Public – To be published on the Trust external website

Title: Clinical Trials Involving Pharmaceutical Products

Ref: PHARM-0002-005-v4

Status: Approved
Document type: Procedure.
Overarching Policy: Medicines Overarching Policy

Contents

1 Introduction

Since April 2016, the Health Research Authority (HRA) has been the governing body for approving all research in the NHS, including that involving Investigational Medicinal Products (IMPs). The HRA approval system draws together the Research Ethics Committee (REC) recommendations and the clinical trial authorisation from the Medicines Healthcare Regulatory Authority (MHRA), the licensing authority.

Tees, Esk and Wear Valleys NHS Foundation Trust (TEWV) must comply with this regulatory framework for clinical trials involving medicines to ensure the safety of our service recruited into clinical trials. The Research Governance Group, a sub-committee of the Quality and Assurance Committee (QuAC) provides corporate assurance that research activity meets the required quality and governance standards.

TEWV hosts clinical trials involving medicines sponsored by pharmaceutical companies, universities, charities, and other bodies. Working in partnership together, the departments of Pharmacy and Research and Development (R&D), ensure the safety, integrity and quality of research is maintained, to be able to contribute to global evidence-based medicine.

This procedure supports Our Journey to Change as set out in the Medicines Overarching Policy.

2 Purpose

Following this procedure will help the Trust to:

- **Ensure the safe and ethical use of IMPs** by our service users.
- **Comply with legal and regulatory requirements** in the authorised supply of IMPs.
- **Ensure that the supply of IMPs to service users** is conducted with the knowledge and approval of both the R&D and pharmacy departments.
- **Ensure compliance with Good Clinical Practice (GCP).**
- **Maintain research integrity and compliance with the General Data Protection Regulations (GDPR).**

3 Who this procedure applies to

This procedure applies to all staff involved in the clinical trial journey aligning to the Trust values so that people affected are treated with compassion and respect.

4 Related documents

This procedure describes what additional requirements are necessary for the safe and ethical use of investigational medicines, in the 'Clinical trials involving pharmaceutical products' section of the Medicines Overarching Framework.

The Medicines Overarching Framework outlines the compliance requirements for prescribing and initiating treatment safely. Before performing the procedures described in this document, you must read, understand, and receive training on these requirements.

The Pharmacy Clinical Trial Service follows its own set of approved Standard Operating Procedures (SOPs) for every step and task involved in managing Clinical Trial Investigational Medicinal Products.

The R&D team work to their own set of approved SOPs, too, covering every step of assessing, confirming, arranging, and participating in clinical trial activity.

Note: external documents such as academic references and codes of practice are recorded in the References section.

5 Clinical Trials in TEWV

5.1 Approval of Research Involving Medicines:

All research, particularly that involving medicines MUST be approved by Research and Development and Pharmacy

- R&D can direct prescribers wishing to undertake their own research to appropriate sources for assistance, for example, with defining the research question, grant applications, and how to submit for ethical approval.
- Research by any practitioner, even if using licensed medicines, MUST be assessed, and approved by R&D from the outset.
- Clinical trials of investigational medicinal products sponsored by pharmaceutical companies, universities, charities, and other bodies will use the national HRA approval process, but still require local R&D and Pharmacy approval before commencement in TEWV.

All staff planning to conduct research should contact the Research and Development department with an initial email contact to tewv.researchanddevelopment@nhs.net to outline their proposal and confirm plans for seeking research approvals.

Research conducted without necessary approvals will be investigated, and the practitioner referred to HR and professional bodies as deemed appropriate.

5.2 Commencement of a Clinical Trial

Once TEWV has accepted a clinical trial involving medicines, R&D and Pharmacy will then undertake a series of checks to ensure the study protocol, documentation, and medicinal products comply with Good Clinical Practice (GCP).

Before recruiting any service users to a study, a study-specific SOP is written for pharmacy colleagues who may need to dispense or check a prescription within the trial. This SOP will detail all the requirements set out in the study for randomisation, labelling, and reconstitution or manipulation that may be required, and details of packaging and any storage or transportation needed. If it is a possibility that a service user recruited into a study may be admitted as an inpatient, then brief guidance for Ward staff on the specific study is prepared, that details what to do if a patient is admitted to a ward on a clinical trial medicine. This includes a summary of the study, how to prescribe, handle and store the investigational medicines, and contact details for the study team.

Most studies will have a mechanism in place for the continued supply of the investigation medicine beyond the end of the study, for those service users who have benefited from the treatment within the study.

Occasionally, a provision for this may not be included within the original protocol. Principal Investigators (PIs) may request to obtain a supply of the trial medicine on an individual basis if this is possible and can be justified. The Drug and Therapeutics Committee should be approached at the commencement of the study if this is deemed likely.

5.3 Storage of Investigational Medicines in Clinics or Departments

Due to logistics, and TEWV's large geography, it may require pharmacy to dispense and deliver a clinical trial medicine to a location remote from the Pharmacy Clinical Trial Service.

The following rules apply to comply with GCP:

- All areas required to store clinical trial medicines must be risk assessed at the outset.
- Clinical trial medicines should be physically separated from other medicines.
- The temperature of the storage area requires regular measurement.
- Access to the investigational products should be restricted to only those persons involved with the study.
- Monthly audit of the security, segregation and temperature monitoring will be undertaken on any remote storage area that holds investigational medicinal products for a specific study.

6 Issues Relating to Clinical Trial Investigational Medicinal Products (CTIMPs)

6.1 Documentation and Record Keeping

For CTIMPs, regulations required that a readily available Trial Master File (TMF) is kept, which must contain the essential documentation relating to that clinical trial and demonstrate compliance with Good Clinical Practice (GCP). The TMF enables the reconstruction of trial activities and facilitates with the appropriate running of the trial.

Pharmacy will hold their own copy of the TMF, tailored to support the functioning of a trial from the perspective of a pharmacy. These are usually called the **Investigator Site File (ISF)**, but sometimes may also be referred to as:

- Pharmacy Site File (PSF)
- Pharmacy Master File (PMF)
- Investigational Product File (IPF)

When the trial ends and the data is ready for archiving, the ISF and will be merged into the TMF and stored – in compliance with both GCP and GDPR – for 25 years after the last patient completes trial medicines.

The ISF serves as a repository for all essential documents related to the conduct of a clinical trial at the investigator site. It ensures compliance with GCP and regulatory requirements. This file should include all relevant documents, such as:

- The trial protocol.
- Investigator brochures.
- Informed consent forms.
- Ethics committee approvals.
- Correspondence.
- Training records.
- Monitoring visit reports.
- Records of IMP accountability.

The Pharmacy Site File will be kept always locked within the Clinical Trials Dispensary when not in-use. For the duration of the trial, the PSF shall not leave the Clinical Trials Dispensary.

6.2 Unblinding

Unblinding should only occur for valid medical or safety reasons.
It is **not** the responsibility of the on-call pharmacist alone to decide whether to unblind a patient within a trial. That decision should only be undertaken by the Principal Investigator (PI), or – in their absence – the sub-investigator, chief investigator, or the trial sponsor.

Some clinical trials involve a placebo arm to the study, and hence some patients may not be receiving the active drug under investigation. Patients and investigators are 'blinded' i.e., unaware as to whether they are receiving the active drug or placebo. Clinical Trials involving placebo controls must contain within the protocol instructions on how to remove the blind, if necessary, in an emergency. This is usually only required in response to a Serious Adverse Event (SAE) or a Suspected Unexpected Serious Adverse Reaction (SUSAR) of an individual patient to enable appropriate treatment choices to be made.

It is expected that the investigator site can un-blind a subject immediately in the case of a medical emergency. Emergency breaking the blind may be undertaken with physical code breaks (for example, envelopes or a scratch panel on the Investigational Medicinal Product (IMP) supply) or via an interactive response technology (IRT) system.

Usually the principal investigator (PI) of the research site has access to these systems and can break the blind when necessary. When receiving a request to unblind a participant within a placebo trial, it should be first assumed that the participant is on active treatment within the trial (in-order to avoid unnecessary unblinding of an active participant.

In the event of an emergency in the out of hours period, there is further information on the shared T drive accessible from a Trust network T:\Intranet Published Documents\Services\Medicines and Pharmacy\Out of Hours\Clinical Trials.

6.3 Troubleshooting Issues

Operating a Clinical Trials dispensary and pharmacy service does not come without issue, and it is impossible to predict and plan for every fault, error or issue that may arise within the normal functioning of any clinical trial dispensary or R&D pharmacy service.

Any problem identified should always be reported to one the of the R&D pharmacy team (their contact details are included below). Some common issues that may occur, include:

1) Non-Compliance with Regulations:
   - This is failing to adhere to GCP guidelines or other regulatory requirements.
   - Non-compliance can result in warnings, fines or even the suspension of clinical trials entirely.

- It is essential that only individuals that are GCP trained, and on the delegation log for a particular clinical trial are involved with any processing of paperwork, CTIMP handling, dispensing, reconstitution, and supply of medicines within the confines of a clinical trial.

2) Documentation Errors:
   - Incomplete, inaccurate, or lost documentation can lead to GCP issues and impact the integrity of the trial.
   - Be open and honest, and report all documentation errors to a member of R&D.
   - Complete an InPhase report if documentation errors are accidently made or discovered.

3) Insufficient Training:
   - Staff not adequately trained on procedures lead to mistakes in trial management.
   - These mistakes jeopardise the integrity of the trial.
   - If unsure, speak up; don't guess and don't feel pressured into doing something that you're not comfortable with.

4) Poor Communication:
   - Miscommunication between team members or with external parties can result in delays or errors.
   - It is preferrable to communicate issues re clinical trials via e-mail. This helps ensure an audit trail. These communications should be printed and filed within the Communications section of the relevant clinical trial.

5) Equipment Failures:
   - Malfunctioning or incorrectly calibrated equipment can affect the accuracy of the trial and jeopardise the integrity of the results.
   - All faulty equipment within the Clinical Trials Dispensary should be promptly reported to R&D, and an InPhase must be completed.
   - Any affected CTIMP should be moved to an appropriate quarantine area (there is a quarantine cupboard and a quarantine fridge within clinical trials). The quarantining of CTIMP should follow SOP CTS009.

6) Medication Errors:
   - Mistakes in dispensing or managing IMPs potentially comprise patient safety and jeopardise the integrity of the trial data.
   - All mistakes **must** be reported to either the Lead Pharmacy Technician or the Lead Clinical Trials Pharmacist.
   - All mistakes **must** be appropriately InPhased.

7) Patient Safety Concerns:
   - Adverse reactions or events not appropriately managed compromise patient safety and risk trial integrity.
   - Patient safety must be prioritised above all else.
   - Follow appropriate SOPs for managing adverse events. If unsure, speak to a member of R&D for assistance.

8) Audits and Inspections:
   - It is vital that we regularly prepare for audits and inspections by ensuring that we always follow GCP and regulatory requirements.

9) Protocol Deviations:
   - Deviations from the approved trial protocol sometimes inadvertently happen. These must always be reported to R&D and the trial sponsor.

6.3.1 Contact Details

Not all possible issues can be listed, and the resolution steps cannot always be followed for each issue the presents itself. Each issue within a clinical trial presents a unique set of obstacles. Remember that there is always someone within R&D to ask for help and/or advice for any issue that occurs within the conduct of a clinical trial. Pharmacy contact details are below:

Clinical Trials Pharmacy E-mail: tewv.pharmacyclinicaltrialservice@nhs.net
Clinical Trials Pharmacy Tel: 0190 4461176

7 Responsibilities of the Pharmacy Department

Pharmacy and R&D will ensure that an adequate skill mix of personnel, are appointed/rostered to the Pharmacy Clinical Trial Service to ensure the safe running of clinical trials involving medicines in TEWV.
The Pharmacy Clinical Trial Service is responsible for ensuring that all clinical trial materials are of an appropriate quality for use in TEWV at the set-up of the trial: this includes both licensed and unlicensed medicines, their labelling, packaging, and patient information leaflets. Pharmacy will ensure that relevant legislation and guidance is followed regarding the investigational medicinal products.
All pharmacy staff involved in approval, dispensing, or checking of any clinical medicines will be provided with training either in-house or via the trial sponsor.
Clinical Trial Investigational Medicinal Products (CTIMPs) must be stored in dedicated temperature controlled and monitored facilities within TEWV, separate from routine pharmacy stock.
The Pharmacy Clinical Trial Service must have standard operating procedures in place covering all aspects of the clinical trial process including approval, receipt, temperature monitoring, storage, dispensing, maintaining, and archiving trial documentation, and issue to service users or research staff.
The Pharmacy Clinical Trial Service is responsible for ensuring up to date information for out-of- hours use, in case of admission of patients participating in a trial, or the need to un-blind a patient in an emergency

Pharmacy Trial Files will be returned to sponsors at the close of the trial. Any patient identifiable data will be obliterated or removed to comply with GCP and General Data Regulation (GDPR). Copies of prescriptions will be retained and archived for **25 years** after the last patient completes the trial medicines.

8 Definitions

Term	Definition
CTIMP (Clinical Trial Investigational Medicinal Product).	• A Clinical Trial of an Investigational Medicinal Product is a research study that tests the effects, risks, and benefits of a new or modified medicinal product on human participants. The goal is to gather data on the product's safety and efficacy before it can be approved for wider use.
GCP (Good Clinical Practice)	• Good Clinical Practice is an international ethical and scientific quality of standards for designing, conducting, recording, and reporting trials that involve the participation of human subjects.
GDPR (General Data Protection Regulation)	• GDPR is a regulation in EU law that focuses on data protection and privacy. It aims to give individuals more control over their personal data and to unify data protection laws across the EU. • This regulation was retained in UK law as the **UK GDPR**, which works alongside the Data Protection Act 2018. The core principles, rights, and obligations remain the same as the EU GDPR.
HRA (Health Research Authority)	• The Health Research Authority is a government agency within the Department of Health and Social Care in the UK. Its core purpose is to protect and promote the interests of patients and the public in health and social care research. • The HRA oversees ethical review, transparency, and data protection.
ISF (Investigator Site File)	• A collection of documents and records maintained at a clinical trial site, containing all essential documents related to a specific trial.
MHRA (Medicines Healthcare Regulatory Authority)	• A UK government agency responsible for ensuring that medicines, medical devices, and blood components meet applicable standards of safety, quality, and efficacy.
PI (Principal Investigator)	• The lead researcher responsible for leading the clinical research team and, along with the other members of the research team, regularly monitors study participant's health to determine the study safety and effectiveness.

R&D (Research and Development)	• The department within TEWV responsible for research and innovation. • They represent TEWV within the National Institute of Health Research.
TMF (Trial Master File)	• This is a comprehensive collection of essential documents and records that are necessary to conduct and management a clinical trial. • It is a critical component of clinical research, ensuring compliance with regulatory requirements and GCP guidelines.

9 How this procedure will be implemented

Implementation will be uploading this document to the policy database within TEWV's intranet and including a hyperlink on the Medicines Optimisation Interactive Guide.

9.1 Implementation action plan

Activity	Expected outcome	Timescale	Responsibility	Means of verification/ measurement
Publication on intranet	Available to all Trust staff	Within 1 month of approval	Deputy Chief Pharmacist	Available on intranet

9.2 Training needs analysis

Staff/Professional Group	Type of Training	Duration	Frequency of Training
Pharmacy Staff Involved with a Clinical Trial	Good Clinical Practice – NIHR e-learning	4 hours	Every 2 – 3 years. (Recommendation is 2, GCP is out-of-date if not refreshed after 3 years).
Pharmacy Staff Involved with a Clinical Trial	Clinical Trial Curriculum Vitae (CV) – *See Appendix 2*	1 hour	Whenever involved with a new clinical trial

10 How the implementation of this procedure will be monitored

Not applicable – individual trials have careful monitoring processes.

11 References

- Professional Guidance on the Safe and Secure Handling of Medicines. (Royal Pharmaceutical Society, 2018)
- Good Clinical Practice Guide (MHRA, 2012)
- Professional Guidance on Pharmacy Services for Clinical Trials. (Royal Pharmaceutical Society, 2019)
- Clinical Trials. (Specialist Pharmaceutical Service)

12 Document control (external)

To be recorded on the policy register by Policy Coordinator

Required information type	Information
Date of approval	28 November 2024
Next review date	28 November 2027
This document replaces	PHARM-0002-005-v3
This document was approved by	Drug & Therapeutics Committee
This document was approved	28 November 2024
This document was ratified by	N/A
This document was ratified	N/A
An equality analysis was completed on this policy on	See generic EA for Pharmacy Documents
Document type	Public

Change record:

Version	Date	Amendment details	Status
1	Nov 2014		Superseded
2	May 2018	Updated to include regulatory and in-house approval frameworks. Updated to include the role of the in-house Pharmacy Clinical Trial Service.	Superseded
3	25 Nov 2021	Updated hyperlink to the Medicines Overarching Framework. Update includes responsibilities and tasks of the in-house dispensary staff. Updates reflect new regulation for storage of records for twenty-five years.	Superseded

4	28 Nov 2024	Corrected all grammatical errors. Renamed section 5 to provide a better description of this section. Introduced section 6 to try and pre-emptively equip colleagues with tools to troubleshoot common issues. Added CV template to appendices. Updated hyperlink. Removed references to fraud (as R&D SOP had been archived).	Published

Appendix 1 – Approval checklist

To be completed by lead and attached to any document which guides practice when submitted to the appropriate committee/group for consideration and approval.

Title of document being reviewed:	Yes / No / Not applicable	Comments
1. Title		
Is the title clear and unambiguous?	Y	
Is it clear whether the document is a guideline, policy, protocol or standard?	Y	
2. Rationale		
Are reasons for development of the document stated?	Y	
3. Development Process		
Are people involved in the development identified?	Y	
Has relevant expertise has been sought/used?	Y	
Is there evidence of consultation with stakeholders and users?	Y	
Have any related documents or documents that are impacted by this change been identified and updated?	Y	
4. Content		
Is the objective of the document clear?	Y	
Is the target population clear and unambiguous?	Y	
Are the intended outcomes described?	Y	
Are the statements clear and unambiguous?	Y	
5. Evidence Base		
Is the type of evidence to support the document identified explicitly?	Y	
Are key references cited?	Y	

Are supporting documents referenced?	Y	
6. Training		
Have training needs been considered?	Y	
Are training needs included in the document?	Y	
7. Implementation and monitoring		
Does the document identify how it will be implemented and monitored?	Y	
8. Equality analysis		
Has an equality analysis been completed for the document?	Y	
Have Equality and Diversity reviewed and approved the equality analysis?	Y	See Generic Pharmacy EIA
9. Approval		
Does the document identify which committee/group will approve it?	Y	
10. Publication		
Has the policy been reviewed for harm?	Y	
Does the document identify whether it is private or public?	Y	
If private, does the document identify which clause of the Freedom of Information Act 2000 applies?	N/A	
11. Accessibility (See intranet accessibility page for more information)		
Have you run the Microsoft Word Accessibility Checker? (Under the review tab, 'check accessibility'. You must remove all errors)	Y	
Do all pictures and tables have meaningful alternative text?	Y	
Do all hyperlinks have a meaningful description? (do not use something generic like 'click here')	Y	

Appendix 2 – Clinical Trial Curriculum Vitae Template

Name:	
Present appointment:	
Address:	
Telephone number:	**Email address:**
Qualifications:	
Professional registration:	
Previous and other appointments:	
Research experience:	
Research training: *(Details of any relevant training in the design or conduct of research, for example in the Clinical Trials Regulations, Good Clinical Practice, consent or other training appropriate to non-clinical research. Give the date of the training.)*	
Relevant publications:	
Signature:	**Date:**