Humber Teaching
NHS Foundation Trust

STANDARD OPERATING PROCEDURE
SETTING UP A CLINICAL TRIAL

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VALIDITY – All local SOPS should be accessed via the Trust intranet

CHANGE RECORD

Version	Date	Change details
1.0	*30/09/22*	*New SOP. Approved at DTG (30/09/22).*

Contents

1. INTRODUCTION

All clinical trials where medicines classed as Investigational Medicinal Products (IMPs) are involved must be reviewed, approved and set-up by the Pharmacy Department prior to the study being approved for conduct in the organisation. This is to ensure that pharmacy can support the trial, taking in to account additional costs, workload and other resource implications and practical aspects of the management of IMPs.

In relation to trials sponsored by Humber Teaching NHS Foundation Trust, pharmacy must be involved in discussions with the Chief Investigator and the Research & Development (R&D) Department at an early stage of protocol development and a formal review will be required.

The purpose of the SOP is to ensure that each trial has an appropriate review and is set-up in a timely manner and within the HRA time period.

2. SCOPE

This SOP should be followed by all members of the clinical trials team within Humber Teaching NHS Foundation Trust.

This SOP should be used as follows:-

- Upon receipt of a clinical trial protocol
- Prior to attending a Site Selection Visit (SSV)
- Setting up a new clinical trial
- To confirm feasibility of a clinical trial
- To review and authorise a clinical trial
- To confirm pharmacy readiness to the R&D Department
- To confirm pharmacy green light

3. DUTIES AND RESPONSIBILITIES

3.1. The Role of Pharmacy

The role of pharmacy in relation to clinical research is:
a) To safeguard subjects, health care professionals and the Healthcare Provider Organisation (HPO) by ensuring that IMPs are appropriate for use and are procured, handled, stored, and used safely and correctly.
b) To ensure that IMPs are managed and dispensed to subjects in accordance with the duly approved current protocol.
c) To ensure that all pharmacy clinical trials procedures comply with relevant guidelines and regulations.

The HPO should have a policy for managing medicines used in clinical trials, including a statement defining the responsibilities that will be delegated to the pharmacy by the investigator. Pharmacy input into the development and review of this policy document is vital to ensure practicability and consistency with other pharmacy procedures.

3.2. Pharmacy Staff

The Chief Pharmacist is responsible for overall service provision although it is expected that a designated member of pharmacy staff will assume operational responsibility for the pharmacy clinical trial service. This individual will usually be the first point of contact within pharmacy when trials involving IMPs are under consideration by the host HPO.

The HPO retains the services of external individuals or organisations to perform IMPrelated duties and functions, the Chief Pharmacist must ensure the individual or organisation is qualified to

perform those IMP-related duties and functions, and must implement processes for assessing their continuing suitability to ensure the integrity of the IMP-related duties and functions.
Designated pharmacy staff providing a clinical trial service must be adequately qualified, trained and experienced to assume clinical research responsibilities and should be able to provide up-to-date training records and/or curriculum vitae.
Pharmacy staff job descriptions should provide clarity with regard to responsibility and accountability for clinical trials.
Pharmacy staff must ensure GCP competence and knowledge commensurate with their roles and responsibilities in relation to CTIMPs.
Pharmacy must hold training records and signature logs for those staff involved in clinical trial activity.
These records may be held in a central location and should be readily available for inspection if required.
Clinical trials pharmacy staff must keep up to date with national guidance relating to clinical trials, GCP, Good Manufacturing Practice (GMP) and medicines management

4. PROCEDURES

When setting up a clinical trial the Pharmacy Clinical Trial Set up Guide (in Appendix A) should be used in conjunction with Pharm/F14 Pharmacy Clinical Trial Set Up form.
There are four main stages of Clinical Trial Set-up:

Stage 1 – Feasibility
This is performed when a Principal Investigator (PI) or Research Nurse has expressed an interest in taking part in a clinical trial (often call an Expression of Interest). There is normally a limited amount of information regarding this study available, so Pharmacy are really assessing whether it is feasible for us to set up this clinical trial.

Stage 2 – Review & Authorisation
This is performed once the site has been selected to open the study. Pharmacy will review the clinical trial protocol and pharmacy manual and confirm that pharmacy are able to proceed with setting up the clinical trial.
Stage 3 – Pharmacy Readiness
Once all of the Pharmacy documents have been created and approved, pharmacy will confirm readiness with the Research Facilitator
Stage 4 – Pharmacy Green Light
Pharmacy Green Light is the confirmation that pharmacy is ready for the first patient to be recruited in to the clinical trial. Pharmacy Green Light may be given at the same time as Pharmacy Readiness if we do not get the initial shipment of IMPs until the first patient is in screening otherwise Pharmacy Green Light is not issued until we have received the IMPs and they are fit for use.

4.1. Stage 1 – Feasibility
Pharmacy will be notified of an Expression of Interest by the R&D Department or by the Research Team.

Upon notification of an Expression of Interest the Pharmacy Clinical Trials Manager/Senior Pharmacy technician for clinical trials will set up an electronic folder on the v:drive in the Expression of Interest folder and transfer any trial related documents to the relevant sub-folders.

The clinical trial name will then be added to the Expression of Interest board which is located in the Clinical Trials office.
Print off a Pharmacy Clinical Trial Set Up Form (Pharm/F14) and complete the trial information on page 1 as far as possible.

Complete Stage 1 – Feasibility on the form. If you do not have all the information at this time to complete stage 1 communicate this to the person who sent you the EOI. Complete the stage 1 at a later date when more information is available.

- **Date of notification of the study and from whom** – the Research Nurse or the Research Facilitator may have notified pharmacy that there has been interest in the study.
- **Date of Site Selection Visit** – some clinical trials will have a Site Selection Visit where the Sponsor will come to the site and meet with the Research Team, The PI and pharmacy.
- **Drugs involved** – this information can be found in the trial summary and the trial protocol (if provided).
- **Who is supplying the IMP/nIMPs** – pharmacy need to obtain the information about where the drugs are being supplied from and if they are being supplied free of charge. If the drugs are being provided from hospital stock or that there is a charge for the drugs, the cost must be compared to the cost of what the treatment a patient would routinely get if they were not taking part in a study. If there is an excess drug cost this must be recorded in this section.
- T**emperature requirements for the storage of IMPs** – What is the storage temperature for the IMP? Do pharmacy have adequate space and are we able to offer storage at the required temperature range?
- **Number of dispensing episodes per patient** – number of items per visit and the total number of visits. Some trials will have a set number of dispensing visits for other trials this may be unknown as the patient may continue treatment until disease progression.
- **Frequency of dispensing** – How often will pharmacy be expected to dispense medication for a patient.
- **Number of patients expected** – how many patients are the Research Nurses planning to recruit into the study?

Do not invest too much time in the study at this point, as it is not guaranteed that we will be selected to open as a site. We are only really checking that it is feasible for pharmacy at this stage.
Any printed documents for this study should be placed in a folder clearly named for that study along with the Pharmacy Clinical Trial Set Up Form (Pharm/F14) in the EOI studies section in the clinical trials dispensary

The Clinical Trials Manager will assess whether it is feasible to undertake the clinical trial and sign the bottom of the Stage 1 form. They will also use the pharmacy study complexity calculator to determine how demanding the study will be for the pharmacy service (the score can be added to the front page and updated as more information is made available). Once stage 1 is complete inform the Research Facilitator by scanning a copy of the completed stage one and sending an email confirming stage 1. Print this email and store with the Pharmacy Clinical Trial Set Up Form (Pharm/F14).

Pharmacy will be notified of the date of the Site Selection Visit (if applicable) and should ensure that a member of the pharmacy clinical trials team can attend (ideally this should be the person who is involved in setting up the clinical trial), so that any questions or queries can be addressed before we are selected as a site. Some Sponsors may wish to visit pharmacy during this visit.

Amend the Expression of Interest board to indicate that stage 1 has been completed.

4.2. Stage 2 – Review & Authorisation

Stage 2 will commence once the site has been selected by the Sponsor and pharmacy have been notified by the R&D Facilitator. The Research Facilitator will send a confirmation email to confirm that pharmacy are to progress with stage 2. The Pharmacy Clinical Trials Manager will nominate a member of staff to complete stage 2. The trial details should be removed from the Expression of Interest board and added to the Pending Trials board.

Move the electronic trial folder that is currently in the Expression of Interest folder to the Pending (in set-up) section of the v:drive. As electronic documents are received they will need to be saved in the electronic trial folder and then printed and filed in the file marked for that study which should be stored in the Pending Trials section in the clinical trial dispensary/office

Complete Stage 2 of the Pharmacy Clinical Trial Set Up form (Pharm/F14).

- **Date of when site was selected** – this can be found on correspondence confirming that the site has been selected.
- **Any additional drug cost** – if pharmacy are having to procure any drugs that are not standard of care that the sponsor is not reimbursing.
- **Any additional cost to pharmacy** – e.g are we having to provide taxis to transport the drug?
- **Additional equipment required** – fridges, denward loggers, cool bags etc.
- **Commercial costing template reviewed and approved** – only applicable to commercial studies, check that dispensing fees, set up fees are correct, this will then need to be approved by the Pharmacy Clinical Trials Manager/Principal Pharmacist (this can be done at the same time that the Pharmacy Clinical Trials Manager/Principal Pharmacist signs off stage 2)
- **Open label/single blind/double blind** – if blinded how will drugs be allocated at each dispensing, will it involve an IXRS system or a randomisation list held within pharmacy
- **Is pharmacy involved with unblinding** – will pharmacy have to unblind, if so how is this done?
- **Drug supply after completion** – who will fund the study drug after completion of the trial, this may not be applicable to all trials.
- **IXRS/IWRS/other web based program to be used by pharmacy, if yes what for?** – will pharmacy acknowledge receipt or dispensing
- **Is manual ordering involved** – will pharmacy have to complete order forms for initial and further supplies of medication.
- **Additional sponsor training required** – Are pharmacy staff expected to perform on-line training for study specific training, and the estimated time for each staff to complete the training. Are there any additional funds available for training if the training will take longer than one hour per staff member.
- **Estimated date of opening** – confirm with the Research Team and the Research Facilitator the date planned for opening, considering HRA time limits and the date of the Site Initiation Visit (SIV).
- **Trial Monitoring Company** – if different from Sponsor.
- **Details of Trial CRA or Monitor** – Name, email and telephone of CRA or Monitor
- **IMP dispensing requirements** – any tear-off labels to be applied to the accountability logs, controlled drug etc.
- **Stability/storage requirements of reconstituted IMP** – after aseptic preparation, or a liquid that has been reconstituted with water the expiry date and storage will differ from the original. Consider if any additional paperwork will be required to maintain the coldchain. For Scarborough trials consider the transportation between sites if Aseptics are involved.

Create a plan for setting up the pharmacy site file, review what documents will need to be created, for example:

- Dispensing Instructions
- Drug Maintenance
- Trial Summary/Unblinding
- Accuracy/ Clinical Checking Checklist
- Master Labels
- Accountability Logs
- Prescriptions

Once Stage 2 of the Pharmacy Clinical Trial Set Up form has been completed the Pharmacy Clinical Trials Manager will sign, print and date.
Scan a copy of the completed stage two and send an email confirming stage 2 to the Research Facilitator. Print this email and store with the Pharmacy Clinical Trial Set Up Form (Pharm/F14). Amend the Pending Trials board to indicate that Stage 2 has been completed.

4.3. Stage 3 – Pharmacy Readiness

The Research Facilitator will send a confirmation email to confirm that pharmacy are to progress with stage 3 or it will be discussed at a prioritising studies meeting. The Pharmacy Clinical Trials Manager will nominate a member of staff to complete stage 3.

Complete Stage 3 of the Pharmacy Clinical Trial Set Up form with the following:

- **Date Pharmacy Site File was requested** – contact the trial CRA/Monitor and request the Pharmacy Site File, if the file is not available as yet ask for all the relevant documents to be sent to pharmacy.
- **Date Pharmacy Site File was received** – in the event that the Sponsor will not be providing a Pharmacy Site File, ensure that all of the trial related documents have been sent to pharmacy and a local file constructed.
- **Date of Site Initiation Visit (SIV) –** This is the date by which we should have everything written and approved by, so that Pharmacy readiness could be issued.
- **Are the accountability logs supplied by the sponsor, if not, date they were created** – this will include drug inventory and patient specific drug accountability logs, if logs are created ensure there is version controlled on each one.
- **Date IB received** – if applicable record the date the Investigator Brochure was received.
- **Date Master labels were created** – create master labels using SOP Pharm/S105.
- **How will QP/Batch/C of As releases/certificates be sent to site** - confirm with the Sponsor the process for receiving QP/Batch releases or any Certificates of Analysis that are required for the IMPs.
- **Date Trial Summary & Unblinding instructions were completed** – the date which they were written.
- **Date Trial Dispensing instructions were completed** – the date which they were written.
- **Date Trial Drug Management instructions were completed** – the date which they were written.
- **Is a prescription supplied, if not date completed (for Chemocare prescriptions include date requested)** – if a prescription is supplied, is it suitable for use (NHS Number, allergy status etc). If we have to get the prescription amended, ask the Sponsor if they can do it as they will then be responsible for version control. If we have to amend this prescription we will have to remove the Sponsor's version control and add our own.
- **Has the Pharmacy Site File been set up according to Appendix 2** – The file should be indexed according to Appendix 2 and the Sponsor's original index should be filed in the superseded section of the file so that we can archive it in its original order if we are asked to.
- **Have Pharmacy staff signed the main site delegation log** – all pharmacy clinical trials staff should sign the site delegation log (unless specified not to).
- **Have pharmacy received a copy of the completed site delegation log** – The completed delegation log should have all staff signed off by the PI.
- **Procedure for initial supply of IMPs/nIMPs** – pharmacy need to confirm whether IMP will be sent before the greenlight has been given or if the initial supply will be released once the first patient is being screened.
- **Has the codebreak/unblinding procedure been tested** – For blinded studies where pharmacy are expected to unblind, the unblinding process has to be tested and this is recorded on form Pharm/F50 "Code Break Test Form".
- **Date documents have been reviewed and approved** – when the documents have been reviewed by a second person (Pharmacy Clinical Trials Manager or a delegate) and approved by a third person (Principal Pharmacist Clinical Research/Clinical Trials Pharmacist)

Once Stage 3 of the Pharmacy Clinical Trial Set Up form has been completed the Pharmacy Clinical Trials Manager will sign, print and date.
Scan a copy of the completed stage three and send an email confirming stage 3 to the Research Facilitator. Print this email and store with the Pharmacy Clinical Trial Set Up Form (Pharm/F14).
Complete the Check-list for study set-up (last page of the Pharmacy Clinical Trial Set Up form) as you work through the preparation of the pharmacy site file. Before stage 4 is issued ensure the final check of pharmacy site file is complete and sign and date the relevant section of the check list.

4.4. Pharmacy Green Light

Once the IMPs have been delivered to site and are suitable for use (i.e no temperature excursions occurred during shipping) and all Pharmacy staff training has been done complete stage 4 of the Pharmacy Clinical Trial Set Up form.

Once stage 4 of the Pharmacy Clinical Trial Set Up form has been completed the Pharmacy Clinical Trials Manager/Senior Pharmacy Technician will email the Research Facilitator and other relevant parties that everything is place in pharmacy for recruitment to begin. Print the email and store in the relevant section of the pharmacy site file. Also store the completed Pharmacy Clinical Trial Set Up form in the pharmacy site file with all the other pharmacy stages emails.

The Research Facilitator will then send an email confirming that recruiting can now start into the trial.

5. REFERENCES

Pharmacy Clinical Trial Set up Guide
Pharm/F14 Pharmacy Clinical Trial Set Up form
Pharm/F50 “Code Break Test Form

Appendix A: Pharm/F14 Pharmacy Clinical Trial Set Up form

Short Trial Name/Number	
EudraCT Number	
R&D Reference	
Sponsor	
PI	
Lead Research Nurse	
Site	
Study Phase	
Date Protocol received	
Version No. of protocol received	
Speciality	
Indication	
Commercial or non-commercial study	
Is it CRN/NIHR supported?	
Research Facilitator responsible for this trial	
Complexity calculator score	

Trial Title:

Stage 1 – Pharmacy feasibility

Date of notification of the study and from whom	
Date of site selection visit	
Drugs Involved (IMP and nIMPs)	
Who is supplying IMP/nIMPs	
Storage & Temperature requirements for the IMP/nIMPs	
Aseptic involvement	
Satellite Unit involvement	
No. of dispensing episodes per patient	
Frequency of dispensing	
Number of patients expected	

Completed by ……

Are pharmacy happy to proceed with this study with the documentation, information we been provided with at this time Yes/No

Sign……. Print ……Date ……

Pharmacy Feasibility (Stage 1) email sent to Research Facilitator

Date ……..

Trial Title:

Stage 2 – Pharmacy Review/Authorisation

Date of receipt of Research Facilitators email ……

Date of site selected	
Any additional drug costs	
Any additional costs to pharmacy	
Additional equipment required	
Commercial costing template reviewed and approved (commercial studies only)	Reviewed by: Approved by:
Open label/single blind/double blind	
Drug supply after trial completion	
IXRS/IWRS/other web based program to be used by pharmacy, if yes what for?	
Is manual ordering involved. If so, how will it be done?	
Is pharmacy involved with unblinding. If yes, how?	
Additional Sponsor training required	
Estimated date of site opening	
Aseptic approval, if applicable	Sign: Print: Date: (or state if email confirmation is attached)
Trial Monitoring Company	
Details of Trial CRA or Monitor	
IMP dispensing requirements	
Stability/ Storage requirements of reconstituted IMP	

Completed by ……..

Are pharmacy happy to give authorisation for this study? Yes/No

Sign……Print ……..Date ……

Pharmacy Review/Authorisation (Stage 2) email sent to Research Facilitator

Date ……..

Trial Title:

Stage 3 – Readiness

Date of receipt of email from Research Facilitator to commence Stage 3 ……..

Date Pharmacy Site File was requested	
Date Pharmacy Site File was received	
Date of Site Initiation Visit (SIV)	
Are the accountability logs supplied by the sponsor, if not, date they were created and the date approved by Sponsor	
Date IB received	
Date Master labels were created	
How will QP/Batch/C of As releases/certs be sent to site?	
Date Trial Summary & unblinding instructions completed	
Date trial dispensing instructions completed	
Date trial drug management instructions completed	
Is a prescription supplied, if not date completed (for ChemoCare prescriptions date requested)	
Has the pharmacy site file been set up according to SOP Pharm/S45, appendix 2?	
Have pharmacy staff signed the main delegation log	
Have we received a copy of the completed delegation log	
Procedure for initial supply of IMPs/nIMPs	
Has the codebreak/unblinding procedure been tested	
Date documents have been reviewed & approved	
Record of Labels printed logs prepared	

Completed by ……

Does pharmacy have all the relevant documentation in place and able to give readiness? Yes/No

Sign…….....Print ……Date ……

Pharmacy readiness (Stage 3) email sent to Research Facilitator Date ……..

Trial Title:

Stage 4 – Pharmacy Green Light

Initial supply of IMPs/nIMPs received	
Date initial supply received	
Date Pharmacy training completed	

Completed by …….

Pharmacy Green Light given? Yes/No

Sign……Print ……..Date ……

Pharmacy Green Light (Stage 4) email sent to Research Facilitator Date ……..

Date of receipt of confirmation from Research Facilitator that recruitment can begin …….

Trial Title:

Check-list for study set-up

Stage Complete		
	Complete and Sent to RDF	Email Filed in PSF
Stage 2		
Stage 3		
Stage 4		

Documents to create							
	Written	Checked	Printed	Authorised	All wet signatures	Laminated	Final copy stored in electronic folder
Trial Summary							
Stock Maintenance							
Dispensing							
Accuracy Grid							
Master Label							
Prescription							
Master Accountability							
Subject Accountability							
File Notes for blank sections							
Record of labels printed Log							
SOP version control forms							
Signs for boxes							
Signs for files							

Pre-created Documents to Include		Documents to request from R&D	
	Printed and Filed		Printed & Filed
Contents List		Delegation Log	
File Dividers		Trust Set Up approvals	
Patient Log			
Staff Signature Log			
Amendment Log			
File note Log			

Final check of pharmacy site file	
All sections of the pharmacy site file contents have been checked and completed or a file note created for blank none applicable sections.	
Checked by:	Date:

Appendix 2 – Pharmacy Clinical Trial File Contents

Pharmacy Clinical Trial File Contents

Section Number	Title
1	Pharmacy Trial Instructions (including information for unblinding / code break if applicable)
2	Master labels, label record forms and if applicable, a copy of the sponsor-provided label
3	Patient log
4	Sample prescription and prescription risk assessment form (if applicable)
5	Pharmacy staff signature log
6	Delegation log
7	Patient prescriptions, subject specific drug accountability logs and master drug accountability logs
8	Drug orders, receipts and shipping records
9	QP release documents / Certificate of Analysis
10	Drug returns / drug destructions / IMP recall
11	Sponsor monitoring visit log and associated documents
12	Current approved protocol
13	Investigator Brochure / Summary of Product Characteristics
14	Pharmacy manual and any IWRS reference documents
15	Pharmacy Set-Up form and sponsor and trust set-up approvals
16	Temperature records and related documentation
17	Transfer documents and pharmacy monitoring forms (if applicable, for studies where IMP is stored outside of Pharmacy)
18	Unblinding and Code break documentation if applicable
19	Training documents and records, and CV and GCP certificates
20	File note log
21	Amendment documents
22	Miscellaneous documents and general correspondence
23	Superseded documents