Royal Papworth Hospital
NHS Foundation Trust

Document Title: Transport, Storage and Environmental Monitoring of IMP's (Investigational Medicinal Products)

Document Number: R&D SOP076

Staff involved in development: *Job titles only*	Senior R & D Manager, R&D Operational Manager, Clinical Project Managers, Clinical Trials Pharmacist
Document author/owner:	Senior R&D Manager
Directorate:	Research and Development
Department:	Research and Development
For use by:	NHS Staff Trust-Wide
Review due:	June 2027

Summary of Amendments

Version Number	Modification:
Version 5.0	**Minor amendments in Section 4.0**
Version 4.0	**Minor amendments throughout** **Section 4.1 Addition of Risk Assessment** **Section 4.3 Addition of information regarding importation following UK exit from EU** **Section 4.6 Addition of direct to patient supply** **Section 4.10 Clarification of sponsor role with respect to temperature excursions**

Key Points of this Document

- To describe the procedure for the supply, transport and storage of investigational medicinal product (IMP) in accordance with the principles of Good Clinical Practice (GCP) Good manufacturing Practice (GMP) annex 13 and in compliance with the UK regulations UK Medicines for Human Use (Clinical Trials).

- This SOP applies to all trial personnel involved in or overseeing the handling or ordering of IMPs.

1 Purpose and Contents

a. To provide guidance on appropriate supply, transport and storage of IMPs where Royal Papworth Hospital is acting as the sponsor or co-sponsor of the trial.

b. To inform researchers and pharmacy staff of the necessary steps required before an IMP supply can be ordered and processed through pharmacy.

c. To inform researchers and pharmacy staff of the appropriate transport arrangements for IMP from manufacturer to site and, in the case of a multi-centre trial, onwards from Royal Papworth Hospital to other trial sites.

d. To outline the considerations required for the storage of IMPs within the pharmacy department and (only where necessary), outside of the pharmacy department, in a pharmacy audited IMP storage and supply area.

e. To describe, in the event of a temperature deviation, the steps to be taken to ensure that IMP is appropriately managed, according to the sponsor's requirements.

2 Roles and Responsibilities

a. It is the responsibility of the trial sponsor to ensure that the site has suitable storage facilities for any IMP, including space, adequate temperature monitoring and secure access. This may be delegated to an appropriately qualified individual: usually the clinical trials pharmacist or technician. This should be established at the site selection visit or as early on in the process as possible – wherever possible the pharmacy should be used as the storage site for IMPs. Areas outside of pharmacy may be used where the trial protocol requires storage facilities

that pharmacy are unable to provide or where access to the IMP is required urgently and outside of usual working hours.

b. The Investigator is responsible for ensuring agreed storage arrangements are adhered to during the course of the trial – this may be delegated to either the pharmacy team or another member of the research team when the IMP is not stored within pharmacy.

c. The investigator may delegate aspects of this role to the pharmacy clinical trials team.

d. Pharmacy clinical trials staff are responsible for the overall management and for the routine checking of the temperature monitoring system within pharmacy only. Areas outside of pharmacy should have their own temperature monitoring systems and associated procedures; these areas should be audited and approved by pharmacy prior to trial commencement.

e. This SOP applies to all personnel that are conducting research at the Trust.

3 Policy

a. This SOP is mandatory and, as per the Trust's Information Governance and Records Management framework, non-compliance with may result in disciplinary procedures.

b. IMP's must be supplied, transported and stored at sites in a manner that maintains the integrity of the product at all times until destruction or return. The sponsor must ensure that documentation is provided and maintained to show that these procedures have been followed for the supply, storage and transport of all IMP.

4 Procedure

4.1 Pharmacy will undertake an IMP risk assessment (CT004A) for all CTIMPs.

4.2 For Royal Papworth Sponsored studies this should be submitted for discussion at RGPAS.

4.3 Prior to Clinical Trials Application (CTA) submission and grant submission the researcher should read this SOP and consult with the pharmacy clinical trials team to ensure that all issues regarding IMP supply, storage and transport are identified, and correct actions taken.

4.4 Supply of IMP to site

a. At the initial meeting with the investigator (or delegate) and the pharmacy clinical trials team, the supply of IMP should be discussed along with the ordering and purchasing arrangements

b. Supplies may be sourced through a number of routes:

1. Commercial supply – for licensed products that do not require repackaging general pharmacy stock purchased via usual routes may be suitable. NB if the product is supplied as generic stock item (where the manufacturer may vary) the sponsor should consider whether or not it is suitable for use in the trial or if a single supplier/brand should be identified.

2. Commercial supply - where a manufacturer has agreed to supply stock of a licensed medicine free of charge (FOC) for trial purposes but where the manufacturer is not the sponsor. In this scenario the manufacturer must verify that the trial has the appropriate authorisations and that the products have been manufactured in accordance with GMP. An agreement should be set up defining the division of responsibilities prior to supplies being made.

3. Non-commercial supply – for products without a manufacturing authorisation which need to be released by a Qualified Person (QP) for trial specific use. A third party subcontractor may be required if any manufacturing activity is required before the IMP can be used for trial purposes see SOP066; Subcontracting of Research Activities. A technical agreement should be in place before any supplies are obtained.

Where IMP sourced from a non-commercial supply requires importation from the EU or EEA (listed countries) or from countries outside of these areas, an MIA (IMP) license is required. QP oversight is required for assurance only of QP certification for IMP coming from a listed country. For IMP coming from an unlisted country full QP certification is required from a UK resident QP. It is the sponsor responsibility to ensure the correct process for importation is followed.

c. All IMPs should be supplied to the hospital pharmacy clinical trials department who will provide acknowledgement of receipt to the supplier and file a copy of this in the Pharmacy File. Once IMP is received it should not be released by the pharmacy until Sponsor Green Light has been issued. Any IMP received ahead of Sponsor Green Light must be placed into quarantine (SOP075).

4.5 Transport of IMP to site (single site trials)

a. Shipments of IMP will be received by pharmacy staff for a contents and documentation check, and signing for receipt of the product. There is usually a requirement for temperature monitors to be accessed and data downloaded to ensure that there have been no temperature excursions during transit. Follow the IMP specific procedure.

b. Upon receipt of IMP, pharmacy staff will check the IMP status (approved or not approved), any importation documents, QP release, batch certifications and labelling prior to releasing to the investigator (please see SOP073: Sourcing of clinical trial investigational medicinal products for Royal Papworth sponsored studies: manufacturing, assembly and labelling).

c. Shipping documentation should be filed in the Pharmacy File along with all other relevant documentation pertaining to the quality of the product. Any missing documentation should be queried with the supplier and the product quarantined until all appropriate documentation is received.

d. Accountability documentation must be completed as soon as the product is confirmed as suitable for use – see SOP072; Supply of Clinical Trials Investigational Material: Dispensing, Returns and Accountability.

4.6 Transfer of IMP across investigational sites (multi-centre trials)

a. 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 will be in charge of this process and the transfer process must be fully documented. Specific IMP handling guidelines should be produced to cover this process.

4.7 Direct to Patient (DTP) IMP supply

a. Consideration should be made early on in protocol development as to the need for IMP to be posted or couriered to patients.

b. Any process for DTP supply must be fully risk assessed and documented for each study (SOP084)

4.8 Storage of IMP at site

a. The pharmacy clinical trials department has a designated, temperature monitored; secure area for the storage of IMPs and this location should be used where possible. If an alternative storage area is required to facilitate timely access to the IMP, or because pharmacy are unable to accommodate the IMP, then a designated IMP storage area should be identified and agreed with pharmacy at the planning stage of the trial.

b. Designated IMP storage sites outside of pharmacy must be approved and audited annually by the Pharmacy Clinical Trials Team to maintain their approval (see Pharmacy SOP: CT015 Authorisation of IMP storage areas outside of the Pharmacy Clinical Trials Department)

c. Detailed IMP handling guidelines (including receipt of product, dispensing, record keeping and temperature monitoring) should be produced by pharmacy to facilitate safe IMP handling

4.9 Storage requirements:

a. Storage requirements should be established early on in the trial set up to ensure appropriate facilities can be sourced in a timely manner.

b. IMP should be maintained at the specific storage conditions dictated by the IMP labelling and IB/IMPD. Where the product is already licensed and in routine use the Summary of Product Characteristics (SmPC) will detail any specific storage requirements.

c. Storage facilities should not be accessible to the general public and should be lockable when not in use.

d. The storage area should be maintained so that it is dry, not at risk of flood and has a backup electricity supply in case of main power failure; the risks of fire, pest infestation and structural damage are minimised.

e. IMP should be stored in a defined area and, if required, the IMP should be stored in labelled boxes or baskets to contain it and prevent items becoming lost.

f. Any IMP (i.e. used IMP, unused IMP and IMP packaging) returned from a patient should be returned to pharmacy as soon as possible and stored separately from unallocated stock; if it is not possible for pharmacy to hold the returns for a particular study then an approved and secure area should be identified and authorised for use. However if it is possible for pharmacy to hold the returns then this should be the course of action. For all IMP study returns see SOP072; Supply of Clinical Trials Investigational Material; Dispensing, Returns and Accountability for handling of returns.

g. Temperature monitoring should be carried out according to the protocol and/or the IMP handling guidelines written by pharmacy.

4.10 Temperature monitoring:

a. Ambient temperature will be maintained within the range of 15-25 °C.

b. Refrigerated temperature will be maintained within the range of 2-8°C.

c. Frozen temperature monitoring will be trial specific, please see IMP specific documentation.

d. Different trials will have different temperature monitoring requirements as specified by the trial protocol or the pharmacy manual; where the study is Royal Papworth Hospital sponsored, temperature monitoring should be part of the IMP risk assessment.

e. Temperature monitoring can range from:

1. No additional monitoring other than that required for general stock supplies e.g. where IMP is held in a standard location as part of routine care.

2. Daily recordings using calibrated maximum/minimum thermometers e.g. in areas where only small amounts of a single IMP are stored. A process should be defined for how the temperature will be checked prior to dispensing IMP from such areas.

3. Continuous recording using automated and alarmed systems e.g. where large volumes of IMP are stored or where there are a number of IMPs with differing storage requirements and/or detailed monitoring requirements.

4. Each temperature monitoring system should be calibrated according to the manufacturer's recommendations and at least annually; a record of calibration will be kept centrally within the pharmacy.

4.11 Temperature Deviations outside of recommended ranges

a. All temperature logging systems should trigger an audible or visual alarm should temperatures fall out of range

b. A local procedure for action should be identified for each area where IMP is stored in case of deviations outside of recommended storage.

c. Follow SOP075; Quarantine of CTIMPs (clinical trial investigational medicinal products) and contact pharmacy clinical trials for advice.

d. Where dual monitoring is available and a temperature deviation is recorded on one device but not the other, consideration should be given as to the location of the monitoring device and small temperature variations within the room. If there is any doubt then the material should be quarantined per SOP075, and the study manager and PI/CI contacted.

e. Pharmacy clinical trials staff should inform the study managers and PI/CI by the beginning of the next working day of the batches and quantities affected and the duration for which the medications were stored outside of requirements. Data from the logging systems should be made available.

f. The pharmacy clinical trials team should contact the manufacturer of the product directly. A sponsor representative in conjunction with the chief investigator should authorise the decision to use or discard stock; this will be based upon the information provided from the manufacturer and the potential risks to the patient and study.

1. For studies where IMP supply is provided free of charge from a commercial company then speak with their representative first about obtaining new stock

g. All research staff of the affected studies should be informed by the beginning of the next working day that patient supply may be affected and necessary actions required with respect to patient visits.

h. If appropriate, a DATIX should be completed and appropriate actions taken immediately to minimise the risk of future temperature excursions, involving estates where necessary to replace or install equipment.

i. All correspondence pertaining to a temperature deviation should be filed in the relevant Pharmacy File.

5 Risk Management/Liability/Monitoring and Audit

5.1 Equipment Failure

a. In the event of equipment failure which would result in the failure to implement this SOP, appropriate local procedures should be in place to provide backup storage facilities as soon as possible.

5.2 Staffing

a. Where no suitable trained staff members are available to undertake the roles described in the SOP the chief investigator should be informed and appropriate staff identified for training.

5.3 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 Site File, Pharmacy File and Sponsor 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 (2023)
Key related documents:	Trust Research Policy GCP (Good Clinical Practice) GMP (Good Manufacturing Practice) SOP066 Subcontracting of Research Activities SOP072 Supply of Clinical Trials Investigational Material: Dispensing, Returns and Accountability. SOP075 Quarantine of CTIMPs (clinical trial investigational medicinal products)

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	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Review date:	June 2027