

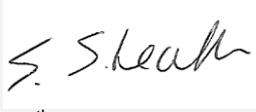
Storage and dispensing of Investigational Medicinal Products outside of Pharmacy

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This SOP will normally be reviewed every 3 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	12 th September 2013
2.0	12 th April 2015	
3.0	20 th December 2019	Change of author, Change of link to R&D website. Updated to include supporting documentation, removed repeated sections, updated to reflect current practice. Made reference throughout to adapt SOPs/documentation based on the individual needs of a trial. Expiry dates will be checked as part of pharmacy monitoring visits. Monitoring visits changed to once a month. Pharm/F91 has been adapted so that Pharm/F92 and Pharm/F93 can be made obsolete. Added in section about storage at Scarborough site.

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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). The area should be assessed and a study-specific SOP or suitable documentation should be produced to ensure all requirements are met to ensure the IMP is stored appropriately.

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 pharmacy clinical trials team within the Pharmacy Department of York Teaching Hospital NHS Foundation Trust.

3 When this SOP Should be Used

This SOP should be used to create a study-specific SOP or documentation, 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.

4 Procedure(s)

For each clinical trial involving an IMP stored and dispensed outside of Pharmacy, a study-specific SOP/documentation should be created. This will be created by the Pharmacy clinical trials team using a similar lay out

to R&D/T08; however sections should be altered to ensure relevance. The SOP may need to cover the following subjects depending on the requirements for the trial;

- 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
- Preparation of IMP

The study-specific SOP is controlled by the Pharmacy clinical trials team, and will be approved by the Pharmacist overseeing the pharmacy clinical service. The most current version will be stored in the pharmacy site file, and additional copies will be created for other storage locations, e.g. in a file on the ward near where the IMP is kept. If changes need to be made to the study-specific SOP then all copies must be updated and old copies superseded and all parties using the study-specific SOP informed/trained on the changes.

Other documentation may also be needed to support the storage of IMP outside of pharmacy. This may present in the form of a poster, picture instructions of how to use a temperature devices or checklists for cupboard/fridge doors that bullet point a clear and quick accurate guide. These can be created as needed and designed specifically for the use in an individual trial. Ensure a version control is added to any documents used and copies updated when required.

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.

Sponsors may want to be sent the study-specific SOP prior to opening to approve the process. Check with the sponsor if this is required.

Pharmacy Confirmation of Readiness/ Green light will not be issued until all individuals involved in the supply and issue of 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 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. If for any reason the two weeks of monitoring cannot take place due to the impending opening of the trial then seek confirmation from the sponsor if they will be happy to have the IMP stored in the location with a reduced temperature monitoring period.

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 or has good air flow, 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 site file.

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 form;

Pharm/F108 – Daily Clinical Trials Temperature Checks

This should be used to document the specific temperature monitoring requirements for the products used in the trial.

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 unless the sponsor has provided their own temperature monitoring device.

A member of the pharmacy clinical trials team will visit the storage location of the IMPs approximately once a month, this might be more frequent if additional support is needed. During this visit, Pharmacy will collect or download the temperature logger, and produce a graph to show the temperature of the area since the previous pharmacy monitoring visit. The temperature graph should be stored in the study specific pharmacy site file. The logger should be replaced or reset.

The study-specific SOP will 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 and communicated with the relevant parties. The Pharmacy clinical trials team will seek approval to use the drug from the Sponsor, or arrange a drug shipment as soon as possible.

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. If required the receipt of the medication should 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.

Pharmacy may also have an accountability log; this will need updating with the transactions of receiving and moving IMP.

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

4.5 Transfer of IMP to and from a storage location

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 use of the following form should be when transferring IMP between two locations one of which is outside of pharmacy; Pharm/F91 – Transfer of IMP between Pharmacy clinical trials and a storage location outside of Pharmacy clinical trials

Accountability logs will need to be completed to reflect sending and receipt of the IMP.

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.

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 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 in relation to the requirements of the study. This may 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. Each study will have their specific requirements so this should be tailored to suit the needs of the study.

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. Common practice would be for 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. However this will need to be in consideration of how the trial will operate in practice and the needs of the study. Adapt the procedures in conjunction with Trust guidance and trial specific protocol.

4.8 Expiry date checks

The research team will perform a check of all IMP expiry dates prior to administration or giving out IMP in line with standard practice. If any are found to be out of date they should be returned to Pharmacy and accounted for on the appropriate IMP accountability logs.

During pharmacy monitoring visits the expiry of all stock should be checked. If expired or damaged the stock should be and returned to pharmacy and seek further instruction from the sponsor to destroy. Return IMP to pharmacy using Pharm/F91 – Transfer of IMP between Pharmacy clinical trials and a storage location outside of Pharmacy clinical trials.

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.

This process should be tailored to suit the requirements of the specific study.

An accountability log may also be maintained in the trials specific pharmacy site file.

4.10 Returns

Medication that needs to be returned to pharmacy or empty containers should be stored in a dedicated, locked cupboard, and should be kept separate from unused IMP available for dispensing. A member of the Pharmacy clinical trials team will bring/or arrange suitable transport for the returned medication/empty containers to Pharmacy during a planned Pharmacy monitoring visit.

If the IMP is to be returned from a location within the main hospital sites (York or Scarborough sites) then the returned medication/empty containers can also be brought direct to pharmacy clinical trials for storing by a member of the research team.

For stock kept outside of the main hospital sites (York or Scarborough sites) this should be documented through the use of Pharm/F91 – Transfer of IMP between Pharmacy clinical trials and a storage location outside of Pharmacy clinical trials and suitable transportation of the IMP back to pharmacy arranged.

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

A member of the pharmacy clinical trials team will visit a storage location outside of the pharmacy department approximately once a month. This might need to be increased in frequency if support is needed.

The following tasks may be required to be completed by a member of the pharmacy clinical trials team during a monitoring visit, however each study will have different requirements so adapt what is needed to be monitored as study requirements dictates;

- Collect or reset the temperature logger and download the temperature data and save accordingly.
- 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 (if required)
- Any other tasks deemed necessary to maintain the trial

The study-specific SOP will document what activities will be conducted during the monitoring 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/T53 – Trial Specific Pharmacy Monitoring Visit Form Template should be created by adapting the criteria required to be checked during a pharmacy monitoring visit depending on the requirements of the individual trial.

Once the form has been completed and approved (by completing the version control on the bottom of the form). It can be used each time the location is monitored. Once forms are completed these need to be stored in the monitoring section of the trials specific pharmacy site file. It is the responsibility of each team to ensure that their actions raised are completed in a timely manner.

4.12 Storage of IMP at the Scarborough site

The Scarborough pharmacy is used as a pick up point for prescriptions that have been dispensed on the York site where the pharmacy clinical trials team is based.

Dispensed IMP is packaged and sent on routine hospital transport and received into the pharmacy stores at the Scarborough site. It is sent in a secure transportation bag and sent with a temperature logger which is checked on arrival. Pharm/F84 - Transporting IMP between York and Scarborough Sites Form should be used to track the movement of the IMP between sites. As each Scarborough based study will have direct requirements on how its IMP needs to be transported refer to the pharmacy site file of the study for details on how to package and send the dispensed IMP.

The dispensed IMP will then be stored in a designated temperature controlled location within pharmacy at Scarborough. Temperatures are checked remotely on a daily basis (Monday to Friday (excluding bank holidays) with the routine temperature checks conducted by the pharmacy clinical trials team.

The research nurses collected the medication from the Scarborough pharmacy and complete the relevant sections on the accompanying paper work before handing out to the patient.

A member of the pharmacy clinical trials team will visit Scarborough when required to send patient returns back to the York site for processing. This should be done by packaging the returns in a secure transportation box and placing on the next available transport to York. No temperature device will be needed unless started by the sponsor.

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/T53	Trial Specific Pharmacy Monitoring Visit Form Template
Pharm/F61	Pharmacy Training Record
R&D/T08	Study-Specific SOP Template
Pharm/F89	Assessing an area for Investigational Medicinal Product storage outside of Pharmacy
Pharm/F91	Pharm/F91 – Transfer of IMP between Pharmacy clinical trials and a storage location outside of Pharmacy clinical trials
Pharm/F108	Daily Clinical Trials Temperature Checks
Pharm/F84	Transporting IMP between York and Scarborough Sites