MANCHESTER 1824
The University of Manchester

Standard Operating Procedure

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Title:	Pharmacy Support for CTIMPs		
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Author:	Beatriz Duran	**Review Date:**	18/SEP/2026
Reviewed by:	Mohammed Zubair	**Approved by:**	Prof Terence O'Neill
Position:	Research Governance, Ethics and Integrity Manager	**Position:**	Deputy of Clinical Trial Management Group
Signature:		**Signature:**	Approved via email

Version	Date	Summary of Changes
1.0	Jun 2018	First Draft
1.1	Dec 2018	First Live Version
2.0	Sep 2024	Align with National Guideline- The role of the sponsor pharmacist. Published in SPS and MFT Sponsor pharmacist SOP

1 Introduction

The EU Good Clinical Practice (GCP) Directive 2001/20/EC was introduced to establish standardisation of research activity in Clinical Trials throughout the European Union. It was transposed into UK law as the Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 2004/1031) which came into force on 1st May 2004. The Medicines for Human Use (Clinical Trials) Regulations together with subsequent amendments will be referred to as the Regulations in the rest of this document.

Regulation 3, as amended by Statutory Instrument 2006/1928, requires that research which falls under the regulation has a "Sponsor". As stated in the Regulations, the Sponsor "in relation to a clinical trial, [is] the person who takes responsibility for the initiation, management and financing (or arranging the financing) of that trial". Therefore all proposed research which falls within the scope of the Regulations must have a confirmed Sponsor.

As sponsor the University of Manchester will ensure that appropriate written arrangements are in place before any trial is given Sponsor green light. As part of this sponsor pharmacist oversight of clinical trials of investigational medicinal products (CTIMPs) is provided.

2 Scope

This SOP describes the process by which the University of Manchester will ensure that there is appropriate oversight of the pharmacy related aspects of the trial from a Sponsor point of view. This is not the same as the day to day management of pharmacy related aspects of the trial, which is the responsibility of the clinical trials lead pharmacist at each site.
This SOP only concerns studies that fall into (or potentially fall into) the category of a CTIMP or a clinical investigation of a medical device, as defined by the Clinical Trials Regulations.

3 Responsibilities

3.1 Role of the Chief Investigator and Sponsor Trial Lead Pharmacist
The CI is expected to identify and detail all the relevant pharmacy-related support required for the setting-up and running of a CTIMP. The University expects the CI to work closely with a UKCRC registered clinical trials unit (CTU) (or equivalent) and the sponsor pharmacist, to ensure that all pharmacy areas where the support required, by the CI and the trial team, are identified, detailed and costed appropriately. This will include (but is it not confined to) all aspects of IMP management (including the purchase, packaging, labelling, distribution, and quality control of active drugs and placebo).

The University will support the CI with identifying pharmacy related activities at the pre-funding stage by providing access to a Sponsor Lead Pharmacist . On In occasions, the CI and the lead NHS trust R&D may identify ied the sponsor pharmacist for a specific trial based at their NHS site. The roles and responsibilities and financial agreement will be reflected in an Service Leverl Agreement with the University for the service provided for the specific trial. The role of the Sponsor Lead Pharmacist is not the same as the role of the Site Trial Lead Pharmacist. The Site Trial Lead Pharmacist should be approached via the lead NHS Trust R&D in the first instance. If no agreement is reached between the University and the lead NHS Trust R&D the Sponsor may outsource this activity subject to a financial agreement being reached with the lead Trust and research team

3.2 Costs of IMP management
The CI must ensure that all the costs related to the site pharmacy activity and Sponsor Lead pharmacist, related to IMP management have been obtained and included in the funding application by the relevant Research Support Manager. This may include identifying potential vendors in order to obtain costs. The CI must share this information with the Sponsor, CTU or equivalent and the Sponsor Lead Pharmacist before submitting a funding application.

3.3 Role of the sponsor Lead Pharmacist
The role of the Sponsor Lead Pharmacist is to oversee all activities related to IMP management for quality assurance to the Sponsor (see Appendix 1). The role of the Sponsor Lead Pharmacist will be described in the Pharmacy Delegation of Duties for Individual Trials (see Appendix 12)

4 Related Documents

Reference Number	Document Title
24/A	Division of Responsibilities
24/B	IMP Risk Assessment

5 Procedures

5.1 Delegation of Duties
The University expects a Pharmacy Delegation of Duties for Individual CTIMPs to be agreed with the lead NHS R&D Trust for each CTIMP (variable depending on the specific requirements of the CTIMP) as detailed in Appendix 1.

5.2 Key areas and responsibilities for the Sponsor Pharmacist

5.2.1. Identification of whether the proposed research falls under the clinical trial legislation must be performed using the CTIMP algorithm provided at the MHRA website,

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/317952/Algothrim.pdf. This is usually done in conjunction with the sponsorship team and it will also be discussed in the sponsor oversight committee meetings. The type of trial as per risk adapted approach and phase of the CTIMP will also be discussed and agreed in those meetings.

5.2.2. Sponsor lead pharmacist will support funding applications in order to confirm the IMP management associated costs for the trial have been considered.

Costs for activities related but not limited to the following must be included as per Attribution of costs for research and development (AcoRD):

- Sourcing, manufacturing (including IMPD production) and distribution of IMP
- QP certification (incorporating importation and regulatory requirements)
- Host site pharmacy set up, close out
- Host site IMP management of the trial

Excess treatment costs must be calculated at this stage.

5.2.3. The sponsor lead pharmacist must write/review the IMP related sections of the protocol for safety and integrity of the research purpose, this is done by cross checking with the safety reference document available (Investigator brochure (IB) or summary of product characteristics (SmPC)) and the investigational medicinal product dossier when available.

Protocol sections related to IMP management include but are not restricted to:

- inclusion/exclusion criteria
- IMP section
- concomitant medication
- supportive medications
- side effects, pharmacovigilance
- blinding procedure
- IMP supplies
- IMP related quality management

5.2.4. The sponsor pharmacist will identify any pharmaceutical and IMP management risk by assessing the protocol with the sponsor IMP risk assessment form, Appendix 2. This is usually performed in parallel to writing/reviewing the protocol, IB, PIS and IMPD. When appropriate an IMP risk assessment should be performed.

Access to the IMP at the end of the trial exit strategy for the participants should be clarified at this point.

Any issues identified will be asked to be clarified or modified prior or during the sponsor oversight committee meetings Based on the issues identified it may be

necessary to modify other trial documentation / monitoring plan etc. In parallel the overall trial risk assessment will also take place.

Note: The IMP risk assessment will feed back to the general risk assessment, and it should be amended if a substantial amendment is approved that has the potential to change the previous identified risks.

5.2.5. The sponsor pharmacist may be asked to support/complete the IMP section of the clinical trials IRAS application form to the authorities (which is completed by the sponsor, usually delegated to the CI).
- All clinical trials of medicinal products in human subjects require an authorisation by the competent authority (MHRA) and a favourable opinion by an ethics committee and HRA. The authorisation is granted in the form of a clinical trials authorisation (CTA).

5.2.6. The content of the CTA includes:
(Underlined sections: where sponsor pharmacist will be involved either producing the documents or reviewing them)

- Receipt confirmation of the EudraCT Number/ ISRCTN Registry or ClinicalTrials.gov
- Covering letter
- Application form
- Protocol
- Investigator brochure (or SmPC)
- Investigational medicinal product dossier (or SmPC)
- TSE certificates
- Copy of labels or justification for its absence
- Copy of the manufacturer's authorisation
- Copy of the QP declaration of GMP (when IMP is manufactured in a third country outside the EU)
- Copy of the importer's authorisation (when importing IMP)
- Proof of payment

The sponsor pharmacist will review the patient information sheet that will have to be summited as part of the application to MHRA and Ethics.

5.2.7. The sponsor pharmacist may oversee/manage the IMP supply. A pharmacy manual or IMP management document will be written/review by the sponsor pharmacist. This document will be updated through the lifespan of the trial depending on the changing landscape of the trial and alterations to the protocol, IMP supply chain or manufacturing etc.

5.2.8. The sponsor pharmacist should agree the specification for the IMP. A vendor assessment is required where IMP manufacturing, importation, labelling and distribution are delegated to a third party. Where the vendor assessment deems that an audit is necessary to assess the manufacturer, depending on the level of experience/complexity of the IMP, the expertise of a QP auditor should be engaged.

When appropriate, the sponsor pharmacist will write/contribute to the report and send it to the sponsor.

5.2.9. Technical Agreements, also called quality agreements, must be put in place when outsourcing the IMP manufacturing and distribution or any other IMP management activity. This is agreed between the sponsor and the vendor to document respective responsibilities and must include the quality standards that will be adhered to (e.g. GCP, GMP, GDP), it must be reviewed by CT sponsor pharmacy. The Sponsor Lead Pharmacist must check the technical agreement(s) in place for the IMP supplies; this includes manufacturing and distribution of IMP. This must be done in accordance to Good Manufacturing Practice. The SPS technical/quality agreement template should be used when required. This provides a list of roles and responsibilities to be considered. Note these may vary depending on the nature of the product and specific arrangements of the trial

5.2.10. For multicentre trials the sponsor pharmacist should review the pharmacy feasibility of setting up clinical trials at participant sites. A feasibility form will be sent to the site pharmacies, the responses and any associated SOPs sent by the host pharmacies will be reviewed to ascertain the feasibility of setting up of clinical trials at participant sites (from a pharmacy point of view). Follow SPS guidance on the role of the sponsor pharmacist if a template is required.
During initiation of a site, the Sponsor will request the following documents from a participating pharmacy site. The Sponsor Lead Pharmacist (or other Sponsor delegated team) must review the following SOPs from the local site pharmacies where applicable:

- temperature monitoring system, out of hours procedures for temperature deviations, annual calibration certificates
- blinding and unblinding procedures, out of hours procedures when applicable
- recall Standard Operational Procedure (SOP)
- destruction SOP or waste policy for the site

When required, depending on risk assessment:

- dispensing / checking procedures, including prescriptions, accountability logs, etc.

When there are inadequacies at a participating site identified by the Sponsor that might put the safety of the participants or the validity of the research at risk, an action plan must be put in place. This must be completed by the host site prior to giving Sponsor green light to the site. Sponsor lead pharmacist should advise on the mitigations required in these instances where appropriate.
Oversight of the delivery of the CTIMP:
Sponsor Pharmacy representatives should attend the regular Sponsor trial management meetings, safety review committees and any other meetings on behalf

of the Sponsor as required. They will have a key role in any regulatory inspections for the trial.

6 References

UK Policy Framework for Health and Social Care Research UK Clinical Trials Regulations 2004/2006
https://www.sps.nhs.uk/articles/the-role-of-the-sponsor-pharmacy-in-clinical-trials-of-investigational-medicinal-products-ctimps/#:~:text=sponsor%20pharmacist