

Product Recall Flow Chart

Purpose: The purpose of this document is to describe the procedure to be followed to manage and document IMP/NIMP recall.

Background: The Sponsor should ensure that the responsibilities of all parties are defined in the appropriate agreements. The trial specific technical agreement and division of responsibilities defines the responsibilities of the different parties involved in a recall. The parties involved in a recall for the University of Manchester may include but are not confined to: the Sponsor, manufacturing company, randomisation provider, the clinical trials unit managing the study site pharmacies.

Drug accountabilities are instrumental to determine what medication was received by the site, received by the study participant, returned to the Sponsor or destroyed.

The Defective Medicines Report Centre (DMRC) is a unit of the Inspection, Enforcement & Standards Division of the MHRA, in the UK. The role of the DMRC is to minimise the hazard to patients arising from the distribution of defective medicines by providing an emergency assessment and communication system between manufacturers, distributors, regulatory authorities and users.

Aim: This document provides an overview of the different types of recall and a flow chart for the Sponsor to follow in the event of a recall.

Who originates the recall?

The ultimate responsibility for product recalls lies with the Sponsor, but may be delegated. Sources of IMP/NIMP supply may vary depending on the trial arrangements. The medicinal products used in the trial may come from standard commercial supply, provided to the investigator from a pharmaceutical company or another marketing authorisation holder. A third party vendor may be employed for IMP management purposes including labelling and packaging of the product.

- For authorised products: The Manufacturer Authorisation Holder (MAH) will initiate the recall. The Sponsor will be notified indirectly by the supplier, if the supplier is not the MAH.
- The University of Manchester is signed up for e-mail alerts on recalls initiated by the MHRA and the lead clinical trials pharmacists for the different trials should also receive alerts via the NHS pharmacy systems.

Before a recall for a trial is initiated by the Sponsor it is recommended that the relevant MHRA department named: "the Clinical Trials Unit and the Defective Medicines Report Centre" is notified, as discussions could lead to a different decision for the trial-related product.

RECALL FLOWCHART

Medication Recall Classification:

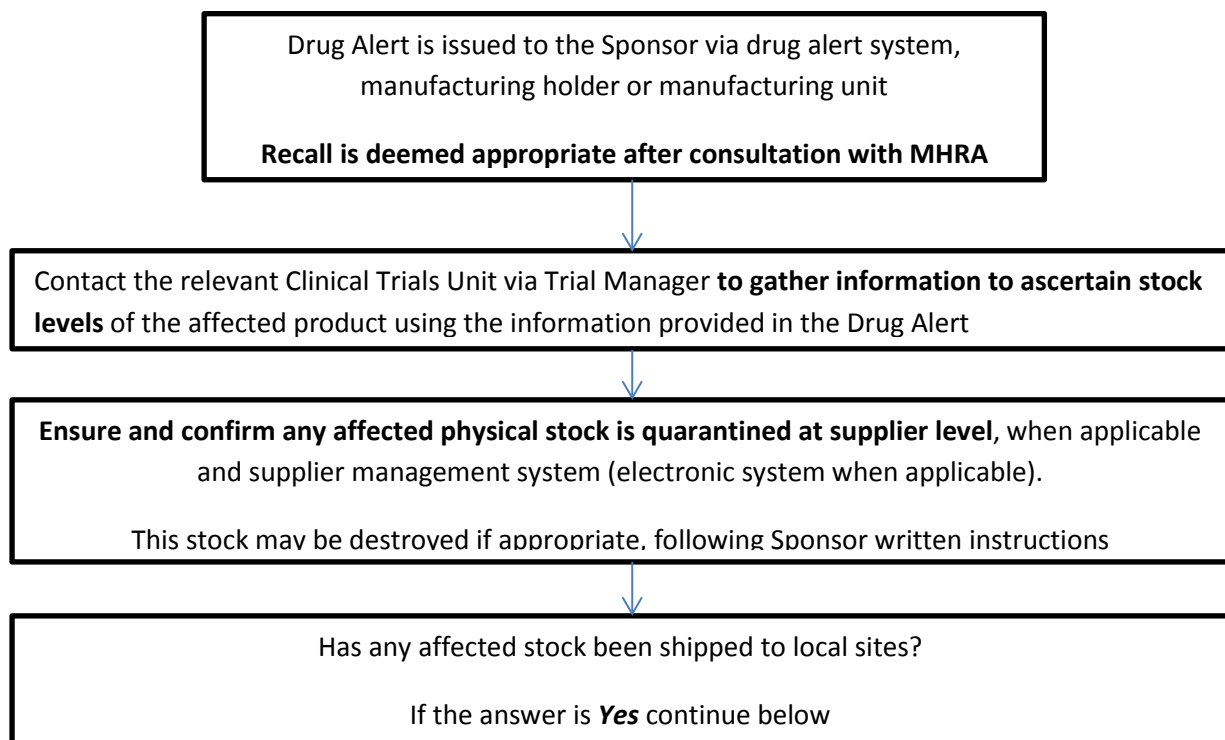
Below is the MHRA recall classification and guidelines on action timelines depending on the risk to participants.

Class 1: The defect presents a life threatening or serious risk to health. Immediate action.

Class 2: The defect may cause mistreatment or harm to the patient, but it is not life-threatening or serious. Recall within 48 hours.

Class 3: The defect is unlikely to cause harm to the patient, and the recall is carried out for other reasons, such as non-compliance with the marketing authorisation or specification. Action to be taken within 5 days.

The MHRA also issues “Caution in Use” notices which are called **Class 4** Drug Alerts, where there is no threat to patients or no serious defect likely to impair product use or efficacy. Alerts advise caution to be exercised when using the product



SINGLE SITE CTIMP

Obtain information on any affected stock dispensed to any trial participant.

Write clear instructions to send to the local site about how to contact the participants to bring any product back to the trial site when required; this should be done in collaboration with the CTU.

Obtain written confirmation that this has happened



Write clear instructions to quarantine/destroy any remaining affected stock on shelf and obtain written confirmation from the site when this has been done

MULTICENTRE SITE CTIMP

Obtain information on any affected stock sent and dispensed to any trial participant for all active sites.

Write clear instructions to send to the local site about how to contact the participants to bring any product back to the trial sites when required; this should be done in collaboration with the clinical trials unit.

Obtain written confirmation that this has happened for each site



Write clear instructions to quarantine/destroy any remaining affected stock on shelf and obtain written confirmation from the site when this has been done