University of Nottingham UK | CHINA | MALAYSIA	**Sponsor Standard Operating Procedure**

Title: **SERIOUS GCP BREACH REPORTING**

SOP ref: **TA016** **Version and date:** **1.5 12th January 2018** **Superseded version and date:** **1.0 30th March 2011**	**Effective from date :** **26th January 2018** **Review cycle:** **2 yrs after effective date**

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Document history:	**Modification to previous version:**
1. V1.0 30th March 20111	1. Update to hyperlinks throughout. 2. Mandatory use of MHRA standard form, section 4.3

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1. PURPOSE and SCOPE

PURPOSE:
To describe the procedures for the reporting of serious GCP breaches that may occur in clinical trials of investigational medicinal products, in compliance with all applicable government directives, UK legislation and European guidance and directive documents.

SCOPE:
This SOP is applicable to all researchers conducting clinical trials that are governed by the Medicines for Human Use (Clinical Trials) Regulations, SI 2004, 1031, its subsequent amendments and/or the Department of Health Research Governance Framework, 2005.

2. NOTES

2.1 The definition of a serious GCP breach as given in the Medicines for Human Use (Clinical Trials) Amendment Regulations, SI 2006, 1928, shall be adopted within all clinical study protocols:

''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.''

2.2 ''The Sponsor of a clinical trial (*of an investigational medicinal product*) shall notify the licensing authority (*MHRA*) 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 form time to time in accordance with regulations 22 to 25,
within 7 days of becoming aware of that breach.''

2.2.1 In practice it is the Chief Investigator whom shall have responsibility for the reporting. The Sponsor must be kept informed at all stages. See 2.5

2.3 Subject to 2.2 the protocol shall make clear distinction between protocol violations or deviations and serious GCP breaches. A protocol violation or deviation is a change or departure from the clinical trial protocol and/or GCP that does not result in harm to the trial subjects or significantly affect the scientific value of the trial. Such deviations should be documented (e.g. in a case report form for the trial or trial master file) in order for appropriate corrective and preventative actions to be taken.

2.4 Serious GCP breaches occurring in the UK must be reported to the Research Ethics Committee (REC) for the trial within the same time-frames.
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.

2.5 Serious GCP breaches must be reported immediately to the Sponsor. Although the Sponsor delegates the responsibility of reporting to the MHRA, REC and other investigators as required to the Chief Investigator or nominated deputy, the Sponsor shall be kept informed and be sent copies of all documentation relating to the breach.

2.5.1 Reporting of the breach to the Trial Steering Committee and Independent Data Monitoring Committee may also be appropriate depending on the nature of the breach.

2.6 Assessment of seriousness and any requirement for expedited reporting is the overall responsibility of the Chief Investigator. This duty may not be delegated. A deputy must be nominated.

2.6.1 The Chief Investigator and/or any investigator and the treating doctor must take appropriate urgent safety measures in order to protect the subjects of a clinical trial against any immediate hazard to their health or safety.

2.6.2 If such measures are taken these should be reported immediately to the Chief Investigator who shall **inform the Sponsor** and any Principal Investigators no later than 3 days from the date the measures are taken. Where appropriate (the event is related to an Investigational Medicinal Product or directly to the trial procedures), the Chief Investigator shall give written notice to the MHRA and the relevant REC of the measures taken and the circumstances giving rise to those measures.

2.6.3 Events that lead to the suspension of the trial are classed as a substantial amendment and must therefore be notified to the MHRA and REC within fifteen days of the trial being suspended. See SOP TA013, Protocol Amendments.

2.7 For international trials the UK Chief Investigator (CI) has overall responsibility for safety assessment for the trial and will report to the appropriate international study committee and national competent authorities and ethics committees as required.

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

3. CROSS REFERENCES

3.1 Statutory Instrument 2004 No.1031, The Medicines for Human Use (Clinical Trials) Regulations 2004.
3.2 Statutory Instrument 2006 No.1928: The Medicines for Human Use (Clinical Trials) Amendment Regulations 2006
3.3 Notification of a Serious GCP Breach form https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/633795/Notification_of_serious_breaches_of_GCP_or_the_trial_protocol_form.doc
3.4 Protocol Amendments SOP TA013

4. PROCEDURE

4.1 All clinical and trials staff at the locations where the trial is conducted are responsible for identifying serious GCP breaches The Principal Investigator must ensure that appropriate procedures are in place locally to provide assurance that such breaches are recognised and that staff are appropriately trained to fulfil the reporting requirements.

4.2 Trial staff are obliged, immediately upon knowledge of the event, to notify their Principal Investigator. In practice this should be within 24 hours of event onset of the event being suspected of being a serious GCP breach.

4.3 The Principal Investigator shall notify the Chief Investigator immediately of knowledge of the event. Notification shall be by writing a GCP Breach Report. This shall follow the MHRA guideline using the Notification of Serious Breaches of GCP or Trial Protocol Form:

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/633795/Notification_of_serious_breaches_of_GCP_or_the_trial_protocol_form.doc

and include the following:

Name of reporter
Name of the organization (University of Nottingham)
Contact details of the reporter
Study identifiers: title, Sponsor's reference, EudraCT number, CTA number
Date the breach was identified
Details of the individual or organization committing the breach (i.e. where it happened and by whom)
Details of the breach
Action taken

4.3.1 In the first instance a verbal report may be given e.g. telephone, in order to discuss the event and make provision for patient safety and any emergency measures necessary. The Principal Investigator in consultation with the Chief Investigator and other colleagues as needed, must determine seriousness and causality of the event as soon as possible and define as such on the GCP breach report.

4.3.2 The initial report must be signed by the local Principal Investigator or deputy and sent to the Chief Investigator immediately (fax or email – use a scanned signature if using this route) for corroboration and authorisation. Retain a copy locally in the Trial Site File (TSF).

Note: In the event of the CI or a deputy not being available for initial consultation regarding the severity and causality of the event then the PI shall take responsibility for the assessment and take appropriate action depending on the assessment. In this instance the CI must be informed as soon as possible.

The **Chief Investigator** shall:

4.4 Assess the event for seriousness, causality and impact on the trial conduct and continuation.

4.4.1 If the event is deemed not serious then that decision shall be recorded on the GCP breach report and authorised by signature. No further expedited reporting is required.

4.4.2 If the event is deemed a serious GCP breach the CI shall corroborate the report and send either that report or a completed new one with further details to the MHRA:

GCP.SeriousBreaches@mhra.gov.uk

4.4.2.1 Inform the Sponsor: via telephone or email to sponsor@nottingham.ac.uk. Add your contact details and any relevant supporting information to the email.

4.4.3 The Chief Investigator or 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.

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

4.4.5 Amend the trial protocol as necessary following SOP TA013, Protocol Amendments, citing the reason for the amendment as following the actions taken to correct a serious GCP breach.

4.4.6 Inform any other trial committee or organisation that needs to be informed according to the trial protocol or as appropriate.

4.4.7 Retain all copies of all documentation in the Trial Master File (TMF).

MHRA response

4.5 Upon receipt of a serious breach notification, the MHRA will log and review the notification, and a variety of actions may be taken, depending on the nature of the breach and its potential impact:

4.5.1 Acknowledgement of receipt, but no immediate action e.g. if appropriate action has already been taken by the Sponsor. The case may be examined during future MHRA inspections.
4.5.2 Request for additional information from and investigation by, the Sponsor. If insufficient information is provided in the initial notification to assess the impact of the breach, follow-up information will be requested.
4.5.3 Sharing of information with other concerned parties, in accordance with the regulations and applicable agreements e.g. to concerned Ethics Committees, other competent authorities, MHRA Clinical Trials Unit.
4.5.4 Investigation by the MHRA, for example, triggered inspection(s).
4.5.5 Implementation of urgent safety measures, where appropriate.
4.5.6 Suspension or termination of a clinical trial authorisation, where appropriate.
4.5.7 Referral for enforcement action e.g. infringement notices, criminal investigation.
4.5.8 Referral to professional bodies e.g. the General Medical Council.

4.8 Copies of all correspondence to and from the MHRA must be retained in the TMF. Where further information and/or action is requested by the MHRA the Sponsor shall be included in the response and kept informed at all stages.

5. FLOW CHART

Not applicable.