UNIVERSITY OF LINCOLN

CLINICAL GOVERNANCE - STANDARD OPERATING PROCEDURE

SERIOUS BREACH REPORTING

CG-QMS SOP CG11

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Approved by: Signature:	UREC See original

Version History	**Reason for change**

NOTE: All SOPs are subject to regular review.

Please ensure that the version of this SOP is the most up-to-date.

OUT OF DATE DOCUMENTS MUST NOT BE USED AND HARD COPIES SHOULD BE DESTROYED

1. PURPOSE

To outline the process for the notification of serious breaches of GCP or the approved trial protocol for clinical trials sponsored by the University of Lincoln or supported by the Lincoln Clinical Trials Unit (LinCTU).

2. SCOPE

This SOP applies to all UoL sponsored clinical research or where LinCTU are providing support in Trial Management for clinical trials that are governed by the Medicines for Human Use (Clinical Trials) Regulations.

3. BACKGROUND

3.1 Regulation 29A of the 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:

> ***"29A.** (1) The sponsor of a clinical trial shall notify the licensing authority in writing of any serious breach of -*
>
> *(a) the conditions 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.*
>
> *(2) 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".*

3.2 The requirement was implemented in UK legislation in order to:

- *Enhance the safety of trial subjects/patients by seeking to ensure that the licensing authority is promptly informed of such serious breaches, in order to take appropriate action in response to the breach; and/or*
- *To take the information regarding serious breaches into account when assessing future applications for clinical trial authorisation, and applications for marketing authorisation, which include data from trials affected by serious breaches.*

Source: Guidance for the Notification of Serious Breaches of GCP or the Trial Protocol Version 6, 08 Jul 2020

3.3 It is the responsibility of the trial Sponsor or a person legally authorised by the Sponsor to carry out the notification procedure within 7 days of becoming aware of the breach.

Note: this activity may be delegated to the Chief Investigator or LinCTU, but the sponsor must be kept informed. The Chief Investigator is not permitted to delegate this responsibility, but a deputy may be nominated.

3.4 The protocol should make clear the distinction between a protocol violation, deviation and serious GCP breaches.

3.5 Minor deviations from clinical trial protocols and GCP can occur in clinical trials. The majority of these instances are technical deviations that do not result in harm to the trial participants or significantly affect the scientific value of the reported results of the trial. These cases will be documented in the monitoring visit reports and explained in File Notes filed within the Trial Master File or Investigator Site File and corrective and preventative actions taken where appropriate.

3.6 Protocol "waivers" or deviations to inclusion/exclusion criteria are NOT permitted and are considered a serious breach. However, not every deviation from the protocol needs to be reported to the MHRA/REC as a serious breach.

3.7 The judgement of whether a breach is likely to have a significant impact on the scientific value of the trial depends on a variety of factors e.g. the design of the trial, the type and extent of the data affected by the breach, the overall contribution of the data to key analysis parameters, the impact of excluding the data from the analysis etc.

3.8 It is the responsibility of the Sponsor* to assess the impact of the breach on the scientific value of the

trial.

3.9 Note: If a potential serious breach is identified by or reported to LinCTU the Sponsor Organisation shall be notified immediately.

3.10 *The sponsor may consult with the Chief Investigator / expert as necessary.

3.11 Serious GCP breaches occurring in the UK must also be reported to the Research Ethics Committee (REC) for the trial within the same timeframes.

3.12 Non-UK breaches do not need to be reported to the REC but must be reported within the member state concerned according to local legislation.

3.13 It is the responsibility of the local investigator in any UK NHS Trust to comply with the reporting guidelines for that NHS Trust.

3.14 All clinical and trials staff at the locations where the trial is conducted are responsible for identifying serious and reporting GCP breaches to the Sponsor / Chief Investigator.

4. CROSS REFERENCES

4.1 ICH GCP

4.2 Clinical Trial Regulations - SI 2004/1031 The Medicines for Human Use (Clinical Trials) Regulations 2004 and any subsequent amendments

4.3 Trial / Study Protocol

4.4 CG-QMS SOP CG07 Trial Master / Site File

4.5 CG-QMS SOP CG12 Amendment

4.6 MHRA Guidance for The Notification of Serious Breaches of GCP or the Trial Protocol

4.7 Notification of serious breaches of GCP or the trial protocol form

5. PROCEDURE

5.1 Follow MHRA Guidance for The Notification of Serious Breaches of GCP or the Trial Protocol also available at https://www.gov.uk/guidance/good-clinical-practice-for-clinical-trials.

5.2 The Sponsor may initially contact the MHRA Inspectorate by telephone to discuss the breach and follow up with a written notification within 7 days of the Sponsor becoming aware of the breach.

5.3 The Sponsor, Chief Investigator or authorised LinCTU staff should assess the event for seriousness, causality and impact on the trial conduct and continuation.

5.4 Complete MHRA form for notifications of serious breaches to the MHRA notification of serious breaches of GCP or the trial protocol form.

5.5 If the event is deemed not serious then that decision shall be recorded on MHRA form for notifications of serious breaches. No further expedited reporting is required.

5.6 If the event is deemed a serious GCP breach the MHRA form for notifications of serious breaches shall be sent to the following email address:

GCP.SeriousBreaches@mhra.gov.uk

5.7 Inform the REC that approved the study. Send a copy of the GCP breach report with a covering email.

5.8 Inform any other trial committee or organisation as required.

5.9 Following the breach, the trial protocol should be amended as necessary in accordance with SOP CG12 Amendments outlining any actions taken to correct a serious GCP breach and/or the MHRA's response.

5.10 The Sponsor should be copied into all correspondence and kept informed at all times. A copy of all MHRA correspondence MUST be retained in the TMF and ISF in accordance with SOP CG07 Trial Master / Site File.

6. FLOW CHART

Not required.