University of Leicester and University Hospitals of Leicester NHS Trust joint Research Support Office Standard Operating Procedures

University of Leicester Research Governance Office
SOP S-1013 UoL

Identifying and Reporting Deviations and Serious Breaches of GCP and/or the Protocol for Trials Sponsored by the University of Leicester

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Office Base

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Effective Date: October 2023

This SOP will be implemented in line with this document's effective date for all UoL Sponsored research still in set up. For active clinical research that is already in the recruitment phase (or further) at the time of implementation, this SOP must be implemented within 3 months of the effective date.

Please note the appendices associated with this SOP may be subject to interim changes. Please ensure that appendices are downloaded from the RGO webpages prior to use to ensure the latest version of the document is being used. For active studies there is no requirement to update appendices to the latest version.

1.0 Introduction and Scope

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 study protocol in all studies sponsored by the University of Leicester (UoL).

The outcome is that the management of all serious breaches or deviations are documented and, where necessary, an appropriate Corrective and Preventative Action (CAPA) is undertaken.

2.0 Definitions

File Note: A 'File Note' is a documented note which is used to provide additional context and explanation around events, deviations, decisions and things that affect participant safety/data integrity. These are considered source data and should be signed by the Principal Investigator to provide evidence of oversight. (See Appendix 3). We recommend the use of a File Note Log (Appendix 4) to maintain an overview of the different File Notes which have been created.

Note to File: A 'Note to File' should be considered more of a navigational document and may be used to highlight the location of a document if stored elsewhere e.g. if referring out to the Sponsor Standard Operating Procedures webpage, or electronically stored meeting minutes. These notes do not relate to participant safety or data integrity and therefore do not require PI review. (See Appendix 5)

Protocol Deviation: Is any unintended change or departure from the protocol, which does not result in harm to the study subjects or does not significantly affect the scientific value of the study (e.g., clinic visits occurring outside of a specified window).

Serious Breach (of the Protocol and/or GCP): A breach which is **likely** to affect to a significant degree:
a) The safety or physical or mental integrity of the participants of a study; or
b) The scientific validity of the study

Urgent Safety Measure (USM): An action that the Sponsor or Investigator may take in order to protect participants in a research study from any immediate hazard to their health or safety.

Corrective and Preventative Action (CAPA): Improvements to processes which are made to overcome and eliminate the cause of a non-conformity. The corrective action is the action taken to immediately correct the issue which has occurred whereas the preventative action is the action taken to prevent reoccurrence.

3.0 Procedure

3.1 Serious Breaches

3.1.1 Notification

A potential Serious Breach may be identified by any member of a Study Team. Where a Serious Breach is suspected, it must be reported to rgosponsor@le.ac.uk by the Chief Investigator (CI) or their delegate immediately and within 24 hours of them becoming aware of the breach.

The email should detail the name of the study, the 4-digit Sponsor reference number and, within the body of the email, provide a brief outline of the suspected breach. Attached to the email the CI or delegate must also submit an initial 'Serious Breach Notification Form' (Appendix 1).

3.1.2 Sponsor Assessment

The Sponsor will make contact with the CI or delegate to assess the potential Serious Breach and determine whether or not the event is indeed categorised as a serious breach or should be considered a protocol deviation or an USM. Where a serious breach is confirmed, the Sponsor will work with the study team to identify its cause, potential remedial actions, and will give guidance on the completion of a CAPA in line with the CAPA SOP (S-1012). Note a CAPA plan may also be appropriate where the issue is not eventually defined as a Serious Breach.

3.1.3 Reporting

Where the Sponsor confirms the assessment of a Serious Breach, The Medicines for Human Use Regulations require the Sponsor of a Clinical Trial to inform the Medicines and Healthcare Products Regulatory Agency (MHRA)/competent authority in writing within 7 calendar days of becoming aware of a Serious Breach. It is recommend that the MHRA 'Notification of serious breaches or GCP or the trial protocol' form is used to ensure all the required information is submitted. In the UK, the Health Research Authority (HRA) also requires a Serious Breach to be reported to the relevant REC within 7 calendar days of awareness. The Sponsor will also notify the R&D/I at the site as appropriate within 7 days of becoming aware of the breach and will update all parties as required following the completion of a CAPA. All actions and documentation resulting from the CAPA must be filed in the Trial Master File (TMF) and Investigator Site File (ISF) as appropriate.

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

3.2 Protocol Deviations

Protocol Deviations not deemed to be serious, and not resulting in Urgent Safety Measures, do not need to be reported to the Sponsor but must be recorded on a Protocol Deviation Tracking Log, an example log is available in Appendix 2, and a copy of the Protocol Deviation Tracking Log must be retained in the TMF/ISF. Where further documentation of a deviation is required, additional details should be recorded in a Site File Note (Appendix 3) and, where required, a CAPA plan must be created in accordance with SOP S-1012 in order to avoid reoccurrence of the deviation.

3.3 Data Protection Breaches

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

4.0 Responsibilities

Responsibility	Undertaken by	Activity
CI/Investigating Team/ Clinical Trial Monitor	CI/Investigating Team/Clinical Trial Monitor	Identify and document all protocol deviations on a Protocol Deviation Tracking Log which should be retained in the TMF/ISF as appropriate. Where appropriate further detail should be provided in the form of a Site File Note and where required a CAPA plan should be created.
CI/Investigating Team/ Clinical Trial Monitor	CI/Investigating Team/Clinical Trial Monitor	Report all potential serious breaches of the protocol and/or GCP to rgosponsor@le.ac.uk immediately and within 24 hours of awareness using the Sponsor 'Serious Breach Notification Form' (Appendix 1).
Sponsor	Head of Research Governance or 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'
Sponsor	Head of Research Governance or delegate	The completed notification form must be forwarded to GCP.SeriousBreaches@mhra.gov.uk within 7 days of becoming aware of the breach.

5.0 Development and approval Record for this document

This table is used to track the development and approval of the document.

Author	Job title	Reviewed by	Approved by	Date approved
Cat Taylor	Head of Research Governance	UoL Research Management and Operations Group (RSMOG)	Professor Nigel Brunskill 	28/09/2023

6.0 Review Record

This table is used to track the changes made on revised/reviewed versions.

Date	Issue number	Reviewed by	Description of changes (If any)
Oct 2013	2	Wendy Gamble	Version 1 revised following review of Sponsor processes
June 2015	3	Wendy Gamble	Version 2 revised to bring in line with UHL SOP.
Oct 2016	4	Wendy Gamble	Version 3 revised following implementation of HRA processes
Sept 2021	4.1	Cat Taylor	Administrative changes
September 2023	5.0	Cat Taylor	Accessibility changes Administrative changes Major updates to the wording Removal of distribution record Appendices – administrative changes and minor updates to wording. New Appendices added (Appendix 4 – Note to File Template, Appendix 5 - File note tracking log)