dispense any potential trial prescriptions.

b. Outside of pharmacy when no suitable staff are available to dispense for a clinical trial then the visit should be delayed or the medication dispensed in advance if possible of the collection visit. If possible and time allows then other members of the research team could be trained to dispense IMP and added to the delegation log.

8.2 Monitoring and Audit

a. The R&D SOP Committee will ensure that this SOP and any future changes to this document are adequately disseminated.

b. The R&D Department will monitor adherence to this SOP via the routine audit and monitoring of individual clinical trials and the Trust's auditors will monitor this SOP as part of their audit of Research Governance. From time to time, the SOP may also be inspected by external regulatory agencies (e.g. Care Quality Commission, Medicines and Healthcare Regulatory Agency).

c. In exceptional circumstances it might be necessary to deviate from this SOP for which written approval of the Senior R&D Manager should be gained before any action is taken. SOP deviations should be recorded including details of alternative procedures followed and filed in the Investigator and Sponsor Master File.

d. The Research and Development Directorate is responsible for the ratification of this procedure.

Further Document Information

Approved by: *Management/Clinical Directorate Group*	Research and Development Directorate
Approval date: *(this version)*	Current approved version date
Ratified by Board of Directors/ Committee of the Board of Directors:	STET
Date:	N/A
This document supports: *Standards and legislation*	Medicines for Human Use (Clinical Trials) Regulations 2004 and all associated amendments. UK Policy Framework for Health and Social Care Research (2018)
Key related documents:	Trust Research Policy Trust Policy DN1 Document Control Procedures

Equality Impact Assessment: Does this document impact on any of the following groups? If YES, state positive or negative, complete Equality Impact Assessment Form available in Disability Equality Scheme document DN192 and attach.

Groups	Disability	Race	Gender	Age	Sexual orientation	Religious & belief	Other
Yes/No	NO	NO	NO	NO	NO	NO	NO
Positive/Negative							

Review date:	November 2023

I certify the contents of this SOP has been reviewed and ratified

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Signed by Dr Ian Smith, Clinical Director of R&D

30th November 2020

Date

SOP Release Date: 9th December 2020

APPENDIX 1

IMP Handling Guidelines

IMPORTANT: Only members of pharmacy staff on the delegation log are able to randomise. Dispensing, accuracy and clinical checking may be done by any appropriately qualified permanent member of staff once this document has been read and the signature log has been signed.

Clinical Trial - _____

Sponsor

Principle drug involved

Study design

Investigator

-

Sub-Investigators

-
-
-

Treatment Period

-

R&D Confirmation of Capacity and Capability

Date received: __/__/20__

Reference Number: P_____

Study Medication Description

Product Risk Assessment and Handling Requirements

To include any special precautions such as cytotoxic, wear gloves, COSHH, etc.

Dosage Regime

Schedule of Dispensing Visits

Visit 1: Week __, Day __, (± __ days)
Dispense __ box/pack/card/kit as confirmed by the ____ IVRS/IWRS/SBIR/IRT report

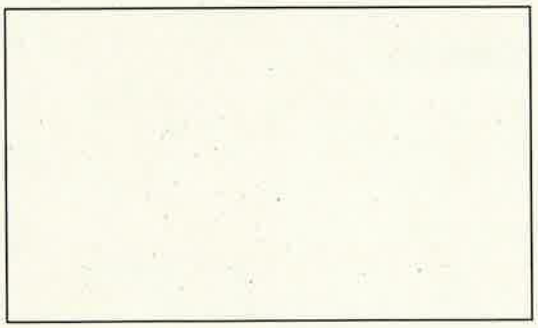
Visit 2: Week __, Day __, (± __ days)
Dispense __ box/pack/card/kit as confirmed by the ____ IVRS/IWRS/SBIR/IRT report

Visit 3: Week __, Day __, (± __ days)
Dispense __ box/pack/card/kit as confirmed by the ____ IVRS/IWRS/SBIR/IRT report

Unscheduled Visits
Dispense the required box(es)/pack(s)/card(s)/kits(s) as confirmed by the ____ IVRS/IWRS/SBIR/IRT report

Dispensing and Labelling Procedure
On receipt of the prescription:

- Confirm that all the prescription details have been completed and the subject details match previous prescriptions if applicable
- Check that the prescriber has signed the delegation log and has been authorised by the investigator to prescribe the trial medication
- Select the box/pack/card/kit number(s) requested on the prescription and check that these box/pack/card/kit number(s) match the attached ____ IVRS/IWRS/SBIR/IRT report
- Peel back the box/pack/card/kit label(s) to reveal the English translation on page __
- Enter the subject number, investigator's name and dispensing date on the label on the front of the box/pack/card/kit
- Complete and attach the following dispensing label on each box/pack/card/kit. Ensure that the patient's name, subject number and dispensing date is entered:



- Complete the ____ log and affix the peel off label
- Complete the Master Drug Accountability Log

- Complete the prescription endorsements
- Ensure that you have signed the signature log at the front of this file if this is the first time you have dispensed for this trial
- Forward the prescription to a pharmacist for final checking

Checking Procedure

- Perform an accuracy check on the dispensed clinical trial medication and ensure that the above dispensing and labelling procedure above has been followed
- Initial the pharmacy label to confirm that the item has been checked
- Sign the accountability logs next to the dispenser's initials
- Sign the prescription in the checked by section
- Ensure that you have signed the signature log at the front of this file if this is the first time you have checked for this trial

NB: Only a pharmacist is permitted to accuracy check a clinical trial prescription. Locum pharmacists and ACT's are not permitted.

Storage Requirements

- Store in the Clinical Trials Room/Fridge between __°C and __°C
- Temperature will be monitored remotely via the Tutela Genesis II wireless system
- Promptly report any temperature excursions to the monitor/CRA and follow procedure 'SOP075 Quarantine of CTIMPs'
- In the event of a constant ambient/fridge temperature excursion or a fridge failure then any suitable and secure location within the pharmacy department that meets the trial temperature monitoring requirements may be utilised in the short term until the issue is resolved e.g. CD room, Goods-In fridge
- At each monitoring visit, the relevant temperature records will be printed and filed in the sponsor file

Handling of Returns

The study medication returns will be stored in the grey returns box in the Clinical Trials Room until an accountability check can be performed. When ready to process the returns:

- Blank out the patient's name on the dispensing label with a black marker pen
- Enter the details of the returned medication on the _____ log
- Store in the relevant returns container for the sponsor/monitor to review

Ordering and Receipt

- Automatic via ____ IVRS/IWRS/SBIR/IRT
- Acknowledge receipt via ____ IVRS/IWRS/SBIR/IRT and enter the shipment details on to the _____ log
- An e-mail notification for shipment receipt and activation will be sent. Print a copy of this e-mail and file it together with the delivery paperwork

- Follow any temperature logging requirements received with the shipment
- For Royal Papworth sponsored studies ensure QP batch certification is present.

Product Recalls

- Follow the specific instructions provided by the sponsor/CRA in conjunction with the 'Handling of Product Recalls of CTIMP or Other Trials Related Drugs' procedure
- Quarantine the stock as per procedure: 'SOP075 Quarantine of CTIMPs'

Unblinding Requests

- Follow procedure: 'SOP069 Code Breaking/Un-Blinding of Clinical Trials, training and procedure testing'
- Only the Investigator has been assigned access to unblind in an emergency situation. Pharmacy has no access

Monitor/CRA

Name:
Telephone Number:
Fax Number:
Mobile Number:
E-mail address:

Research Nurse/Study Co-ordinator

Name:
Extension Number:
Bleep Number:
E-mail address:

	Name	Position	Date
Author			
Approved by			
Reviewed by Monitor/CRA*			

*See attached e-mail confirmation of review

Version	Date	Written/Updated By	Reason for change
1.0			New document