York and Scarborough Teaching Hospitals NHS Foundation Trust R&D Unit
Standard Operating Procedure
R&D/S68

Urgent Safety Measures or Safety Concerns requiring a temporary or permanent halt to a study

IT IS THE RESPONSIBILITY OF ALL USERS OF THIS SOP TO ENSURE THAT THE CORRECT VERSION IS BEING USED

All staff should regularly check the R&D Unit's website and/or Q-Pulse for information relating to the implementation of new or revised versions. Staff must ensure that they are adequately trained in the new procedure and must make sure that all copies of superseded versions are promptly withdrawn from use unless notified otherwise by the SOP Controller.

The definitive versions of all R&D Unit SOPs appear online. If you are reading this in printed form check that the version number and date below is the most recent one as shown on the R&D Unit website: https://www.research.yorkhospitals.nhs.uk/sops-and-guidance-/ and/or Q-Pulse

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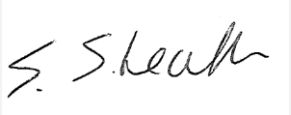
	Signature:	
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This SOP will normally be reviewed every 3 years unless changes to the legislation require otherwise

Version History Log

This area should detail the version history for this document. It should detail the key elements of the changes to the versions.

Version	Date Implemented	Details of significant changes
1.0	24th August 2017	
2.0	4th February 2021	Change of link to R&D Unit website. Updates to notification to R&D unit procedure.

Contents

1 Introduction, Background and Purpose

Clinical Trials of Investigational Medicinal Products (CTIMPs) are legally regulated by the Medicines for Human Use Act 2004 and regulations made by statutory instrument under that Act. [1]

The Regulations require immediate action in the event of an urgent safety measure (USM). An urgent safety measure is an action that the study sponsor and/or investigator may take in order to protect the subjects of a trial against any immediate hazard to their health or safety. The MHRA and REC are required to be notified immediately in this event. The procedure for ensuring the necessary reporting is required to be robust and is therefore described in this SOP.

For non-CTIMPs there is a requirement to report USM to REC.

2 Who Should Use This SOP

This SOP applies to staff working on CTIMP and non-CTIMP research studies taking place in the Trust.

3 When this SOP Should be Used

This procedure should be used in situations where a sponsor/investigator must take urgent action in order to protect the subjects of a trial against any immediate hazard to their health or safety.

This SOP should be used in conjunction with the other related SOPs listed in section 5. *Note: This SOP does not cover the procedure for amendments that are not urgent safety measures or notifying the end of a trial that has not closed prematurely.*

4 Procedure(s)

4.1 What is an urgent safety measure

During the course of a study, new safety information may necessitate an immediate change in study procedures or a temporary halt to the study to protect clinical trial subjects from any immediate hazard.

If time does not allow for an amendment to be authorised by the MHRA (CTIMP studies only), REC (CTIMP and non-CTIMP studies) and sponsor (CTIMP and non-CTIMP studies), this change in procedure can be implemented as an Urgent Safety Measure (USM), by the Chief Investigator (CI), Principal Investigator at a site (PI) or Sponsor.

[1] The Medicines for Human Use (Clinical Trial) Regulations 2004 and the Medicines for Human Use (Clinical Trial) Amendment Regulations 2006, the Medicines for Human Use (Clinical Trials) Amendment (No.2) Regulations 2006, the Medicines for Human Use (Clinical Trials) and Blood Safety and Quality (Amendment) Regulations 2008, and the Medicines for Human Use (Miscellaneous Amendments) Regulations 2009.

4.2 Who should submit an urgent safety measure

Where the CI or a PI implements a USM responsibility for notifying MHRA and/or the REC is delegated to the CI. In exceptional circumstances this may be done by a PI. For a sponsor implemented USM, notification will be done by the R&D Unit as sponsor representative.

Immediately following implementation USMs must be notified to:

1. MHRA (CTIMP studies only)
2. REC (CTIMP and non-CTIMP studies)
3. R&D Unit (CTIMP and non-CTIMP studies)
4. CI (if PI is making notification).

4.3 How to notify that an urgent safety measure has been implemented

The Investigator or sponsor representative must immediately telephone:

(i) The Clinical Trials Unit at the MHRA on 020 3080 6456 to discuss the issue with a safety scientist, ideally within 24 hours. The MHRA's safety scientist will request information that must be provided on the call or, where this is not available, it must be provided as soon as possible afterwards.

(ii) The REC (that gave the favourable ethical opinion for the study) .

Details of the telephone conversation(s) must be documented in the Investigator Site File / Trial Master File (ISF/TMF).

If the reporting has been done by an Investigator s/he must then immediately complete a Notification of Urgent Safety Measure Report Form (See Section 5) and email to the R&D Unit using the mailbox (research.governance@york.nhs.uk) In accordance with the SOP on R&D Unit handling of notifications (see Section 5) the R&D Unit will acknowledge receipt by noon of the next working day. It is the responsibility of the Investigator reporting the USM to ensure a receipt is received and to contact the R&D Unit immediately by telephone (Tel: 01904 726996) if a receipt is not received within this timescale.

The R&D Unit will contact the Investigator reporting the USM immediately or the next working day at the latest. If the reporting Investigator will be unavailable s/he must discuss the matter fully with a delegated individual and give that person's contact details on the USM report form. Such delegation should only be done in exceptional circumstances - the reporting Investigator should make him/herself available to discuss the matter if at all possible.

The Investigator or sponsor representative implementing the USM shall then immediately, and no later than 3 days from the date the measures are taken, give written notice to MHRA and/or the REC detailing the measures taken and the circumstances giving rise to them, including the name of the medical assessor contacted and any supporting documents.

The Notification of Urgent Safety Measure Report Form used to notify the R&D Unit (see above) may also be used for this purpose. This notification must be emailed to clinicaltrialhelpline@mhra.gov.uk. At the same time, a substantial amendment must also be submitted. Submission of the amendment must not be delayed by any additional changes being incorporated. The substantial

amendment must address the urgent safety measures only. The written notification should be:

1. Sent to the MHRA
2. Sent to the main REC – details will be held in the ISF/TMF.
3. Copied to the CI if the USM is reported by a PI or sponsor representative.
4. Copied to the hosting Trust's own R&D Office

An acknowledgement of USM notification should always be requested and followed up if not received. This acknowledgement and any other correspondence relating to the USM should be filed in the ISF/TMF.

4.4 Temporary Halt to a Research Study

When a study is halted temporarily for a reason involving risk to participants' health or safety the halt should be reported as a USM (see Section 4.1).

Where a study is halted temporarily for any other reason the CI or sponsor representative must notify the MHRA (CTIMP studies) and/or REC (CTIMP and non-CTIMP studies) immediately and within 15 days from the date of the temporary halt. The notification should be made as a substantial amendment and should clearly explain exactly what has been halted (e.g. stopping recruitment and/or interrupting treatment of subjects already included) and the reasons for this action.

If the sponsor needs to halt a study temporarily (e.g. in light of issues highlighted in a monitoring report) the sponsor representative will notify the necessary regulatory authorities.

Substantial amendments relating to temporary halts should be:

1. Submitted to MHRA
2. Submitted to the REC
3. Sent to the R&D Unit by email (research.governance@york.nhs.uk)
4. Copied to the CI if the temporary halt is submitted on behalf of the sponsor
5. Copied to the hosting Trust's R&D Office

A copy of the complete application must be retained in the ISF/TMF together with evidence of submission Any correspondence relating to the temporary halt from the MHRA, REC and/or sponsor must be retained in the ISF/TMF. Correspondence from the MHRA and/or REC must be copied to the R&D Unit.

4.5 Restarting a study that has been halted

Restarting a halted study is a substantial amendment. The procedure set out in the Amendments SOP (see Section 5) should be followed. As with any substantial amendment it must be approved by the sponsor before submission to the necessary regulatory authorities. The application made by the CI should include evidence that it is safe to restart the study.

If the sponsor decides not to recommence a temporarily halted study responsibility will be delegated to the CI to notify the REC and/or MHRA within 15 days of this decision, using the End of Trial Declaration form.

5 Related SOPs and Documents

R&D/S05 Research Related Adverse Event Reporting Procedure

R&D S74 Making Amendments to Trust Sponsored Research Studies

R&D/F20 Notification of Urgent Safety Measure (USM) Form

R&D/S12 Receiving and Acknowledging Safety Notifications to the R&D Unit