

Standard Operating Procedure R&D/SOP003

Serious Breach of Protocol or GCP in CTIMPs

1. Scope

This SOP applies to Clinical Trials of Investigational Medicinal Products (CTIMPs) sponsored by the Trust or where the Trust is a participating site regulated by the UK regulations on Clinical Trials: The Medicine for Human Use (Clinical Trials) Regulations 2004 and its amendments.

2. Purpose

This SOP outlines the procedure for managing breaches in Clinical Trials of Investigational Medicinal Products (CTIMPs).

Regulation 29A of the UK Medicines for Human Use (Clinical Trials) Regulations 2004 [Statutory Instrument 2004/1031], as amended by Statutory Instrument 2006/1928, contains a requirement for the notification of "serious breaches" of GCP or the trial protocol to the MHRA.

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

3.1. Definitions

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

3.2. Abbreviations

Abbreviation	Meaning
CI	Chief Investigator
CTIMP	Clinical Trial of Investigational Medicinal Product
GCP	Good Clinical Practice
MHRA	Medicines and Healthcare products Regulatory Agency
PI	Principal Investigator
R&D	Research and Development Department

4. Undertaken by

Research staff, monitors, auditors, staff of the R&D Department and the Cambridge Clinical Trials Unit who may identify a breach of GCP or the protocol.

5. Items Required

MHRA Serious Breach Report Form

<http://www.mhra.gov.uk/Howweregulate/Medicines/Inspectionandstandards/GoodClinicalPractice/Background/index.htm#5>

6. Summary of Significant Changes

Replaces R&D/S/050

7. Method

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

7.1. A breach of GCP and/or Protocol

- A breach is defined as **serious** when it is likely to affect to a significant degree:
 - The safety, physical or mental integrity of the subjects in the trial
 - The scientific value of the trial

7.2. Examples of Serious Breach

- Proof of fraud relating to clinical trial records or data
- Persistent or systematic non-compliance with GCP or protocol that has a significant impact on the integrity of trial subjects or the scientific value of the trial
- Failure to control investigational medicinal product(s) such that trial subjects or the public are put at significant risk or the scientific value of the trial is compromised
- Failure to report adverse events, serious adverse events or SUSARs in accordance with the legislation such that trial subjects or the public are put at significant risk

7.3. Identification of a Serious Breach

- Not all breaches from protocols are considered to be serious. However all deviations from the approved protocol should be documented by researchers in the Trial Master File/Investigator Site File for affected sites
- Breaches can be identified by anyone who is conducting, managing or monitoring a trial
- It is the responsibility of the person who identifies a suspected serious breach to notify the R&D Department of any SUSPECTED serious breaches of GCP.

- The R&D Department must be notified of any suspected serious breaches within 24 hours of the breach being identified
- The notification can be by email or in person and must detail the following:
 - Trial details
 - Name of CI or Investigator and site
 - How the breach was identified
 - Full details of the breach
 - An assessment of the impact that the breach will have on the subjects and/or scientific integrity
 - Details of any corrective actions planned or taken
- R&D staff who receive notification of the breach should immediately inform the R&D Manager

7.4. Assessment of a Serious Breach

- Upon receipt of the initial report the R&D Manager will:
 - Promptly discuss with relevant research and R&D staff and confirm the seriousness of the breach
 - Gather any further documentation/supporting evidence
 - The final decision of whether the breach meets serious breach of the protocol and or GCP will be made by the Director of R&D
 - Documentation of the review of all associated documents and the final decision must be signed, dated and filed within the relevant R&D file and Trial Master File
 - Assess in collaboration with the Director of R&D and the CI/PI, whether any Urgent Safety Measures may need to be implemented
 - In the case of studies sponsored by the Trust agree with the CI any remedial actions required if the breach does not warrant notification to the MHRA and REC
 - In the case of studies where the Trust is a participating site agree with the PI whether the Sponsor and Ethics should be notified of the breach

7.5. Notification of a Serious Breach to the MHRA

- If it is clear that a serious breach has occurred in a study sponsored by the Trust the MHRA must be informed within 7 days of the Trust becoming aware of the serious breach
- This can be by telephone initially, followed up by written notification
- A Sponsor representative in the R&D Department will complete the Notification of a Serious Breach Form from the MHRA website
- The form should be sent by email to the MHRA (GCP.SeriousBreaches@mhra.gsi.gov.uk) within 7 days
- Any further information required by the MHRA should be provided by R&D and/or the CI when requested
- Any corrective and preventative measures should be implemented as appropriate

- If Urgent Safety Measures have been taken these should be notified to the MHRA and Ethics within 3 days of the action taken. Refer to CCTU/SOP019 Urgent Safety Measures
- All correspondence and documentation relating to the breach should be retained in the TMF, Investigator Site Files and R&D 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.

10. Associated Documents

The MHRA web-pages on Serious Breaches should always be consulted when using this SOP and MHRA form:

<http://www.mhra.gov.uk/Howweregulate/Medicines/Inspectionandstandards/GoodClinicalPractice/Background/index.htm>

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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