Document Title: Urgent Safety Measures

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Staff involved in development: *Job titles only*	Senior R&D Manager, R&D Operational Manager, Clinical Project Managers
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Department:	Research and Development
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Summary of Amendments

Version Number	Modification:
Version 4.0	Updated to reflect latest HRA guidance
Version 3.0	Minor procedural changes throughout

Key related documents:	Trust Research Policy

Key Points of this Document

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 safety measures (USMs) 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: Clinical trials for medicines: manage your authorisation, report safety issues - GOV.UK (www.gov.uk)

1. Purpose and Contents

a. This document defines the Trust's procedures for reporting and implementing Urgent Safety Measures for a clinical trial (CTIMP or device trial) that is either managed by Papworth Trials Unit Collaboration or sponsored by Royal Papworth Hospital NHS Foundation Trust.

b. An Urgent Safety Measure is defined as *an action that the sponsor and investigator may take in order to protect the subjects of a trial against any immediate hazard to their health or safety (for example, an organisation identifies that there is a significantly higher incidence of death at one UK site, and as a result suspends recruitment at that site as an USM).*

2. Roles & Responsibilities

a. This Policy applies to all personnel that are conducting research at the Trust.

b. All members of the research team are responsible for reporting to the Principal Investigator and /or sponsor or delegated party, if they identify a safety concern.

c. The Sponsor and Chief Investigator (CI) have the responsibility to take appropriate urgent safety measures.

3. Policy

a. This SOP is mandatory and, as per the Trust's Information Governance and Records Management framework, non-compliance with may result in disciplinary procedures.

4. Procedure

4.1 Informing the MHRA (Papworth Sponsored Studies) CTIMPs only

a. In order to determine whether the action you are taking is an Urgent Safety Measure (USM) please refer to regulation 30 of the Statutory Instrument (SI) 2004 Number 1031 (as amended). The Medicines for Human Use (Clinical Trials) Regulations 2004 (legislation.gov.uk)

b. The MHRA (and REC) must be informed immediately and, in any event, within 3 days that such a measure has been taken and the reason why it has been taken.

c. Call the MHRA's Clinical Trials Unit on 020 3080 6456 to discuss the issue with a medical assessor, ideally within 24 hours of measures being taken. Please call no later than 3 days from the date the measures are taken.

d. Information you will be asked for on the call:

1. The IRAS ID and/or the EudraCT number of; a. The trials for which USM action has been taken, b. Other ongoing trials with the same Investigational Medicinal Product(s) (IMP(s)) c. Trials run by a different Sponsor affected by the USM action
2. The affected IMP(s) - commercial or developmental names
3. Nature of the safety concern and whether it has been reported as a SUSAR
4. Which USMs have been taken and when
5. 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

6. Contact details in case of further questions

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

f. After discussing the USM with the MHRA assessor via phone you must provide the MHRA with written notification of the measures taken and discussed with the medical assessor, within 3 days from the date the measures were taken. For trials not approved via Combined Review you will be instructed to send an email to the medical assessor who assessed the USM over the phone, clintrialhelpline@mhra.gov.uk.

g. If at least one of the trials covered by the USM has gone through the Combined Review process, then the USM written notification should be submitted via the Integrated Research Application System (IRAS). More information can be found on the Health Research Authority (HRA) website.

4.2 Informing the REC and HRA (Papworth Sponsored Studies) – all types of studies

a. **For studies not submitted via combined review**

The research ethics committee (REC) must be notified by email within three days. The notice should set out that such measures have been taken and the reasons why. Where an urgent safety measure (USM) requires an amendment to study documents, this should be submitted as a substantial amendment as soon as possible. The amendment should be marked as being in response to urgent safety measures and a copy of the USM notification should be submitted with the amendment.

Copies of the information should be provided to the REC that approved the study using the appropriate REC safety reporting cover sheet (see below).

b. **For CTIMPs submitted via combined review**

An urgent safety measure (USM) notification should be submitted in IRAS. No additional notification is required to the REC. Where an urgent safety measure (USM) requires an amendment to study documents, this should be submitted as a substantial amendment as soon as possible. The amendment should be marked as being in response to urgent safety measures.

4.3 Informing the Sponsor (Non-Royal Papworth Sponsored Studies)

a. If the CI / PI is based at Royal Papworth, he/she must inform the Sponsor immediately and report the urgent safety measure in accordance with this SOP or the Sponsor's SOP.

4.4 Notifying participating sites and the research team (Royal Papworth Sponsored Studies)

a. Upon implementation of USM the CI must notify the senior manager of R&D and the clinical director of R&D in their capacity as sponsor representative.

b. The CI or delegate should inform all participating sites and Principal Investigators immediately of the implementation of the urgent safety measure and follow this up in writing/email within three days. An acknowledgment of receipt must be requested.

c. Further actions required associated with notification to trial Data Safety and Monitoring Boards; Trial Steering Committee; Quality Assurance and Trial Management team will be agreed and completed once regulatory notifications have been finalised.

4.5 Notifying Trial Participants

a. The measures to be taken to inform trial participants must be detailed in the supporting documents sent to the Research Ethics Committee, who will review the appropriateness of the plans to contact participants.

b. The trial participants should be informed of the urgent safety measures and be given the option to either continue or withdraw from the trial. The participants should be informed in writing or as instructed by the Sponsor of:

i. The rationale for the urgent safety measures
ii. The steps taken or new procedures required to minimise the risks
iii. There may be a requirement to re-consent to an amended participant information and consent sheet

5.0 Risk Management / Liability / Monitoring & Audit

a. The R&D SOP Committee will ensure that this SOP and any future changes to this document are adequately disseminated.

b. The R&D Department will monitor adherence to this SOP via the routine audit and monitoring of individual clinical trials and the Trust's auditors will monitor this SOP as part of their audit of Research Governance. From time to time, the SOP may also be inspected by external regulatory agencies (e.g. Care Quality Commission, Medicines and Healthcare Regulatory Agency).

c. In exceptional circumstances it might be necessary to deviate from this SOP for which written approval of the Senior R&D Manager should be gained before any action is taken.

SOP deviations should be recorded including details of alternative procedures followed and filed in the Investigator and Sponsor Master File.

d. The Research and Development Directorate is responsible for the ratification of this procedure.

Approved by: *Management/Clinical Directorate Group*	Research and Development Directorate
Approval date: *(this version)*	Current active version approved date
Ratified by Board of Directors/ Committee of the Board of Directors:	STET
Date:	N/A
This document supports: *Standards and legislation*	Medicines for Human Use (Clinical Trials) Regulations 2004 and all associated amendments. UK Policy Framework for Health and Social Care Research (2023)

Equality Impact Assessment: Does this document impact on any of the following groups? If YES, state positive or negative, complete Equality Impact Assessment Form available in Disability Equality Scheme document DN192 and attach.

Groups	Disability	Race	Gender	Age	Sexual orientation	Religious & belief	Other
Yes/No	NO	NO	NO	NO	NO	NO	NO
Positive/Negative							

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