Sponsor Investigational Medicinal Product (IMP) / Intervention Management

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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 investigational products.

1.3 This SOP does not cover the requirements for dispensing Investigational Medicinal Products (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). For the purpose of this SOP, IMP may also refer to a substance for example human blood cells, food products, medical devices or imaging agents in the context of a non-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 (QA) and Monitoring staff as well as UoE Research Governance personnel, who have oversight of IMPs in clinical trials sponsored by NHSL and/or UoE.

3.4 This SOP applies to CTIMPs and any clinical research for which a Combined Risk Assessment is deemed appropriate (e.g. first-in-man, invasive, experimental or complex research).

4 Responsibilities

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

4.2 The Sponsor Reviewer 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.
- Review of trial specific pharmacy manual before first Site Initiation Visit (SIV) for compliance with manufacturer's Summary Product Characteristics (SPC)/Investigator's Brochure (IB) and protocol IMP and/ or NIMP instructions.
- Determining the extent of IMP accountability checks that will be required for a trial, and reviewing site specific accountability logs and trial specific prescriptions 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. The PI, or designee, is also responsible for ensuring the integrity of IMP during transfers between hospital sites within the same Board/Trust, and filing the associated documentation.

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 Sponsor Reviewer will ensure that all necessary agreements are in place prior to authorisation to start the trial.

5.1.2 The Sponsor Reviewer will ensure that where required, a QP certifies that the IMP has been manufactured to Annex 13 of Volume 4 of The Rules Governing Medicinal Products: Guideline to Good Manufacturing Practices (GMP) (January 2010) 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 Sponsor Reviewer will provide written authorisation to start the clinical trial ('Regulatory Checks Complete') to the Chief Investigator (CI), once a Research Ethics Committee (REC) favourable opinion and a CTA has been granted in the applicable territory(ies). 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 will provide the 'Regulatory Green Light' to sites as delegated in the study specific Co-Sponsorship Agreement.

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

5.1.6 Where the IMP is an off-the-shelf product, Technical Release and Regulatory Green Light are not required. Required checks are still performed by the Clinical Trials Monitor and will be documented through SATO (CM001 Site Initiation and Sponsor Authorisation).

6 Site Pharmacy Procedures

6.1 Pharmacy Manual

6.1.1 Where a pharmacy manual/IMP handling instruction is required, the document will be sent to the clinical trial monitor for review. The review will take place in accordance with GS010-T04 (Pharmacy/IMP handling checklist). As an example the pharmacy manual may detail:

- Summary of trial design
- Description of IMP or agent
- Manufacturer of drug
- Drug label
- Pharmacy set up process
- IMP Storage conditions including temperature excursion procedure
- Ordering Process
- Prescription, dispensing, returns and destruction process
- Unblinding information
- Pharmacy file and monitoring requirements

6.1.2 GS010-T04 sign off is required before CM001-T03 (regulatory green light) is issued (if required) or CM001-T02 (SATO) is issued if regulatory green light is not required.

6.1.3 If, due to trial design, it is anticipated that pharmacies will need to dispense IMP which will expire during the treatment course the associated risks must be considered and documented in the Combined Risk Assessment (GS002) and mitigated where possible. These mitigations must be reflected in the pharmacy manual where appropriate.

6.1.4 If, due to logistical reasons, it is essential to dispense IMP which will expire during the treatment course as a temporary measure to ensure continued supply the plan to ensure IMP will be returned or stock finished by participants prior to the expiry date

must be agreed with the Sponsor in advance of dispensing. The pharmacy manual must be updated to reflect the agreed plan where appropriate.

6.2 Labelling of IMP

6.2.1 For IMPs used out with the terms of its Marketing Authorisation (MA), the product should be labelled in compliance with the requirements provided in Annex 13 of Volume 4 of The Rules Governing Medicinal Products: Guideline to GMP (January 2010). Documentation of the labelling requirements will be detailed in the necessary Co-sponsorship and/or Technical agreement.

6.3 IMP Storage

6.3.1 The PI, or designee, will ensure the IMP is stored under the conditions detailed in the trial protocol and/or trial pharmacy manual and/or SPC/IB.

6.3.2 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.

6.3.3 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.

6.3.4 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.

6.3.5 The Clinical Trial Monitor will determine, in consultation with the study specific QP, PI and the Sponsor Reviewer (where necessary), whether the quarantined IMP can be released for use or must be destroyed.

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

6.3.7 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 local risk assessment is carried out for the assessment and approval of the storage area, shipping arrangements and the

dispensing and record keeping processes. This risk assessment will be reviewed by the Clinical Trials Monitor as part of SATO (ACCORD SOP CM001).

6.4 IMP Accountability

6.4.1 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).

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

6.4.3 The Clinical Trials Monitor will review study/site specific accountability logs and prescriptions prior to SATO using GS010-T02 (Accountability Log Review Checklist) and GS010-T03 (Prescription Review Checklist). As an example, the accountability log may detail;

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

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

6.5 Transfer of IMP

6.5.1 The Co-Sponsors may permit transfer of IMP from one trial site to another under exceptional circumstances. For example, where the safety of the participant is jeopardised if supplies are not provided from another site in accordance with Annex 13 of Volume 4 of The Rules Governing Medicinal Products: Guideline to GMP (January 2010)

6.5.2 In situations where the transfer of IMP is required, the PI, or designee, or the Trial Manager must seek advice and approval from the Sponsor Reviewer in advance of the transfer.

6.5.3 The Sponsor Reviewer 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).

6.5.4 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.

6.5.5 The Trial Manager, or designee, must ensure that written approval for IMP transfer is obtained from the Sponsor Reviewer prior to each transfer.

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

6.5.7 The Sponsor Reviewer 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

6.5.8 Transfer of IMP between hospital sites in the same Health Board/Trust does not meet the criteria for site to site transfer requirements. There will be a formalised local procedure in place at site to conduct such transfers. Consideration will be given to the following (as directed by the relevant Clinical Trials Pharmacist):

- Temperature monitoring during transfer.
- Process/documentation (e.g., accountability logs).
- Record of transfers kept at local pharmacies.

Documentation required, as per the local procedure, will be retained and filed in the Investigator Site File (ISF).

7 References and Related Documents

- GS010-T01 Rationale and Procedures for Site to Site Transfer of IMPs
- GS010-T02 Accountability Log Review Checklist
- GS010-T03 Prescription Review Checklist
- GS010-T04 Pharmacy Manual/IMP Handling Instructions Review Checklist
- 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.
  The Rules Governing Medicinal Products in the European Union: EU Guideline to GMP (Volume 4, Annex 13) (January 2010)

8 Document History

Version Number	Effective Date	Reason for Change
1.0	11 JUN 2018	New SOP
2.0	10 DEC 2019	Addition of GS010-T02 (Accountability Log Review Checklist) and GS010-T03 (Prescription Review Checklist). At section 5.1.3: 'Regulatory Release' has been renamed 'Regulatory Checks Complete'. Clarification added that the scope of this SOP includes studies subject to risk assessment (i.e. non-CTIMPs). Section 4.2 responsibility updated from Clinical Research Facilitator to Sponsor Reviewer. Update to SOP title. Change of author.
3.0	30 JUN 2020	Addition of GS010-T04 (Pharmacy manual/IMP handling instruction review) under new section 6.
4.0	14 FEB 2023	Added at section 5.1.2 and 6.5.1 'annex 13 Jan 2010' as EU has updated to 31 Jan 2022 but until UK has own regulations MHRA will inspect to Jan 2010. Addition of section 6.5.8 to outline considerations for transfer of IMP between hospital sites within the same Board/Trust. PI responsibilities expanded at 4.4 to ensure integrity of IMP during these transfers.
5.0	20 MAY 2025	Addition of sections 6.1.3 and 6.1.4 relating to IMP expiry. Minor updates to grammar and clarifications throughout. SOP transferred to new ACCORD

		template. GS010-T01, T02, T03 and T04 also transferred to new template (all updated to v2.0).

9 Approvals

Sign	Date
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Paul Dearie Paul Dearie (May 1, 2025 12:18 GMT+1) APPROVED: Paul Dearie, Clinical Research Facilitation Manager, UoE, ACCORD	01/05/2025
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