

# Standard Operating Procedure CCTU/SOP019

## Urgent Safety Measures for CTIMPs

### 1. Scope

This SOP applies to Clinical Trials of Investigational Medicinal Products (CTIMPs) regulated by the UK Regulations on Clinical Trials (The Medicine for Human Use (Clinical Trials) Regulations 2004 and its amendments).

If unexpected events relating to the conduct of a trial (or the development of the IMP) sponsored by the Trust occur, there must be arrangements in place for taking appropriate Urgent Safety Measures to protect participants against any immediate hazard.

### 2. Purpose

This Standard Operating Procedure (SOP) details the procedures to be followed when a study needs to be urgently amended or halted for reasons relating to the safety of participants.

### 3. Definitions and Abbreviations

The headings below contain the definitions of terms and meaning of abbreviations used within the document.

Common abbreviations and definitions can be found in CCTU/INF001 Common Abbreviations and Definitions.

Term	Definition
Trust-Sponsored	Sponsored by Cambridge University Hospitals NHS Foundation Trust (CUH) or sponsored by CUH jointly with The University of Cambridge

#### 3.1. Abbreviations

Abbreviation	Meaning
...	...

### 4. Undertaken by

Active research staff and staff of the R&D Department and the Cambridge Clinical Trials Unit (CCTU) whenever an Urgent Safety Measure needs to be taken in order to protect the subjects of a clinical trial against any immediate hazard to their health or safety.

The Chief Investigator (CI) of a Trust sponsored CTIMP has been delegated the responsibility to take appropriate urgent safety measures. The CI must inform the MHRA, main REC and the CCTU acting on behalf of the Sponsor within 3 days.

## 5. Items Required

MHRA website for up to date reference

<http://www.mhra.gov.uk/Howweregulate/Medicines/Licensingofmedicines/Clinicaltrials/Safetyreporting-SUSARsandASRs/index.htm#10>

## 6. Summary of Significant Changes

Replaces R&D/S/010

## 7. Method

The following sections provide a description of the processes to be followed when implementing this document's procedures.

**The MHRA web-pages on Urgent Safety Measures should always be consulted when using this SOP**

### 7.1. 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
- The urgent safety measures should be taken immediately
- There is no need to wait for MHRA or ethics approval but such safety issues need to be reported in writing to the MHRA, main REC, and the CCTU within 3 days.

#### Examples

- Single case reports of an expected serious adverse reaction (SARs) with an unexpected outcome (e.g. a fatal outcome)
- An increase in the rate of occurrence of an expected serious adverse reaction, which is judged to be clinically important
- Post-study Suspected Unexpected Serious Adverse Reactions (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

### 7.2. Actions

- The Chief Investigator (CI) of Trust sponsored CTIMP's is delegated the responsibility to take appropriate urgent safety measures
- The CI must inform the MHRA, main REC and CCTU within 3 days.
- The MHRA, main REC and CCTU should be provided with complete details of the events that gave rise to the urgent safety measures together with the reasons why, and an indication of any proposed further action to be taken

- 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 Competent Authorities and relevant Ethics Committee must be informed **as soon as possible**

### 7.3. Notifying the MHRA

- The CI should telephone the Clinical Trial Unit at the MHRA and discuss the issue with a medical assessor immediately
  - This conversation should be documented and filed within the TMF (Trial Master File) for future reference
  - The CI must notify the MHRA, in writing, of the Urgent Safety Measure taken and the reason for the measures within three days
  - This notification should include:
    - A covering letter detailing the measures taken
    - The reason for them
    - The name of the medical assessor contacted
    - Any supporting documents
- 1) Sent by email to [clintrialhelpline@mhra.gsi.gov.uk](mailto:clintrialhelpline@mhra.gsi.gov.uk)) marked 'Urgent Safety Measure' and
  - 2) Sent as PDF documents on disk to: Information Processing Unit, Area 6, Medicines & Healthcare products Regulatory Agency, 151 Buckingham Palace Road, Victoria, London. SW1W 9SZ
- If the urgent safety measure merits a substantial amendment this must be submitted according to current procedures

### 7.4. Notifying the REC

- The CI should send notification in writing within 3 days
- The notification should set out the reasons for the urgent safety measures and the plan for further action

### 7.5. Notifying the Sponsor

- The CI should inform the CCTU (acting on behalf of the Sponsor) **within 3 days** with details of the measures taken, the reasons why and confirm that the MHRA and main REC have been informed
- If the urgent safety measure merits a substantial amendment this must be submitted according to current procedures
- The CI should keep CCTU informed of the progress, outcome or resolution of the actions taken

### 7.6. Notifying all Sites

- The CI should inform all participating sites and principal investigators of the Urgent Safety Measures immediately or within a maximum of three days
- The local principal investigator must carry out the actions at participating sites
- In some instances an Urgent Safety Measure may require suspension or termination of the trial (or all trial studies using the same IMP)

- In some circumstances, a substantial amendment to the trial documentation may be required

### 7.7. Documents to 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 sponsor's trial files.

## 8. Monitoring Compliance with and the Effectiveness of this Document

### a. Process for Monitoring compliance and Effectiveness

As part of routine monitoring visits, audit and inspection

### b. Standards/Key Performance Indicators

This process forms part of a quality management system. Documents are reviewed every two years

## 9. References

The Institute of Clinical Research, 2008, Abbreviations used in Clinical Trials.

Notification of Amendment form available from EudraCT:

<https://eudract.emea.europa.eu/document.html>

Please note: The MHRA web-pages on Urgent safety measures should always be consulted when using this SOP:

<http://www.mhra.gov.uk/Howweregulate/Medicines/Licensingofmedicines/Clinicaltrials/Safetyreporting-SUSARsandASRs/index.htm#10>

## 10. Associated Documents

None

## 11. Equality and Diversity Statement

This document complies with the Cambridge University Hospitals NHS Foundation Trust service equality and diversity statement.

## 12. Disclaimer

It is the user's responsibility to check against the electronic library that this printed out copy is the most recent issue of this document.

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