RD&I	NHS University Hospitals Plymouth NHS Trust **STANDARD OPERATING PROCEDURE**

DO NOT USE THIS SOP IN PRINTED FORM WITHOUT FIRST CHECKING IT IS THE LATEST VERSION

The definitive versions of all UHNPT RD&I Dept SOPs appear online, not in printed form, to ensure that up to date versions are used. 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 Trust's website: https://www.plymouthhospitals.nhs.uk/research-sops

Urgent Safety Measures

SOP No: T7

Version No: 3.1

Effective Date: Jan 2019

Supersedes: Version 3.0, Aug 2017

Page: **1** of **9**

Last Review Date: Jan 2019 Next review date: Dec 2022

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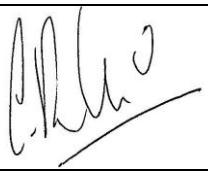
Signature:	
Date:	21st Jan 2019

1 Purpose and Scope

If unexpected events relating to the conduct of a clinical trial or the development of the Investigational Medicinal Product (IMP) occur, there must be arrangements in place for taking appropriate urgent safety measures to protect participants against any immediate hazard.

This Standard Operating Procedure (SOP) details the process to be followed when a study needs to be urgently amended or halted for reasons relating to the safety of participants. Such safety issues need to be reported to the Medicines and Healthcare products Regulatory Agency (MHRA), the Research Ethics Committee (REC) and Sponsor in an expedited manner.

In scope: research hosted by, and/or sponsored by University Hospitals Plymouth NHS Trust (UHNPT).

Definitions

PI	Principal Investigators
CI	Chief Investigator
CTIMP	Clinical Trial of an Investigational Medicinal Product
GCP	Good Clinical Practice
HCA	Health Care Assistants
HRA	Health Research Authority
MHRA	Medicines and Healthcare products Regulatory Agency
REC	Research Ethics Committee
RD&I	Research Development & Innovation
RO	Research Office
SOP	Standard Operating Procedure
UHNPT	University Hospitals Plymouth NHS Trust

2 Who should read this document?

All staff involved in setting up and conducting research e.g. Chief Investigators (CI), Principal Investigators (PI), Research Nurses & Midwives, Health Care Assistants (HCA), RD&I Managers and Clinical Trial Administrative staff

3 Procedure to Follow

Any urgent safety measure relating to an IMP trial must be notified to the study Sponsor, Research Ethics Committee and MHRA within three days of the action being taken. The notification should describe the event, the measures taken and justification for the measures taken. The MHRA can be contacted *via* email at clinicaltrialshelpline@mhra.gsi.gov.uk by titling the email 'Urgent Safety Measures'. The ethics committee will need to be informed in writing with a copy to the sponsor.

MHRA website for up to date reference on Urgent Safety Measures and temporary halt: https://www.gov.uk/guidance/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues

HRA website for up to date reference for Urgent Safety Measures: http://www.hra.nhs.uk/research-community/during-your-researchproject/safety-reporting/

3.1 When to take Urgent Safety Measures

- Urgent Safety Measures should be taken in a clinical trial when it is considered that they are required in order to protect clinical trial subjects from any immediate hazard to their health and safety
- Urgent Safety Measures should be implemented immediately, approvals are not required prior to implementation

3.2 Examples of when Urgent Safety Measures may be required

- Single case reports of an expected SARs with an unexpected outcome (e.g. a fatal outcome)
- An increase in the rate of occurrence of an expected SAR, which is judged to be clinically important
- Post-study SUSARs that occur after the subject has completed a clinical trial
- A new event relating to the conduct or the development of the IMP likely to effect the safety of the subjects e.g.;
    - A serious event which could be associated with the trial procedures and which could modify the conduct of the trial
    - Lack of efficacy of an IMP used for the treatment of a life-threatening disease

- A major safety finding from a newly completed animal study

3.3 Actions

- The CI is delegated the responsibility to take appropriate Urgent Safety Measures
- The CI must notify the MHRA, REC and Sponsor as detailed in sections 3.3.1 to 3.3.3 below
- If necessary treatments and patient recruitment should be put on hold until there is evidence to suggest that the trial is safe to recommence see section 3.5.
- If Urgent Safety Measures need to be taken during a period in which a disease is pandemic and is a serious risk to human health or potentially a serious risk to human health then the MHRA, REC and Sponsor must be informed as soon as possible.

3.3.1. Notifying the MHRA

- The CI should telephone the Clinical Trial Unit at the MHRA and discuss the issue with a safety scientist immediately. Phone the MHRA's Clinical Trial Unit on 020 3080 6456 to discuss the issue with a safety scientist, ideally within 24 hours.
- A medical assessor may contact the CI should further clarification be required
- This conversation should be documented in a file note and filed within the TMF for future reference
- The CI must notify the MHRA of the Urgent Safety Measures taken, in the form of a substantial amendment within three days of implementation
- This notification should include:
  - A covering letter detailing:
    - The measures taken
    - The reason for them
    - The name of the safety scientist contacted
    - A notice of substantial amendment form
    - Any supporting documentation

Submit PDF documents *via* the CESP portal.

3.3.2. Notifying the REC

- The CI should make initial notification to the REC by telephone
- The CI must notify the REC of the Urgent Safety Measures in writing by email within 3 days of implementation of measures, setting out:
  - The reasons for the Urgent Safety Measures

- The plan for further action
- If the urgent safety measure merits a substantial amendment to the documentation approved by the REC this must be submitted within 3 days of implementation.

3.3.3. Notifying the Sponsor

- The CI must notify the Sponsor by telephone and in writing by email, immediately following implementation of measures, setting out:
  - A description of the safety issue
  - The details of the measures taken
  - The reasons for the measures
  - Confirm that the MHRA and REC have been informed
  - Confirm that other PI's have been contacted as required
  - The substantial amendment must be submitted immediately
  - The CI should keep Sponsor informed of the progress, outcome or resolution of the actions taken.

3.3.4. Notifying all Sites

The CI should inform all participating sites and Principal Investigators of the implementation of Urgent Safety Measures immediately or within a maximum of three days in writing by email

The local Principal Investigator must carry out the actions at participating sites

3.3.5. Notifying Trial Subjects

Trial subjects must be informed of the Urgent Safety Measures and be given the option to continue in the trial with the modified trial procedures or withdraw.

Trial subjects must be informed in writing of:

- The rationale for the Urgent Safety Measures
- The steps taken or new procedures required to minimise the risks. The necessary actions must be appropriate to the measures implemented and will be determined by the CI in conjunction with the Sponsor, for example:
  - Requirement to re-consent to an updated patient information sheet and/or
  - Provision of study update letter to subject *in lieu* of an updated PIS

3.4 Documents that must be retained

All communications relating to the measures should be retained e.g. emails, memos, faxes or letters and filed in the TMF and the local ISF.

3.5. Temporary Halt of a Trial

- Temporary halt to a trial is sometimes necessary for various reasons, including Urgent Safety Measures
- Temporary halt can apply to the whole trial or at individual site(s), or to all Trust-Sponsored trials using the same IMP; and can halt recruitment and/or interrupt treatments of active subjects
- The notification of temporary halt should:
  - Be submitted to both the REC and MHRA as a substantial amendment within 15 days from when the trial is temporarily halted
  - Detail what is being halted and reasons for the temporary halt
  - When there is evidence to suggest the trial is safe to recommence:
    - A request to re-start the trial should be submitted as a substantial amendment. Providing necessary evidence to back-up the request.

3.6 Permanent Halt of a Trial

- Should the Sponsor or Investigator decide the trial will not recommence after temporary halt, an end of trial notification must be submitted within 15 days of the decision.

4 Document Ratification Process

The review period for this document is set as ***default of three*** years from the date it was last ratified, or earlier if developments within or external to the Trust indicate the need for a significant revision to the procedures described.

This document will be approved by the ***RD&I Manager or their Deputy***.

Non-significant amendments to this document may be made, under delegated authority from ***a Senior RD&I manager***, by the nominated author. These must be ratified by ***a Senior RD&I manager***.

Significant reviews and revisions to this document will include a consultation with ***appropriately knowledgeable staff***. For non-significant amendments, informal consultation will be restricted to ***staff*** who are directly affected by the proposed changes.

Dissemination and implementation

4.1. Dissemination of this SOP

4.1.1. New SOPs and new versions of existing SOPs: The Research Governance Manager will be responsible for ensuring authorised SOPs are uploaded on the RD&I intranet site. Internal Trust Staff are expected to use the RD&I intranet site to access latest versions of SOPs and to check the website regularly for updates.

Notice of new or amended procedural documents that have undergone a major amendment will be given *via* the following routes:

- Inclusion in the Trust weekly e-bulletin Vital Signs
- Direct email to Trust Researchers and or teams

4.2. Training in this SOP

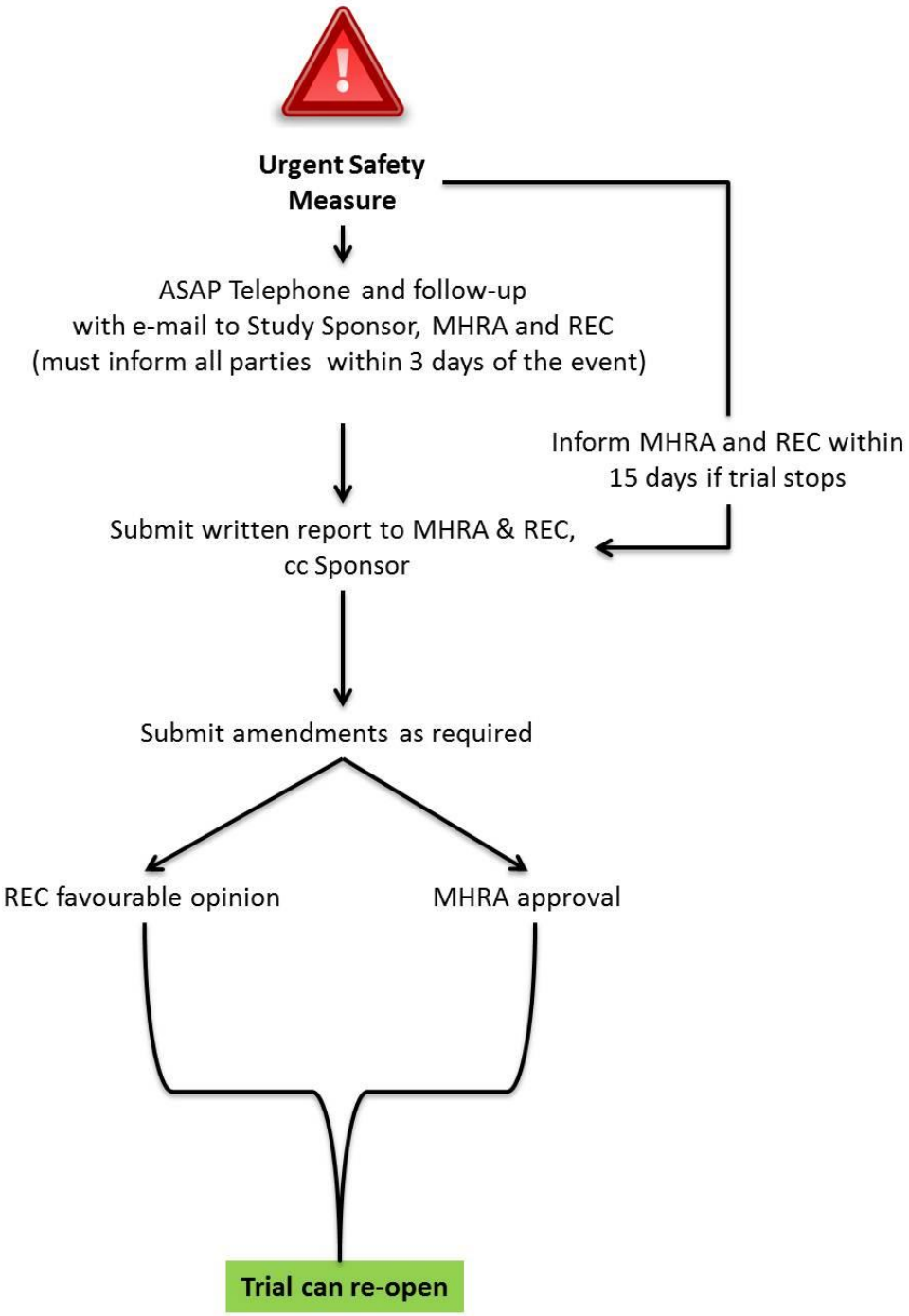
4.2.1. All staff whose activities are subject to this SOP should ensure that they read and understand the content of the SOP.

5 Reference material

MHRA website for up to date reference on Urgent Safety Measures and temporary halt: https://www.gov.uk/guidance/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues

HRA website for up to date reference for Urgent Safety Measures: http://www.hra.nhs.uk/research-community/during-your-researchproject/safety-reporting/

Appendix: Urgent Safety Measures — Appendix 1



6 Amendment History

Version Number:	3.1
Date Of Amendment:	Jan 2019
Details Of Amendment:	Updated Trust and Dept. name. Reduce signature requirement to single senior RD&I Manager.

Version Number:	3.0
Date Of Amendment:	Aug 2017
Details Of Amendment:	Updated SOP template and numbering system. Reviewed and updated SOP.

Version Number:	2.1 (minor amendment)
Date Of Amendment:	Mar 2012
Details Of Amendment:	Cover page - Change of SOP location address.

Version Number:	2.0
Date Of Amendment:	Dec 2009
Details Of Amendment:	Page 3 section 6 Procedure 6th paragraph - Medicines for Human use Regulatory Authority changed to MHRA.