Reference Number: UHB040 **Version Number: 4**	**Date of Next Review:** *01/09/2026* **Previous Trust/LHB Reference Number: T363**

Investigational Medicinal Product (IMP) Management

Standard Operating Procedure

Introduction and Aim

The purpose of this procedure is to inform trial sponsors and trial investigators of the role of pharmacy in the approval and management of IMPs for clinical trial use within Cardiff and Vale University Health Board (UHB).

Objectives

To inform sponsors and investigators of pharmacy requirements for the safe management of IMPs approved by the UHB.

To define and clarify the role of pharmacy and its responsibilities with regard to the review of clinical trials and the management of IMPs within Cardiff and Vale UHB.

Scope

This procedure applies to all of our staff in all locations including those with honorary contracts working within the field of clinical trials.

Equality Impact Assessment	An Equality Impact Assessment has been completed. (The Equality Impact Assessment completed for this procedure found there to be no impact.)
Health Impact Assessment	A Health Impact Assessment (HIA) has not been completed as it has no impact.
Documents to read alongside this Procedure	Research Governance Standard Operating Procedure (UHB 457). Cardiff Joint Research Office (JRO) standard operating procedures of relevance to the reader. Pharmacy Clinical Trials standard operating procedures of relevance to the reader.
Approved by	Joint Research Governance Group

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Summary of reviews/amendments			
Version Number	**Date of Review Approved**	**Date Published**	**Summary of Amendments**
1	*October 2010*	25th March 2011	Replacement of trust version 363 to UHB040.
2	*September 2015*		The document has been transferred to the UHB corporate template.
3	*26 April 2016*	04 Aug 2016	The document has been re-formatted and the layout amended to improve its presentation. A list of sections has been introduced. Section 3 The content of the section remains largely unchanged. Roles and responsibilities have been specified to Sponsor, Investigator and Pharmacy. Duplicated information has been removed. Section 4 This section remains largely unchanged, duplicated information has been removed. Phrasing has been made more concise. Section 7 introduction of Incidents and Errors. Section 8 (previously section 7 implementation). Section 9 (previously section 8 Equality Impact and Assessment). Section 10 - Introduction of Audit. Section 11 - previously section 10 distribution. Distribution has been amended to via the UHB Intranet. Section 12 The title has been changed to information sources and the references have been removed from the text but the reference sources used have been listed. The pharmacy R&D form has been removed as a new Support in Principle form is being used by R&D and supported by pharmacy.

4	*September 2023*	18/07/2024	Procedure updated to reflect the change from Cardiff and Vale UHB R&D Office to Cardiff Joint Research Office (JRO). Procedure updated to remove references to CaRRS (Cardiff and Vale Research Review Service), which has been replaced with obtaining capacity and capability (C&C) confirmation for research to start. Procedure reviewed and updated to ensure correct terminology used and information sources are still relevant Procedure reformatted to current Cardiff and Vale SOP format.

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SECTION 1. INTRODUCTION

The role of the pharmacy service in relation to clinical trials is to safeguard patients, healthcare professionals at Cardiff and Vale University Health Board (UHB) by ensuring that any Investigational Medicinal Product (IMP) used in a trial is appropriate for use and procured, handled, stored, used safely and disposed of appropriately.

In May 2004 the Medicines for Human Use (Clinical Trials) Regulations came into force. These impose legal standards on the conduct of all interventional clinical trials involving medicines. Pharmacy must ensure that procedures are in place to comply with the regulations and subsequent amendments and relevant guidelines and directives e.g. Good Clinical Practice (GCP) for clinical trials

The use of medicines in interventional trials must be covered by a Clinical Trial Authorisation (CTA) issued by the Medicines and Healthcare products Regulatory Agency (MHRA). Whilst some clinical trials will involve the use of existing marketed products used within their licensed indications, others will use new medicines, formulations or methods of administration unfamiliar to staff handling them. The clinical trial medicines may also be blinded to prevent ready identification by investigator or patient. Extra precautions need to be taken to ensure safety and security in their use.

This procedure sets out the standards required for IMP management within C&V UHB. It applies to all interventional trials involving medicines, including advanced therapy trials (ATIMPs), but excludes wound dressing and blood product clinical trials. This procedure encompasses all phases of clinical trials from Phase 1 human volunteer studies to Phase IV post-marketing studies. These may be non-commercial (including investigator-initiated) or commercial trials.

SECTION 2. OVERARCHING STATEMENT

The management of clinical trial medicines must comply with legislation and all relevant Cardiff Joint Research Office (JRO) policies.

All medicines used in clinical trials within Cardiff and Vale UHB should be stored and dispensed by the pharmacy department and managed to the same standards as other medicines used therapeutically. IMP must not be stored in offices, clinics or ward areas unless by prior arrangement with pharmacy and only where appropriate risk management processes and standard operating procedures (SOPs) are in place as outlined in this procedure. IMP must only be used in patients recruited to the trial.

SECTION 3. RESPONSIBILITIES OF THE SPONSOR, INVESTIGATOR AND PHARMACY DURING STUDY SET UP

3.1 Sponsor/Investigator responsibility (or person(s) with delegated duty to act) with regards to the registration of new hosted trials involving IMPs and their role during the approval and initiation process.

- For all trials involving an IMP, a copy of the protocol and any documents relevant to pharmacy (e.g. pharmacy manual) must be submitted to the pharmacy clinical trials team at the same time that the trial is registered with Cardiff JRO.
- All clinical trials involving IMPs are feasibility reviewed by the Cardiff JRO. As part of this process, a clinical trials pharmacist will assess if pharmacy has the capacity and capability to host the trial.
- Pharmacy must be kept informed regarding the trial progression, before it is officially submitted for capacity and capability review. Protocols will be kept for 2 years from the anticipated start date. They will then be destroyed, if there has been no communication from the trial research team.
- The sponsor should provide copies of all approvals to the pharmacy clinical trials team before a clinical trial involving medicines can commence (Research Ethics Committee, Medicines and Healthcare Products Regulatory Agency (MHRA), Health Research Authority (HRA)/Health and Care Research Wales (HCRW) Approval, Cardiff JRO confirmation of capacity and capability).
- An initiation meeting must be held between the sponsor and a member of the clinical trials pharmacy team.
- Confirmation must be agreed with pharmacy regarding the arrangements for emergency unblinding.
- Confirm with the pharmacy clinical trials team that pharmacy is ready to start the trial before the first patient is seen.
- Supply pharmacy with a copy of the completed delegation log, the pharmacy clinical trials team should be included on the log.
- Provide pharmacy with an updated Investigators Brochure (IB) or SmPC on an annual basis, or every time it is updated, whichever is sooner.
- Inform pharmacy when the trial has been completed and is ready for close down.

3.2 CTIMPs for which CAVUHB or CU is Sponsor

- The JRO sponsorship team will inform the clinical trial pharmacists if and when a UHB or Cardiff University sponsored CTIMP is being planned. All potential sponsor pharmacist requests should be received via the JRO.

- An initial meeting with the research team and trial unit may be required to gather more information about the trial and to ascertain the type and level of pharmacy support required.

- All clinical trials involving IMPs that are sponsored by Cardiff University or Cardiff and Vale UHB, will be assessed by a panel of specialist pharmacists including a qualified person (QP) and a pharmacist with regulatory expertise. The aim of this assessment is:
    - To establish the type and level of pharmacy support needed
    - Establish whether Cardiff and Vale UHB pharmacy has the capacity and capability to provide the level of support the trial will need.

- Depending on the complexity of the trial the following activities may need to be considered:
    - Sourcing, manufacturing and distribution of IMP
    - Ensure accuracy of IMPD (investigational medicinal product dossier)
    - QP certification (incorporating importation and regulatory requirements)
    - Host site pharmacy set up, close out
    - Host site IMP management of the trial
    - Writing and/or reviewing IMP related sections of the protocol
    - Writing or reviewing the pharmacy manual
    - Establishing monitoring requirements at participating sites

- If Cardiff and Vale pharmacy department has the capacity and capability to act as a sponsor pharmacy, then a quote for the pharmacy costs for the life span of the trial will be provided. The CI should include the quote provided by pharmacy in any grant applications.

- If pharmacy has the capacity and capability to support the trial and the grant is successfully awarded, an agreement will be put in place to confirm the roles and responsibilities for the pharmacy development of the trial and predicted timescales.

- Any subsequent significant amendments to the trial protocol will require a reassessment of the pharmacy requirements of the trial and if pharmacy still has the capacity and capability to support the trial.

- The clinical trials pharmacists may be asked to give feedback on the Schedule of Events Cost Attribution Template (SoECAT), to ensure appropriate pharmacy costs are included in grant applications for host sites. This is not an agreement to act as a sponsor pharmacy.

3.3 Pharmacy responsibility regarding the capacity and capability peer review of clinical trials involving IMP

Pharmacy review of clinical trials involving IMP forms an integral part of the Cardiff JRO obtaining capacity and capability process. Refer to SOP UHB 448 Obtaining Capacity & Capability Confirmation for Research to Start for further information.

- This review is conducted by a clinical trials pharmacist, some trials may also be reviewed by a specialist pharmacist.

- Wherever possible, the clinical trials pharmacist will liaise with the investigator/sponsor to address any IMP issues prior to the start of the capacity and capability confirmation process.

- The clinical trials pharmacist will submit comments to Cardiff JRO within 10 days of the capacity and capability request for pharmacy review being emailed out by Cardiff JRO.

3.4 Pharmacy responsibilities during approval and initiation of clinical trials involving IMPs

- The clinical trials pharmacist will carry out risk assessments, in collaboration with the investigator, for each clinical trial and put procedures in place to minimise risk and safeguard patients and staff.

- Members of the pharmacy clinical trials team will ensure that all clinical trial medicines provided or procured for use in trials are manufactured and labelled in accordance with Good Manufacturing Practice for IMPs.

- Commercial trials will be assigned a cost based on the National Institute for Health Research (NIHR) interactive Costing Tool and will be agreed between the sponsor, pharmacy and the commercial trials team at Cardiff JRO. The approved pharmacy charges will be included in the UHB Clinical Trials Agreement with the sponsor.

- Following the pharmacy clinical trials team initiation meeting, a trial specific dispensing procedure will be prepared.

- At least two weeks is required between the initiation meeting and the first patient dispensing, but pharmacy will aim to reduce this time period where possible.

- All staff involved with the day to day dispensing and management of a clinical trial will receive in-house training.

SECTION 4. Responsibility for IMP management during active trials and following trial discontinuation and closedown.

For the majority of clinical trials run within Cardiff and Vale UHB all trial IMPs will be stored within pharmacy.

However, in exceptional circumstances for some trials it may be necessary for the investigator to hold a small stock of IMP outside of pharmacy. If the need for storage of IMP outside of pharmacy is identified during the protocol review the clinical trials pharmacist will highlight this in the capacity and capability report. The storage of IMP outside of pharmacy needs to be approved by the trial sponsor as part of the Cardiff JRO capacity and capability confirmation process.

In very exceptional circumstances, the clinical trials pharmacist, principal investigator (PI) and trial sponsor may decide that it is more appropriate for all the IMP management to be performed by the PI with no pharmacy involvement (see section 4.3).

4.1 All IMP held in pharmacy

The pharmacy clinical trials team will be responsible for:

- All pharmacy clinical trial deliveries will be initially received in pharmacy stores who will transfer clinical trial deliveries to the pharmacy clinical trials office. On receipt in the clinical trials office, deliveries will be correctly received and recorded.
- Ensuring all IMP is stored at the correct temperatures and appropriate temperature monitoring records are kept.
- Dispensing IMP against an appropriate prescription following a trial specific dispensing procedure.
- Accountability of IMP received, stored and dispensed in pharmacy including patient returns.
- Ensuring that the blind is maintained throughout the trial and code break envelopes or codes (if applicable) are returned to the sponsor or investigator at the end of the trial. Code break envelopes or randomisation lists will only be released to the trial sponsor (or investigator) when written evidence from the sponsor has been provided to the clinical trials pharmacist that the final locked dataset has been verified.
- Emergency unblinding supported by pharmacy (where applicable), according to an agreed procedure.
- Provision of appropriate facilities for trial monitoring by pre-arranged appointments.

4.2. IMP held in pharmacy with small stock supplied to PI

- The pharmacy clinical trials team will retain responsibility for the IMP held in pharmacy as outlined above.

- Pharmacy will keep up to date details of any IMP held outside pharmacy.

- The PI will be responsible for the appropriate storage, temperature monitoring and accountability of IMP held outside of pharmacy. This may include procuring new equipment. Pharmacy staff can provide advice about suitable storage areas, temperature monitoring and accountability processes and assist the PI in preparing the relevant procedures.

- Before full Cardiff JRO capacity and capability is confirmed, a member of the pharmacy clinical trials team will inspect the PI facilities for storing IMP and the relevant procedures will be approved by pharmacy.

- The pharmacy clinical trials team will perform a trial monitoring visit of the IMP storage and accountability three months after the trial starts. Items to be monitored are:

    - Storage conditions of IMP including temperature monitoring records
    - Balance of IMP held by PI
    - Adequate completion of accountability records

- Cardiff JRO will be informed of the results of the monitoring visit in the event of any deficiencies.

- The frequency of future monitoring will be based on the results of the first monitoring visit.

- If the trial is sponsored by an external organisation (e.g. pharmaceutical company), the sponsor may take responsibility for inspecting the PI storage facilities before the trial starts and also routinely inspect storage facilities, drug accountability and monitoring records during the course of the trial.

- If the temperature in the PI storage area goes outside the approved range, the PI must return all stock to pharmacy if pharmacy has suitable storage facilities. The pharmacy clinical trials team will follow an internal procedure and quarantine the stock until further information is obtained from the trial sponsor. New stock will not be released by pharmacy until the temperature has returned within the acceptable range.

- In the event of a recall of the IMP by the trial sponsor, the pharmacy clinical trials team will follow an internal standard operating procedure and inform the PI that the IMP must be returned to pharmacy.

- Before the IMP is due to expire the pharmacy clinical trials team will contact the PI (or delegate) to arrange timely return of expiring IMP and resupply. The expiring IMP will be stored in the clinical trials returns section until permission for destruction is granted by the trial sponsor.

4.3. All IMP held by PI with no pharmacy involvement

- In this case the PI has taken overall responsibility for IMP management. This will be documented on the site delegation log.

- Duties may include:

    - Correct receipt and recording of deliveries by a responsible person.
    - Proper safe handling, storage, dispensing of IMP
    - Ensure all IMPs are packaged and labelled according to GMP requirements and regulations, and are legible and understandable to patient/carer.
    - Issue against an appropriate prescription.
    - Maintain drug accountability records.
    - Reconciliation of delivery records with usage and return of unused stock.
    - Safe storage of used and returned IMP before dispatch to external sponsor for disposal.
    - Safe keeping of randomisation code envelopes (if applicable) and the provision of 24-hour emergency unblinding.
    - Archiving of clinical trial documentation.

- Pharmacy staff can provide advice about suitable storage areas, temperature monitoring and accountability processes and assist the PI in preparing the relevant procedures.

- Before full Cardiff JRO capacity and capability is confirmed either the trial sponsor or UHB pharmacy staff will inspect the PI facilities for storing IMP and approve the relevant procedures.

- Ongoing IMP monitoring arrangements during the trial will be agreed with the trial sponsor.

- If the sponsor or another external organisation (e.g. CRO) is not monitoring IMP on a regular basis, the pharmacy clinical trials team will perform a trial monitoring visit of the PI IMP storage and accountability three months after the trial starts as detailed in pharmacy internal standard operating procedures.

4.4 Trial discontinuation and closedown

- The Sponsor or their delegate will inform pharmacy when a trial has been discontinued and requires closedown.

- Pharmacy will follow their internal procedure to ensure this process is completed.

- The process will include:
    - Disposal of IMP
    - Checklist of documentation
    - Anonymising of patient details where appropriate
    - Archiving of study file with the investigator site files

SECTION 5. RESOURCES

This procedure provides advice and information for staff. It is therefore unlikely that any additional resource will be required.

SECTION 6. TRAINING

Appropriate training for staff involved in clinical trials is available online through Health and Care Research Wales and the National Institute for Health and Care Research (NIHR), IMP management specific courses are available. Pharmacy staff will receive training as deemed appropriate through the value-based appraisal process.

SECTION 7. INCIDENTS AND ERRORS

All incidents and errors which affect the quality of the IMP or patient safety will be investigated in accordance with pharmacy internal procedures and reviewed by the Cardiff JRO Research Governance Group. Refer to SOP UHB 235 Managing Breaches of GCP or the Study Protocol for further information, or another appropriate SOP which replaces this in future.

SECTION 8. IMPLEMENTATION

The Cardiff and Vale UHB pharmacy clinical trials team, Cardiff JRO and JRO Research Governance Group will endeavour to ensure that this procedure is implemented. This will be re-enforced within clinical boards by local clinical governance arrangements.

SECTION 9. EQUALITY IMPACT AND ASSESSMENT

This procedure has had an equality impact assessment which has shown that there should be no adverse effect on or discrimination against any particular individual or group.

SECTION 10. AUDIT

It will be necessary to ensure compliance to the requirements of this procedure. Audit of compliance against the guideline and GCP can be undertaken periodically by internal and external inspectors as applicable.

SECTION 11. DISTRIBUTION

This procedure will be available on the pharmacy and Cardiff JRO SharePoint pages.

SECTION 12. INFORMATION SOURCES

1. Professional Guidance on Pharmacy Services for Clinical Trials. National Pharmacy Clinical Trials Advisory Group (endorsed by Royal Pharmaceutical Society) Version 2.1 April 2019 PRACTICE GUIDANCE ON PHARMACY SERVICES FOR CLINICAL TRIALS (rpharms.com) (accessed 22/06/2023)

2. Medicines for Human Use (Clinical Trials) Regulations 2004 The Medicines for Human Use (Clinical Trials) Regulations 2004 (legislation.gov.uk) (accessed 22/06/2023).

3. Principles and detailed guidelines for good clinical practice as regards IMPs for human use, as well as the requirements for authorisation of the manufacturing or importation of such products. European Commission Directive on Good Clinical Practice 2005/28/EC. April 2005.

4. The Medicines for Human Use (Clinical Trials) Amendment Regulations 2006 (SI 2006/1928) implementing Commission Directive 2005/28/EC The Medicines for Human Use (Clinical Trials) Amendment Regulations 2006 (legislation.gov.uk) (accessed 22/06/2023)

5. Annex 13 Manufacture of IMPs. Eudralex Volume 4. Good Manufacturing Practice (GMP) guidelines Dec 2017. EudraLex - Volume 4 (europa.eu) (accessed 22/06/2023)

6. The role of the sponsor pharmacy in clinical trials of investigational medicinal products (CTIMPS) Dec 2022 The role of the sponsor pharmacy in clinical trials of investigational medicinal products (CTIMPs) – SPS - Specialist Pharmacy Service – The first stop for professional medicines advice (accessed 22/06/2023)