DIVISION OF RESEARCH AND INNOVATION

Clinical Research Facility

Document Number: GOSH/ICH/SOP/CRF/001	Version Number: 03
Title: Ordering, Storage and Administration Of Medicines In The CRF	
Effective Date:	30-Jun-2021

	Name	Position
Authored by:	Rebecca Norton	QA/R&D Officer
Approved by:	Lorraine Hodsdon	Head of Nursing & Patient Experience Research & Innovation

1. Scope

This SOP describes the process for the storage and administration of medicinal products, including advance therapies, Investigational Medicinal Products (IMPs) and controlled drugs (CDs), in the Clinical Research Facility (CRF). IMPs may include Advanced Therapy Investigational Medicinal Products (ATIMPs).

This SOP applies to all staff that are required to order, store and/or administer medicinal products in the CRF.

2. Purpose

The purpose of this SOP is to outline the process for:

- The safe and secure storage and handling of medicinal products in the CRF.
- The administration and checking of medicinal products in the CRF.

3. Definitions/Abbreviations

- Advanced Therapy medicinal products: Medicines for human use that are based on genes, tissues or cells.
- Controlled Drugs: medicines controlled in Schedules 2 and 3 of the Misuse of Drugs Act 1971 and Regulations made under the Act. Potassium injections (NPSA, 2002), strong Sodium Chloride injection and Sildenafil are also treated as controlled drugs.
- Investigational Medicinal Products (IMP): a licensed or unlicensed medicinal product or matching placebo, which is being tested or referenced in a clinical trial involving human subjects.
- Temperature excursion: The storage temperature as measured by the CRF temperature monitoring system is outside the allowed range for longer than 15 minutes, or there is a fault with the monitoring system that means such an event cannot be ruled out. The British Pharmacopoeia defines ambient allowed range as 15°C - 25°C, and refrigerated allowed range as 2°C - 8°C.

4. Responsibilities

Duties may be delegated but the responsibility always remains with those listed.

4.1 CRF Sister(s) are responsible for:

- The safe and secure storage and handling of medicinal products in the CRF. This includes controlling access to medicinal products and the maintenance of controlled drug records.
- Ordering medicines from pharmacy to maintain ward stocks and to meet the needs of individual patients (with the ward pharmacist).
- Ensuring compliance with medicine policies, procedures and guidelines.

4.2 Nurse in Charge is responsible for:

- The day to day safe and secure storage and handling of medicinal products in the CRF and overall responsibility in the absence of the CRF sister(s). This includes controlling access to medicines, the maintenance of controlled drug records and the ordering of medicines from pharmacy.

- Responding to temperature alarms during CRF working hours.

- Checking the Connected Automated Monitoring + formally known as Tutela system for unacknowledged temperature alarms when the CRF opens or prior to the first participant dosing for that day, whichever is earlier.

- Ensuring compliance with medicine policies, procedures and guidelines.

4.3 CRF Pharmacist is responsible for:

- Monitoring the ordering and storage of medicinal products on the CRF.

- Ordering medicines from pharmacy to maintain ward stocks and for individual patients (with the CRF sister/Nurse in Charge). They are responsible for ensuring that this is done by an authorised person.

- Assessing if quarantined stock is safe to use following a temperature excursion and notifying the relevant study Sponsor(s), PI(s) and lead research nurse(s) if IMP is impacted by a temperature excursion.

- Monitoring prescriptions and ensuring prescribers and those administering medicines follow the appropriate guidelines.

- Advising in the event of any query regarding medicinal products.

4.4 All staff who are required to order, store and administer medicinal products in the CRF are responsible for:

- Ensuring their practice meets the requirements of this SOP and the Medicine Management – Code of Practice policies found on the GOSH web.
- Responding to temperature monitoring alarms in accordance with this SOP.

5. Procedure

5.1 Medicinal Product Storage

The Trust Medicines Ordering and Storage Policy must be followed.

All medicinal products must be stored in their original packaging and in accordance with the product information (i.e. the Summary of Product Characteristics (SmPC), Investigator's Brochure (IB), product label or similar).

Medicinal products (including IMPs and controlled drugs) used in the CRF must be kept in the Treatment Room (room M1023) cupboards or refrigerator when not in use. Access to the treatment room is by swipe proximity reader only.

Access to the treatment room is restricted to clinical professional staff and a limited number of none clinical staff where access to specified rooms on wards are essential to their work. A list of staff that have access will be kept by the nurse in charge.

The Nurse in Charge may delegate the holding of the Drug Keys and/or Controlled Drugs (CD) Keys to an authorised person when holding the keys personally would cause delays or difficulties in making medicines available. The person responsible for a key must know its whereabouts at all times. Best practice is to return the key to the Nurse in Charge as soon as possible.

Refrigerators and cupboards designated for the storage of medicinal products must be used solely for this purpose.

The air conditioning unit in the Treatment Room must be set to keep the room temperature between 15°C-25°C.

Generally, IMPs are to be stored in the Pharmacy Clinical Trials Office (within the Pharmacy Dispensary) and managed by the Trust Pharmacy Clinical Trials team. In extenuating circumstances, IMPs may be stored in the CRF (e.g. if required for an

early study visit). IMPs must be stored separately from other medicinal products in the designated IMP areas.

- IMP Ambient area – Cupboards 9 or 10
- IMP Refrigerated area – Refrigerator top shelf

The storage temperatures must be monitored (see section 5.2).

The 'IMP STORAGE LOG - Clinical Research Facility (CRF) Treatment Room' must be completed for all IMP stored in the CRF Treatment Room (including returns).

For storage of controlled drugs, see section 5.5.

Emergency medicines are to be stored in the Clinical Emergency Trolley (in accordance with Trust Medicines, Ordering and Storage Policy and Trust Resuscitation Policy).

5.2 Temperature Monitoring

The ambient storage allowed temperature range is 15°C - 25°C and the refrigerated storage allowed temperature range is 2°C - 8°C (in accordance with Procedure for Monitoring Refrigerator and Freezer Temperatures in Wards, Theatres and Outpatient Departments Policy).

The Connected Automated Monitoring + Wireless Monitoring System is used for monitoring the temperature of storage areas in the Treatment Room. The system will alarm and automatically contact key personnel if the storage temperature goes outside of the allowed range or a problem is detected.

Connected Automated Monitoring + is accessed through the GOSH Homepage , using 'Client Login' and entering a user name (Trust email address) and password.

The Connected Automated Monitoring + system is the source data for temperature records in the CRF. Temperature records should only be printed in exceptional circumstances and after discussion with the CRF QA Manager.

Connected Automated Monitoring + temperature records can be viewed in blocks of up to 60 days. Records will be accessible on the live system for 5 years. Older records are archived and can be accessed by contacting Connected Automated Monitoring + Support.

Records from the previous temperature monitoring system Comark are accessible through Q-Pulse.

5.3 Responding To A Temperature Monitoring Alarm When The CRF Is Open

In the event of an alarm, Connected Automated Monitoring + will call each contact on the cascade until a call is answered. If no calls are answered, an 'unable to contact' email will be sent to the CRF QA Manager, Operations Manager, Assistant Operations Manager, Head of Nursing Clinical Research, Research Matron and QA/CT CRF Pharmacist. The person who receives the alarm call must give their name and this will be recorded on the Connected Automated Monitoring + system. The person who receives the call is responsible for responding to the alarm and ensuring it is resolved.

If a Connected Automated Monitoring + alarm is received, report this immediately to the Nurse in Charge. The Nurse in Charge (or delegate) must take the following actions (unless the reason for alarm is clear):

5.3.1 Review the Connected Automated Monitoring + system to determine the nature of the alarm.

5.3.2 Check the temperature controlled environment is functioning properly and that any doors are closed firmly.

If the temperature controlled environment returns to a normal range as a result of closing the door, acknowledge the alarm and complete the alarm report as soon as possible. In line with Medicines Management – Operational Medicines Policy that can be found on the GOSH web, the responsibility of signing off the alarm report lies with the nursing team, this should be completed by the nurse in charge but may be reviewed by the QA/CT CRF Pharmacist(s) if necessary.

5.3.3 If the door is closed, check the positioning of the probe inside the fixture to determine whether the temperature alert has occurred as a result of items being placed on top of the probe or whether the probe has been pushed towards the side-wall.

If the probe does appear to be out of positon, re-locate it so that it can measure the temperature of the air in the fixture.

If the temperature controlled environment returns to a normal range as a result or moving the probe, acknowledge the alarm and complete the alarm report as soon as possible. The alarm report must be signed off by the nurse in charge but may be reviewed by the QA/CT

5.3.4 If the temperature recorded appears to be improbable (e.g. -80°C) this indicates that the temperature monitoring probe has become detached from the transmitter. Check the connection between the probe and the transmitter, ensuring this is intact.

Re-attach the probe if necessary.

If the temperature controlled environment returns to a normal range as a result or re-attaching the probe, acknowledge the alarm and complete the alarm report as soon as possible. The alarm report must be signed off by the nurse in charge but may be reviewed by the QA/CT
In the event of a temperature excursion (i.e. temperature is outside the allowed range for longer than 15 minutes or there is a fault with the monitoring system that means such an event cannot be ruled out):

5.3.5 CRF Nurse in Charge must be informed and a Treatment Room Temperature Excursion Form must be initiated.

5.3.6 The affected fixture must be kept closed and the CRF Nurse in Charge (or delegate) must immediately label impacted stock as quarantined. The label must read: **'Quarantined – stock not to be used'**

The quarantine time must be recorded on the 'Treatment Room Temperature Excursion Form'.

The quarantine must cover all stock in the affected storage area, e.g. if there is an ambient storage temperature excursion, all ambient medicinal products must be quarantined (including ward stock, IMP and CDs).

Quarantined stock must not be used. If stock is needed imminently, the CRF Nurse in Charge should discuss ordering replacement stock with the CRF Pharmacist.

5.3.7 The CRF Pharmacist must be informed as soon as possible.

The time the CRF Pharmacist was informed must be recorded on the 'Treatment Room Temperature Excursion Form'.

5.3.8 Once the event is resolved, the CRF Pharmacist must assess if the quarantined stock is safe to use or not. This should include a review of the relevant temperature records on the Connected Automated Monitoring + system and may include discussion with the manufacturer.

If stock is safe to use, it should be removed from quarantine. Stock that is not safe to use must be returned to pharmacy for appropriate disposal.

The decision must be recorded on the 'Treatment Room Temperature Excursion Form'.

5.3.9 If IMP is impacted, the CRF pharmacist must notify the relevant study Sponsor(s), PI(s) and lead research nurse(s) as per the Pharmacy Technical Services process.

5.3.10 All actions taken must be recorded on the 'Treatment Room Temperature Excursion Form' by the CRF Nurse in Charge (or delegate) and CRF Pharmacist.

A Datix incident form must be completed. The completed Temperature Excursion Form should be scanned and uploaded to the Datix and a copy filed on Q-Pulse.

5.3.11 Once the temperature controlled environment returns to a normal range, acknowledge the alarm and complete the alarm report as soon as possible. The alarm report must be signed off by the nurse in charge but may be reviewed by the QA/CT CRF Pharmacist.

Refer to the Medicines Management – Code of Practise for supply, storage and disposal of medicines on the GOSH Intranet.

1.1 Responding To A Temperature Monitoring Alarm When The CRF Is Closed

If a temperature alarm occurs when the CRF is closed, it will not be reviewed until the CRF opens. The CRF Nurse in Charge should check the Connected Automated Monitoring + system for unacknowledged temperature alarms when the CRF opens and prior to any patient dosing. If there is an alarm, the steps outlined in 5.3 should be followed IMMEDIATELY.

1.2 Controlled Drugs (CDs)

Controlled drugs must be ordered, received, stored, and monitored in accordance with the Trust Medicines Management – Code of Practise for supply, storage and disposal of medicines on the GOSH Intranet Policy.

The Controlled Drugs cupboard (CDC) is in the Treatment Room. The light on the front of the CDC is green when it is locked. When the CDC is unlocked, the light on the front of the cupboard turns red, a red light will appear in the corridor outside of the Treatment Room door, and the warning notice 'CDC open: M1023' will be displayed on the control panels in the Nurses Office and at Reception.

The CD cupboard may only be opened by a person who may lawfully be in possession of controlled drugs, e.g. a pharmacist or registered person in charge, or a person working under their authority.

CDs must never be left unattended nor the CD cupboard left unlocked.

The stock of controlled drugs must be formally checked:

- At least once a day by two registered nurses.
- Weekly to confirm the exact measured volume of liquid medicines.
- Three monthly by the CRF Pharmacist with the Nurse in Charge

The checks must be done in in accordance with the Medicines Management - Code of Practice for controlled drugs Policy that can be found on the Trust Website and recorded in the back of the Controlled Drug Register.

Controlled drugs must be administered in accordance with the Trust Medicines Administration Policy.

1.3 Products that Involve Genetically Modified Organisms (GMO)

In accordance with the Health and Safety Executive SACGM Compendium of guidance (Part 6: Guidance on the use of genetically modified microorganisms in a clinical setting); a risk assessment must be carried out for all activities involving GMO products, and the approval of the Local GOSH Genetically Modified Organism Safety Committee (GMOSC) and the UCL/UCLH/RFH Genetic Modification Safety Committee (GMSC) obtained in advance of the work commencing. Those completing this risk assessment should be familiar with the Trusts' Policies and the legal requirements.

1.4 Administration of Medicinal Products

The Medicines Management - Code of Practice for Administration of Medicines Policy must be followed.

All medicines must be administered according to the relevant guidelines and policies, including the latest clinical study protocol and risk assessment (if applicable).

All medicines require independent double checking of all the prescription, preparation and administration checks. The required checks are listed in the Trust Medicines Administration Policy.

In addition to the checks listed in the Trusts Medicines Management - Code of Practice for Administration of Medicines Policy, the following information must be independently double checked:

a) Centre and subject numbers

b) Visit number and schedule of events (in current version of the study protocol)

c) Protocol identifier – a minimum of two of these are required (e.g. R&D number, study number/ name/ EudraCT number)

It must not be assumed that the dose is correct because it has been administered by other staff before and/or the drug has been signed as being checked by a pharmacist.

If the person who will be administering the drug has any query however small they must check with the prescriber, the study protocol, the risk assessment (if applicable) and/or pharmacy as necessary before administration.

Medicine administration must be recorded in accordance with the Trust Medicines Administration Policy and any study specific requirements. Every patient receiving an IMP have an anaphylaxis kit prescribed and the kit present in the patient's room.

IMP should be given in normal working hours with adequate medical cover on site. If dosing is expected to occur after 4pm the Nurse in Charge, Research Sister, Research Matrons and PI should be informed with a plan made and appropriate medical and nursing cover ensured with an escalation plan in place.

1.5 Medicinal Products Brought Into Hospital By Participants/Carers

The participant/carer must be asked what, if any, medicinal products they have brought with them to the CRF during the study visit.
Medicinal products brought into GOSH by a participant/carer must not be used until assessed as suitable for use by the CRF Pharmacist (or a registered nurse if the pharmacist is unavailable). The medicinal product must be assessed in accordance with the Trust Medicines, Ordering and Storage Policy.

Once assessed as suitable for use, the medicinal products can be used in accordance with the Trust Medicines Administration by Patients and Carers Policy.

1.6 Waste Disposal and Cleaning

The Trust Medicines Administration Policy, the study protocol and risk assessment (if applicable) must be followed.

Any unused or patient returned IMP must be returned to the Trust Clinical Trials Pharmacy Department at the end of the shift. This is essential for the purpose of IMP accountability.

Medicinal products or the majority of CDs that are no longer required must be given to Pharmacy for disposal in accordance with Medicines Management - Code of practice for supply, storage and disposal of medicines Policy.
CDs that must be disposed of in the treatment room if they are; Part used CD doses, broken or damaged individual doses, dropped solid dosage forms (i.e. tablets/capsules / suppositories/ pessaries), doses prepared but not administered, wastage from prepared doses and discontinued infusions or PCA syringes.

There must be disposed of promptly in a yellow lidded sharps container and be destroyed with a superabsorbent sachet or denaturing kit so that the drug is denatured or rendered unfit for use.
All destruction of CDs **must** be witnessed and signed in the appropriate CD record book.

All waste, including sharps, must be disposed of according to the Trust Waste Management Policy, Code of Practice for CDs, the study protocol and risk assessment (if applicable).

2. Recalls

Pharmacy will organise the recall of medicinal products in the time frame designated by MHRA (as per the Trust Medicines Administration Policy). If CRF staff become aware of a product recall (e.g. from a study Sponsor) they should inform the CRF Pharmacist to ensure pharmacy are aware.

If CRF staff become aware of a medical device alert/recall, they should inform Trust Patient Safety.

2.1 Samples Of Medicinal Products Or Devices

Samples of medicinal products or devices must not be accepted by the CRF. Representatives wishing to leave samples must be referred to the CRF Pharmacist.

2.2 CRF Closure and Drug Keys (Including Overnight, Weekends and Bank Holidays)

Ordinarily; if the CRF is to close for two or more days (including weekends and bank holidays), all IMPs and Controlled Drugs must be returned to Pharmacy prior to closure.

In extenuating circumstances; IMPs or Controlled Drugs may, with the agreement of the CRF Pharmacist and the CRF Sister(s), stay in the CRF provided there is adequate security to prevent unauthorised access to the Treatment Room.

When the CRF is closed (including overnight), the Drugs Keys and the Controlled Drug Cupboard Keys must be locked in the key safe in the CRF Office (M1008). The key (numbered 110) to the key safe must then be given to Trust security.

3. Related Documents

- GOSH/ICH/~~FRM/CRF/001: IMP Storage Log~~
- GOSH/ICH/FRM/CRF/002: Treatment Room Temperature Excursion Form

- Medicines Management - Code of practice for supply, storage and disposal of medicines Policy
- Medicines Management - Code of practice for CDs

- Procedure for Monitoring Refrigerator and Freezer Temperatures in Wards, Theatres and Outpatient Departments. Refrigerator and Freezer Temperature Monitoring for Wards and Outpatient Departments Policy
- Medicines Management - Code of Practice for Administration of medicines Policy

- Trust Resuscitation Policy

- Medicines Administration by Patients and Carers Policy

- Trust Waste Management Policy

4. References

NA