SUSPECTED SERIOUS BREACHES

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1 INTRODUCTION

1.1 The Academic & Clinical Central Office for Research & Development (ACCORD) is a joint office comprising clinical research management staff from NHS Lothian (NHSL) and the University of Edinburgh (UoE).

1.2 The UK clinical trial regulations state:

"The sponsor of a clinical trial shall notify the licensing authority in writing of any serious breach of –

- the conditions and principles of GCP in connection with that trial; or
- 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.

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.

1.3 Serious breach example scenarios can be found in the Medicines and Healthcare products Regulatory Agency (MHRA) Guidance for Notification of Serious Breaches of GCP or the Trial protocol.

2 PURPOSE

2.1 To describe the processes for notification, reporting and appropriate follow-up of suspected serious breaches of GCP and/or the study protocol.

3 SCOPE

3.1 This Standard Operating Procedure (SOP) applies to ACCORD personnel and researchers participating in research studies sponsored by NHSL and/or the UoE, or hosted by NHSL.

4 RESPONSIBILITIES

4.1 On discovery of a potential serious breach, ACCORD staff members or member of the research team are responsible for informing the QA Manager, or designee, or a representative of the sponsor(s) within 24 h.

4.2 The QA Manager, or designee, is responsible for;

- Arranging a meeting of the Serious Breach Review Committee (SBRC) to discuss a suspected serious breach
- Reporting serious breaches to the ACCORD Senior Management team (SMT)
- Reporting serious breaches to the MHRA the appropriate Research Ethics Committee (REC) and the external sponsor for hosted studies (where applicable)
- Ensuring the Corrective and Preventative Action (CAPA) plan is communicated to the CI and that the plan is enacted in a compliant and timely manner.

4.3 The SBRC is responsible for determining if the reported event constitutes as a serious breach and agreeing an appropriate CAPA plan.

5 PROCEDURE

5.1 Notification of a Suspected Serious Breach (Sponsored Studies)

5.1.1 If any ACCORD staff member or any member of a research team conducting a study sponsored by NHSL and/or UoE discovers a potential serious breach, they will inform the ACCORD QA Manager, or designee, or a representative of the sponsor(s) within 24 h.

5.1.2 This initial contact may be made in person, via the telephone (contact details found at www.accord.scot), via e-mail (QA@accord.scot). Anonymous telephone calls or e-mails will be accepted.

5.1.3 This initial report will provide the following details where available:

- The name of Chief Investigator (CI) and Principal Investigator (PI) at the site where the breach occurred
- The full title of the clinical trial
- Details of the breach

5.1.4 The QA Manager, or designee, will record the aforementioned details using form CR003-F01 (Suspected Serious Breach Report).

5.2 Assessment of a Suspected Serious Breach (Sponsored Studies)

5.2.1 The QA Manager, or designee, will convene a SBRC in order to determine if the reported event constitutes a serious breach, in accordance with the definition outlined in the introduction.

5.2.2 The QA manager, or designee, will circulate the Suspected Serious Breach Report to the SBRC prior to the meeting if time allows.

5.2.3 The SBRC will consist of at least one representative of the sponsor(s), the QA Manager, or designee, and the Senior Clinical Trials Monitor, or designee.

5.2.4 The QA Manager, or designee, will inform the CI that a potential serious breach has been reported and invited them to contribute to the decision making process.

5.2.5 The SBRC will discuss the breach in detail and compile evidence to support the decision on classification.

5.2.6 A representative of the SBRC may contact the MHRA to seek clarification or advice regarding serious breach classification if required and appropriate.

5.2.7 If the SBRC determine that the reported event does not constitute a serious breach, in accordance with the definition outlined in the introduction, a CAPA plan will be discussed, in response to the event, and agreed.

5.2.8 If the SBRC determine that the reported event does constitute a serious breach, in accordance with the definition outlined in the introduction, the serious breach will be reported to the ACCORD SMT, and to the MHRA (if applicable) and the appropriate REC, and the CAPA plan will be discussed and agreed.

5.2.9 If the SBRC determine that the reported event may constitute research misconduct, SOP CR014 (Suspected Research Misconduct) will be followed.

5.2.10 The SBRC will assign a sponsor representative to communicate the CAPA plan to the CI, and follow up actions to closure.

5.2.11 The key outcomes of the SBRC meeting will be recorded and filed in the relevant Trial Master file (TMF) and Sponsor File (if applicable).

5.3 Reporting a Serious Breach (Sponsored Studies)

5.3.1 For Clinical Trials of Investigational Medicinal Products (CTIMPs), the QA Manager, or designee, will complete an MHRA 'Notification of Serious Breaches of GCP or the Trial Protocol Form', and e-mail this to GCP.SeriousBreaches@mhra.gsi.gov.uk, within the specified timeframe.

5.3.2 The QA Manager, or designee, will also submit the completed 'Notification of Serious Breaches of GCP or the Trial Protocol Form' to the appropriate REC and the ACCORD SMT within the same timelines, and a copy will be filed in the relevant TMF and Sponsor File (if applicable).

5.3.3 If the opportunity is available within the specified timelines, the QA Manager, or designee, will provide a draft of the serious breach notification to the SBRC members for review before submission.

5.3.4 If further information is requested by the ACCORD SMT, the MHRA or the relevant REC, the QA Manager, or designee, will ensure that a response is

submitted in a timely fashion. If necessary, the QA Manager will re-convene the SBRC to discuss the request.

5.4 Remedial Action (Sponsored Studies)

5.4.1 The CAPA plan, in response to a serious breach or other event, as described in section 5.2, will be communicated to the CI and affected facilities by a representative of the sponsor(s), assigned by the SBRC.

5.4.2 The representative of the sponsor(s) will ensure that the CAPA plan is enacted in a compliant and timely fashion. Evidence of progress and completion of CAPA, via correspondence, bespoke reports and clinical monitoring reports, will be filed in the relevant TMF and Sponsor File (if applicable).

5.5 Hosted Studies

5.5.1 On receipt of a suspected serious breach notification from NHSL staff, the research team or the external Sponsor, the recipient will inform the QA Manager, or designee, who will document the suspected serious breach using form CR003-F01 (Suspected Serious Breach Report).

5.5.2 The QA Manager, or designee, may convene a SBRC in order to discuss the suspected serious breach and decide on appropriate action with regards to NHS Lothian patients and the organisation.

5.5.3 If called, the SBRC will consist of the NHSL Head of Research Governance, or designee, the QA Manager, or designee, and the Senior Clinical Trials Monitor, or designee.

5.5.4 The QA Manager, or designee, will inform the NHSL PI that a suspected serious breach has been reported, and the CAPA plan will be discussed and agreed with the PI.

5.5.5 Documentation related to the suspected serious breach, including the CAPA plan and follow up to closure of actions, will be retained in the relevant Investigator Site File (ISF) and the relevant R&D study file.

5.5.6 The QA Manager, or designee, will inform the external Sponsor and the ACCORD SMT of the suspected serious breach in a timely manner, and will liaise with the Sponsor regarding appropriate actions/ follow up.

6 REFERENCES AND RELATED DOCUMENTS

- CR003-F01 Suspected Serious Breach Report
- MHRA Notification of Serious Breaches of GCP or the Trial Protocol Form

- MHRA Guidance for notification of Serious Breaches of GCP or the Trial

7 DOCUMENT HISTORY

Version Number	Effective Date	Reason for Change
1.0	22 MAR 2011	New SOP
2.0	29 AUG 2016	New title. New SOP template including section 4 on responsibilities. Introduction updated and minor changes to text throughout. The QA Manager, or designee will complete the Suspected Serious Breach Report and report this to the ACCORD SMT as well as MHRA (where applicable) and REC. Serious breach scenarios removed from this SOP and reference made to the MHRA guidance on serious breach reporting. Section 5.5 on Hosted Studies added. Sections on Suspected Research Misconduct removed from this SOP and references made to new SOP (CR014).

8 APPROVALS

Sign	Date
Signature kept on file AUTHOR: Heather Charles, QA Manager, NHSL, ACCORD	
Signature kept on file APPROVED: Susan Shepherd, Head of Research Governance, NHSL, ACCORD	
Signature kept on file AUTHORISED: Lorn Mackenzie, QA Coordinator, NHSL, ACCORD	