STANDARD OPERATING PROCEDURE

SOP 230

Urgent Safety Measures

Version 2.2	
Version date	27/08/2019
Effective date	27/08/2019
Number of pages	8
Review date	01 April 2020
Author	NNUH UEA Joint Research Office
Approved by	Julie Dawson
Role	Research Services Manager
Signature	*Julie Dawson*
Date	*21/08/2019*
Authorised for NNUH and UEA by	Sarah Ruthven
Role	Research Manager UEA
Signature	*Sarah Ruthven*
Date	*27/08/2019*

COPIES PRINTED FROM THE WEBSITE ARE VALID ONLY ON THE DAY OF PRINTING

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 NNUH R&D website for information relating to the implementation of new or revised versions of SOPs. Staff must ensure that they are adequately trained in the new procedure and must make sure that all copies of superseded versions are promptly withdrawn from use.

The definitive versions of all Joint NNUH/UEA health care research SOPs appear online. If you are reading this in printed form please check that the version number and effective date is the most recent one as shown on the NNUH R&D website.

TABLE OF CONTENTS

1 ABBREVIATIONS

CTIMP	Clinical Trial of an Investigational Medicinal Product
CRTU	Clinical Research and Trials Unit
GCP	Good Clinical Practice
HRA	Health Research Authority
ICH	International Conference for Harmonisation
IMP	Investigational Medicinal Product
MHRA	Medicines and Healthcare Products Regulatory Agency
NNUH	Norfolk and Norwich University Hospital
REC	Research Ethics Committee
SAE	Serious Adverse Event
SAR	Serious Adverse Reaction
SOP	Standard Operating Procedure
UEA	University of East Anglia
REN	Research & Enterprise Services

2 INTRODUCTION

The aim of this SOP is to describe the processes to be followed when urgent safety measures need to be put in place in relation to a clinical trial.
During the course of a clinical trial involving an investigational medicinal product new safety information may occur as a result of a serious adverse event (SAE) or information from an external source. In this case, when there is no time to amend the study by the usual process, urgent measures may need to be put in place immediately to protect clinical trial subjects from hazards to their health and safety. These measures may involve temporary halt of the trial and may result in its premature closure.

3 SCOPE

This SOP applies to all healthcare research sponsored by NNUH or UEA which falls within the scope of the Research Governance Framework (2nd edition 2005) or its successor. Where additional legislation applies - for example the Medicines for Human Use (Clinical Trials) Regulations 2004 (and amendments) or the Medical Devices Regulations 2002 - required procedures will be indicated. External sponsors may require use of their own SOPs and this will be specified in site agreements. It is the responsibility of the local PI to ensure that study specific SOPs can be operated without conflict with this SOP and in accordance with all organisational polices related to research.

4 DEFINITIONS

An Urgent Safety Measure – is an action or course of actions that the Sponsor or the investigator may take in order to protect clinical trial participants from immediate hazard to their health and safety. Urgent Safety Measures can be implemented without prior authorization from the REC and MHRA (for CTIMPs).

Examples of situations requiring urgent safety measures 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 that could affect patient safety.

5 RESPONSIBILITY

It is the responsibility of the CI to take appropriate action to protect study participants from any immediate hazard to their health and safety, and to notify the Sponsor of any safety concerns as well as any Urgent Safety Measure implemented.

When the CI is not available it is the responsibility of the PI to introduce and report any urgent safety measures.

It is the responsibility of the Sponsor to ensure that any necessary Urgent Safety Measures are being implemented, that the MHRA and the HRA REC have been notified within the specified timelines (see below) and that hosting organisations are aware of the need to implement Urgent Safety Measures.

It is the responsibility of the study team to notify the CI / PI immediately after they have become aware of any issues that may put health and safety of participants at risk.

In the event that the Sponsor representative is unavailable to report an Urgent Safety Measure within the timelines (e.g. due to office closures over a long bank holiday) then the CI/PI is responsible for notifying the MHRA and REC, and should contact the Sponsor as soon as possible to confirm this.

6 PROCEDURE

6.1 Reporting Urgent Safety Measures

For CTIMPs and Medical Device Studies both the MHRA and the REC must be notified of an Urgent Safety Measure. For non CTIMPs notification must be sent to REC.

Any correspondence with the Sponsor, regulatory bodies or hosting organizations must be clearly documented in the TMF, e.g. email correspondence between Sponsor and the MHRA, a copy of completed Substantial Amendment form, etc.

6.1.1 Reporting for CTIMPs and Medical Device Studies

On discovering the safety issues the Investigator must contact the Sponsor immediately to discuss further action. This should be done in person via phone and followed up by an email.

The sponsor or investigator may take appropriate urgent safety measures in order to protect research participants against any immediate hazard to their health or safety, without prior authorisation from a regulatory body. However Sponsor or investigator must inform the REC and MHRA immediately (via phone) and in writing within 3 days by submitting a form for substantial amendment.

According to the MHRA website, reviewed on 12 July 2016, the following procedures should be followed when reporting an urgent safety issue:

1. Sponsor or trial investigator, to act immediately when identifying a safety issue during a clinical trial to protect subjects from any immediate threat to their health and safety.

2. Sponsor or investigator to phone the MHRA's Clinical Trial Unit on 020 3080 6456 to discuss the issue with a safety scientist, ideally within 24 hours of identifying safety issue.

3. Sponsor or investigator must then follow up in writing within 3 days of the incident. The notification should be in the form of a substantial amendment and should describe the event, the measures taken and justification for the measures taken.

Should further clarification be required, the Sponsor or Investigator will be contacted by a MHRA medical assessor.

If urgent safety measures include unblinding a patient's allocation to treatment, SOP 835 should be followed.

The Sponsor or Investigator must also notify the HRA REC (the REC which issued the favorable ethical opinion) immediately by phone and in writing within 3 days. This should be done in the form of a substantial amendment. The notification should include details of what measures have been taken, and the reason for those measures.

Additional information can be found on HRA website and by following The Safety and Progress Reports (CTIMPs) Procedural Table: http://www.hra.nhs.uk/

6.1.2 Reporting for Studies which are not CTIMPS

The Sponsor must notify the HRA REC (the REC which issued the favorable ethical opinion) immediately by phone and in writing within 3 days. This should be done in the form of a substantial amendment and using the Safety and Progress Reports Table (non-CTIMPs) as a guide. This notification should include details of what measures have been taken, and the reason for those measures.

Additional information can be found on HRA website and by following The Safety and Progress Reports Table (non-CTIMPs): http://www.hra.nhs.uk/

6.2 Temporary halt of a trial

When a decision has been made by the Sponsor to halt a trial temporarily, the REC and MHRA should be notified immediately, and at least within 15 days from when the trial is temporarily halted. The notification should be made as a substantial amendment using the notification of amendment form, and should clearly explain what study activities have been halted (e.g. stopping recruitment and/or interrupting treatment of subjects already included) and the reasons for the temporary halt.

All forms are available on the HRA website: http://www.hra.nhs.uk/

To restart a trial that has been temporarily halted, the Sponsor should make the request as a substantial amendment using the notification of amendment form and providing evidence that it is safe to restart the trial.

If a Sponsor decides not to recommence a temporarily halted trial, the MHRA and REC should be notified within 15 days of this decision, using the End of Trial Declaration form available from the HRA website and including a brief explanation of the reasons for ending the trial (http://www.hra.nhs.uk/)

6.3 Premature trial closure

If a trial is terminated before the date specified for its conclusion (in the application), the Sponsor should notify the MHRA and REC within 15 days of the date of termination by submitting a declaration of the end of a clinical trial form. This form can be found on the HRA Website: http://www.hra.nhs.uk/.

6.4 Notification to host institutions

For multisite studies the Sponsor will be responsible for notifying hosting sites of the need to implement Urgent Safety Measures. This will be done by contacting the local R&D department or PI directly.

6.5 Notification to Joint Research Governance Committee

For studies sponsored by UEA and NNUH the JRGC must be notified of any urgent safety measures, halt of the trial or premature trial closure as a consequence of implantation of urgent safety measure.

For studies sponsored by the NNUH the responsibility to report urgent safety measure to JRGC will be with the Research Services Manager or Research Governance Co-ordinator.

For studies sponsored by the UEA the responsibility of reporting urgent safety measures to JRGC will be with Research Manager or Head of Research at REN.

For a clinical trial sponsored by UEA and hosted by the NNUH, the Sponsor's representative should send notice of urgent safety measures, temporary halt or premature closure to the NNUH R&D Office who will record details on the office study database and report to the Joint Research Governance Committee.

7 REFERENCES

MHRA website: Clinical trials for medicines: Safety reporting - SUSARs and SARs link http://www.mhra.gov.uk/

MHRA website: MHRA Good Clinical Laboratory Practice: http://www.mhra.gov.uk/

Detailed guidance on the request to the competent authorities for authorisation of a clinical trial on a medicinal product for human use, the notification of substantial amendments and the declaration of the end of trial (CT-1) : 31/3/2010 Official Journal of the European Union C82/1

NIHR Clinical Trials Toolkit – Safety measures: http://www.ct-toolkit.ac.uk/

Eudra CT: European Clinical Trials Website: https://eudract.ema.europa.eu/

Research Governance Framework (2nd edition 2005) or its successor.

Medicines for Human Use (Clinical Trials) Regulations 2004

Medical Devices Regulations 2002

8 RELATED DOCUMENTS

SOP 205 Identifying, Recording and Reporting Adverse Events for Clinical Trials of Investigational Medicinal Products

SOP 206 Identifying, Recording and Reporting Adverse Events for Healthcare Research Studies that are not CTIMPs

SOP 210 Breaches of Good Clinical Practice of the Trial Protocol

SOP 835 Clinical Data Management System: EMERGENCY UNBLINDING

9 LIST OF APPENDICES

Appendix 1: Change Control, Revision and Review Sheet

Appendix 1: Change Control Revision and Review Sheet

Revision Form: SOP 230				
Version No	Change Date	Reason for Change	Reviewer	Signature and Date
1.1	21/03/2011	Updated to reflect UEA/NNUH joint working arrangements.		
1.2	06/11/2013	Updated to extend review period by two months.		
2.0	01/01/2014	Updating of links and references. Combining of SOP control and revision sheets.	**Noreen Cushen** Lead Research Nurse CRF Manager	***Noreen Cushen 17th December 2013***
2.1	30/12/2015	Websites and links reviewed and remain current Addition of NIHR Clinical Trials Toolkit web address	**Adele Cooper** Senior Clinical Research Nurse	**Adele Cooper 30th December 2015**
2.1	*27.03.2017*	Addition of "or its successor" following Research Governance Framework (2nd edition 2005). General formatting Update of the SOP in accordance to updated MHRA guidelines (JULY 2016), clarification of responsibilities of CI, Sponsor and study team. Clarification of the term Urgent Safety Measure.	**Leodie Alibert QA Lead (NCTU / UEA)** **Basia Brown Research Governance Co-coordinator (NNUH)**	***Leodie Alibert Basia Brown*** **6th Jan .2017**
2.2	14/08/2019	Extension of review deadline 12 month from existing review date, no content changes made.	**Francesca Dockerty- Clinical Trial Monitor NNUH**	***Francesca Dockerty*** ***08/08/2019***