MANCHESTER 1824
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 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 rewording. Updated references

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1 Background

The EU Good Clinical Practice (GCP) Directive 2001/20/EC was introduced to establish standardisation of research activity in Clinical Trials throughout the European Community. It was transposed into UK law as the Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 2004/1031) which came into force on 1st May 2004. The Medicines for Human Use (Clinical Trials) Regulations together with subsequent amendments will be referred to as the Clinical Trial Regulations in the rest of this document. Medical Device trials are also subject to requirements for reporting of 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 subjects from any immediate hazard to their health and safety.
If time does not allow for an amendment to be authorised 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 applicable to Clinical Trials involving an Investigational Medicinal Product and Medical Device trials, where the University of Manchester (UoM) is Sponsor. The use of the term “urgent safety measure” throughout this SOP includes serious health threats that arise during the course of medical device trials. Urgent safety measures for medical device trials follow the same procedure described in this SOP (unless otherwise stated), in accordance with ISO 14155: 2020.

3 Roles and Responsibilities

Sponsor
Ensures urgent safety measures are reported to competent authorities and REC
Review and approval of substantial amendment
Reporting to Competent Authority and REC (Clinical Trials only) unless delegated

CI
Identifying the requirement for urgent safety measure
Informing the Sponsor and Funder
Ensuring the urgent safety measure is implemented at sites
Preparation and submission of substantial amendment (Clinical Trials only)

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 (Medical Device Trials only)
Reporting to competent authorities, REC, and Sponsor
Preparation and submission of substantial amendment

All members of the trial team
Informing the CI immediately on 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 may be followed. However, the process must be reviewed by the Sponsor at the point of vendor assessment for compliance with minimum requirements and UoM expectations, as outlined in 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.***

4 Definitions

CTIMP	Clinical Trial of an Investigational Medicinal Product
Competent Authority	The national body responsible for regulating clinical trials and/or medical device trials. 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 authorisation by the Competent Authority, main REC and Sponsor(s) in order to protect trial participants from any immediate hazard to their health and safety.

5 Procedure

5.1 When to implement an Urgent Safety Measure

If the Principal/Chief Investigator becomes aware of information that trial subjects 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.

5.2 Notifying the University of Manchester

The University Research Governance, Ethics and Integrity Team (RGEIT) must be notified immediately of the urgent safety measure by telephone (0161 275 2725) or via 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 of time greater than 3 days (for example at Christmas and Easter), the Chief Investigator will be responsible for notifying the Competent Authority and REC as per section 3.3 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 should 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. That organisation will be responsible for notifying the Competent Authority and REC.

5.3 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. See the MHRA website (in references) for details of the information that the MHRA will request.

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 multi-national trials, the relevant Competent Authorities outside 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 amendment to the Competent Authority no later **than 3 days** from the date the urgent safety measures were implemented. The substantial amendment should detail the measures taken, the reasons for implementing such measures as well as detailing the medical assessor contacted.

The REC which issued the favourable 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).

5.4 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.

5.5 Temporary Halts

If a study is temporarily halted for any reason, (e.g. stops recruitment of new subjects and/or interrupts the treatment of subjects 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 amendment. A further substantial amendment will be required to re-start the study. The Chief Investigator may not recommence the study until the main REC has given a favourable opinion and the Competent Authority has not raised grounds for non-acceptance of the recommencement.

5.6 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 substantial amendment form submissions.

6 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/2004-*?title=Clinical%20Trials%20Regulations

Clinical investigation of medical devices for human subjects — Good clinical practice
https://www.iso.org/standard/71690.html

7 Appendices

None