The University of Manchester

Standard Operating Procedure

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Title:	**Urgent Safety Measures**		
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Version	Date	Summary of changes
2.0	January 2013	Update of weblinks and office details
2.1	May 2014	Addition of version control statement for SOP
3.0	October 2015	Update of weblinks and office details
4.0	August 2016	Update of weblinks and office details
5.0	March 2018	Update to reflect current processes
6.0	November 2021	Added considerations for medical device trials and multi-national trials throughout. New sections 4 and 5.4 were added. Updated section headers in line with SOP template v6.0. Added requirement to ensure communication of urgent safety measures to sites is acknowledged. Reordering of text and minor re-wording. Updated references.
7.0	June 2026	Minor changes for clarification.

When using this document please ensure that the version you are using is the most up to date either by checking on the Research Governance, Ethics and Integrity Office website (https://www.staffnet.manchester.ac.uk/rbe/ethics-integrity/) for any new versions or contacting the author to confirm the current version.

1 Background

All clinical trial activities conducted under this SOP are in line with the applicable UK legislation governing clinical trials of investigational medicinal products and/or medical devices. This includes, but is not limited to, the Medicines for Human Use (Clinical Trials) Regulations 2004 and any subsequent amendments or replacement legislation, such as the Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025, effective from 28 April 2026. All procedures will be carried out in accordance with current guidance issued by the Medicines and Healthcare Products Regulatory Agency (MHRA), the Health Research Authority (HRA), relevant Research Ethics Committees (RECs), and updated GCP standards. This SOP will be reviewed annually or upon significant changes to the regulatory framework to ensure continued compliance.

Medical Device trials are also subject to requirements for reporting urgent safety measures, in accordance with the Medical Devices Regulations 2002 (SI 2002 No 618, as amended) in the UK, and the Medical Device Regulations (2017/745) in the EU.

During the course of a trial, new safety information in the form of a Serious Adverse Event or information received from an external source may necessitate an immediate change in the study procedures or a temporary halt to the study in order to protect trial participants from any immediate hazard to their health and safety.
If time does not allow for an modification to be authorized by the Competent Authority (the Medicines and Healthcare Regulatory Authority (MHRA) in the UK) and main Research Ethics Committee (REC), this change in procedure can be implemented as an **Urgent Safety Measure**, as detailed in this standard operating procedure (SOP).

2 Purpose and Scope

This SOP is to be followed when an urgent safety measure has to be implemented and it is applicable to Clinical Trials involving an Investigational Medicinal Product and Clinical Investigations of Medical Devices, where the University of Manchester (UoM) is the sponsor.

2.1 Roles and Responsibilities

Sponsor

- Ensure urgent safety measures are reported to the competent authorities, the REC and the Data Monitoring Committee
- Review and approval of subsequent substantial modification resulting from the Urgent Safety Measure.

CI

- Identifying the requirement for the urgent safety measure
- Informing the Sponsor and Funder immediately
- Ensuring the urgent safety measure is implemented at all sites

- Preparation and submission of substantial modification

N.B. When the CI is not available, it is the responsibility of the PI to introduce and report any urgent safety measures. The Sponsor can also implement this change.

Manufacturer of the Investigational Medical Device (Clinical Investigations of Medical Devices only)

- Reporting the Urgent Safety Measures to competent authorities, REC, DMC and Sponsor

All members of the trial team

- Informing the CI or PI immediately on the awareness of any immediate hazard to participant health and safety

Where The University of Manchester has delegated responsibility for Urgent Safety Measures to another organisation, such as a Clinical Trial Unit (CTU), or the manufacturer of a medical device, the SOP of that organisation should be followed for this process. However, the SOP must be reviewed by the Sponsor at the point of vendor assessment for compliance with minimum requirements and UoM expectations, in line with this SOP. ***Regardless of the SOP followed, The University of Manchester must still be notified (as set out in 3.2 below) where any Urgent Safety Measures have been implemented.***

3 Definitions

CTIMP -Clinical Trial of an Investigational Medicinal Product
Competent Authority- The national body responsible for regulating clinical trials and/or **Medical Devices**: In the UK, this is the Medicines and Healthcare Products Regulatory Agency (MHRA).
Urgent Safety Measure: A procedure not defined by the protocol that is put in place prior to approval by the Competent Authority, main REC and Sponsor(s) to protect trial participants from any immediate hazard to their health and safety.

4 Procedure

When to implement an Urgent Safety Measure:

If the Principal/Chief Investigator becomes aware of information that trial participants may be at risk of harm, he/she must take immediate action to make the required changes in study procedure or temporarily halt the study in order to protect clinical trial participants from any immediate hazard to their health and safety.

It must be ensured that any communication to sites regarding implementation of urgent safety measures is acknowledged by the sites.

Notifying the University of Manchester:

The University Research Governance, Ethics and Integrity Team (RGEIT) must be notified immediately of the urgent safety measure by email to clinicaltrials@manchester.ac.uk (marking the email Urgent and including the subject “Urgent Safety Measure”). Full information must be provided, including details of the decision-making process leading to the implementation of the urgent safety measure.

If the Research Governance, Ethics and Integrity Office is closed for a period greater than 3 days (for example at Christmas and Easter), the Chief Investigator will be responsible for notifying the Competent Authority and REC as detailed below and must copy the RGEIT into all correspondence (clinicaltrials@manchester.ac.uk).

If there is a co-sponsor for the study, the co-sponsor must also be notified. Where the University of Manchester has delegated responsibility for Urgent Safety Measures to another organisation, the Investigator should follow the SOP of that organisation. The delegated organisation will be responsible for notifying the Competent Authority, REC, and DMC.

Notifying the Competent Authority and REC:

The Sponsor (RGEIT), or the organisation/individual delegated to report urgent safety measures, must inform the MHRA immediately (ideally within 24 hours) by contacting the Clinical Trial Unit at the MHRA by phone (on 020 3080 6456) and discussing the issue with a medical assessor. This should then be followed up in writing within 3 calendar days of the action being taken via a substantial modification.
Information you will be asked for on the call to the MHRA:

- the IRAS ID and the EudraCT number of:
- the trials for which USM action has been taken
- other ongoing trials with the same investigational medicinal product(s) (IMP(s))
- trials run by a different sponsor affected by the USM action
- the affected IMP(s) - commercial or development names
- the nature of the safety concern and whether it has been reported as a SUSAR
- which USMs have been taken and when
- the number of UK participants who are currently receiving the IMP, the number of participants who received it and the number affected by the USM
- contact details in case of further questions

During periods where the MHRA phone is not accessible, an email should be sent to clintrialhelpline@mhra.gov.uk providing an overview (or devices.regulatory@mhra.gov.uk for medical device trials). This should then be followed up with a phone call to the MHRA the next day; the phone lines are open (Monday – Friday 08.30-16.30).
For multinational trials, the relevant Competent Authorities outside of the UK must be notified in line with their requirements.

The Sponsor (or delegate) must then submit a written notification in the form of a substantial modification to the Competent Authority no later than 3 days from the date the urgent safety measures were implemented. The substantial modification should detail the measures taken, and the reasons for implementing such measures as well as detailing the medical assessor contacted.

The REC which issued the favorable ethical opinion must also be notified in line with the Competent Authority reporting schedule (immediately and in any event within three days,

detailing the measures taken and the reasons why).

For CTIMPs via Combined Review:

Notification of Urgent Safety Measures should be submitted via IRAS. The Sponsor (or their delegate) must navigate to the Reporting section within My Studies – My Projects and select the Urgent Safety Measures report from the available options. All required details should be completed and submitted along with the cover letter.
The MHRA will communicate the outcome of the USM via email, and it will also be accessible through IRAS. If a USM is accepted, applicants may proceed to submit a substantial modification, clearly indicating that it is associated with the approved USM. There is no requirement to report USMs separately to the REC.

Other Notifications and non-CTIMPs:

Where applicable, oversight committees (such as the Data Monitoring Committee) should review information relating to urgent safety measures and report any recommendations to all relevant parties.

The funder should be updated on all developments and actions as soon as possible.

For non-CTIMP research, the Chief Investigator must notify the main REC immediately of any urgent safety measures and in any event within three days. NHS R&D offices will also require notification in accordance with local policies/procedures.

Temporary Halts:

If a study is temporarily halted for any reason (e.g., stops recruitment of new participants and/or interrupts the treatment of participants already included in the trial), the sponsor must notify the Competent Authority and the main REC as soon as possible and not later than 15 days as a substantial modification. A further substantial modification will be required to re-start the study. The Chief Investigator may not re-commence the study until the main REC has given a favorable opinion, and the Competent Authority has not raised grounds for no objection of the recommencement.

Documenting the Urgent Safety Measure:

All correspondence with the Sponsor, Competent Authority and REC must be filed in the Trial Master File (TMF) including copies of any substantial modification form submissions.

5 References

MHRA website guidance on Urgent Safety Measure reporting
https://www.gov.uk/guidance/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues#urgent-safety-measures

Clinical trials toolkit
https://www.ct-toolkit.ac.uk/routemap/urgent-safety-measures/

The Medical Devices Regulations 2002
https://www.legislation.gov.uk/uksi/2002/618/contents/made

UK Clinical Trial Regulations

https://www.legislation.gov.uk/uksi/2004/1031/regulation/30

Combined review submission
https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/clinical-trials-investigational-medicinal-products-ctimps/combined-review/step-step-guide-using-iras-combined-ways-working-cwow/#usm

6 Appendices

None