SOP 230 Urgent Safety Measures

For Use in:	Research
By:	All staff
For:	All staff involved in the conduct of research
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This Standard Operating Procedure (SOP) is available on the Research & Development pages on the NNUH website

Copies printed from the website are only valid on the day of printing.

1. Contents

2. Definitions of Terms Used / Glossary

CI	Chief Investigator
CESP	Common European Submission Portal
CTIMP	Clinical Trial of an Investigational Medicinal Product
EudraCT Number	European Union Drug Regulating Authorities Clinical Trials Number
HRA	Health Research Authority
IMP	Investigational Medicinal Product
JRGC	Joint Research Governance Committee
MHRA	Medicines and Healthcare Products Regulatory Agency
PI	Principal Investigator
R&D	Research and Development
REC	Research Ethics Committee
RGC	Research Governance Coordinator
RIN	Research Innovation Services
RSM	Research Services Manager
SAE	Serious Adverse Event
SAR	Serious Adverse Reaction
SOP	Standard Operating Procedure
SUSARs	Suspected Unexpected Serious Adverse Reactions
TMF	Trial Master File
USM	Urgent Safety Measures

3. Objectives

To have a clear and robust procedure for when urgent safety measures (USM) need to be put in place during a clinical trial.

4. Scope

During the course of a clinical trial involving an investigational medicinal product (IMP) / device trial, new safety information may occur as a result of a serious adverse event (SAE) or information from an external source or Sponsor

- If there is no time to amend the study protocol by the usual process, urgent measures may need to be put in place immediately to protect clinical trial subjects from hazards to their health and safety. These measures could involve a temporary halt of the trial and may result in its premature closure

- USM's can be implemented without prior authorisation from the Health Research Authority (HRA), Research Ethics Committee (REC) and Medicines and Healthcare Products Regulatory Agency (MHRA

Examples of situations requiring USM's might include:

- An expected Serious Adverse Reaction (SAR) with an unexpected outcome (e.g. death)
- An increase in the number / frequency of SARs which is deemed clinically important
- A new event or information relating to the IMP / Device that could affect patient safety.

For further information please see the Medicines and Healthcare Products Regulatory Agency (MHRA) website: https://www.gov.uk/guidance/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues#urgent-safety-measures

5. Purpose

This SOP describes the process to be followed when Urgent Safety Measures (USM) need to be put in place in relation to a clinical trial.

6. Responsibilities

- The Chief Investigator (CI) must take appropriate action to protect study participants from any immediate hazard to their health and safety, and to notify the Sponsor of any safety concerns as well as any USM's implemented.

- If the CI is not available, it is the responsibility of the Principal Investigator (PI) to introduce and report any USM's

- The Sponsor must ensure that any necessary USM's are being implemented, the MHRA and REC have been notified within the specified timelines and hosting organisations are aware of the need to implement USM's

- The study team must notify the CI / PI immediately once aware of issues that may put health and safety of participants at risk

In the event that the Sponsor representative is unavailable to report an USM within the timelines:

- The CI/PI is responsible for notifying the MHRA and REC and should contact the Sponsor as soon as possible to confirm the action

7. Procedure

7 .1 Reporting USM's

For Clinical Trials of an Investigational Medicinal Product (CTIMP) / Device Studies the MHRA and REC must be notified of an USM.

For non CTIMPs notification must be sent to REC.

Any correspondence with the Sponsor, regulatory bodies or hosting organisations must be clearly documented in the Trial Master File (TMF), e.g. email correspondence between Sponsor and the MHRA, a copy of completed Substantial Amendment form

7.2 CTIMPs and Medical Device Studies

In accordance with the MHRA website (see link on page 3 of this SOP):

On discovering the safety issue, the Investigator must contact the Sponsor immediately to discuss further action. This must be done in person or via the phone and followed up by an email.

The Sponsor or Investigator must call the MHRA's Clinical Trials Unit on 0203 080 6456 to discuss the issue with a safety scientist, ideally within 24 hours of measures being taken. Please call no later than 3 days from the date the measures are taken. If they need more information a medical assessor will contact you.

Information you will be asked for on the call:

1. European Union Drug Regulating Authorities Clinical Trials Number (EudraCT number) of the trials for which USM action has been taken. Include information of other trials which may potentially be affected

2. EudraCT number of other ongoing trials with the same Investigational Medicinal Product

3. Whether any other trials with a different sponsor may be impacted and whether the concerned investigators have been made aware
4. The affected IMPs (including alternative / Commercial names)
5. Nature of the safety signal, and whether there have been any SUSARs
6. What immediate safety actions have been taken and when
7. The number of UK subjects who are currently receiving the IMP, the number of subjects who received it and the number affected by the USM
8. Contact details in case of further questions

Where this information is not available during the initial call it should be provided as soon as possible afterwards

	• Inform MHRA no later than 3 days from the date the measures are taken by email to clintrialhelpline@mhra.gov.uk
	• Written notification in the form of a substantial amendment is also required
	• The substantial amendment covering the changes made as part of the USM is expected within approximately 2 weeks of notification to the MHRA
	• The substantial amendment covering the changes made as part of the USM is anticipated expected within approximately 2 weeks of notification to the MHRA
	• Submission of the substantial amendment should not be delayed by additional changes outside of those taken and required as an USM. Unrelated and unacceptable changes may result in rejection

If USM's include unblinding a patient's allocation to treatment, follow **SOP 835 Clinical Data Management System – Emergency Unblinding.**

7.3 Notification to REC

The Sponsor or Investigator must also notify the REC (this should be the REC which issued the favorable ethical opinion) immediately by phone and in writing within 3 days. This should be done in the form of a substantial amendment. The notification shall include details of what measures have been taken and the reason for those measures.

Additional information can be found on HRA website: https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/safety-reporting/ and follow the Safety report form and The Safety and Progress Reports (CTIMPs) Procedural Table links.

7.4 Non CTIMP Studies

Procedure within 7.3 of this SOP should be followed for any non CTIMP studies.

7.5 Temporary Halt of a Trial

If you suspend a trial temporarily you must notify MHRA and the Research Ethics Committee (REC) immediately or at least within 15 days.

The notification must be made as a substantial amendment using the notification of amendment form, clearly explaining what has been stopped and the reasons for the suspension.

Substantial amendments relating to temporary suspension and urgent safety measures must be submitted using the Common European Submission Portal (CESP).

To restart a trial that has been temporarily suspended, you must make the request as a substantial amendment using the notification of amendment form, providing evidence that it is safe to restart the trial.

7.6 Premature trial closure

If a trial is terminated before the date specified for its conclusion (in the application), the Sponsor will notify the MHRA and REC within 15 days of the date of termination by submitting a declaration of the end of a clinical trial form. This form can be found on the HRA Website: http://www.hra.nhs.uk/.

See **SOP 335 Research Project Closure (Including Procedure for Project Suspension or Early Termination**.

7.7 Notification to Host Institutions

For multisite studies the Sponsor will be responsible for notifying host sites of the need to implement USM. This will be done by contacting the local R&D department or PI directly.

7.8 Notification to Joint Research Governance Committee (JRGC)

For studies sponsored by UEA and NNUH the JRGC must be notified of any urgent safety measures, halt of the trial or premature trial closure as a consequence of implementation of urgent safety measures.

For studies sponsored by the NNUH the responsibility to report urgent safety measures to JRGC will be with the Research Services Manager (RSM) or Research Governance Coordinator (RGC).

For studies sponsored by the UEA the responsibility of reporting urgent safety measures to JRGC will be with Research Manager or Head of Research at Research Innovation Services (RIN).

For a clinical trial sponsored by UEA and hosted by NNUH, the Sponsor's representative shall send notice of urgent safety measures, temporary halt or premature closure to the

rdsae@nnuh.nhs.uk inbox who will record details on the Edge the database and report to the JRGC.

8. References and Related Documents

SOP No.	SOP Title
SOP 335	Research Project Closure (Including Procedure for Project Suspension or Early Termination
SOP 835	Clinical Data Management System – Emergency Unblinding.

9. Approval

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10. Reason for new version and Training Implication

This SOP replaces the previous version number V3

Changes made	
Reason	• Revision in procedure
Training Implication	Yes
Actions required	• Matrix to be updated