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JOINT RESEARCH SUPPORT OFFICE

STANDARD OPERATING PROCEDURES

UHL Research Support Office
SOP S-1013 UHL V9 April 2020

Standard Operating Procedure for Identifying and Reporting Deviations and Serious Breaches of GCP and/or the Protocol/ Clinical Investigation Plan for Clinical Trials sponsored by University Hospitals of Leicester NHS Trust (UHL)

PGC Reference No: C16/2014

OFFICE BASE

Research & Innovation
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1. Introduction

This Standard Operating Procedure (SOP) describes the process for the identification and reporting of serious breaches or deviations of Standard Operating Procedures (SOPs), Data Protection Regulations, International Conference on Harmonisation of Good Clinical Practice(GCP) and/ or the approved Protocol/Clinical Investigation Plan (CIP) in all research studies sponsored by the University Hospitals of Leicester NHS Trust (UHL).

The outcome is that the management of all Serious Breaches or Deviations of SOPs, GCP and / or Protocol/ CIP Deviations are documented and appropriate Corrective Action and Preventative Action (CAPA) undertaken.

2. Scope

This SOP applies to all researchers conducting research studies sponsored by the UHL.

3. Definitions

Protocol/ CIP deviation: A protocol/ CIP deviation is any un-intended change or departure from the protocol/ CIP, e.g. a protocol/ CIP visit date deviation, which does not result in harm to the trial subjects or significantly affect the scientific value of the trial.

Serious breaches of the protocol/ CIP and / or GCP: For the purposes of this regulation, a "serious breach" is a breach which is **likely** to effect 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

Urgent safety issues: A protocol deviation/change may be implemented in response to an immediate hazard to a trial subject without prior approval from the Sponsor/HRA/MHRA/REC. This is defined as an urgent safety measure under UK Regulation 30. Urgent safety measures are covered in a separate **SOP S-1026 UHL**

4. Procedure

In each case, all serious breaches must be reported to the Sponsor by the Chief Investigator (CI) or any member of the research team within 24 hours of them becoming aware of the breach. Protocol/ CIP deviations not resulting in urgent safety measures, do not need to be immediately reported to the Sponsor.

4.1 Serious Breaches

The initial report to the Sponsor may be by email to UHLSponsor@uhl-tr.nhs.uk. The email must detail the name of the study, and give a brief outline of the suspected breach identified.

The C I or member of the research team must submit an initial report by email attaching the Serious Breach Notification Form (Appendix 1) to the Sponsor\ via UHLSponsor@uhl-tr.nhs.uk within 24 hours of becoming aware of the breach. The Sponsor will make contact with the C I to discuss the nature of the breach, and to give guidance on completion of a CAPA in line with the **CAPA SOP S-1012 UHL.**

In addition the Sponsor will satisfy it's responsibilities under Regulation 29A of the Medicines for Human Use (Clinical Trials) Regulations 2004 [SI 2004/1031]: "29A (1) The Sponsor of a clinical trial shall notify the licensing authority in writing of any serious breach of –

a) The condition and principles of GCP in connection with that trial; or
b) The protocol relating to that trial, as amended from time to time in accordance with regulations 22 to 25, within 7 days of becoming aware of that breach.

Further guidance can be found on the MHRA website, Guidance for notification of serious breaches of GCP or the trial protocol: MHRA Guidance

The Sponsor will allocate a number to the serious breach. The Sponsor will notify the MHRA, HRA, R&I at the site & REC as appropriate within 7 days of becoming aware of the breach and will update as required following completion of a CAPA. All actions and documentation resulting from the CAPA must be filed in the Trial Master File (TMF)/Investigator Site File (ISF) and relevant Sponsor files.

The Sponsor will add information about the serious breach using the relevant workflows on EDGE.

All files relating to the serious breach must also be uploaded to EDGE

4.2 Protocol/ CIP Deviation

Single deviations that are not deemed to be serious do not need to be reported to the Sponsor but must be documented in the Case Report Form and TMF / ISF for multi-centre studies, using a signed and dated file note available (Appendix 2) on the R&I web pages. All protocol/ CIP deviations must also be logged on the Protocol/ Clinical Investigations Deviation Tracking Log (Appendix 3) which must be retained in the TMF / ISF. Where required and particularly when a deviation is noted on more than one occasion, appropriate corrective and preventative action must be taken in accordance with **CAPA SOP S-1012 UHL** in order to avoid reoccurrence of the deviation.

4.3 Data Protection Regulations

Breaches of data protection regulations should be managed in accordance with the Sponsor / host organisation policies and procedures.

5. Multi-Centre Studies

The instructions detailed in 4 above must be followed. It is expected that the CI will coordinate collation of information from the sites. The Sponsor will track the information flow on the appropriate EDGE workflow. It is expected that Protocol/ CIP deviations will be reported to the Sponsor at regular quarterly intervals.

6. Responsibilities

	Responsibility	Undertaken by	Activity
1	CI/Investigating Team/ Clinical Trial Monitor	CI/Investigating Team/Clinical Trial Monitor	Identify and document all protocol deviations in the CRF and Master/Site File, in order for appropriate corrective and preventative actions to be taken.
2	CI/Investigating Team/ Clinical Trial Monitor	CI/Investigating Team/ Clinical Trial Monitor	Report all potential serious breaches of the protocol/ clinical investigations plan and/or GCP to the Sponsor within 24 hours of becoming aware of the breach, supplying as much information as possible
3	Sponsor	Head of Research Operations or their delegate	If the breach is confirmed as 'serious' according to the MHRA definition, the Sponsor must complete a 'Notification of Serious Breach of GCP or Trial Protocol Form'
4	Sponsor	Head of Research Operations or their delegate	The completed notification form must be forwarded to GCP.SeriousBreaches@mhra.gsi.gov.uk OR GCP Inspectorate, MHRA, 2a Hunter house, 57 Goodramgate, York, YO1 7FX within 7 days of becoming aware of that breach

7. Legal Liability Statement

Guidelines or Procedures issued and approved by the Trust are considered to represent best practice. Staff may only exceptionally depart from any relevant Trust guidelines or Procedures and always only providing that such departure is confined to the specific needs of individual circumstances. In healthcare delivery such departure shall only be undertaken where, in the judgement of the responsible healthcare professional it is fully appropriate and justifiable – such a decision to be fully recorded in the patient's notes and in the research site file.

This table is used to track the development and approval of the document and any changes made on revised / reviewed versions

DEVELOPMENT AND APPROVAL RECORD FOR THIS DOCUMENT		
Author / Lead Officer:	Carolyn Maloney	**Job Title:** Head of Research Operations
Reviewed by:	R&I Management Meeting	
Approved by:	**Nigel Brunskill**	**Date Approved:** 1/10/20

REVIEW RECORD			
Date	**Issue Number**	**Reviewed By**	**Description Of Changes (If Any)**
April 2015	3	Carolyn Maloney	Updated Logo and change of corporate identity
June 2015	4	Carolyn Maloney	Changes to process
August 2016	5	CM, LW, JJ	Addition to Protocol Deviation, consistency checks.
February 2017	6	Carolyn Maloney	Updated Logo
March 2018	7	CM	Added processes for EDGE. Amended process for Protocol Deviations and added in SOP breaches/deviations.
September 2018	8	CCL JJ	Updated R&I logo Added wording to account for medical devices/ Clinical Investigation Plan
April 2020	9	JJ LW AM	Consistency check

DISTRIBUTION RECORD:			
Date	**Name**	**Dept**	**Received**

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Serious Breach Notification Form

Name of person reporting Breach:	Contact Details:	Date Breach Identified:
Study Number : IRAS Number: EudraCT Number: Study Title:		Principal Investigator:

Include details of the breach; include the rationale (e.g. patient safety/data integrity issue and relevant legislation if known).

Details of Breach	Action Taken

CI/PI Name: …… CI/PI Signature …… Date ……

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NHS University Hospitals of Leicester NHS Trust

Site File Note

Study Title	
Study Number:	IRAS Number:
Reason for File Note	Explanatory/Other ☐ Deviation ☐ Serious Breach ☐ If deviation is this from the Protocol ☐ GCP ☐ SOP ☐ Other ☐ N/A ☐
Date of incident	
Details	
Corrective Action(s)	
Preventative Action(s)	
Impact on Patient Safety	
Impact on Research Integrity	

Title	Name	Signature	Date
Author			
CI/PI			
Sponsor informed: Yes ☐ No ☐ N/A ☐		Date sponsor informed:	

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Protocol/ Clinical Investigation Plan (CIP) Deviation Tracking Log

Study Title:	Study Number: (EDGE ID)	IRAS Number
Principal Investigator:	Site:	

Protocol/ CIP Deviation: A protocol/ CIP deviation is any un-intended departure from the protocol/ CIP, e.g. a protocol/ CIP visit date deviation, which does not result in harm to the trial subjects or significantly affect the scientific value of the trial. These do not need to be reported to the Sponsor but must be documented in the CRF and Trial Site/Master. Appropriate corrective and preventative action must be taken

***If the deviation has an impact on patient safety or study outcomes this may constitute a serious breach and should be reported to the sponsor as per SOP S-1013 UHL.**

Event No.	Event Date	Participant ID/Initials	Description of Deviation	Deviation Code	Corrective /Preventative Action taken to avoid recurrence e.g. protocol amendment

Investigator Signature_____ Date _____

Deviation Codes: A. Consent procedure. B. Inclusion/Exclusion criteria, C. Serious Adverse event reporting/Unanticipated adverse device effect
D. Randomization Procedures/study drug dosing E. Study Procedures F. Laboratory assessments/procedures G. Visit schedule/Interval H. Other

Protocol/ Clinical Investigation Plan Deviation Tracking Log - Tool guidance document

Purpose of this document:

To record all protocol/ CIP deviations that occurs at a study site.

This tracking log should provide a comprehensive list of all protocol deviations that occur at a study site. It is required for both observational and interventional clinical research studies

The tool is complementary to, and does not replace, the requirement to report potential serious breaches of the Protocol to the Sponsor and Regulatory Authorities as per SOP S-1013 UHL.

Completion of the log:

- Ensure Study Title/Study Number/ Sponsor/PI and site details are completed on all forms
- Record protocol/ CIP deviations in the tracking log as they occur, to ensure completeness and accuracy of data.
- The site PI should sign each form after it has been completed.
- The Deviations should be reviewed and corrective preventive action completed and recorded. (i.e. amendment to the Protocol).
- Events should be numbered sequentially, commencing with no 1.
- The log should be filed in the Essential Documents Folder (i.e. Trial Master File/Site File) in either a specific labelled section (Protocol/ CIP Deviations) or with the trial protocol.
- Pages should be filed in reverse chronological order, with the newest pages of the log placed at the front of the section.
- At the conclusion of the study, ensure all forms are complete and signed by the Principal Investigator.