



**Royal  
Pharmaceutical  
Society**  
of Great Britain

## **PRACTICE GUIDANCE ON PHARMACY SERVICES FOR CLINICAL TRIALS**

This guidance was prepared on behalf of the Practice Division of the Royal Pharmaceutical Society of Great Britain and the Institute of Clinical Research.

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This practice guidance on pharmacy services for clinical trials has been produced jointly by the Institute of Clinical Research and the Royal Pharmaceutical Society of Great Britain and should be used by pharmacy staff involved with the provision of clinical trials services at policy, strategic and operational levels.

The guidance applies to all clinical trials that are regulated by the Medicines for Human Use (Clinical Trials) Regulation 2004. This includes commercial and non-commercial clinical trials and investigator initiated clinical research.

The generic terms "pharmacy" or "pharmacy staff" encompass pharmacists and pharmacy technicians, although it is recognised that pharmacists and pharmacy technicians may have different professional roles in relation to the provision of clinical trials services.

The pharmacy department may support clinical trials involving medicines, biological substances, gene therapy or radio-pharmaceuticals. Specific guidance and regulations exist for the management of these products. It is the responsibility of the pharmacy staff involved to ensure compliance.

When a clinical trial is taking place in a hospital all Investigational Medicinal Products (IMPs) should be stored and dispensed by the hospital pharmacy and managed to the same standards as licensed medicines. IMPs must not be stored in offices, clinics or ward areas unless by prior agreement with pharmacy.

For clinical trials conducted within the primary care sector the principles of this practice guidance should be adhered to where possible.



## 1. THE ROLE OF PHARMACY WITHIN A NHS TRUST

### 1.1

The role of the pharmacy in relation to clinical research is:

- a) To safeguard subjects, health care professionals and the Trust by ensuring that IMPs are appropriate for use and are procured, handled stored and used safely and correctly. (2,5,6,8)
- b) To ensure that IMPs are managed and dispensed to patients in accordance with the protocol.
- c) To ensure that all pharmacy clinical trials procedures comply with relevant guidelines and regulations. (1,3,4,8)

### 1.2

It is good practice for a NHS Trust to issue a policy document covering the safe handling of medicines used in clinical trials, including a statement listing the responsibilities the clinical trial investigator will delegate to the pharmacy department. The pharmacy department must have input into this policy document and its regular review (5,8).

## 2. PHARMACY STAFF

### 2.1

A designated member of pharmacy staff must be appointed who will have overall responsibility for the pharmacy clinical trial service.

### 2.2

Designated pharmacy staff providing clinical trial services 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 (3,4) Pharmacy staff job descriptions must provide clarity with regard to responsibility and accountability for clinical trials.

### 2.3

Pharmacy must hold training records and signature logs for those staff involved in any clinical trial activity. (8) Staff training records for an individual clinical trial must be archived with the pharmacy study file to ensure that these records are available for audit or regulatory inspection.

### 3. PHARMACY FACILITIES

#### 3.1

Pharmacies must have facilities that allow for IMPs to be stored separately from normal pharmacy stock in an area with restricted access. IMPs that are returned by patients or have expired must be stored separately from unused IMPs. (3)

#### 3.2

Regular temperature monitoring of IMPs storage facilities must be undertaken and these records archived. Fridges and freezers should be fitted with thermometers that record minimum and maximum temperatures and with an alarm system to alert staff if the temperature falls outside the specified range. The pharmacy should have written procedures in place for what actions to take when the storage conditions are outside the specified range.

#### 2.3

Suitable archiving facilities will be required for pharmacy trials files. The system used for archiving should allow for prompt retrieval of any pharmacy study file or of non-study specific documentation (such as pharmacy standard operating procedures, original pharmacy temperature monitoring records and training records of pharmacy staff) (3).

## 4. PHARMACY AND RESOURCES

### 4.1

Pharmacy should ensure that adequate resources are available to provide a pharmacy clinical trial service so that research does not inappropriately divert pharmacy NHS resources from the provision of patient care (4).

### 4.2

Pharmacy should receive fees for providing clinical trials services. These fees should reflect the workload and cover costs involved. This pharmacy fee is separate to the prescription charge. (12,13,19)

### 4.3

In NHS Trusts that have adopted the model clinical trials agreement (CTA) for industry sponsored trials, the pharmacy should ensure that:

- The appropriate fee for pharmacy clinical trial services are included in annex 5 of the agreement.
- The required pharmacy resources are available and appropriate for the clinical trial.

It is desirable that a management system is established within a NHS Trust whereby pharmacy is contacted in advance to the Trust agreeing and signing the model CTA. (14,15)

### 4.4

When the pharmacy is not included within the trial agreement the pharmacy should set up a separate agreement with the sponsor. The Trust's Research and Development (R & D) department should be consulted.

## **5. PRESCRIPTION CHARGES**

### 5.1

Prescription charges apply to clinical trial medicines unless the subject is exempt or the clinical trial is placebo controlled . (7)

A sponsor may choose to pay the prescription charges on behalf of the subjects in a clinical trial. These charges must be handled separately from clinical trial payments as per department policy.



## **6. COMMUNICATION WITHIN AND OUTSIDE THE NHS TRUST**

### **6.1**

The pharmacy should ensure that an effective working relationship is established with the site investigators, research personnel, the R&D department and other support services to provide a comprehensive process for delivering the pharmacy clinical trial service.

A good working relationship should also be established and maintained with sponsors, monitors, auditors and regulatory authorities:

- To ensure the safe supply of IMPs to clinical trial subjects.
- To ensure that all data and documentation (e.g. pharmacy study file, standard operating procedures) associated with a study are accurate, up-to-date and available for audit or inspection by an appropriate authority. (1,3)
- To ensure that medicines management systems for IMPs within a Trust are adequate.
- To represent and uphold the interests of the pharmacy and pharmacy professionals in clinical research.
- To ensure that the confidentiality and security of information and data about the subjects and the clinical trial are maintained and respected.

### **6.2**

Pharmacy staff should be aware of legislation and local requirements for the reporting of suspected fraud, misconduct or other incidents. If pharmacy staff become aware of any of these they should notify the investigator, sponsor or the local research and development department at the earliest opportunity.

## 7. PHARMACY AND THE R&D DEPARTMENT

### 7.1

The clinical trial pharmacy staff should foster a good working relationship with their local R & D Department. The pharmacy staff will be able to advise on issues such as:

- a. The source and quality of IMPs including comparators to be used.
- b. The cost of IMPs.
- c. The acceptability of the packaging and labelling of IMPs.
- d. The regulatory approval process providing support and assistance where necessary.
- e. The identification of possible clinical risk issues, and address these where the use of an IMP may differ from normal routine practice.
- f. The regulations and guidelines on good clinical practice and good manufacturing practice.
- g. The Trust's clinical risk assessments of individual clinical trials and with internal clinical trials systems and procedures.
- h. Health and safety aspects of drug handling, dispensing and reconstitution.

### 7.2

Where appropriate pharmacy should be involved in the Trust peer review process of clinical trial protocols. Where there is a conflict of interest for the pharmacy department, it must be declared.

## **8. ETHICS COMMITTEE**

### **8.1**

Ethics committees that are reviewing clinical trials involving IMPs should have a pharmacist as a member. The pharmacist must be aware of, and where appropriate, must declare any possible conflict of interest between her/his role on the ethics committee and involvement in providing pharmacy clinical trials services or in the clinical trial as a researcher/investigator. (16,17)

## 9. SET-UP OF A STUDY

### 9.1

Designated pharmacy staff must review each protocol, assess the feasibility of the study, cost the work to be undertaken by the pharmacy department and where appropriate assess the impact for the Trust.

### 9.2

Pharmacy clinical trials staff should participate in the investigator meeting or the site selection visit and initiation meeting. Pharmacy staff should use their professional expertise to review the protocol and explain the correct use and storage of any IMPs to other health professionals (e.g., investigators and research nurses) who may not be familiar with these.

### 9.3

IMPs must be manufactured in a licensed production unit, authorised by the Medicines and Healthcare Products Regulatory Agency (MHRA), in accordance with Good Manufacturing Practice (GMP) and labelled in accordance with Annexe 13 (GMP), these IMPs must be released for use by a Qualified Person (QP (IMP)) (1,6). The distinction between manufacturing, assembly and dispensing, and the circumstances where a (QP (IMP)) is not required are defined in The Medicines for Human Use (Clinical Trials) Regulations 2004. (1)

### 9.4

Pharmacy should request actual samples of the packaging and labelling of IMPs in advance of the commencement of recruitment of subjects to the clinical trial. Sufficient time should be allowed for a risk assessment of the product and for additional pharmacy labels to be produced if necessary prior to any dispensing (9).

Pharmacy must check the packaging and labels of IMPs to ensure they comply with Good Manufacturing Practice (GMP) requirements and regulations and ensure that they are legible and understandable for the subject (1,6).

9.5

Where drug accountability forms, prescription forms and other associated forms are supplied by the sponsor, the pharmacy department should review these with regard to the data they are designed to capture and their suitability for use within the pharmacy department. The pharmacy department should provide this documentation for non-commercial clinical trials using IMPs (9).

9.6

Prior to the commencement of a clinical trial it should be determined whether the IMPs will be made available to the subjects when the clinical trial has finished.

9.7

Pharmacy should agree with the sponsor whether unused IMPs and used IMPs returned by clinical trial subjects are to be returned to the sponsor or destroyed locally, in accordance with the sponsor's instructions and Trust procedures (9).

9.8

The pharmacy should, where possible, hold the code breaks. In circumstances when the pharmacy does not hold the code break the pharmacy should ensure that there is a system in place for providing 24-hour cover to access the code-break for a clinical trial (8).

## 10. APPROVALS

### 10.1

Prior to the commencement of a clinical trial and the dispensing of any IMPs the pharmacy must be satisfied that clinical trials have:

- appropriate regulatory documentation in place i.e. Clinical Trial Authorisation
- been given a favourable opinion by the appropriate Research Ethics Committee(s).
- been approved by the local R & D Department.

In addition, the pharmacy department must be in receipt of the final copy of the protocol and any amendments and the latest version of the investigator brochure prior to dispensing any IMPs.

## 11. IMP MANAGEMENT

### 11.1

The pharmacy must have written clinical trials standard operating procedures (SOPs) to cover the following procedures (3,10,11):

- Receipt and recording of the safe delivery of IMPs.
- Safe handling and storage of IMPs.
- Code breaking
- Preparation and dispensing of IMPs in accordance with professional standards (including dispensing against an appropriate prescription, maintaining drug accountability records and ensuring that all IMPs are labelled with the appropriate pharmacy label).
- Return and disposal of unused IMPs.
- Reconciliation of IMPs.
- Maintaining a pharmacy study file.
- Training of clinical trial pharmacy staff.
- Archiving of clinical trials documentation.

SOPs should be authorised and reviewed at regular intervals (e.g., annually). SOPs and other documents produced by pharmacy should be version-controlled to ensure that the correct documents are used. Superseded documents should not be destroyed.

### 11.2

Pharmacy is responsible for keeping accurate records with sufficient information to provide a full audit trail from the receipt of the IMPs to their removal from site or destruction (3).

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## 11.3

It is good practice for pharmacy staff to assess whether any IMPs brought into hospital by a patient are suitable for use. Where possible the pharmacy staff should notify the investigator and sponsor of any unplanned hospital admissions.

## 11.4

IMPs should always be labelled with the patient's name and date dispensed however to maintain confidentiality, the patient identity must be removed before it is returned to the sponsor.

## 11.5

Clinical trial subjects should be counselled on the correct use of the IMP in addition to any written information which is provided e.g. clinical trial patient information sheet or the Patient Information Leaflet (PIL).

## 11.6

Pharmacy staff should promptly notify all reported, possible adverse events experienced by patients in a clinical trial to the investigator and sponsor.

## 12. PRESCRIPTIONS FOR CLINICAL TRIALS

### 12.1

Only qualified and registered medical practitioners and health care professionals who are supplementary prescribers\* can prescribe IMPs. The IMPs must be prescribed on a hospital drug chart or on a prescription form which is signed by a prescriber who is recognised as participating in the clinical trial.

*\*A supplementary prescriber can prescribe unlicensed medicines if part of a clinical trial. If a supplementary prescriber prescribes for a clinical trial, then the pharmacy department should be provided with written confirmation of this arrangement which is signed by the local investigator and the sponsor. This document should be included in the pharmacy study file. (<http://medicines.mhra.gov.uk>) April 2005*

### 12.2

Study-specific clinical trial prescription forms should be used to facilitate the prompt identification of the clinical trial and dispensing procedures and to reduce the risk of dispensing errors.

### 12.3

It is essential that prescriptions for IMPs clearly identify the clinical trial, the subject and medication required. When an IMP is prescribed for an in-patient, the medicine chart should clearly identify the clinical trial and the IMP and include the words "Clinical Trial"

### 12.4

Prescription charges may apply see section 5.

# Glossary

**GLOSSARY OF TERMS** (For full explanation for each term consult the appropriate references):

**ETHICS COMMITTEE:** An independent body consisting of healthcare professionals and lay members, whose responsibility it is to protect the rights, safety and well being of human subjects involved in a trial and to provide public assurance of that protection by, among other things, expressing an opinion on the trial protocol, the suitability of the investigators and the adequacy of facilities, and on the methods and documents to be used to inform trial subjects and obtain their informed consent (1).

**INVESTIGATOR:** An authorised health care professional responsible for the conduct of a clinical trial at a clinical trial site. If this trial is conducted by a team of authorised health professionals at a clinical trial site, the investigator is the leader responsible for that team (1). Often the investigator within the hospital setting is a medically qualified consultant and in primary care, a medically qualified general practitioner.

**INVESTIGATOR BROCHURE:** A compilation of the clinical and non-clinical data on the investigational product(s) which is relevant to the study of the investigational products in human subjects. (3)

**INVESTIGATIONAL MEDICINAL PRODUCT (IMP):** A pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical trial (1).

# Glossary

**MONITOR:** A person who has been trained to oversee the progress of a clinical trial, and to ensure that the clinical trial is conducted in accordance with the clinical trial protocol, standard operating procedures, good clinical practice and applicable regulatory requirements (3).

**PHARMACY STUDY FILE:** Contains all the documents pertaining to a specific clinical trial. This usually includes, but is not limited to: clinical trials protocol and amendments, investigator brochure, copies of documents from relevant ethics committees, regulatory authority, financial agreements with investigator and/or sponsor, list of pharmacy and sponsor responsibilities in relation to the trial, pharmacy dispensing procedures, pharmacy signature list, monitoring visit log, drug accountability forms, receipt and return of IMPs, code-break procedure, contact number of monitor, investigator and other key personnel, subject I.D. logs and any relevant correspondence (including hard copies of e-mails).

**PROTOCOL:** A document that describes the objective(s), design, methodology, statistical considerations, and organisation of a trial. The protocol usually also gives the background and rationale for the trial, but these could be provided in other protocol reference documents. (3)

**SPONSOR:** A sponsor is, in relation to a clinical trial, a person who takes responsibility for the initiation, management and financing (or arranging the financing) of that clinical trial (1,3,17).

# References

## REFERENCES:

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2. Crown Copyright. Control of Substances Hazardous to Health Regulations (COSHH) 1999. Statutory Instruments. No 437. The Stationery Office
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16. Central Office for Research Ethics Committees (COREC) [www.corec.org.uk](http://www.corec.org.uk)
17. Department of Health. EU Clinical Trial Directive: Sponsorship responsibilities in publicly funded trials - Medicines for Human Use (Clinical Trials) Regulation 2004. 5 April 2004.
18. Department of Health. Governance Arrangements for the NHS Research Ethics Committees. July 2001
19. NHS Research and Development Forum and the ABPI Guidance to Facilitate the Conduct of Commercially Funded Research in the National Health Service (Secondary Care). January 2005

# Internet

## Useful web addresses

Central Office for Research Ethics Committees (COREC)  
[www.corec.org.uk](http://www.corec.org.uk)

Department of Health  
[www.dh.gov.uk](http://www.dh.gov.uk)

Department of Health and Medical Research Council. Clinical Trials Tool Kit.  
[www.ct-toolkit.ac.uk](http://www.ct-toolkit.ac.uk)

Institute of Clinical Research (has information on pharmacy clinical trials services including a question and answering section that are updated regularly)  
[www.instituteofclinicalresearch.org](http://www.instituteofclinicalresearch.org)

Medicines and Healthcare products Regulatory Agency (MHRA - formally the MCA )  
[www.mhra.gov.uk](http://www.mhra.gov.uk)

Research and Development Forum  
[www.rdforum.nhs.uk](http://www.rdforum.nhs.uk)

National Cancer Research Network  
[www.ncrn.org.uk](http://www.ncrn.org.uk)

The Medical Research Council  
[www.mrc.ac.uk](http://www.mrc.ac.uk)

Royal Pharmaceutical Society of Great Britain  
[www.rpsgb.org.uk](http://www.rpsgb.org.uk)