

**STANDARD OPERATING PROCEDURE**

**Serious Breach of GCP or Protocol**

**R&D/S/005/3.0**

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

The definitive versions of all the R&D Department's SOPs also appear online. A printed version will be available for reference only. 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: [http://www.cuh.org.uk/research/researchers/document\\_library.html](http://www.cuh.org.uk/research/researchers/document_library.html)

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Date

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## **Serious Breach of GCP or Protocol**

### **1. PURPOSE AND SCOPE**

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.

This SOP outlines the procedure for managing such breaches in Clinical Trials of Investigational Medicinal Products (CTIMPs) sponsored by Cambridge University Hospitals NHS Foundation Trust (Trust) or jointly sponsored with the University of Cambridge, or where the CTIMP is conducted at the Trust, whereby the Trust is a participating site.

### **2. ASSOCIATED DOCUMENTS**

Appendix 1: MHRA Notification of Serious Breaches Form Version 2, 25-09-09

Please note: 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>

### **3. APPLICABILITY**

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 2006, 2008 and 2009) and to research staff, monitors, auditors and staff of the R&D Department and the Clinical Trials Office (CTO) who may identify a breach of GCP or the protocol.

### **4. PROCEDURES**

#### **4.1 DEFINITIONS**

A breach of GCP and/or protocol is defined as **serious** when it is likely to affect to a significant degree –

- (a) the safety or physical or mental integrity of the subjects of the trial; or
- (b) the scientific value of the trial.

#### **4.2 EXAMPLES OF SERIOUS BREACHES**

- 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 in the UK or on the scientific value of the trial
- Failure to control investigational medicinal product(s) such that trial subjects or the public in the UK 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, in the UK are put at significant risk

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### **4.3 IDENTIFICATION OF A SERIOUS BREACH**

- 4.3.1 Not all breaches from protocols will be considered to be serious. However, all deviations from the approved protocol should be documented by researchers in the Trial Master File/Investigator File.
- 4.3.2 Breaches can be identified by anyone who is conducting, managing or monitoring the 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.
- 4.3.3 All suspected serious breaches MUST be notified to R&D Department within 24 hours of the breach being identified.
- 4.3.4 Reporting can be by email or in person and should inform of:
- 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
- 4.3.5 R&D staff who receive notification of the breach should immediately inform the R&D Manager.

### **4.4 ASSESSMENT OF SERIOUS BREACH**

- 4.4.1 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 Research and Development. Documentation of the review of all associated documents and the final decision must be signed and dated and filed within the relevant R&D file and Trial Master File
  - Assess in collaboration with the Director of Research and Development and the CI/PI, whether any urgent safety measures may need to be introduced.
  - In the case of studies sponsored solely by the Trust or jointly with the University, agree with the CI any remedial actions to be taken 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

### **4.5 CTIMP STUDIES SPONSORED BY THE TRUST: NOTIFICATION OF SERIOUS BREACH TO MHRA**

- 4.5.1 If it is clear that a serious breach has occurred in a study sponsored solely by the Trust or jointly with the University, the MHRA must be informed

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within 7 days of the Trust becoming aware of the serious breach. This can be by telephone initially, followed up by written notification.

- 4.5.2 A Sponsor representative in the R&D Department should complete the Notification of a Serious Breach of GCP or the Protocol Form (Appendix 1).
- 4.5.3 The form should be sent by email to the MHRA (GCP.SeriousBreaches@mhra.gsi.gov.uk) within 7 days.
- 4.5.4 Any further information required by the MHRA should be provided by R&D and/or the CI when requested.
- 4.5.5 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.
- 4.5.6 All correspondence and documentation relating to the breach should be retained in the TMF, Investigator and R&D files.

### **5. ILLUSTRATIONS/APPENDICES**

APPENDIX 1 – MHRA Notification of Serious Breaches of GCP or Protocol Form

### **6. CHANGES SINCE LAST VERSION**

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#### **Description of changes**

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<i>Section Ref:</i>	<i>Brief description of change</i>
<i>All</i>	<i>Update of MHRA breach e-mail address Addition of the standard MHRA reporting form Requirement to notify ethics of Serious Breach Requirement for R&amp;D Director to make the final decision of whether a breach of the protocol or GCP is serious and requires reporting to MHRA and Ethics Removal of R&amp;D breach notification form replaced with MHRA template</i>
<i>4.3.3</i>	<i>Deleted "in writing" because in conflict with 4.3.4</i>

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### Serious Breach of GCP or Protocol

<b>FOR MHRA USE ONLY:</b>	
<b>GCP Unique ID:</b>	
<b>Triaging Inspector</b>	

### Notification of Serious Breach of Good Clinical Practice or Trial Protocol

(Ref: UK Statutory Instrument 2004/1031 Regulation 29A, as amended by 2006/1928)

Please forward this notification to [GCP.SeriousBreaches@mhra.gsi.gov.uk](mailto:GCP.SeriousBreaches@mhra.gsi.gov.uk)

OR

GCP Inspectorate, MHRA, 2a Hunter House, 57 Goodramgate, York, YO1 7FX.

<b>Your Name:</b>		<b>Your Organisation:</b>	
<b>Your Contact Details:</b>		<b>Date Breach Identified by Sponsor:</b>	
		<b>Date Breach Notified to MHRA:</b>	
<b>Details of Individual or Organisation committing breach:</b>		<b>Details of related study (if applicable):</b> (e.g. EudraCT No, CTA number, study title)	
<b>Report:</b> Tick appropriately	<b>Initial Report</b> <input type="checkbox"/>	<b>Follow-up Report</b> <input type="checkbox"/>	
<b>Please give details of the breach</b>			
<b>Potential impact to patient safety and/or data credibility:</b>			
<input type="checkbox"/> Patient safety	<input type="checkbox"/> Patient confidentiality	<input type="checkbox"/> Approval Issues	<input type="checkbox"/> IMP
			<input type="checkbox"/> Scientific value / data credibility
			<input type="checkbox"/> NA/None
			<input type="checkbox"/> Other Non-compliances (specify)
<b>Background:</b>			
<i>(continue on additional sheets if required)</i>			
<b>Other relevant information:</b> <i>(i.e. study status, site(s), ethics, trust, CRO /sponsor details etc.)</i>			
<i>(continue on additional sheets if required)</i>			

**Breach of GCP or Protocol**

**Please give details of the action taken:**

*This should include: Any investigations by your organisation, details of investigations by other organisations (e.g. CRO/ethics/trust), the results and outcomes of the investigations (if known or details of when they will be available/submitted), how it will be reported in the final report/publication, the corrective & preventative action implemented to ensure the breach does not occur again.*

*(continue on additional sheets if required)*

**Actual impact to patient safety and/or data credibility:**

- |  |  |
|--|--|
| <input type="checkbox"/> Patient safety          | <input type="checkbox"/> Scientific value / data credibility |
| <input type="checkbox"/> Patient confidentiality | <input type="checkbox"/> NA/None                             |
| <input type="checkbox"/> Approval Issues         | <input type="checkbox"/> Other Non-compliances (specify)     |
| <input type="checkbox"/> IMP                     |  |