

A Guide to Pharmacy Documentation For Clinical Trials

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The following guidance is based on Individual Trust requirements, the requirements of GCP / GMP and the results of a recent MHRA Inspection.

The Pharmacy Department in an NHS Hospital is responsible and accountable for Pharmacy Services to that Hospital through the Chief Pharmacist.

Supply of Clinical Trial Material / IMP to NHS patients who participate in studies in NHS premises are governed by the requirements for those NHS pharmacy services together with any additional requirements for conducting clinical studies.

Documentation is essential covering not just an individual CT but more importantly the Pharmacy Service providing CT support.

Documentation covering Pharmacy Clinical Trials Service

Pharmacy Services that may be need to be provided

- Dispensing
- Assembling
- Manufacturing
- Quality Assurance
- Receipt
- Storage
- Returns

Documentation covering Pharmacy Clinical Trials Service

- Procedure for writing Clinical Trials procedures
- Decision Tree for assessing whether an undertaking is a clinical trial
- A list of all documents relating to clinical studies
- Who has access to documents and how
- Evidence of document author and date of writing
- Evidence of Trust Approval for documentation (when appropriate)
- Evidence of Date for review / update

Documentation covering Pharmacy Clinical Trials Service

- **Location map for current department study documents**
- **Location map for individual Trial Folders (and also Trial Material)**
- **List of Key Staff directly responsible for clinical trials and their responsibilities**
- **List of all pharmacy staff (past and present) who may be involved in C.T.'s in any way.**
- **Evidence of Individual training (CV / CPD etc) in clinical trials procedures**
- **Training Procedure, including retraining and accreditation / re-accreditation**
- **List of staff generally involved in clinical trials (and their signatures) and contact details**

Documentation covering Pharmacy Clinical Trials Service

- Evidence of staff trained in specific clinical trials
- Evidence of staff trained in specific clinical trial procedures / manipulations e.g. Aseptic preparation.
- Log of location of documentation for all closed studies. (including PI, and start / closure dates)
- Pharmacy standards for clinical studies
- Protocol for Pharmacy approval of individual studies
- Risk assessment process for individual studies
- Pharmacy Trust approved charges and basis of those charges

Documentation covering Pharmacy Clinical Trials Service

- Log of all current studies
including starting dates and closing dates and researchers
- List of all known pending studies
and expected starting dates
- List of external key personnel involved in clinical studies
e.g. R&D and Ethics Committee contacts and their responsibilities.
- General procedures for dealing with emergency situations
– e.g. Lack of Telephones, Internet
- Description of IMP / CTM and licensed products
detailing how to distinguish and different trial requirements
- List of reference documents and how to access and websites (MHRA / ICR etc)

Documentation covering Pharmacy Clinical Trials Service

Some of the required evidence may be combined to form a composite with other evidence in individual protocols or SOPS

Whatever method of documentation is used, the evidence must be readily extractable and available if requested.

Documentation covering Pharmacy Clinical Trials Service

General Procedures

There should be general procedures covering all the areas listed below .

- Individual protocols or SOP's may also be necessary for individual study.
- In many cases the individual studies will include these as part of official documentation.
- Specific procedures should usually detail how to undertake a single process.
- General procedures should provide pharmacy staff with information on the who / what and why of when they would be expected to undertake more common procedures.

An example is code break – many studies specify that this can only be via a Researcher and a phone call using IVRS. This is seen by the MHRA as 'poor' GCP and Pharmacy would be expected to have a procedure covering a situation where if a researcher was not available that would permit a code break to be undertaken in a timely fashion by pharmacy.

Documentation covering Pharmacy Clinical Trials Service

IMP / CTM Movement

- Receipt of IMP/ CTM *1
- Transfer from receipt to storage
- Storage
- Temperature control for Freezer / Refrigeration room temperature
- Adverse temperature procedure
- Preparation / assembly procedure (if appropriate)
- Dispensing / issuing procedure
- Returns procedure
- Storage of Returns procedure
- Return to Sponsor of IMP/CTM
- Disposal and / or Destruction procedure (if applicable)

Documentation covering Pharmacy Clinical Trials Service

*1

Receipt

The Receipt Procedure must include a procedure for dealing with incomplete / faulty deliveries and also detail who is authorised to 'receive' IMP/CTM.

It would also be appropriate to include in this a process for dealing with inadequate temperature control (or lack of evidence of) during transit

Documentation covering Pharmacy Clinical Trials Service

- Drug Recall procedure (for stored IMP/ CTM)
- Code Break Procedure for Pharmacy Staff *2
- Code Break access – a list of all code break access points for residency / emergency use
- Procedure for dispensing / issuing errors
- Recovery process for incorrectly dispensed IMP / CTM or recalled IMP/CTM
- Ordering of IMP/CTM –including emergencies
- Re-ordering of IMP/CTM – including emergencies
- Storage of IMP/CTM assembled prior to dispensing
- Ward / Department storage prior to administration

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*2 The Code Break procedure should detail circumstances under which pharmacy staff may need to undertake code break in an emergency.

It should detail how and when to arrive at that decision, how to undertake the code break and what follow up should then be undertaken.

It must be possible for pharmacy to undertake a code break in an emergency. The MHRA consider that Pharmacy being denied access to code breaks does not meet GCP requirements and could consider such lack of access as inadequate support for a study.

Some code breaks (and drug re-order processes) rely on IVRS and / or internet access. A procedure should be in place that deals with situations where IVRS / internet access is unavailable

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IMP / CTM Quality

The following documentation is essential for non-commercial IMP/CTM and may also be essential for commercially sponsored studies :-

- Release documentation for each batch of CTM / IMP and /or
- QPIMP specification of quality of each individual batch of product. This is essential if source is non-EU
- Evidence supporting any change of storage conditions / expiry date
- Import License if product sourced from non-EU country direct to study site (Not required if obtained through importer)
- Evidence that import is to licensed importer (If above does not apply)
- Protocol for assessing CTM / IMP Suppliers

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- **Temperature logs for transit / delivery** *3
- **Temperature logs for storage at site**
- **Copies of any SPC's for IMP/CTM (if available)**
- **Translations of any SPC's for IMP / CTM not written in English (If available)**
- **Internal (i.e. obtained by Pharmacy) QPIMP**
- **Assessment and release of product – particularly if non EU sourced** *4
- **Audit of trial stock – expiry dates etc. The procedure should detail process for dealing with short expiry dates etc.**

Documentation covering Pharmacy Clinical Trials Service

*3 Surprisingly temperature logs are not requested for ambient temp transit but this may be important for products where temperature variations above or below a certain range are critical.

It is insufficient to have a statement from Sponsor / Transporter that storage was at suitable temperature. Some companies do try and state that storage was adequate and they are responsible. However the Pharmacy is responsible for validating that temperature control during transit was adequate and this cannot be done without the appropriate evidence.

Ideally the study folder and supporting documentation should be able to provide a temperature log from the point of assembly to the point of issue to a participant.

Documentation covering Pharmacy Clinical Trials Service

*4 Evidence for the quality of a product is essential. In the EU, manufacturers spec, especially for licensed products, may be adequate.

For unlicensed IMP/ CTM, release documentation and or QPIMP documentation is necessary.

It may also be felt necessary to identify the releasing officer for each received batch and their qualifications in relation to IMP/ CTM .

If the storage or preparation of an IMP / CTM changes, then evidence of why that change is necessary or has been approved is also required – not simply a notification that it has.

This is no less important where storage requirements are relaxed. Where storage conditions become more restrictive, questions should be raised on previous issues and the potency or risk of the product when used prior to the change

Documentation covering Pharmacy Clinical Trials Service

The Clinical Trial Folder

- **Index / Concordance for trial folder**
- **Initiation date and possible closing date**
- **Study folder marked with its location in Dept.**
- **Current Protocol with version number etc.**
- **All official communications between Pharmacy / Sponsor / Investigator**
- **Ethics approval letter**
- **R&D Approval letter**
- **Pr. Researcher, Chief Researcher and Sponsor contact details**
- **Responsible Pharmacy Staff – including signatures where necessary**

Documentation covering Pharmacy Clinical Trials Service

- **All receipts for IMP/CTM**
- **Copies of all protocol variations and significant amendments (with official approvals)**
- **Local SOP with version number, author and revision date**
Must be updated to cover any protocol variations
- **All Batch QC data**
- **Record of all Dispensings (suitably dated and signed including checkers)**
- **Record of all dispensing errors and how they were resolved**
There is a recommendation that a central record of all errors is maintained and should cover any retraining etc. to minimise such errors. This depends on level / frequency
- **All Patient Returns logged and dated**
- **All Returns to Supplier**

Documentation covering Pharmacy Clinical Trials Service

- Code break envelopes and / or IVRS process for code break.
- Records of any code breaks together with an explanation
- Destruction process and log of all authorised destructions and copy of destruction certificates.
- Current Patient Information Sheet.
- Product SPC or Clinical information in particular detailing any known SE / AE
- Record of any withdrawals due to SE/ AE (If known to pharmacy)
- Information on how to deal with overdose and or SE / AE (If known)
- Local SOP covering essentials of individual study that require any supplementation to general SOP's standard.
- Risk assessment by pharmacy for the specific study.

Documentation covering Pharmacy Clinical Trials Service

Summary

Pharmacy may not necessarily produce specific documentation but is responsible for both its availability and relevance within the Pharmacy Department Clinical Trials Service.

The purpose of a Protocol for writing CT protocols is essentially to ensure there is a formal process in place for conducting CT's in Pharmacy

Documentation must be readily available and accessible and so there should be one or more points where a list of the current documentation is available. Examples include a web page on the Trust Intranet and also a written list in Medicines Information and the CT area itself.

Documentation covering Pharmacy Clinical Trials Service

There should be a concordance within the study documentation that allows extraction of Investigator names and the studies they are involved in, drugs involved in studies, etc. (in case of a drug recall / withdrawal).

There should also need to be procedures for dealing with unusual situations such as what happens when a researcher leaves and no named researcher replaces that researcher. (e.g. a Locum is appointed).

Where there is a recommendation that records are maintained for rare events – e.g. code breaks, there should be evidence that there is cover for such events even if none have occurred.

Documentation covering Pharmacy Clinical Trials Service

There should be a list of current official documents relating to clinical studies – e.g. from MHRA , current EU directives / RPSGB / ICR Practice guidance etc. and this should include such as the MHRA application form , IMP definition Declaration of Helsinki etc. and details of how to access these.

Documentation covering Pharmacy Clinical Trials Service

Pharmacy are a professionally regulated body that have clinical responsibilities towards the patients to whom they provide services and clinicians who utilise that service

Clinical Trial documentation should be such as to demonstrate that Pharmacy has in place the appropriate standards and facilities to provide and monitor such services

While documentation is clearly aimed at meeting regulatory requirements, the aim of those requirements is to ensure that Patients as participants, Clinicians as researcher and Pharmacists are part of and are provided with a service that meets the required standards.

Documentation covering Pharmacy Clinical Trials Service

Main Reference Sources

MHRA

COREC

ICR

RPSGB