Document Title: Handling of medicine recalls of Investigational Medicinal Products (IMPs) or other trial related drugs

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Summary of Amendments

Version Number	Modification:
Version 3.0	**Minor procedural changes throughout**

Key Points of this Document

- This document sets out the procedures to be followed by all Royal Papworth Staff who are involved in the handling of drug alerts and recalls of IMPs or other drugs used in the context of clinical research.

1 Purpose and Contents

a. To describe the process for responding to a recall or drug alert of an IMP or any drug used within a clinical trial that is sponsored by Royal Papworth Hospital NHS Foundation Trust or managed by Papworth Trials Unit Collaboration.

2 Roles and Responsibilities

a. The responsibility for product recalls lies with the sponsor. Before a recall for a trial is initiated by a sponsor, it is recommended that MHRA (Clinical Trials Unit and Defective Medicines Report centre) is notified.

b. A technical agreement should exist that defines the roles for the different parties (i.e. sponsor, vendor, CTU) in the event that a product recall is required.

c. All research active staff with responsibility for IMP management must read this SOP. Failure to follow this SOP may result in disciplinary procedures

d. For commercially available IMPs used within clinical trials, drug recalls and alerts are usually cascaded via pharmacy departments who should have an appropriate system in place to cascade this information to rest of the hospital (see section 4a below).

e. For IMPs without a marketing authorisation, the initial knowledge of a recall may be received by the Chief investigator whose responsibility it will be to contact PIs and pharmacy department accordingly.

f. If a research team member becomes aware of a recall or drug alert they must inform the Chief Investigator (CI) and Pharmacy department who will cascade this information

3 Policy

a. This policy complies with the requirement of the Medicines for Human use (Clinical Trials) Regulations 2004 and subsequent amendments.

4 Procedure

a. Notification of a defect in a medicinal product or withdrawal of a drug can be issued from:

1. The manufacturer (Marketing Authorisation Holder)
2. The MHRA
3. The trial sponsor or delegate (i.e. the CRO)

b. Medicines recalls from the MHRA are classified according to their severity and impact on patient safety:

1. Class 1 (recall - action now including Out of Hours). Will also be classed as a National Patient Safety alert (risk of death or disability)
2. Class 2 (recall- action within 48 hours) May be classed as National Patient Safety Alert
3. Class 3 (recall - action within 5 days)
4. Class 4 (medicines notification, caution in use, no recall required)

c. Medicines recalls in classes 1-3 require the affected batches of medication to be recalled

d. The MHRA is also responsible for disseminating National patient safety alerts which will replace the Dear Doctor letters (and which also cover medical devices), and Field Safety Notices (specific to devices) to healthcare professionals.

e. Medicines recalls or safety information are currently sent by email and online via the MHRA website / CAS alert system. Healthcare professionals can sign up to these bulletins on the MHRA website. There is a process between pharmacy and the trust Risk management department to ensure relevant alerts are followed up via the CAS system. The clinical trials pharmacist is included in the email chain from Risk management.

f. For licensed products used off the shelf the Pharmacy department will usually receive the email and follow trust procedure DN211 (Procedure for Drug recall) ;in this instance, the pharmacy clinical trials team will notify the investigator and follow any required actions below.

g. For trial products that do not have a marketing authorisation the manufacturers or vendor must contact the sponsor representative and CI directly who should liaise with pharmacy and follow this procedure.

h. Where RPH is the sponsor: On receipt of a drug recall for an IMP the information should be emailed to the relevant team members including pharmacy – pharmacy will initiate completion of the form "Drug Recall Handling" FRM033.

i. Where RPH is not the sponsor for the trial then Sponsor specific procedures and paperwork should be followed.

j. On receiving notification of a drug recall/withdrawal involving an IMP or a product currently used within a trial at Papworth the pharmacy clinical trials team will ascertain whether the affected batch has ever been in stock at Papworth for CTIMP (Clinical Trial of an Investigational Medicinal Product) use by checking the accountability logs or delivery notes.

k. Where IMP is stored outside of pharmacy, a member of the pharmacy team or a delegated member of the research team must check stock holdings (past and present) using the accountability logs. The delegated staff members should inform pharmacy when this is done.

l. Any affected product identified within stock should be immediately quarantined according to SOP075 Quarantine of CTMPs and DN211 as appropriate.

m. The recall must be documented in the Pharmacy Trial File (PTF) and in the Trial Master File (TMF) along with any action taken using the form Drug Recall handling. It should be circulated via email to all relevant members of the research team. It is the Chief investigators (CI) responsibility to ensure this is done either by themselves or via a delegated representative i.e. Pharmacy.

n. For recalls to the patient level the accountability logs should be used to identify patients who received the medication. This list should be passed onto the PI. The CI, PI (Principal Investigator) or delegate will be responsible for contacting participants.

o. The CI, PI or delegate should supply timely and accurate information to affected participants. This may include definition of symptoms, what to do if they experience symptoms, what to do with the affected batch (return to pharmacy) and what the arrangements are for treatment or re-supply in line with trials specific procedures.

p. The CI, PI or delegate will order new stock for the trial as required.

q. The quarantined product must remain so until further instruction is received from the manufacturer/sponsor.

r. For Papworth Sponsored multi-site trials:

1. Before initiating a recall for an authorised product from a MAH (Marketing Authorisation Holder) contact the MHRA clinical trials unit to discuss as the circumstances of the trial may mitigate some risks identified in the recall (NB Class 1 recalls must be actioned immediately) (Good Clinical Practice Guide p208)

2. If a recall is deemed necessary all the above actions should be followed. The recall handling form (FRM033) should be distributed to the relevant pharmacies at each site with the recall information and actions required. This should be completed by the CI in conjunction with Pharmacy clinical trials staff who will support the distribution of the documents.

s. The CI is responsible for communicating any further actions as a result of the recall to sites outside of Papworth, such as scheduling of any additional visits now required.

5 Risk Management / Liability / Monitoring & Audit

5.1 Staffing

a. During the running of a CTIMP trial there should always be a member of staff trained in the management of IMP available and documented on the delegation log. Where there is not then the investigator should take responsibility.

5.2 Monitoring and Audit

a. The Pharmacy Clinical Trials staff should review compliance to this SOP by reviewing their own practices on an annual basis; they should also be aware of any areas outside of the pharmacy where IMP is stored and maintain oversight of the practices in these areas.

b. The R&D SOP Committee will ensure that this SOP and any future changes to this document are adequately disseminated.

c. The R&D Department will monitor adherence to this SOP via the routine audit and monitoring of individual clinical trials and the Trust's auditors will monitor this SOP as part of their audit of Research Governance. From time to time, the SOP may also be inspected by external regulatory agencies (e.g. Care Quality Commission, Medicines and Healthcare Regulatory Agency).

d. In exceptional circumstances it might be necessary to deviate from this SOP for which written approval of the Senior R&D Manager should be gained before any action is taken. SOP deviations should be recorded including details of alternative procedures followed and filed in the Investigator and Sponsor Master File.

e. The Research and Development Directorate is responsible for the ratification of this procedure.

R&D SOP074: Handling of drug alerts and recalls of IMPs or other trials related drugs

Further Document Information

Approved by: Management/Clinical Directorate Group	Research and Development Directorate
Approval date: (this version)	Current approved version date
Ratified by Board of Directors/ Committee of the Board of Directors:	STET
Date:	N/A
This document supports: Standards and legislation	Medicines for Human Use (Clinical Trials) Regulations 2004 and all associated amendments. UK Policy Framework for Health and Social Care Research (2018)
Key related documents:	Trust Research Policy MHRA website DN211 – Procedure for Drug recall SOP075 – Quarantine of CTIMPs (clinical trial investigational medicinal products) FRM033 Drug Recall Handling

Equality Impact Assessment: Does this document impact on any of the following groups? If YES, state positive or negative, complete Equality Impact Assessment Form available in Disability Equality Scheme document DN192 and attach.

Groups	Disability	Race	Gender	Age	Sexual orientation	Religious & belief	Other
Yes/No	No	No	No	No	No	NO	NO
Positive/Negative	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Review date:	March 2024

I certify the contents of this SOP has been reviewed and ratified

..... 24th March 2021

Signed by Dr Ian Smith, Clinical Director of R&D — Date

SOP release date: 7th April 2021