Management and Accountability of Investigational Medicinal Products in the King’s Clinical Research Facility

Document Detail

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<td>Related documents</td>
<td>KCH Medicines Management Policy</td>
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Change History

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<tr>
<td>23rd December 2013</td>
<td>1. Amended text in SOP title from “Clinical Research Facilities” to “King’s Clinical Research Facility”</td>
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<td>2. Amended name of Director to reflect new Director</td>
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<td>6. Removed reference to SOP for Controlled Drugs and Substances- SOP now obsolete</td>
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1.0 Background

1.1 An ‘investigational medicinal product’ (IMP) is defined as:

A pharmaceutical form of an active substance or placebo being tested, or to be tested, or used, or to be used, as a reference in a Clinical Trial, and includes a medicinal product which has a marketing authorisation but is, for the purposes of the trial -

a) used or assembled (formulated or packaged) in a way different from the form of the product authorised under the authorisation,

b) used for an indication not included in the summary of product characteristics under the authorisation for that product, or

c) used to gain further information about the form of that product as authorised under the authorisation. (Clinical Trials Toolkit)

1.2 Current clinical trial legislation details the requirements for the manufacture and importation of IMPs. Under the legislation, clinical trials involving IMPs (CTIMPs) require the IMP to be manufactured according to Good Manufacturing Practice (GMP) and Good Clinical Practice (GCP) should also be adhered to.

1.3 All protocols for CTIMPs should detail the IMP requirements, including a description of the trial treatment, provision of the IMP, labelling, packaging, storage, dispensing, accountability, route of administration, the dosing regimen and any risks and related safety assessments.
2.0 Purpose

2.1 This Standard Operating Procedure (SOP) describes the procedures in place for the management and accountability of IMP for trials conducted within the King’s Clinical Research Facility (CRF).

3.0 Scope

3.1 This SOP applies to all CRF core staff and users of the CRF who are involved in the management, handling and accountability of IMP within the CRF.

3.2 The CRF encompasses the Clinical Trials Facility (CTF), the Experimental Medicine Facility (EMF) and the Cell Therapy Unit (CTU). CRF SOPs will apply to the CTF and EMF only and staff working in those areas should work to all relevant CRF SOPs. The CTU will continue to control and use their own policies and SOPs to ensure compliance with Good Manufacturing Practice (GMP).

3.3 This SOP focuses on IMP activities which may be undertaken for CTIMPs within the King’s CRF and is not an exhaustive operating procedure on all aspects concerning IMPs in clinical trials.

3.4 This SOP will not cover in depth the dispensing of IMPs or pharmacy accountability of IMPs, as these processes fall under the remit of the specific Trust pharmacy departments involved in the trial.

4.0 Responsibilities

4.1 It is the responsibility of the trial Sponsor to have procedures in place to ensure that the manufacturing, packaging, labelling, releasing, and distributing of the IMP is conducted according to the principles of Good Manufacturing Practice (GMP) and Good Clinical Practice (GCP), delegating specific responsibilities accordingly.

4.2 It is the responsibility of the relevant local Trust pharmacy, either King’s College Hospital (KCH) or South London and the Maudsley Hospital (SLaM), unless delegated to another department/pharmacy, to be responsible for the receipt, storage, accountability, management, return and destruction of IMPs, in accordance with the trial protocol and Sponsor requirements.
4.3 Responsibility for IMP storage, administration, accountability (and also possibly receipt and/or destruction) may be delegated to the CRF for a particular trial. CRF staff listed on a specific trial’s Delegation Log as having responsibility for any of these procedures are responsible for managing them appropriately, ensuring that all procedures are conducted in accordance with the trial protocol and Sponsor requirements.

4.4 The relevant local Trust pharmacy and the CRF Manager, or appropriate delegate, are responsible for reviewing and agreeing the procedure for the dispensing of the IMP to the CRF research nursing staff prior to commencement of the trial.

5.0 Procedure

5.1 IMP Distribution and Receipt

5.1.1 When all the required regulatory and local approvals and documentation is in place for the local site, and usually after the site initiation visit (SIV) has been conducted, the IMP will normally be released by the Sponsor of the study to the relevant local Trust pharmacy.

5.1.2 The Senior Clinical Trials Pharmacist from the relevant local Trust pharmacy will be responsible for managing and documenting the receipt of the IMP, code envelopes and randomisation lists, as well as for the storage, dispensing, return and destruction of the IMP for the duration of the study, as agreed with the Sponsor or delegate.

5.1.3 The Sponsor or delegate should ensure that written procedures are provided to the relevant local Trust pharmacy and CRF which document the procedures for the handling and storage of the IMP and include adequate documentation. The procedures should address receipt, handling, storage, dispensing, recall, unblinding, expiry date extensions, temperature excursions, retrieval of unused product from trial subjects, and return of any unused IMP to the relevant local Trust pharmacy (or alternative disposition if authorised by the Sponsor and in compliance with the applicable regulatory requirements).

5.2 Dispensing of IMP to CRF Staff

5.2.1 If possible, the IMP should remain in the relevant local Trust pharmacy until the day of administration to the trial participant. However, if required by the trial protocol, or if the IMP is to be administered out of normal pharmacy
working hours, an IMP for a trial subject may be dispensed by the relevant local Trust pharmacy to CRF research nursing staff after obtaining the prescription from the Chief Investigator (CI) / Principal Investigator (PI). It must then be stored securely within the CRF until administered. The normal working hours of the KCH and SLaM pharmacies are 09.00-17.30hrs, Monday-Friday.

5.2.2 Upon receipt of a trial subject’s IMP, the CRF research nurse must carefully check that all details on the IMP packaging match that of the prescription (trial ID, dosage, formulation etc). Expiry dates should also be double checked. Where possible, this should also be checked by a second member of clinical staff.

5.2.3 Dispensing of any IMP which meets the definition of a controlled drug or substance should comply with the KCH Controlled Drugs Policy.

5.2.4 All drug dispensing procedures should comply with the KCH Medicines Management Policy.

5.3 IMP storage within the CRF

5.3.1 IMPs will be stored within pharmacy until as near to dosing of study subjects as possible, unless agreed with pharmacy, the Sponsor and the CRF that an IMP can be stored within the CRF.

5.3.2 If IMP is to be stored within the CRF for a specified time period prior to dosing, it must be stored in a secure location appropriate for the defined storage conditions (fridge, freezer or appropriate drug cupboard) which is accessible only to CRF nursing staff and/or appropriate CRF users.

5.3.3 The temperatures of all CRF fridges and freezers are monitored and recorded 24 hours a day (see CRF-QA-SOP-11: The Tutela Temperature Monitoring System in the King’s CRF), to ensure that IMPs are stored within the parameters detailed in the trial protocol and the Summary of Product Characteristics (SmPC) or Investigator’s Brochure (IB).

5.3.4 If temperature parameters are breached, this must be documented and reported to the CI/PI, Sponsor and pharmacy as soon as possible, and the affected stock quarantined immediately until further instruction is provided by
pharmacy and the Sponsor. All quarantined IMP should be labelled clearly as QUARANTINED STOCK and stored in a separate area from any remaining stock. It can be returned to pharmacy if required.

5.3.5 IMPs which are logged in and out of CRF storage locations (eg: drug cupboard, fridge) must be documented using CRF-STU-FRM-1: IMP Storage Accountability Log, unless another form is provided by the Sponsor in which case this form should be used.

5.3.6 Any IMP which meets the definition of a controlled drug or substance must be stored within the CRF Controlled Drugs cupboard and recorded in compliance with the KCH Controlled Drugs Policy.

5.4 IMP Administration within the CRF

5.4.1 The number of subjects dosed for a study within the CRF on any one occasion, and the interval between dosing individual subjects and cohorts of subjects, will depend on the type of IMP, the route of administration and the phase and type of trial.

5.4.2 The Sponsor must provide clear, written instructions detailing the IMP dosage, dosage frequency, route of administration, frequency of dose escalation (if applicable) and any other relevant instructions such as expected adverse drug reactions. These should be reviewed at regular intervals as required.

5.4.3 IMPs will be administered to trial subjects in the CRF as detailed in the trial protocol, prescription and relevant SOPs. Personnel who are dosing trial subjects must check that subject identifiers, study title, visit number, dose, formulation, frequency, route of administration and quantity of IMP match the prescription. The administration of the IMP to the subject must be documented on the relevant page(s) in the trial’s Case Report Form, according to the trial protocol and Sponsor’s instructions.

5.4.4 Any deviations to the IMP administration procedures for subjects dosed within the CRF must be reported to the CI/PI, pharmacy and Sponsor as soon as the CRF becomes aware of the event.
5.4.5 The Sponsor will assess whether or not a serious breach of GCP or of the trial protocol has occurred as a result of a deviation of IMP administration, and will be responsible for reporting to the Competent Authority (MHRA) within the required timelines if required and as per regulatory requirements. Any deviation of IMP administration that meets the KCH definition of an ‘adverse incident’ (AI) must be reported via Datix (see CRF-QA-SOP-5: Safety Reporting and Pharmacovigilance in the King’s CRF).

5.5 IMP Accountability

5.5.1 The Sponsor and CI/PI must ensure that responsibility for IMP accountability is clearly stated on the Delegation Log for the trial.

5.5.2 The relevant local Trust pharmacy will be responsible for maintaining accountability records relating to the delivery of the IMP to the local site, (shipment and receipt dates) inventory at the site, use by each subject, return of unused IMP from subjects and return of unused IMP to the Sponsor or delegated department/organisation. If the CRF is to take responsibility for this, it must be clearly documented in the trial protocol and agreed in advance with the CRF Manager, Sponsor and relevant pharmacy.

5.5.3 Pharmacy accountability records should include the IMP name, strength, form, quantities, batch/serial numbers, expiration dates and the unique code numbers assigned to the investigational product(s) and trial subjects (if applicable), as well as temperature monitoring records which document that the IMP was stored as specified by the Sponsor whilst in the pharmacy.

5.6 Emergency Unblinding

5.6.1 If applicable to the trial, the Sponsor or delegate must have a written procedure in place for rapid unblinding of trial subjects. The procedure must be secure, readily available at all times during the trial, and not allow breaks of the blinding to go undetected.

5.6.2 CRF staff and users of the CRF must follow instructions detailed in the trial protocol in the event of an emergency situation occurring within the CRF which requires a trial subject to be unblinded.
5.6.3 No blinded CTIMP trial will be allowed to be conducted within the CRF without robust 24-hour unblinding emergency procedures in place which are agreed by the Sponsor and the relevant local pharmacy.

6.0 Related documents & References

6.1 KCH Controlled Drugs Policy [http://kingsdocs/Pages/Home.aspx]
6.3 CRF-STU-FRM-1: IMP Storage Accountability Log
6.4 CRF-QA-SOP-5: Safety Reporting and Pharmacovigilance in the King’s CRF
6.5 CRF-QA-SOP-11: The Tutela Temperature Monitoring System in the King’s CRF

7.0 List of Appendices

N/A

8.0 Approval and sign off

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