



UNIVERSITY OF
LEICESTER

**University of Leicester and University Hospitals of Leicester NHS
Trust joint Research Support Office Standard Operating Procedures**

**University of Leicester (UoL) Research Governance Office
SOP S-1029 UoL**

**Urgent Safety Measures for Studies Sponsored by University of
Leicester**

Version 4.0, September 2023

Office Base

Research Governance Office
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Effective Date: October 2023

This SOP will be implemented in line with this document's effective date for all UoL Sponsored research still in set up. For active clinical research that is already in the recruitment phase (or further) at the time of implementation, this SOP must be implemented within 3 months of the effective date.

Please note the appendices associated with this SOP may be subject to interim changes. Please ensure that appendices are downloaded from the RGO webpages prior to use to ensure the latest version of the document is being used.

1.0 Introduction and Scope

This Standard Operating Procedure (SOP) details the procedures to be followed where Urgent Safety Measures (USMs) are required to protect study subjects against any immediate hazard to their health and/or safety in all studies sponsored by the University of Leicester (UoL).

USMs do not require prior approval or authorisation before being implemented however, the Sponsor and appropriate bodies must be notified immediately and within the required timeframes as detailed below. The implementation of an USM must be followed by a request for a substantial amendment.

The Chief Investigator (CI)/Principal Investigator (PI) has the delegated responsibility to take appropriate USMs.

2.0 Definitions

Combined review: Combined review is the way in which research teams seek approval for Clinical Trials of Investigational Medicinal Products (CTIMPs) and combined medicine device trials. A single application is made using a new part of IRAS (Integrated Research Application System), which goes to both the Medicines and Healthcare products Regulatory Agency (MHRA) and a Research Ethics Committee (REC) at the same time.

Urgent Safety Measure (USM): An action that the Sponsor or Investigator may take in order to protect participants in a research study from any immediate hazard to their health or safety.

Investigator: Is the authorised health professional for the conduct of a trial at a trial site. For UoL Sponsored studies this will always be the Principal Investigator (PI).

3.0 Procedure

Actions to protect participants from any immediate hazard to their health or safety can be implemented immediately. Notification and/or approvals are not required prior to their implementation but must be actioned immediately afterwards.

Upon identifying a hazard to research participants which requires an USM the investigator should;

- Report the hazard and measures taken immediately to the CI
- Document the hazard and actions taken on the USM Reporting Form (Appendix 1)
- If necessary, treatments and patient recruitment should be put on hold until there is evidence to suggest that the study/trial is safe to recommence. See section 5.0 below.

The CI must notify the Sponsor, Research Ethics Committee (REC) and Competent Authority (the MHRA in the UK (for CTIMPs)) immediately and within 3 (three) days from the date the USM was implemented. The PI should notify their R&D/I office in accordance with local policies and procedures.

Specific instructions for notifying each regulatory body can be found below, however, **individuals must refer to the MHRA and HRA websites to ensure up to date details for safety reporting are followed.**

3.1 Notifying the Competent Authority

In the UK, the MHRA is the Competent Authority.

For up-to-date instructions on the correct notification procedure for the MHRA in the event of an USM, the following webpage must be consulted: <https://www.gov.uk/guidance/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues#urgent-safety-measures>

Where other Competent Authorities are involved, the relevant website(s) must be consulted.

Upon notice of an implemented USM the CI (or delegate) should;

1. Telephone the MHRA's Clinical Trials Unit on 020 3080 6456 to discuss the issue with a medical assessor **immediately and ideally within 24 hours of the measures being taken.**
2. This conversation should be documented in Appendix 1 and filed within the Trial Master File (TMF) for future reference.
3. After discussing the USM with the MHRA assessor via phone a written notification of the measures taken and discussed with the medical assessor must also be submitted to the Regulatory Authority, **within 3 days from the date the measures were taken.**
 - For CTIMPs not submitted via combined review, the USM notification to the MHRA should be done via email. In addition, a notification to the REC is required as per section 3.2.
 - For CTIMPs submitted via combined review, the USM notification should be submitted in IRAS. No additional notification is required to the REC.
4. If the USM warrants a substantial amendment, this must be submitted **within approximately two weeks of notification to the MHRA.** The amendment should be marked as being in response to a USM and a copy of the USM notification should be submitted with the amendment.
5. A record of all contact with the MHRA must be maintained using the USM Reporting Form (Appendix 1)

3.2 Notifying the REC

For up-to-date instructions on the correct notification procedure for the REC in the event of an USM, the following webpage must be consulted: <https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/safety-reporting/>

1. The CI must notify the REC of the USMs in writing by email **within 3 days from the date the measures were taken** detailing:
 - The measures that have been taken
 - The reasons for the USMs
 - The plan for further action using the appropriate REC safety reporting cover sheet:
 - <https://www.hra.nhs.uk/documents/1086/safety-report-form-ctimps.docx>

- <https://www.hra.nhs.uk/documents/1087/safety-report-form-non-ctimp.docx>
2. If the USM warrants a substantial amendment, this must be submitted **within approximately two weeks of notification to the MHRA** (for CTIMPs) **and as soon as possible** (for non-CTIMPs). The amendment should be marked as being in response to a USM and a copy of the USM notification should be submitted with the amendment.
 3. A record of all contact with the REC must be maintained using the USM Reporting Form (Appendix 1)

3.3 Notifying the Sponsor

The CI must notify the Sponsor immediately following the implementation of a USM setting out:

- A description of the safety issue
- The details of the measures taken
- The reasons for the measures
- Confirmation that the MHRA and REC have been informed
- Confirmation that other PI's have been contacted as required
- The requirement (or not) for a substantial amendment. Where a substantial amendment is required this must be submitted **within approximately two weeks of notification to the MHRA** (for CTIMPs) **and as soon as possible** (for non-CTIMPs). The amendment should be marked as being in response to urgent safety measures
- The CI should keep the Sponsor informed of the progress, outcome or resolution of the actions taken by sending follow-up information.

3.4 Notification of sites in Multi-centre studies

- The CI/delegate must inform all PIs at all collaborating sites of the USM immediately, or within **3 days from the date the measures were taken**. Notification must be in writing (email) and must detail the required actions to be taken by the PIs at each site.
- The PI at each collaborating site must acknowledge and confirm implementation of the USM to the CI/delegate within 3 calendar days of notification. Email confirmation is acceptable.
- The PI must alert their local R&D/I offices to any USMs as per local policies and procedures.
- Details of collaborating sites notification and acknowledgement must be documented on the USM Reporting Form (Appendix 1).
- RGOsponsor@le.ac.uk must be copied into all communication.

3.5 Notifying Study Participants

- The study participants must be informed of the USM and given the option to continue in the study with the modified study procedures or withdraw from the study. 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, USM Reporting Form (Appendix 1), and where applicable in the Case Report Form.
- Participants who are willing to continue in the study, must be re-consented. A full record of all communication with participants must be maintained.

4.0 Examples of when a USM 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 study.
- 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.

5.0 Temporary Halt

In some instances, it may be necessary to halt a trial. A temporary halt can apply to:

- The whole trial
- A specific aspect of a trial e.g, new recruitment
- Individual site(s)
- All UoL Sponsored trials using the same IMP; and can halt recruitment and/or interrupt treatments of active subjects

The notification of temporary halt to the REC, MHRA and R&D/I offices should occur immediately and within 15 days from when the trial is temporarily halted. The notification should be made as a substantial amendment and should clearly detail the reason(s) for the temporary halt.

When there is evidence to suggest the trial is safe to recommence, a request to re-start the trial, alongside the supporting evidence, should be submitted as another substantial amendment. Should the Sponsor or Investigator decide the trial will not recommence after a temporary halt, the REC, MHRA and R&D/I offices must be notified immediately and within 15 days of the decision using the 'end of trial' declaration form.


6.0 Responsibilities

Responsibility	Undertaken by	Activity
Chief Investigator	Chief Investigator or their Delegate	Notify Sponsor via UoL Research Governance Office on identification of the requirement for urgent safety measures implementation
Chief Investigator	Chief Investigator or their Delegate	Notify Pharmacy on identification of the requirement for urgent safety measure implementation
Chief Investigator	Chief Investigator or their Delegate	Notification of the REC and MHRA immediately but within 3 days of urgent safety measures being implemented
Chief Investigator	Chief Investigator or their Delegate	Completion of Urgent Safety Measure Template

Responsibility	Undertaken by	Activity
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
Chief Investigator	Chief Investigator or their Delegate	Keep the Sponsor informed at each stage
Principal Investigator	Principal Investigator or their Delegate	Implement Urgent Safety Measures at site, and confirm implementation to Chief Investigator. Alert local R&D/I offices of USM
Chief Investigator & Principal Investigators	Chief Investigator & Principal Investigators at their site	Notify participants of Urgent Safety Measures, document conversations and re-consenting

7.0 Development and approval Record for this document

This table is used to track the development and approval of the document.

Author	Job title	Reviewed by	Approved by	Date approved
Cat Taylor	Head of Research Governance	UoL Research Management and Operations Group (RSMOG)	Professor Nigel Brunskill 	28/09/2023

8.0 Review Record

This table is used to track the changes made on revised/reviewed versions

Date	Issue number	Reviewed by	Description of changes (If any)
July 2015	2	Wendy Gamble	Clarification of number of calendar days throughout document.
Oct 2016	3	Diane Delahooke	Change logo and address. Minor changes to bring in line with UHL.
September 2021	3.1	Cat Taylor	Administrative changes
September 2023	4.0	Cat Taylor	Administrative Changes Major revisions to wording to aid the clarification of the procedure for actioning and reporting a USM. Changed review schedule to 3 years Major updates to Appendix 1 to aid reporting of a USM. Removal of distribution record

