SOP-QA-15 V4

Title: Management of Medicinal Products used in research

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Document History

Version	Description of update	Date Effective
1	New SOP number for Q-Pulse	2-10-15
2	Reformatted	1-4-17
3	Updated scope and text at 3.2	1-8-20
4	Author updated and 'Pharmacy Manual' added at 3.6	9-8-23

1. Scope

1.1 This SOP applies to research projects involving a Medicinal Product (MP) sponsored by the University of Aberdeen (UoA) and/or NHS Grampian (NHSG), conducted at local or external research site(s).

1.2 Such projects may fall under the Medicines for Human Use (Clinical Trials) Regulations 2004, as amended, or equivalent local legislation outside the UK.

2. Responsibilities

Chief Investigator (CI)	Liaise with Clinical Trial Pharmacist (CTP) throughout the project.
Clinical Trial Pharmacist (CTP)	Oversee the management of any Medicinal Product used in research.

3. Procedure

Project design and funding

3.1 Considerations for use of a MP should start at the earliest stages of project planning. The Chief Investigator (CI) shall consult with the NHSG Clinical Trials Pharmacist (CTP), or delegate, during drafting of the grant proposal. The CTP shall advise on MP supply, whether an external vendor will be required, or if the MP can be sourced from hospital stock; taking into consideration NHSG formulary requirements, storage requirements for released MP and returns. Contact details for the CTP are available on the Grampian Research Office (GRO) website.

3.2 Having consulted with the CTP, the CI shall establish any pharmacy and MP costs involved and, if required, shall obtain an illustrative quote for inclusion into the grant proposal, including arrangements and costs for drug packaging and distribution.

3.3 The CTP shall review the protocol to ensure that all relevant product information and unblinding mechanism (if required) is included. If a randomised trial, the CTP may, in exceptional circumstances, agree to hold the code breaking mechanism and participate in out of hours unblinding (see SOP-QA-18 - Randomisation and blinding for controlled trials).

3.4 The CTP shall be a signatory on any final protocol involving an MP.

3.5 The CTP shall review the content of the Participant Information Sheet/Leaflet, to ensure that all relevant product information is being supplied to the participant, before the information sheet is submitted for appropriate approvals.

3.6 The CTP shall review the product information (ie Summary of Product Characteristics (SmPC/SPC) Investigator Brochure (IB), Pharmacy Manual, Simplified Investigational Medicinal Product Dossier (sIMPD), label text and stability data) for relevance prior to submission for appropriate approvals.

3.7 The CTP may continue to be involved throughout the research project design, to ensure that the proposed arrangements for MP management remain suitable and that blinding mechanisms and emergency unblinding procedures are appropriate.

3.8 The CTP and other parties (as appropriate) may have input into the selection of, and contractual arrangements with, MP suppliers/manufacturers/distributors, as required (see SOP-QA-16 - Selection and management of third-parties and SOP-QA-13 - Generation of contracts).

Initiation of research

3.9 Sponsorship and approvals shall be obtained prior to any research activities commencing (see SOP-QA-4 - Applying for sponsorship, SOP-QA-6 - Study start-up and SOP-QA-10 - Applying for Research Ethics Committee opinion).

3.10 The CI shall not place an order for MP until receipt of required approvals unless this is agreed in advance by R&I. For externally sourced MP, the MP Order Form (TMP-QA-23) shall be used. This MP Order Form includes the approved label text and shall be checked against the MP specification by the CTP. If the external vendor has an appropriate order form, this may be used. It is recommended that the sample label from the external vendor is submitted to the CTP for review; this may prevent unnecessary delays.

3.11 For all orders of MP, consideration shall be given to MP expiry date and expected recruitment rate in order to minimise wastage.

3.12 Advice from the Qualified Person (QP)/manufacturer shall be sought regarding the transportation and temperature monitoring of MP during transit (if required) to pharmacy.

3.13 For research projects involving MP, the Sponsor shall confirm that all required regulatory approvals and the QP release of MP are in place. This must occur prior to authorising the dispensing of any MP for the research project, as detailed in the Regulatory green light form (TMP-QA-19).

3.14 The CTP shall approve any local MP storage areas out with pharmacy before MP can be released.

3.15 The CTP must approve the practice of MP returns from participants to a locally approved storage area (prior to pharmacy return). If storage of returns out with pharmacy will be undertaken, this shall be documented in the protocol and/or an SOP/User Guide prepared by the CI, detailing the procedure for recording compliance and return to pharmacy at appropriate intervals during the project.

3.16 All research projects involving MP require a **pharmacy file**; created by the research team and given to the CTP (see SOP-QA-7 -Trial Master File).

3.17 In consultation with the CTP, all project specific templates related to MP shall be developed, where appropriate, including Local Medicinal Product accountability log (TMP-QA-24), Research project prescription (TMP-QA-25), Unblinding form (TMP-QA-26) and Medicinal Product request form (TMP-QA-27). Templates of these forms are available on the GRO website and can be adapted accordingly for each research project.

3.18 The CI shall delegate responsibilities of MP management to the CTP (as appropriate) using the Delegation Log (TMP-QA-13). The CTP shall delegate responsibilities within the clinical trials pharmacy using the internal pharmacy signature log.

Conduct of research

3.19 The regulatory green light form (TMP-QA-19) shall be signed by the Research Governance Manager (RGM) and the CTP (if appropriate). A copy of the completed form shall be sent to the CI informing them that MP has been received and is available for dispensing.

3.20 MP shall be dispensed to participants on receipt of a signed Research Project Prescription (TMP-QA-25) or transferred to a locally approved storage area, subject to receipt of a signed Medicinal Product request form (TMP-QA-27). Labelling of MP, when required, shall be conducted by pharmacy in accordance with pharmacy SOPs.

3.21 Accountability (including compliance) of MP is the responsibility of **all** delegated research team members. **All** handling of MP shall be recorded in accountability/compliance records, including:

- Case Report Form (CRF)
- Source notes
- Local Medicinal Product accountability log (TMP-QA-24)

Project specific accountability/compliance documentation shall be reviewed by the CTP prior to the research commencing.

3.22 For MP that is dispensed in the Clinical Trials Pharmacy, the CTP/delegated staff shall complete the Local Medicinal Product accountability log (TMP-QA-24) for each dispensing. The completed prescription shall be collected from Pharmacy by a member of the research team, or sent to the designated ward/clinic by a porter; who will sign the pharmacy collection log for receipt of prescription. Where it has previously been agreed, if the MP is being delivered to the participant's home, a courier will collect the MP from CTP. The research team shall complete the Local Medicinal Product accountability log (TMP-QA-24) on each occasion MP is issued from the ward/clinic area to a participant.

3.23 For MP held in a locally approved storage area, delegated research team members are responsible for completing the Local Medicinal Product accountability log (TMP-QA-24) stating who has dispensed, checked and issued MP to the participant.

3.24 Temperature logging and temperature excursions of MP stored within pharmacy shall be managed by pharmacy in accordance with their SOPs.

3.25 For MP held in a locally approved storage area, research team members are responsible for recording the temperature daily using the Temperature monitoring log (TMP-QA-28). The CTP and Sponsor must be informed of any temperature excursions as soon as the research team become aware; the CTP shall advise on any corrective and preventive action (CAPA).

3.26 Expiry management and relabeling, where required, shall be conducted by the CTP in accordance with pharmacy SOPs.

3.27 For randomised research projects, arrangements shall be in place for emergency unblinding. In exceptional circumstances, the CTP may need to be involved in out of hours unblinding. The CTP shall be consulted on all unblinding procedures (see 3.3).

3.28 MP recall, where required, shall be conducted by the CTP in accordance with pharmacy SOPs.

3.29 The CTP shall be given copies of all documents relating to relevant amendments to the research project for information and for filing in the Pharmacy file.

3.30 The CTP shall be consulted during drafting of any amendment which affects management of the MP, or involves the addition of an investigational site which will require supply of MP.

3.31 In exceptional circumstances, MP transfer to another investigational site, where needed, shall be conducted by the CTP in accordance with pharmacy SOPs.

3.32 All MP and/or packaging returned to site eg routine returns, withdrawals, recalls etc. must be documented on the appropriate Local MP handling/compliance form or MP Accountability Log as appropriate. Once recorded, all MP shall be returned to the local pharmacy for accountability and destruction. This will be done in accordance with Pharmacy SOPs, unless otherwise notified.

Close-out

3.33 Once recruitment and any follow up is completed, the research team shall inform the CTP that the project is complete and that the pharmacy file can be archived.

3.34 The CTP, or delegate, shall reconcile the pharmacy file and ensure that all documentation is complete and accounted for. Any unblinding documentation shall remain in the pharmacy file unless requested by the CI.

3.35 The CTP shall reconcile all remaining MP. Any remaining MP that had been stored out with pharmacy must have been returned for destruction along with a copy of the completed Local Medicinal Product accountability log (TMP-QA-24). The CTP shall check that all pharmacy accountability logs are reconciled, completed and signed off. MP shall be destroyed as per pharmacy SOPs. A destruction form shall be completed and signed off by the CTP.

3.36 The pharmacy file shall be archived with the TMF. A member of the research team shall arrange a suitable time to sign for and collect the file from pharmacy and the CTP shall be kept informed of the storage location of the archived TMF; for possible future access (see SOP-QA-32 – Archiving).

4. Abbreviations and definitions

4.1 Medicinal Product - The EU Directive 2001/20/EC (Clinical Trials Directive) defines a medicinal product as:

'A pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical trial, including products already with a marketing authorisation but used or assembled (formulated or packaged) in a way different from the authorised form, or when used for an unauthorised indication, or when used to gain further information about the authorised form.'

CAPA	Corrective Action and Preventive Action
CI	Chief Investigator
CRF	Case Report Form
CTIMP	Clinical Trial of an Investigational Medicinal Product
CTP	Clinical Trial Pharmacist
IB	Investigator Brochure
MP	Medicinal Product
MHRA	Medicines and Healthcare products Regulatory Agency
QP	Qualified Person
REC	Research Ethics Committee
RGM	Research Governance Manager
sIMPD	Simplified Investigational Medicinal Product Dossier
SmPC/SPC	Summary of Product Characteristics
TMF	Trial Master File

5. Related documentation and references

SOP-QA-4	Applying for sponsorship
SOP-QA-6	Study start-up
SOP-QA-7	Trial Master File
SOP-QA-10	Applying for Research Ethics Committee opinion
SOP-QA-13	Generation of contracts
SOP-QA-16	Selection and management of third-parties for CTIMPs
SOP-QA-18	Randomisation and blinding for controlled trials
SOP-QA-32	Archiving
TMP-QA-13	Site delegation log
TMP-QA-19	Regulatory green light form
TMP-QA-23	Medicinal Product order form
TMP-QA-24	Local Medicinal Product accountability log
TMP-QA-25	Research project prescription
TMP-QA-26	Emergency unblinding form
TMP-QA-27	Medicinal Product request form
TMP-QA-28	Temperature monitoring log