

## **1. Introduction**

This Standard Operating Procedure (SOP) details the procedures to be followed by the Sponsor, Chief / Principal Investigators or research teams where Urgent Safety Measures (USM) are required to protect study subjects against any immediate hazard to their health and / or safety in studies Sponsored by the University Hospitals of Leicester NHS Trust (UHL)

An USM can be defined as any action required to be taken by the Sponsor and / or Investigator(s) to protect study subjects from any immediate hazard to their health and / or safety.

## **2. Scope**

This SOP applies to all staff, and any external individual who are associated with any research activity where the UHL are acting as the Sponsor organisation.

## **3. Procedure for Phase I Trials**

USM should be implemented immediately. Notification and / or approvals are not required prior to their implementation but must be actioned immediately afterwards.

### **3.1 When Urgent Safety Measures may be required**

- An increase in the rate of occurrence of an expected Serious Adverse Reaction (SAR) which is judged to be clinically important.
- Single case reports of an expected SAR with an unexpected outcome (e.g. a fatal outcome).
- A new event relating to the conduct or the development of an Investigational Medicinal Product (IMP) likely to affect the safety of the subjects.
- A serious event which could be associated with the study procedures and which could modify the conduct of the trial.
- A lack of efficacy of an IMP used for the treatment of a life-threatening disease
- An organisation identifies that there is a significantly higher incidence of death at one UK site and as a result suspends recruitment at that site

## **4. Reporting Requirements**

The Chief Investigator (CI) or their delegate must notify the Sponsor by telephone, followed up by an email of the USM at the same time or immediately after notifying the Medicines for Healthcare Regulatory Agency (MHRA). In addition, where the USM involves an IMP, the CI / delegate must notify Pharmacy by telephone, followed up by an email copied to the Sponsor.

### **4.1 MHRA Notification (Competent Authority)**

The CI / delegate must inform the MHRA immediately and in any event within 3 days that the USM(s) have been taken and the reason why.

The CI / delegate must phone the Clinical Trial Unit at the MHRA and discuss the issue. The discussion must be recorded using the Urgent Safety Measures Template (Appendix 1). Should further clarification be required the CI / delegate will be contacted by a MHRA Medical Assessor.

The CI / delegate must then contact the Sponsor to give a full appraisal of the conversation with the MHRA. Documentary evidence of this conversation will be required using Appendix 1.

The CI / delegate must work closely with the Sponsor to notify the MHRA and the REC, in writing, of the measures taken and the reason for the measures within three (3) days.

The notification must include:

- A covering letter detailing the measures taken and the reason for them
- Annex II substantial amendment form
- IRAS Substantial amendment form
- Any supporting documentation
- Relevant fee (where appropriate)

Submission details can be found on the [MHRA website](#)

Details of the Urgent Safety measure, copy of the written notification to the MHRA and a completed Urgent Safety Measures Template (Appendix 1) must be saved in the Trial Master File with copies to the Sponsor.

#### **4.2 Health Research Authority (HRA)/ Research Ethics Committee (REC)**

The CI / delegate must inform the HRA/ REC immediately and in any event within three calendar (3) days that USM have been taken and the reason why they have been taken.

The initial notification to the HRA/ REC must be by telephone. Notice in writing must then be sent within three calendar (3) days setting out the reasons for the USM and the plan for further action. Where the study involves an IMP the same documentation submitted to the MHRA may also be submitted to the HRA/ REC.

The HRA/ REC is not required to approve USM, however the Committee will review such notifications and consider whether the measures taken are appropriate in relation to the potential risk to the subjects, and will consider the further action proposed by the Sponsor and Investigator i.e. the submission of substantial amendments to the protocol.

Details of the USM, copy of the written notification to the HRA/ REC and a completed Urgent Safety Measures Template (Appendix 1) must be saved in the Trial Master File with copies to the Sponsor.

#### **4.3 Notification of sites in Multicentre Studies**

The CI / delegate must inform all Principal Investigators (PIs) at all collaborating sites of the USM immediately, or within a maximum of three calendar days of the USM being taken. Notification must be in writing by email and must detail the required actions to be taken by the PIs at each site and must be copied to the Sponsor.

The PI must alert their local R&I/ R&D offices to any USMs.

Written confirmation that these actions have been taken by the PIs at each collaborating site must be obtained by the CI / delegate within three (3) calendar days of notification. Email confirmation is acceptable.

The CI / delegate must confirm receipt of acknowledgement that the measures have been taken by the collaborating site(s) within three (3) calendar days of notification.

Details of collaborating sites notification and acknowledgement must be documented on the Urgent Safety Measures Template (Appendix 1).

#### 4.4 Notifying Study Participants

The study participants must be informed of the USM and given the option to continue in the trial with the modified trial procedures or withdraw from the trial. Study participants may be contacted initially by phone and then informed in writing of the rationale for the USM and the steps taken or new procedures required to minimise the risk.

All correspondence must be documented in the participant medical notes, Urgent Safety Measures Template (Appendix 1), and where applicable in the Case Report Form.

### 5. Amendments following USM

Where USM result in an amendment, SOP S-1017 UHL must be followed.

### 6. Responsibilities

	Responsibility	Undertaken by	Activity
1	Chief Investigator	Chief Investigator or their Delegate	Notify Sponsor via UHL Research Office on identification of the requirement for urgent safety measures implementation
2	Chief Investigator	Chief Investigator or their Delegate	Notify Pharmacy on identification of the requirement for urgent safety measure implementation
3	Chief Investigator	Chief Investigator or their Delegate	Notification of the REC and MHRA immediately but within 3 days of urgent safety measures being implemented
4	Chief Investigator	Chief Investigator or their Delegate	Completion of Urgent Safety Measure Template
5	Chief Investigator	Chief Investigator or their Delegate	Notify all PIs at all sites giving details of the urgent safety measures required, and obtaining confirmation that appropriate action has been taken
6	Chief Investigator	Chief Investigator or their Delegate	Keep the Sponsor informed at each stage
7	Principal Investigator	Principal Investigator or their Delegate	Implement Urgent Safety Measures at site, and confirm implementation to Chief Investigator within three calendar days of notification. Alert local R&I/ R&D offices of USMs.
8	Chief Investigator & Principal Investigators	Chief Investigator & Principal Investigators at their site	Notify participants of Urgent Safety Measures, document conversations and re-consenting

## **7. Supporting Documents and Key References**

SOP S-1026 Appendix 1

SOP S-1017

## **8. Key Words**

Research, Innovation, Volunteers, Participants, USM, Urgent Safety Measures, Investigational Medicinal Product, IMP, HRA, REC

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This table is used to track the development and approval and dissemination of the document and any changes made on revised / reviewed versions

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<b>Author / Lead Officer:</b>	Carolyn Maloney		<b>Job Title:</b> Head of Research Operations
<b>Reviewed by:</b>	UHL Research Management Meeting		
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Date	Issue Number	Reviewed By	Description Of Changes (If Any)
September 2015	3	Carolyn Maloney	Changes to notification procedures at sites.
August 2016	4	Carolyn Maloney	Consistency check
February 2017	5	Carolyn Maloney	Update to logo
September 2018	6	JJ, LW, CCL	Update to R&I logo Included reference to HRA. Specified PI responsibility to alert local R&I of USMs.
February 2021	7	LW CM JJ	Update and review
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