York Foundation Trust R&D Unit
SOP
Pharm/S76

Storage and dispensing of Investigational Medicinal Products outside of Pharmacy

IT IS THE RESPONSIBILITY OF ALL USERS OF THIS SOP TO ENSURE THAT THE CORRECT VERSION IS BEING USED

All staff should regularly check the R&D Unit's website and R&D Newsletter for information relating to the implementation of new or revised versions. Staff must ensure that they are adequately trained in the new procedure and must make sure that all copies of superseded versions are promptly withdrawn from use unless notified otherwise by the SOP Controller.

The definitive versions of all R&D Unit SOPs appear online. If you are reading this in printed form check that the version number and date below is the most recent one as shown on the R&D Unit website: www.northyorksresearch.nhs.uk/sops.html

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This SOP will normally be reviewed every 2 years unless changes to the legislation require otherwise

Version History Log

This area should detail the version history for this document. It should detail the key elements of the changes to the versions.

Version	Date Implemented	Details of significant changes
1.0	July 2013	12th September 2013
2.0	12th April 2015	

Contents

1 Introduction, Background and Purpose

This Standard Operating Procedure (SOP) should be used to create a study-specific SOP documenting the procedures to be followed when an Investigational Medicinal Product (IMP) is being dispensed or stored outside of the Pharmacy department. This may be necessary due to the area outside of Pharmacy providing the equipment required for storing the IMP. It may also be appropriate when a patient is receiving treatment outside of the Pharmacy opening hours, or due to treatment being required immediately (e.g. in the Genito-Urinary Medicine (GUM) clinic or Accident and Emergency department), where the time interval between the diagnosis and IMP administration could be short.

The National Pharmacy Clinical Trials Advisory Group Professional Guidance on Pharmacy Services for Clinical Trials (2013) states that 'where clinical trials take place in a hospital, all IMPs should be stored and dispensed by the hospital pharmacy and managed to the same standards as licensed medicines, in accordance with local medicines management policy. Whenever possible, IMPs should be stored in the pharmacy. However, it may be necessary to store IMPs on wards or in other departments (for example, if IMPs are to be used in emergency situations or for inpatients). If IMPs are to be stored outside of the pharmacy a risk assessment should be performed'. A study-specific SOP should document the requirements to be met to ensure the IMP is stored appropriately. The study-specific SOP should be entitled 'IMP Arrangements for the (insert name of trial) Study'.

The study-specific SOP will ensure that the responsibilities associated with different arrangements to those usually followed are clearly documented and understood by all those involved. The study-specific SOP must be created by the Pharmacy clinical trials team prior to opening the study. This must be authorised by the Clinical Trials Pharmacist and Principal Investigator. For studies sponsored by York Teaching Hospital NHS Foundation Trust, the R&D SOP controller may control the study-specific SOP.

2 Who Should Use This SOP

This procedure should be followed by clinicians authorised to prescribe on clinical trials, research nurses, clinical trial assistants, and all members of the clinical trials team within the Pharmacy Department of York and Scarborough Hospitals, who form part of the York Teaching Hospital NHS Foundation Trust.

3 When this SOP Should be Used

This SOP should be used to create a study-specific SOP, which is to be followed by the research team when IMP is being stored outside of Pharmacy. The SOP will define the responsibilities and tasks that must be completed by the research team, in order to ensure that IMPs are being provided to clinical trial patients in accordance with Good Clinical Practice and section 6 of the York Teaching Hospital NHS Foundation Trust Medicines Code.

Sections of this SOP can be used as a template, and can be copied into the study-specific SOP if appropriate.

4 Procedure(s)

For each clinical trial involving an IMP stored and dispensed outside of Pharmacy, a study-specific SOP should be requested from the R&D SOP Controller. The study-specific SOP will be created by the Pharmacy clinical trials team using R&D/T08, and should cover the following subjects;

- Training
- Storage of IMP
- Temperature monitoring and quarantine procedures
- Order and receipt of IMP
- Transfer of IMP to and from a storage location
- Patient log completion
- Prescribing, dispensing and checking of IMP
- Expiry date checking
- Accountability log completion
- Patient returns
- Pharmacy visit

The study-specific SOP is controlled by the Pharmacy clinical trials team, and will be authorised by the SOP controller, clinical trials Pharmacist and the study Chief/Principal Investigator prior to implementation.

4.1 Training

Pharmacy will provide training in the procedures described in the study-specific SOP to the research team prior to the start of the study. Completion of a Pharmacy Training Record (Pharm/F61) will be required to document that all members of the research team have read and understood the procedures contained within the study-specific SOP.

The Pharmacy clinical trials team will write the Pharmacy Trial Instructions using Pharm/T25 and this will define the responsibilities and tasks to be completed by the Pharmacy clinical trials team. Once authorised, the Pharmacy Trial Instructions will be stored in a trial specific file in the Pharmacy clinical trials dispensary/office.

In accordance with the Training of Pharmacy Personnel SOP (Pharm/S49) and the Pharmacy Trial Assessment and Confirmation of Readiness SOP (Pharm/S41), Pharmacy Confirmation of Readiness (Pharm/T09) will not be issued until all teams involved in supplying the medication have been trained in the trial-specific procedures described in the study-specific SOP.

4.2 Storage of IMP

The proposed area for IMP being stored outside of Pharmacy should be assessed by a clinical trial Senior Pharmacy Technician, Pharmacist or Manager to determine whether it is suitable for the requirements of the trial.

The points described above should be assessed and recorded using Pharm/F89 (assessing an area for Investigational Medicinal Product storage outside of Pharmacy), which will document the proposed storage and temperature monitoring requirements of the IMP. This will involve temperature monitoring the area for a minimum of two weeks to confirm that the storage location remains within the required temperature range. The temperature graphs associated with this monitoring period should be attached to the form.

Consideration should be given as to how the temperature of the storage area will be controlled during the trial. This will involve determining whether or not the area is air conditioned, and how the temperature may change due to seasonal variations.

The suitability of the area and the temperature monitoring arrangements must be discussed and agreed with a member of the research team, and confirmation of the suitability for use should be documented on the form. Once completed, the form should be stored within the trial specific pharmacy trial file.

In accordance with Pharm/S47 (Storage of Clinical Trial Materials and Investigational Medicinal Products), the following information should be documented in the study-specific SOP to describe the storage arrangements of the IMP;

- Required temperature range of the IMP
- Description of where the IMP is stored
- Description of how the area was assessed and deemed acceptable for use
- Description of how to access the storage area (e.g. where are keys located)

4.3 Temperature monitoring and quarantine procedures

Daily temperature monitoring is the responsibility of the research team (or a team delegated the responsibility by the research team). The current temperature, maximum temperature, and minimum temperature must be recorded Monday to Friday (excluding bank holidays) unless otherwise agreed with a member of the Pharmacy clinical trials team prior to the study commencing. The temperature should be recorded using one of the following forms;

Pharm/F36 (Temperature Monitoring Form (Fridge Temperature)) should be used to document fridge monitoring of IMPs requiring storage between 2-8°C.

Pharm/F54 (Temperature Monitoring Form (Ambient Temperature)) should be used to document the monitoring of IMPs requiring storage between 15-25°C (or up to 30°C with prior agreement from the Sponsor).

Pharm/F78 (Temperature Monitoring Form (Frozen Temperature)) should be used to document the monitoring of IMPs requiring frozen storage. The temperature required for the freezer should be agreed prior to storage of IMPs, and Pharm/F78 will need to be completed with the minimum and maximum acceptable temperature range.

The study-specific SOP should state where the IMP is being stored, and the area and frequency of the temperature monitoring required. The Pharmacy clinical trials team will provide the research team with a temperature logger for this purpose.

Pharmacy will visit the storage location of the IMPs at an interval agreed prior to commencing the study, and the agreed frequency will be documented in the study-specific SOP. During this visit, Pharmacy will collect the temperature logger, and produce a graph to show the temperature of the area since the previous Pharmacy visit. The temperature graph should be stored in the Pharmacy clinical trials dispensary, unless otherwise requested by the research team.

The study-specific SOP should advise the research team as to what actions are required should a temperature excursion occur. This will involve contacting the Pharmacy clinical trials team. The affected IMPs should be quarantined to ensure they cannot be used, following SOP Pharm/S59 (Quarantine of IMP). Ensure that Pharm/F42 (Quarantine

notice) and Pharm/F43 (Quarantine log) are also completed. The Pharmacy clinical trials team will seek approval to use the drug from the Sponsor, or arrange a drug shipment as soon as possible.

The study-specific SOP should advise that all forms required for temperature monitoring and quarantining IMP can be found on the York Foundation Trust R&D Unit website www.northyorksresearch.nhs.uk

4.4 Ordering and receipt of the IMP from Pharmacy

IMPs for clinical trials will either be ordered by the Pharmacy clinical trials team, or sent to the Pharmacy department by the Sponsor. All IMPs will be checked upon receipt, and may be transferred to the research team immediately or upon request.

IMPs may be requested by the research team through the use of either a trial-specific prescription or order form. The study-specific SOP should describe who is responsible for ordering stock, and how this is to be done. The SOP should ensure the research team are informed of the documentation they need to accompany their request. This may include a copy of the patient's drug chart, a randomisation fax/email, and a copy of the relevant accountability logs.

Upon receipt of the IMP from Pharmacy, the medication should be promptly taken to the allocated storage area to ensure it cannot be used for patients not involved in the clinical trial. Receipt of the medication must be documented on the appropriate accountability log (either provided by the Sponsor or designed by the Pharmacy clinical trials team), and the study-specific SOP should describe the accountability logs that will require completion, and the information that is required to do so.

Reference should be made to the location for filing the documentation associated with the order. This should be within the Pharmacy trial file, unless otherwise requested by the research team.

4.5 Transfer of IMP to and from a storage location

Refer to section 6.14.3 of the MHRA Good Clinical Practice Guide (2012) for advice regarding site-to-site transfer of IMPs. Consideration should be given to how the IMP will be transferred from Pharmacy to a storage location, and how long the process will take.

As stated in the MHRA Good Clinical Practice Guide (2012), 'if IMP is being transferred between sites for a commercial trial, approval for this activity should be sought from the Sponsor and the QP should have oversight of the procedure for assurance of the quality of the product. If transfer is being conducted for a non-commercial trial, oversight should be managed by appropriate personnel on behalf of the Sponsor (this is generally delegated to Pharmacy).'

The study-specific SOP should describe the use of the following forms to capture the transfer details;

- Transfer of Investigational Medicinal Products from Pharmacy to a storage location outside of Pharmacy (Pharm/F91)

- Transfer of unused Investigational Medicinal Products from a storage location outside of Pharmacy to Pharmacy (Pharm/F92)

- Transfer of patient returned/used Investigational Medicinal Products from a storage location outside of Pharmacy to Pharmacy (Pharm/F93)

The study-specific SOP should describe which accountability logs will need to be completed to reflect receipt of the IMP, and how these should be completed.

4.6 Patient log completion

The study-specific SOP should state who is responsible for completing and maintaining the patient log. This will either be the research team or the Pharmacy clinical trials team. For clinical trials conducted outside of the hospital, it may be necessary for both teams to maintain a patient log, and if so, consideration should be given as to how Pharmacy will be informed of the patient and their details.

The study-specific SOP should describe which team is maintaining the patient log, and what information must be captured. An example of a patient log can be found in the Pharmacy Trial Instructions (Pharm/T25).

4.7 Prescribing, dispensing and checking of IMP

When a patient or subject is recruited into a clinical trial, the IMP should be prescribed by a qualified and registered medical practitioner. The prescriber must be trained on the study, and on the delegation log for the study. Prescribing must comply with section 6 of the York Teaching Hospital NHS Foundation Trust Medicines Code, found on Horizon on the Trust intranet.

Prescribing can occur through the use of a range of prescriptions, such as trial specific prescriptions, hospital outpatient prescriptions, hospital inpatient prescriptions, electronic prescriptions generated by the Sponsor, and electronic prescribing systems.

The study-specific SOP should include a detailed description of how to accurately dispense and check the IMP. This should include a reference to the study drugs involved, what information should be completed on the prescription by the prescriber, how to dispense the IMP, expiry dates, labelling, accountability records, what information should be completed on the prescription by the staff dispensing and checking the medication, and any other tasks specific to the trial. It may be appropriate to follow guidance contained within the Pharmacy Trial Instructions (Pharm/T25) to support completion of the study-specific SOP.

The study-specific SOP should clarify that only delegated members of the research team, who have read the study-specific SOP and have signed the training log, can dispense and check the IMP. A member of the research team should dispense the IMP, and a second qualified person (this does not have to be a member of the research team) should perform a check of the IMP dispensed. This person should be independent of the prescriber and the dispenser.

4.8 Expiry date checks

The research team will perform a check of all IMP expiry dates prior to administration. If any are found to be out of date they should be returned to Pharmacy and accounted for on the appropriate IMP accountability logs. To enable them to do this, the study-specific SOP should clearly state the required expiry according to the patients visit. This may be documented through the use of a table which states the required expiry in accordance to the visit number (if this varies throughout the trial). This may also include 'overage' to allow for the patient clinic visit to be moved if necessary within the protocol mandated study visit windows.

The research team will check the expiry date of all IMP when a new order is received. Any found to be nearing their expiry date will be returned to Pharmacy, and a clinical trial order form or prescription for replacement stock will be completed.

The study-specific SOP should clearly document where the expiry date of the IMP needs to be recorded. This may include the prescription, a patient specific accountability log, or a master drug accountability log.

4.9 Accountability log completion

The research team are responsible for ensuring accurate accountability records are maintained for all IMP being dispensed outside of Pharmacy. These should document the receipt, dispensing and return of medication (as applicable to the trial). This may involve the completion of a patient specific accountability log, ward accountability log, and/or a master accountability log. Accountability logs will either be provided by the Sponsor, or created by the Pharmacy clinical trials team.

The study-specific SOP should describe which accountability logs must be completed, and the information they should be completed with. The SOP should state how accountability logs should be completed for the patient's initial dispensing episode and for every subsequent episode (if this differs).

Compliance will be monitored by the Pharmacy clinical trials team by either requesting a copy of all accountability logs following every dose or before providing any further IMP upon receipt of a request, or by visiting the area the IMP is stored in and monitoring the documentation at a frequency agreed by the research team and Pharmacy clinical trials team.

4.10 Patient returns

For clinical trials occurring within the hospital, the returned medication/empty containers should be returned to Pharmacy for accountability purposes if requested by the Sponsor. The study-specific SOP should describe this, and if the medication cannot be returned to Pharmacy immediately, the IMP should be stored in a dedicated, locked cupboard. The area should be clearly marked as for patient returns, and should be kept separate from unused IMP available for dispensing.

For clinical trials occurring outside of the hospital, the returned medication/empty containers should be stored in a dedicated, locked cupboard. The area should be marked as for patient returns, and should be kept separate from unused IMP available for dispensing. A member of the Pharmacy clinical trials team will bring returned medication/empty containers to Pharmacy during the planned Pharmacy visit. This should be documented through the use of Pharm/F93 (Transfer of patient returned/used IMP from a storage location outside of Pharmacy to Pharmacy).

If the Sponsor has confirmed that the IMP does not need to be returned to Pharmacy, the study-specific SOP should document how the research team should dispose of the IMP, and how this should be documented.

4.11 Pharmacy visit

For clinical trials that are conducted outside of the hospital, Pharmacy must liaise with the research team to discuss how frequently a member of the Pharmacy clinical trials team will visit the research team to ensure the study-specific SOP is being followed and all associated documentation has been maintained. The frequency of the visit should be decided before the study begins.

The following tasks may be required to be completed by the Pharmacy;

- Collection and downloading of the temperature logger
- Check of the expiry date of the IMP
- Collect and return patient returned medication/empty bottles to Pharmacy
- Confirm that the master drug accountability logs and patient specific accountability records are accurate (or complete if required)
- Check the quality of completion of patient prescriptions
- Any other tasks deemed necessary to maintain the trial

The study-specific SOP should document the frequency with which the Pharmacy team will visit the research team, and what activities will be conducted during the visit. If the research team are required to perform

any tasks prior to the Pharmacy visit, the study-specific SOP should describe the activities.

Pharm/F97 (Pharmacy Monitoring Form) should be completed for each planned visit. A copy of this should be sent to the research team, and the original stored in the monitoring section of the pharmacy file. It is the responsibility of each team to ensure that their actions raised are completed in a timely manner.

5 Related SOPs and Documents

York Teaching Hospital NHS Foundation Trust Medicines Code

The MHRA Good Clinical Practice Guide (2012)

National Pharmacy Clinical Trials Advisory Group (NPCTAG) Professional Guidance on Pharmacy Services for Clinical Trials (version 1.0, October 2013)

Pharm/F97	Pharmacy Monitoring Form
Pharm/F61	Pharmacy Training Record
Pharm/S59	Quarantine of IMP
Pharm/F42	Quarantine notice
Pharm/F43	Quarantine log
R&D/T08	Study-Specific SOP Template
Pharm/F36	Temperature Monitoring Form (Fridge Temperature)
Pharm/F54	Temperature Monitoring Form (Ambient Temperature)
Pharm/F78	Temperature Monitoring Form (Frozen Temperature)
Pharm/T25	Pharmacy Trial Instructions
Pharm/S49	Training of Pharmacy Personnel
Pharm/T09	Pharmacy Confirmation of Readiness
Pharm/S41	Pharmacy Trial Assessment and Confirmation of Readiness
Pharm/F89	Assessing an area for Investigational Medicinal Product storage outside of Pharmacy
Pharm/S47	Storage of Clinical Trial Supplies
Pharm/F91	Transfer of IMP from Pharmacy to a storage location outside of Pharmacy
Pharm/F92	Transfer of unused IMP from a storage location outside of Pharmacy to Pharmacy
Pharm/F93	Transfer of patient returned/used IMP from a storage location outside of Pharmacy to Pharmacy