




SOP Number

008

SOP Title

Serious Breach of Good Clinical Practice or the Trial Protocol

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1. PURPOSE

This SOP describes the standard procedures to be followed for handling Serious Breaches of Good Clinical Practice (GCP) or the trial protocol.

2. INTRODUCTION

In the course of a clinical trial, there may be occasions when there are relatively minor protocol deviations or violations (e.g. clinic visits outside of the scheduled time window). Serious Breach, however, has the potential to cause harm to patients or to the integrity of the trial.

The Medicines for Human Use (Clinical Trials) Regulations require the Sponsor of a clinical trial to inform the competent authority (MHRA in the UK), in writing, within 7 calendar days of becoming aware of any Serious Breach. In the UK, for example, the Health Research Authority (HRA) also requires any such Serious Breach to be reported to the relevant REC within 7 calendar days of awareness. Please refer to other country-specific requirements.

3. SCOPE

The scope of this procedure is for all CTIMPs and devices trials sponsored by the University of Oxford, but may also be used for other clinical research studies at the discretion of the unit.

4. DEFINITIONS

Serious Breach

A Serious Breach is a breach which is likely to effect to a significant degree (a) the safety, physical or mental integrity of the subjects of the trial or, (b) the scientific value of the trial.

Corrective and Preventive Action (CAPA)

Improvements to processes made to eliminate causes of non-conformities.

Corrective action is implemented to prevent recurrence of a non-conformity, whilst preventive action is prediction of a problem and actions made to prevent occurrence.

5. RESPONSIBILITIES

Chief Investigator (CI)

Responsible for identifying and/or assessing a potential Serious Breach and reporting to the Sponsor.

Study Team Members

Responsible for identifying a potential Serious Breach and reporting to the CI or delegate, or to the Sponsor.

Sponsor

Responsible for working with the CI and Study Team to assess the potential Serious Breach. If it is categorised as a Serious Breach, then the Sponsor will prepare the report, submit to the competent authority, and to the REC. The Sponsor will then support the development and implementation of CAPA plans.

6. SPECIFIC PROCEDURE

6.1 Receipt of Serious Breach Notification

A potential Serious Breach may be identified by any member of the Study Team by means of meetings, communications, central or site monitoring, audit, or routine review of general non-compliance issues. A Serious Breach may also be identified through allegations by whistleblowers or complainants within or outside the study team.

A member of the team will be identified to be responsible for maintaining written records, whether this be written information received, verbal information recounted, or accounts of discussions.

6.2 Assessment

Information regarding potential Serious Breaches should be treated as confidential. Details and outcomes should be made available to relevant staff on a need-to-know basis. All interviewees and correspondents will be reminded of the need for confidentiality.

Where a Serious Breach is suspected, the Sponsor must be contacted without delay.

The Sponsor will work with the relevant Study Team members to assess the Serious Breach, its cause and potential remedial actions, and to produce a CAPA plan. A CAPA plan must incorporate the specific site, trial, operations of the unit or department and Sponsor where ever these are relevant. A CAPA plan may also be appropriate where the issue is not eventually defined as a Serious Breach.

N.B. Recognition by the Sponsor of a Serious Breach will start the clock at Day 0 of the reporting process.

For multi-national trials, in the absence of country specific guidance being available, Serious Breaches will be assessed against The Medicines for Human Use (Clinical Trials) Regulations 2004 and amendments.

Where there is a difference of opinion between the Sponsor and Study team on whether or not a potential serious breach is a serious breach, it will be reported with reference to this difference of opinion.

6.3 Reporting

The Sponsor will inform the competent authority and REC of relevant participating countries within required reporting timelines. Details of the breach may be reported to third parties as appropriate, and by agreement. This may take the form of an initial report within the specified time, with follow-up details provided later.

Where a Serious Breach occurs outside of the UK and the trial has UK participants, the MHRA will be notified where appropriate with reference to the current guidance.

6.4 Follow-up and Closure

The Sponsor will work with the Chief Investigator and Study Team to provide follow-up information for the competent authority and REC where required, and to support the CAPA plan until case closure. For trial-specific Serious Breaches, related documentation should be filed in the TMF, unless there is confidential information within, in which case its location should be flagged within the TMF. Where a Serious Breach is not specific to a trial, documentation may be filed in a specified location. All relevant documentation will also be retained by the Sponsor.

7. RELATED DOCUMENTS

Notification of Serious Breaches of GCP or the Trial Protocol:

<https://www.gov.uk/guidance/good-clinical-practice-for-clinical-trials#report-a-serious-breach>

8. REFERENCES

The Medicines for Human Use (Clinical Trials) Regulations 2004 (and subsequent amendments)

9. CHANGE HISTORY

Version No.	Effective Date	Significant Changes	Previous Version No.
1.0	01 Jan 2014	First version of SOP	n/a
2.0	02 June 2016	Update to procedure to outline what is required in the event of a Serious Breach occurring outside the UK	1.0
3.0	See page 1	Update to scope and front page in line with changes to SOP template. Clarification in section 6.2 on what would happen in the event of a divergence of opinion between the Sponsor and study team	2.0