UNIVERSITY OF WARWICK

STANDARD OPERATING PROCEDURE 17 Part 3

Urgent Safety Measures

Version:	5.0
Approval Date:	27/04/2026
Effective Date:	11/05/2026
Review Date:	10/05/2028
Review Lead:	WCTU QA Team
WCTU Reviewers:	Beth Norris, Clinical Trials Manager, WCTU
Sponsor Reviewers:	Mathew Gane, Research Governance & QA Manager, R&IS
WCTU approval:	**Natalie Strickland, Head of Operations, WCTU**
Sponsor approval:	**Carole Harris, Assistant Director Research Culture. Governance & Compliance, R&IS**

Revision Chronology:	**Effective date:**	**Reason for change:**
5.0	11 May 2026	Biennial review: Updates to timelines and requirements to align with updated UK Clinical Trial Regulations. Terminology updated from amendment to modification. Timelines updated for written notification of a USM to REC/MHRA from 3 to 7 days. Clarified regulatory requirements vs good practice requirements.
4.0	14 Dec 2023	Biennial review: Flowchart replaced with diagram to summarise requirements and timelines. Consistency check on timelines. Text reviewed to improve flow and reduce duplication. Formatting changes.
3.0	11 Oct 2021	Biennial review: Change to new format. Minor changes to text. Update to timelines. More detail added about discussion with MHRA.
2.0	4 July 2019	Removal of safety reporting process for CTU (now present in parts 1 & 2). Change of title and scope to cover urgent safety measures only. Addition of some specific responsibilities and tasks.
1.6	1 August 2016	Biennial review: Minor clarifications to text. Web links and process flowchart updated.
1.5	26 February 2014	Biennial review: Web links updated. Addition of information on safety reporting for international trials.
1.4	1 December 2011	Update to annual safety reporting requirements. Additional information re: blinding and pregnancy in clinical trials

1.3	1 September 2010	Addition of information re: new MHRA electronic SUSAR reporting system (section 3.3.4.1)
1.2	29 January 2010	Biennial review. Web page links & CTCAE version number updated.
1.1	25 January 2008	Format change. Clarification of reporting process.
Version 1.0	March 2006	

UNIVERSITY OF WARWICK

CONTENTS

1 Purpose and Scope

This SOP describes how to identify if an (USM is required and the process for implementing a USM to protect study participants against any immediate hazard to their health or safety.

It applies to all staff working on UoW sponsored research studies.

For studies not sponsored by UoW but managed by the WCTU, this SOP applies where the responsibility for USMs has been appropriately delegated in an appropriate agreement. Where delegation has not occurred, externally sponsored studies must follow the sponsor's USM process and document any deviations from the procedures in this SOP.

2 Acronyms

CA	Competent Authority
CI	Chief Investigator
CTA	Clinical Trial Authroisation
CTIMP	Clinical Trial of Investigation Medicinal Product
DSUR	Developmental Safety Update Report
IB	Investigator Brochure
ICH-GCP	International Conference on Harmonisation – Good Clinical Practice
IMP	Investigational Medicinal Product
ISF	Investigator Site File
MA	Marketing Authorisation
MHRA	Medicines and Healthcare products Regulatory Agency
PIS	Patient Information Sheet
PI	Principal Investigator
QA	Quality Assurance
R&IS	Research and Impact Services
RSI	Reference Safety Information
SAE/SAR	Serious Adverse Event/Reaction
SOP	Standard Operating Procedure
SPC	Summary of Product Characteristics
SPM	Senior Project Manager
SUSAR	Suspected Unexpected Serious Adverse Reaction
TM/TC	Trial Manager/Trial Coordinator
TMF	Trial Master File
TMG	Trial Management Group
UoW	University of Warwick
WCTU	Warwick Clinical Trials Unit

3 Definitions

Urgent Safety Measure (USM)	A procedure which is not defined by the protocol but put in place with immediate effect to protect study participants from any immediate hazard to their health and safety.

Investigator Location (site)	Clinical trial regulations refer to “investigator location” to reflect the range of settings in which trial activities may be conducted. However, within this SOP and associated procedures, the term “investigator site” is retained where appropriate (including within established acronyms and documentation) and should be considered synonymous with “investigator location” as defined in the regulations.

4 Background

For CTIMPs, The Medicines for Human Use (Clinical Trials) Regulations make provisions for the sponsor and CI to take appropriate USMs to protect a research participant from an imminent hazard to their health and safety. These measures can be implemented before seeking approval from the REC and MHRA.

5 Responsibilities

CI (or delegate)	• Contact MHRA Clinical Trials Unit and discuss the event with a safety scientist (as required for CTIMPs). • Discuss event with sponsor to determine if a temporary halt to the study is required. • Prepare substantial modification to detail the USM. • Notify sponsor, REC, MHRA, investigator sites,funder, and other parties such as DMC, as applicable. • Monitor implementation of all aspects of the USM. Notify NHS R&D offices in accordance with local procedures.
PI	• Notify the sponsor/CI immediately (if USM is instigated by the PI/study site). • Confirm implementation of USM at site. • Document conversations with participants. • Undertake and document actions taken to fulfil the USM.
Sponsor	• Retain responsibility and oversight for ensuring USMs are implemented appropriately.
REC	• Receive and review USM information and modifications. • Consider whether the measures taken are appropriate in relation to the potential risks to the participants.
MHRA	• Receive and review USM information and modifications. • Consider whether the measures taken are appropriate in relation to the potential risks to the participants.
Data Monitoring Committee(DMC)	• Review information relating to USMs and report recommendations to all relevant parties.
TMG	• Discuss and document decisions made regarding implementation of a USM. • Prepare an implementation action plan.
QA Team	• Support study team to review potential USMs and take appropriate actions.

6 When

USMs may be identified and implemented at any time during a study. Initial notification upon the identification of a potential USM should be made to the Sponsor. Once confirmed, the USM must be notified in writing within seven calendar days to:

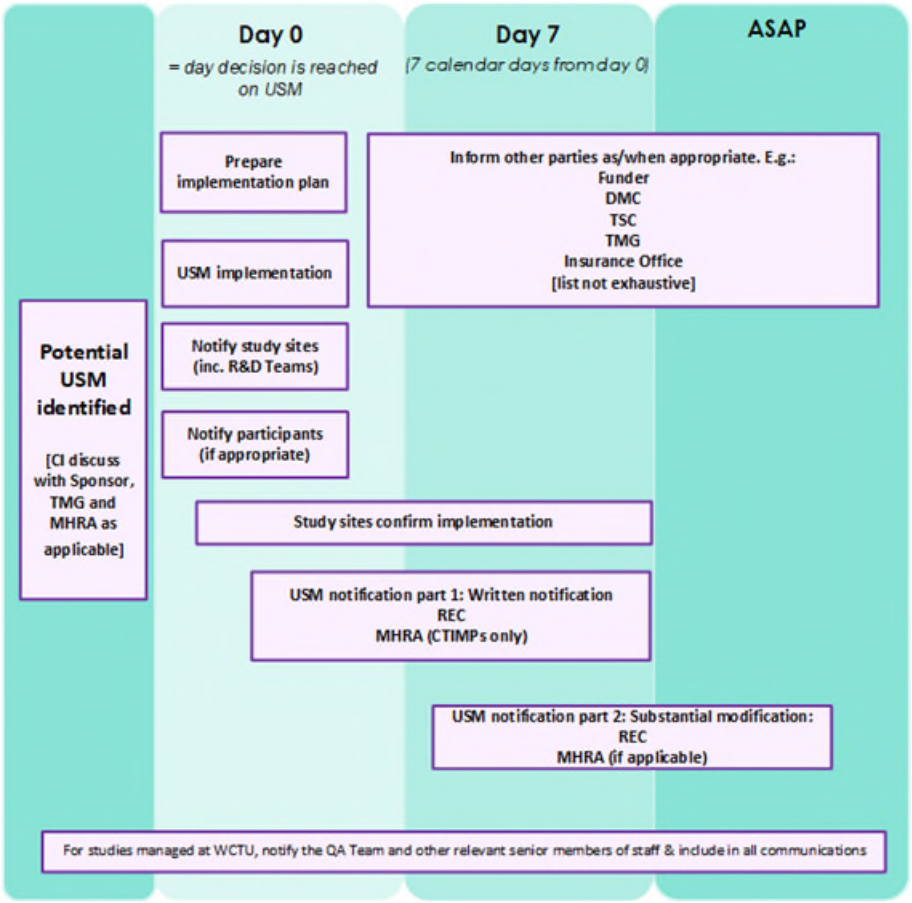
- The REC who provided the favorable opinion
- The MHRA (for CTIMPs)

This should be followed by submission of a substantial modification as soon as possible following notification.

Although the clinical trial regulations do **not** require telephone notification to the MHRA or REC, and the HRA explicitly confirms that sponsors are *not required* to notify the REC by phone, the Sponsor may choose to make telephone contact as a matter of good practice in urgent or complex situations where rapid discussion would support participant safety. This is optional and does not replace the requirement to provide written notification within the statutory seven day period.

7 How

The process is outlined below. Further details can be found in the relevant sections:



7.1 Identification of potential USM

A USM may be required when new information indicates an immediate hazard to participant safety. Examples include:

- Increased frequency or severity of expected SAEs.
- A SAR with an unexpected outcome.
- An event arising from study conduct or operational procedures.
- An issue related to the delivery or administration of the IMP.
- Evidence of lack of efficacy of an IMP in a life-threatening condition.
- A significantly higher incidence of serious outcomes (including death) in one trial arm or at a specific site.

This list is not exhaustive. Any information suggesting a potential immediate safety risk must be escalated to the Sponsor immediately for assessment.

7.2 Decision on USM

Relevant members of the TMG, the Sponsor's representative (and where applicable) the WCTU QA team should review the safety information, agree whether a USM is required, and document all discussions, decisions, and actions. The DMC may also be consulted where appropriate. Once the Sponsor determines that a USM is necessary, this constitutes 'day zero' and the measures must be implemented immediately to protect participant safety. It is good practice to prepare a short implementation action plan. The Sponsor (or delegate) should then prepare the substantial modification to notify the REC and MHRA (CTIMPs) within seven calendar days. The Sponsor may also choose to contact the MHRA or REC by telephone for urgent operational clarification; however, telephone notification is not a regulatory requirement and does not replace the mandatory written notice.

7.3 Implementation of USM

A USM must be implemented immediately when required to eliminate an immediate hazard to participant safety. This may be done without the prior agreement or approval from the REC and MHRA. At the study design stage, the trial team should plan how urgent information will be communicated to sites, participants and other relevant parties. This may include maintaining up-to-date contact lists, defining rapid communication methods, and ensuring responsibilities are clearly described in contracts and study documents.

7.4 Notification to investigator sites

The CI or delegate must immediately notify all PIs by email. The notification must include:

- Reason for USM
- Required actions
- Timelines for implementation
- Request for written confirmation to state that the required actions have been undertaken.

The CI or delegate must retain all notifications and site confirmations in the TMF and must inform the Sponsor (and QA team, where applicable) once notifications have been issued and acknowledgements received.

7.5 Notification to participants

Participants may need to be notified of a USM, depending on the study design, nature of the safety concern, and where the study is being conducted. Participants who are actively receiving the intervention should be informed as quickly as possible using the most rapid and appropriate communication method. Participants must be advised of:

- any additional visits, tests, or procedures required,
- the timelines for these actions, and
- any implications for their ongoing participation

All actions, discussions, and participant communications must be documented in the medical notes and relevant trial records.

Additional considerations include:

- Whether some or all affected participants require re-consent, and how will this be documented.
- Whether study participants who are not currently receiving the intervention need to be informed and the urgency of doing so. For participants not receiving the intervention at the time of USM, whether to seek advice from the Legal and Compliance team or ethical advice on the appropriate communication approach.

PIs or delegated investigator site staff must provide written confirmation that the required USM actions have been implemented. Once all sites have confirmed completion, the CI/delegate should inform the Sponsor (and WCTU QA if applicable) and store evidence of the confirmations in the TMF.

Any site that does not respond within the given deadline must be followed up immediately and continued non-response escalated promptly by the CI or delegate to ensure full and timely implementation of the USM.

7.6 Written notification of USM

Sponsors must provide written notification of any implemented USM to both the MHRA and REC within seven calendar days. Written notifications must clearly describe the measures taken and the reasons for them.

For international CTIMPs, reporting requirements may vary between CAs. These requirements must be identified at study setup and documented in the study-specific procedures.

The REC and MHRA do not approve USMs prior to implementation but will review the measures taken to assess whether they were appropriate in response to the identified immediate hazard.

For studies approved under combined review, notification can be done using IRAS. Those submitted via non-combined review, you should seek advice from HRA and MHRA websites on the best mechanism for notification.

7.7 Substantial modification

Formal notification of substantial modification should be submitted to REC and MHRA (for CTIMPs) as soon as possible to update all the necessary documentation that needs to be modified as a result of the USM. This is separate from the written notification detailed above. Submission of the substantial modification should be via IRAS and include a copy of the USM notification.

Details regarding submission of substantial modifications for USMs are available via:

HRA/REC:

https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/safety-reporting/

MHRA:

https://www.gov.uk/guidance/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues

All substantial modifications should be reviewed and approved by the sponsor (and the QA Team for all WCTU managed studies).

Upon submission of the substantial modification to the REC and MHRA, sites (including R&D) should be provided with the information for their ISF.

Where suspension or early termination of the study occurs, refer to SOP 5 Part 3: Communications with Approval Bodies for further details.

7.8 Notification to other parties

If not already involved, the funder, DMC, TSC and Insurance Office should be informed of the details of the USM as soon as possible, and documentation of the notification to these bodies must be retained in the TMF.