SPONSOR INVESTIGATIONAL MEDICINAL PRODUCT (IMP) MANAGEMENT

1 INTRODUCTION

1.1 The Academic & Clinical Central Office for Research & Development (ACCORD) is a joint office comprising clinical research management staff from NHS Lothian (NHSL) and the University of Edinburgh (UoE).

1.2 The Medicines for Human Use (Clinical Trials) Regulations SI 2004/1031 (as amended) describe Sponsor responsibilities in relation to the manufacture, assembly, importation and labelling of IMPs.

1.3 This SOP does not cover the requirements for dispensing IMPs as this may be the responsibility of pharmacy departments at Investigator sites. Under these circumstances, processes will be detailed in local SOPs with any specific arrangements detailed in the clinical trial protocol where required.

2 PURPOSE

2.1 The purpose of this SOP is to describe IMP management activities that NHSL and/or UoE may undertake as Sponsors of a Clinical Trial of an Investigational Product (CTIMP).

2.2 This SOP will not capture specific issues pertaining to the manufacture, assembly, packaging, labelling, supply and storage of IMPs. This will be discussed and documented at the ACCORD combined risk assessment (ACCORD SOP GS002) and captured in the study protocol and appropriate study specific agreements.

3 SCOPE

3.1 This SOP applies to the Principal Investigator (PI), or designee, responsible for the management of IMP at their site.

3.2 This SOP applies to individuals delegated IMP management tasks by NHSL and/or UoE as Sponsors of a clinical trial.

3.3 This SOP also applies to ACCORD Quality Assurance and Monitoring staff as well as UoE Research Governance personnel, who have oversight of IMP in clinical trials sponsored by NHSL and/or UoE.

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4 RESPONSIBILITIES

4.1 The Sponsor has ultimate responsibility for the conduct of a clinical trial, including IMP management.

4.2 The ACCORD Clinical Research Facilitator, or designee, is responsible for;
   - Providing written authorisation to start the trial, ensuring all necessary agreements are in place.
   - Reviewing and approving the use of documents for site-site IMP transfers and providing written authorisation for any transfers.

4.3 The ACCORD Clinical Trials Monitor, or designee, is responsible for Sponsor oversight activities in relation to IMP management for studies sponsored by NHSL and UoE including;
   - Providing written authorisation for the release of IMP to sites for single centre studies.
   - Providing Sponsor Authorisation to Open (SATO).
   - Contacting the manufacturer of the IMP, where appropriate, in light of an IMP storage temperature deviation.
   - Determining the extent of IMP accountability checks that will be required for a trial, and reviewing site specific accountability logs prior to SATO, where applicable.

4.4 The PI will be responsible for the IMP management at their site, although tasks associated with IMP management at site are often delegated to pharmacy departments.

4.5 The Trial Manager, or designee, will be responsible for providing the release of IMP to sites for multi-centre studies. In addition, the Trial Manager, or designee will be responsible for coordinating and documenting IMP site-site transfers, where applicable.

5 PROCEDURE

5.1 Authorisation to Start the Trial

5.1.1 The Clinical Research Facilitator, or designee, will ensure that all necessary agreements are in place prior to authorisation to start the trial.

5.1.2 The Clinical Research Facilitator, or designee, will ensure that where required, a QP certifies that the IMP has been manufactured to EU Good Manufacturing Practice (GMP) standards and in accordance with the Clinical Trials Authorisation (CTA) and Product Specification File.

5.1.3 Following ‘Technical Release’ from the QP (section 5.1.2), the Clinical Research Facilitator, or designee, will provide written authorisation to start the clinical trial (‘Regulatory Release’) to the Chief Investigator (CI), once a
Research Ethics Committee (REC) favourable opinion and a Clinical Trial Authorisation (CTA) has been granted, as well as NHS Lothian R&D Management approval being in place. Written authorisation to start the trial will be documented on the Facilitation Checklist as per ACCORD SOP FA001 (Facilitating a Regulated or Complex Research Project) and written confirmation will be provided to the trial team in the form of an e-mail.

5.1.4 For single centre studies, the Clinical Trials Monitor will provide authorisation to release the IMP to site (‘Regulatory Green Light’) as per ACCORD SOP CM001 (Site Initiation and Sponsor Authorisation). For multi-centre studies, the Trial Manager with provide the ‘Regulatory Green Light’ to sites as delegated in the study specific Co-Sponsorship Agreement as per ACCORD SOP CM001.

5.1.5 Once IMP is available at site, the Clinical Trials Monitor will provide Sponsors Authorisation to Open (SATO) as per ACCORD SOP CM001 (Site Initiation and Sponsor Authorisation).

5.2 Labelling of IMP

5.2.1 For IMPs used out with the terms of its MA, the product should be labelled in compliance with the requirements provided in Annex 13 of Volume 4 of The Rules Governing Medicinal Products in the EU: Good Manufacturing Practices. Documentation of the labelling requirements will be detailed in the necessary Co-sponsorship and/or Technical agreement.

5.3 IMP Storage

5.3.1 The PI, or designee, will ensure the IMP is stored under the conditions detailed in the trial protocol and/or Summary Product Characteristics (SPC)/Investigator’s Brochure (IB).

5.3.2 If there is a requirement to monitor the storage temperature, the PI or designee, will ensure a temperature log is maintained with temperatures recorded by a calibrated temperature-recording device. Where possible, this device should be linked to an alarm system should temperatures fall out of range.

5.3.3 Where a temperature deviation is recorded, the PI or designee, will quarantine the affected IMP under the appropriate storage conditions, and inform the Clinical Trials Monitor.

5.3.4 Where necessary, the Clinical Trials Monitor, or designee, will contact the manufacturer of the IMP to determine whether there is stability data to support storage of the IMP out with the conditions specified in the clinical trial protocol or SPC.
5.3.5 The Clinical Trial Monitor will determine, in consultation with the study specific QP, PI and the Clinical Research Facilitator (where necessary), whether the quarantined IMP can be released for use or must be destroyed.

5.3.6 Temperature deviations will be documented in accordance with ACCORD SOP CR010 (Management of Protocol and GCP Deviations and Violations).

5.3.7 If IMP is stored on the ward, out with Pharmacy, this should be stored separately from clinical stock. The PI, or designee, will ensure a risk assessment is carried out for the assessment and approval of the storage area, shipping arrangements and the dispensing and record keeping processes.

5.4 IMP Accountability

5.4.1 Where necessary, the Clinical Trial Monitor will determine the extent of IMP accountability checks required (based on risk) on a study specific basis. This will be detailed in the study specific Monitoring and/or Source Data Verification Plans prepared by the Clinical Trials Monitor in accordance with ACCORD SOP CM004 (Developing a Monitoring and SDV Plan).

5.4.2 The PI, or designee, will maintain drug accountability logs for their site, where necessary.

5.4.3 The Clinical Trials Monitor will review study/site specific accountability logs prior to SATO. As an example the accountability log may detail:

- Subject ID
- IMP bottle number
- Date dispensed
- Dose
- Quantity dispensed
- Batch number
- Date returned (if applicable)
- Quantity returned
- Destruction date (if applicable)
- Recorder's initials

5.4.4 The PI, or designee, will ensure that any unused or expired IMP will be managed in accordance with the study protocol and that destruction of IMP will only be conducted with the Sponsors approval.

5.5 Transfer of IMP

5.5.1 The Co-Sponsors may permit transfer of IMP from one trial site to another under exceptional circumstances. For example, where the safety of the subject is jeopardised if supplies are not provided from another site in accordance with EU GMP guidelines.
5.5.2 In situations where the transfer of IMP is required, the PI, or designee, or the Trial Manager must seek advice and approval from the Clinical Research Facilitator, or designee, in advance of the transfer.

5.5.3 The Clinical Trial Facilitator, or designee, will ensure that the process for the transfer is agreed with the study specific QP and documented in the Rationale and procedures for site to site transfer of IMPs (GS010-T01).

5.5.4 The Trial Manager, or designee, will follow steps detailed in the Rationale and procedures for site to site transfer of IMPs (GS010-T01) when managing a site to site transfer.

5.5.5 The Trial Manager, or designee, must ensure that written approval for IMP transfer is obtained from the Clinical Research Facilitator, or designee, prior to each transfer.

5.5.6 The PI, or designee, will retain the necessary transfer paperwork in the Investigator Site File (ISF).

5.5.7 The Clinical Research Facilitator, or designee, will retain the necessary transfer paperwork in the Sponsor File. They will also advise the Trial Manager/PI or designee, if the product is to be quarantined if there are any missing documents.

6 REFERENCES AND RELATED DOCUMENTS

- GS010-T01 Rationale and Procedures for Site to Site Transfer of IMPs
- SOP GS002 Combined Risk Assessment
- SOP FA001 Facilitating a Regulated or Complex Research Project
- SOP CR010 Management of Protocol and GCP Deviations and Violations
- SOP CM001 Site Initiation and Sponsor Authorisation
- SOP CM004 (Developing a Monitoring and SDV Plan).

7 DOCUMENT HISTORY

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<th>Effective Date</th>
<th>Reason for Change</th>
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<td>1.0</td>
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8 APPROVALS

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