York Foundation Trust R&D Unit
Standard Operating Procedure
Pharm/S58

Actioning a Clinical Trial Investigational Medicinal Product Recall

IT IS THE RESPONSIBILITY OF ALL USERS OF THIS SOP TO ENSURE THAT THE CORRECT VERSION IS BEING USED

All staff should regularly check the R&D Unit's website and R&D Newsletter for information relating to the implementation of new or revised versions. Staff must ensure that they are adequately trained in the new procedure and must make sure that all copies of superseded versions are promptly withdrawn from use unless notified otherwise by the SOP Controller.

The definitive versions of all R&D Unit SOPs appear online. If you are reading this in printed form check that the version number and date below is the most recent one as shown on the R&D Unit website: www.northyorksresearch.nhs.uk/sops.html

SOP Reference:	Pharm/S58
Version Number:	3.0
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Implementation date of current version:	23rd November 2015

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This SOP will normally be reviewed every 2 years unless changes to the legislation require otherwise

Version History Log

This area should detail the version history for this document. It should detail the key elements of the changes to the versions.

Version	Date Implemented	Details of significant changes
1.0	1st June 2010	
2.0	23rd August 2013	Removal of references to the North and East Yorkshire R&D Alliance. Change of SOP Controller. Addition of Scarborough Hospital as a site working to this SOP. Assurance that Medicines held in the Experimental Medicine Unit will be checked upon a Recall.
3.0	23rd November 2015	Amendment of references to Experimental Medicine Unit to York Clinical Research Facility. Addition of reference to SOPCST7 which now covers responding to MHRA drug alerts across both York and Scarborough Hospitals.

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1 Introduction, Background and Purpose

This SOP describes the actions to be taken in the event of an instruction to recall a product used within a clinical trial.
This SOP works alongside the Trust wide product recall procedure described in the Pharmacy SOP (SOPCST7) – Responding to a Medicines and Healthcare Products Regulatory Agency (MHRA) drug alert.
For studies sponsored by York Teaching Hospital NHS Foundation Trust, Section 6.11 of the MHRA Good Clinical Practice Guide should be referred to for guidance on the responsibilities of the Sponsor for product recall. Where York Teaching Hospital NHS Foundation Trust are procuring Investigational Medicinal Product to be used in a trial they are sponsoring, it is important that the Technical agreement produced contains the responsibilities of each party involved, i.e. IMP manufacturer and Sponsor, in relation to product recall. Refer to Pharm/S43 – How to Procure an Investigational Medicinal Product for more detail.
This procedure also ensures that medications stored within the York Clinical Research Facility (YCRF) at York Teaching Hospital NHS Foundation Trust are also checked as part of the recall process.

2 Who Should Use This SOP

The responsibilities for responding to a MHRA drug alert are listed in the Pharmacy SOP – SOPCST7.

The Pharmacy clinical trials team is responsible for checking clinical trial stocks of medicines affected by each Drug Alert and documenting any action taken.

The Pharmacy clinical trials team is responsible for co-ordinating the response to a drug recall initiated by a trial sponsor.

The Pharmacy clinical trials team is responsible for notifying investigators if any trial participants have received an affected batch of Investigational Medicinal Product (IMP) and reconciliation of returned IMPs.

The Investigator and Research Nurses will be responsible for contacting patients who have been supplied with IMP from the affected batch.

The Pharmacy clinical trials team are responsible for informing the York Clinical Research Facility (YCRF) of any Product recall notifications.

The York Clinical Research Facility (YCRF) team are responsible for confirmation as to whether products held within the York Clinical Research Facility (YCRF) are affected by a Product recall.

This SOP is applicable to York and Scarborough Hospital which form part of York Teaching Hospital NHS Foundation Trust.

3 When this SOP Should be Used

This procedure is applicable to the recall of licensed medicines used in clinical trials and Investigational Medicinal Products supplied by pharmaceutical companies and trial sponsors.

4 Procedure(s)

The following procedure(s) must be followed as appropriate:

4.1 Drug Alerts from the MHRA

Drug alerts from the MHRA will relate to medicines with a UK Marketing Authorisation.

4.1.1 Notification

A member of the Pharmacy team will notify the clinical trials team following receipt of a national drug alert notification. They will provide a copy of the MHRA alert and product details, and will state the urgency of the alert and the necessary action to be taken (including recall of the affected batches).

4.1.2 Checking Stock

This, and sections 4.1.3 and 4.1.4 are the responsibility of a member of the Pharmacy clinical trials team.

- Identify a lead person from the clinical trials team to be the point of contact for other departments while the IMP recall is actioned. Record this as required on the Trial Drug Recall Summary Sheet if necessary (Pharm/F41).
- Identify if the product is used as an IMP in any trials hosted by York Teaching Hospital NHS Foundation Trust by checking the Pharmacy file of the clinical trial, or the trial status inventory list, located in the trials dispensary or the clinical trials office/room. Also contact the YCRF to request them to check whether they have any stock of the affected product.
- If the product is NOT used as an IMP in the Trust (and not held as stock in the YCRF):
    - Confirm to the member of the Pharmacy team who is actioning the alert.
    - Sign and date the York Pharmacy Recall Record and confirm the action required.
    - Please note: The York Pharmacy Recall Record will be filed as per SOPCST7.
- If the product is used as an IMP in the Trust (or is held as stock in the YCRF):
    - Check trial files and any ring-fenced stock to identify whether any of the affected batches have been received. The batch number of IMP will be recorded on receipt and usually on the prescription and accountability log. Details of when the

affected batch was placed on the market can be found from the drug alert.

- Identify all areas where the affected IMP is stored in pharmacy, wards, clinics, theatres, emergency departments, external units e.g. Genito Urinary Medicine (GUM) clinic and the York Clinical Research Facility (YCRF).
- Withdraw all affected stock from use and place in quarantine (see Pharm/S59).
- Record details of any recalled product identified on the trial specific Trial Drug Recall Summary Sheet (Pharm/F41). Use one sheet for each trial.
- Obtain a print out of the Drug Alert and accompanying email and attach to the Trial Drug Recall Summary Sheet (Pharm/F41).
- Normal dispensary stock of the product (i.e. not ring-fenced trial stock) will be identified and checked by the designated personnel for the dispensary.

- In ALL cases, report back to the person responsible for coordinating the recall, the outcome of the recall. Sign, date and time the York Pharmacy Recall record to confirm action has been taken. The Trial Drug Recall Summary sheet (Pharm/F41) should be filed in the relevant Pharmacy clinical trial file (together with a copy of the standard York Pharmacy Recall Record).

4.1.3 Informing Investigators and Clinical Trial Participants

- For each trial, a member of the clinical trials team will identify and list (on the Trial Drug Recall Summary Sheet (Pharm/F41)) all patients that have received IMP from the recalled batch.
- A member of the clinical trials team will inform the Principal Investigator (PI) for each trial affected by the drug alert and forward a photocopy of the Trial Drug Recall Summary Sheet (Pharm/F41) to the PI and Research Nurse they designate responsibility to. It is the responsibility of the Principal Investigator to contact the clinical trial patients affected by the recall as appropriate. Under normal circumstances this responsibility will be delegated to the Research Nurse.
- The Research Nurse will contact patients who have been supplied with IMP from the affected batch, if appropriate.
- The Research Nurse will request that the patient returns their trial medication to Pharmacy as soon as possible for checking and replacement with alternative stock if available. They will return their copy of the Trial Drug Recall Summary Sheet (Pharm/F41) to Pharmacy after completing section E. A photocopy of the Trial Drug Recall Summary Sheet should be filed in the Trial Master file to show evidence of the patients being contacted.
- A member of the clinical trials team (usually the lead person) will document all actions taken on the original trial specific Trial Drug Recall Summary Sheet (Pharm/F41) completing section F, attach

the copy returned from the Research Nurse containing confirmation of patients being contacted and file in the pharmacy trial file.

- It is the responsibility of the Pharmacy lead person to reconcile the IMP returned from the patients against the list of patients on the Trial Drug Recall Summary Sheet (Pharm/F41) and take appropriate action if IMP is not returned. In this circumstance, the Research Nurse should be contacted to ask them to contact the patient again.

4.1.4 Quarantine of Recalled IMP

- Withdraw all affected stock from all storage areas if necessary.
- Place all defective stock into quarantine according to Pharm/S59 - Quarantine of IMPs.
- Record details of quarantined stock on the Trial Drug Recall Summary Sheet (Pharm/F41).
- Contact the Research Nurse to confirm if there is sufficient IMP for patient visits expected in the near future.
- Contact the trial sponsor to inform them of the action taken and request further stock if necessary.
- Establish what further action is required regarding return or destruction of the recalled product. Replacement stock or credit may be available through the trial sponsor, manufacturer or wholesaler.

4.1.5 Central alerts system (CAS) reporting

- If the drug alert is received through the central alerts system (See Central alerts system policy on York Staff Room), assurance that action has been taken should be reported to the Senior Management Team within Pharmacy. They will confirm via the DATIX system that they are aware of the alert and have taken action.

4.2 Drug Recalls Initiated by a Trial Sponsor

4.2.1 Notification

The trial sponsor will notify all trial site pharmacies and investigators of an IMP recall according to their SOPs. This notification may be by letter, e-mail or fax and may be followed up by a telephone call if the recall is urgent and requiring immediate action.

If York Teaching Hospital NHS Foundation Trust are the Sponsor, notification will be received from the R&D unit and the following process will be followed upon receipt.

4.2.2 Checking Stock

This, and sections 4.2.3 and 4.2.4 are the responsibility of a member of the Pharmacy clinical trials team

- To locate the stock and trial file it may be necessary to refer to the trials status inventory list which is displayed in the Clinical Trial dispensary/room. Additional information may be obtained through the

clinical trials team or Directorate Pharmacists. The York Clinical Research Facility (YCRF) should be contacted to ascertain whether they have affected stock.

- Once the trial file has been located, check the IMP receipt documentation to ascertain whether the affected batch of IMP has been received. The batch number of IMP will be recorded on receipt and usually on the prescription and accountability log.
- If the affected batch of IMP has NEVER been received:
    - Document this on the IMP recall notification.
    - Follow the trial Sponsor's procedure for faxing this information back or confirming this with them.
    - File all related documentation in the trial specific pharmacy file (supply/receipt section).
- If the affected batch of IMP has been received:
    - Identify all areas where the affected IMP is stored in pharmacy, wards, clinics, theatres, emergency departments, external units e.g. GUM clinic and the YCRF.
    - Follow the instructions provided by the trial sponsor with regard to withdrawal of affected stock from use and quarantine procedures.
    - Record details of any recalled product identified on the trial specific documentation provided by the sponsor.
    - If the sponsor has not provided instructions or documentation, withdraw all affected stock from use and place in quarantine (see Pharm/S59) until further instructions are received.
    - Record details of any recalled product identified on the trial specific Trial Drug Recall Summary Sheet (Pharm/F41). Use one sheet for each trial.

4.2.3 Informing Investigators and Clinical Trial Participants

- From the dispensing records, a member of the clinical trials team will identify all patients that have received IMP from the recalled batch. Follow the instructions provided by the trial sponsor regarding recall of IMP from trial participants. Record on Pharm/F41 as appropriate.
- A member of the Pharmacy clinical trials team will inform the Principal Investigator for each trial affected by the recall notice and forward a photocopy of the Trial Drug Recall Summary Sheet (Pharm/F41) to the PI and Research Nurse they designate responsibility to. It is the responsibility of the Principal Investigator to contact the clinical trial patients affected by the recall as appropriate. Under normal circumstances this responsibility will be delegated to the Research Nurse.
- The Research Nurse will contact patients who have been supplied with IMP from the affected batch, if appropriate.
- The Research Nurse will request that the patient returns their trial medication to Pharmacy as soon as possible for checking and replacement with alternative stock if available. They will return their

copy of the Trial Drug Recall Summary Sheet (Pharm/F41) to Pharmacy after completing section E. A photocopy of the Trial Drug Recall Summary Sheet (Pharm/F41) should be filed in the Trial Master file to show evidence of the patients being contacted.

- A member of the Pharmacy clinical trials team will document all actions taken on the original trial specific Trial Drug Recall Summary Sheet by completing section F (or complete documentation provided by the trial sponsor), attach the copy returned from the Research Nurse containing confirmation of patients being contacted and file in the pharmacy trial file (in the supply/receipt section).
- It is the responsibility of the Pharmacy lead person to reconcile the IMP returned from the patients against the list of patients on the Trial Drug Recall Summary Sheet (Pharm/F41) and take appropriate action if IMP is not returned. In this circumstance, the Research Nurse should be contacted to ask them to contact the patient again.

4.2.4 Quarantine of the IMP

- Withdraw all affected stock from all pharmacy clinical trial storage areas.
- Place all defective stock into quarantine according to Pharm/S59 - Quarantine of IMP.
- Record details of quarantined stock on the Trial Drug Recall Summary Sheet (Pharm/F41).
- Contact the Research Nurse to confirm if there is sufficient IMP for patient visits expected in the near future.
- Contact the trial sponsor to inform them of the action taken and request further stock if necessary.
- Establish what further action is required regarding return or destruction of the recalled product. Replacement stock should be available through the trial sponsor.

4.3 Out of Hours

If the on call pharmacist receives an MHRA Drug alert, they will follow the procedures outlined in the Pharmacy department SOP - SOPCST7 – Responding to a MHRA drug alert.

In the case of the drug being an Investigational Medicinal Product, this alert should be given to a member of the clinical trials team to action at 8.45am the next working day as no IMP will be dispensed from Pharmacy out of hours. The clinical trials Team will then proceed to follow the ‘during normal working hours’ process as described in section 4.1 above.

The same process applies to receipt of an IMP recall initiated by the sponsor of a clinical trial out of hours.

The only exception to the above would be a drug alert or recall for studies where IMP’s are stored outside the Pharmacy. The details of these can be found on the Trial Status Inventory List in the clinical trials dispensary/room. In these cases, the Principal Investigator of the study should be contacted immediately by the on call Pharmacist and the process for ‘during normal

working hours' followed as detailed above, as the IMP is at risk of being dispensed.

4.4 Testing the IMP Recall process

This should be conducted by a member of the Pharmacy clinical trials team and a Research Nurse/Principal Investigator from the relevant speciality.

Testing of this process should be conducted on a yearly basis.

The process should be tested on two trials. The trials tested should be selected from a different medical speciality each year and this should be documented on the IMP Recall Test Form – Pharm/F49.

Of the two trials selected for testing, one should be commercially sponsored and one non-commercially sponsored where possible.

If an actual MHRA drug alert or IMP recall is actioned during the year, the requirement for testing will be reduced accordingly.

Follow the procedure detailed below and record actions on the IMP Recall Test Form (Pharm/F49):

- Select an active trial from the Trial Status Inventory List.
- Locate the accountability log and select a batch number of the medication listed (which has been dispensed).
- Follow the relevant part of the Standard Operating Procedure listed above using the batch number and medication selected as a test recall notice.
- Complete the Trial Drug Recall Summary Sheet (Pharm/F41) as required. Write 'TEST' in the recall details section of the form in capital letters. Attach this form to the IMP Recall Test Form (Pharm/F49) after the process has been completed.
- The Research Nurse should complete section E once all the patient contact numbers have been obtained/verified as present. IT IS NOT NECESSARY TO CONTACT THE ACTUAL PATIENTS.
- The process should be reviewed by the Pharmacy clinical trials team and the Research Nurse/Principal Investigator after the test.
- The outcome of the test and any further actions should be agreed and documented on the IMP Recall Test Form (Pharm/F49).
- The IMP Recall Test Form (Pharm/F49) should be filed in the relevant Pharmacy Trial File and held centrally to provide evidence of compliance with this SOP.

5 Related SOPs and Documents

Pharm/F41	Trial Drug Recall Summary Sheet
Pharm/S59	Quarantine of IMP
Pharm/F49	IMP Recall Test Form

SOPCST7 (Internal Pharmacy SOP on q pulse)	Responding to an MHRA Drug alert
Risk & Legal Services	Central alerts system Policy, November 2009
Pharm/S43	How to Procure an Investigational Medicinal Product
MHRA	Good Clinical Practice Guide (the grey guide)
Appendix 1 of SOPCST7	York Pharmacy Recall Record