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).

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 research participants; or
(b) the scientific value of the research.

It is a requirement that serious breaches of Good Clinical Practice (GCP) or the trial Protocol are reported to the Sponsor, the Medicines and Healthcare products Regulatory Agency (MHRA), and the Research Ethics Committee (REC)) as applicable.

The Sponsor must carry out the notification procedure within 7 days of becoming aware of the breach.

1.2 Serious breach example scenarios can be found in the Medicines and Healthcare products Regulatory Agency (MHRA) Guidance for the Notification of Serious Breaches of GCP or the study 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 (see Appendix 1 for a process overview diagram for locally sponsored trials).

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 suspected 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 hours.

4.2 The QA Manager, or designee is responsible for;

- Informing the CI, Trial Manager of the suspected serious breach
- Arranging a meeting of the Serious Breach Review Committee (SBRC) to discuss a suspected serious breach
- Reporting suspected and serious breaches to the ACCORD Senior Management Team (SMT)

4.3 Reporting serious breaches to the MHRA, the appropriate REC and the external sponsor for hosted studies (where applicable)

- Ensuring the Corrective and Preventative Action (CAPA) plan is enacted in a compliant and timely manner.

4.4 In the absence of the QA Manager, the Head of Research Governance (NHSL) or a member of staff assigned by the ACCORD Senior Management Team (SMT) will fulfil the role of designee.

4.5 The QA Coordinator, or QA Admin Officer, will add details of the CAPA plan to the Serious Breach tracker in the QA folder on the ACCORD SharePoint.

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

5 Procedure

5.1 Identification of a Suspected Serious Breach (Sponsored Studies)

5.1.1 If any ACCORD staff member or any member of a research team conducting, managing or monitoring a study sponsored by NHSL and/or UoE discovers a non-compliance (SOP CR010 Management of Protocol and GCP Deviations and Violations) that may

have the potential to be a serious breach (see Section 1), they will inform the ACCORD QA Manager, or designee, or a representative of the sponsor(s) within 24 hours.

5.1.2 This initial contact may be made in person, via the telephone, MS Teams or 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 suspected breach occurred
- The full title of the clinical trial
- Details of the suspected breach

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

5.1.5 Where the ACCORD QA team are notified of a non-compliance and believe that the event meets the criteria of a suspected serious breach, the QA Manager or designee will follow this process from section 5.1.4 onwards.

5.1.6 The QA Manager, or designee, will e-mail the CI and Trial Manager informing them that a suspected serious breach has been reported to the Sponsor. This communication will include, as a minimum;

- Summary of the reported incident,
- Site(s) involved, if any,
- A copy of SOP CR003 (Suspected Serious Breaches) and confirmation that a SSBC will be convened and they will be invited to attend,
- Reporting requirements if event meets serious breach criteria e.g. REC, MHRA (if applicable) and timelines.

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, including the CI and Trial Manager 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 a Senior Clinical Trials Monitor, or designee. If the CI and/or Trial

Manager is unable to attend the meeting, they may provide additional information/input in advance of (or after) the meeting via e-mail communication with the QA Manager or designee.

5.2.4 The SBRC will discuss the reported event in detail and the evidence to support the decision on classification.

5.2.5 The QA Manager, or designee, may contact the MHRA to seek clarification or advice regarding serious breach classification if required and appropriate.

5.2.6 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.

5.2.7 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 MHRA (if applicable) and the appropriate REC, and the CAPA plan will be discussed and agreed The ACCORD SMT will also be informed (see section 5.3)..

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

5.2.9 If the SBRC determine that the reported event may constitute a data breach, Policy POL003 (Data Protection and Confidentiality) will be followed.

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.gov.uk, within the specified timeframe.

5.3.2 For CTIMPs, 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.

5.3.3 The QA Manager, or designee, will consider whether there are any other relevant MHRA units that should be notified to comply with other legislation e.g. notification to the Clinical Trials Unit (CTU) if the breach constitutes an urgent safety measure or if a substantial amendment is required due to a temporary halt in the study or to the

Defective Medicines Report Centre if the breach involves defective medicines or IMP recall. The notification will be sent to other MHRA units where deemed appropriate.

5.3.4 For non-CTIMPs, a copy of CR003-F01 (Serious Breach Report) will be sent to the appropriate REC and ACCORD SMT within specified timelines (e.g. 7 days of becoming aware of breach).

5.3.5 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 including the CI and Trial Manager for review before submission. A final copy of the serious breach report will be provided to the SBRC, CI and Trial Manager.

5.3.6 A copy of the completed serious breach report and any accompanying correspondence will be filed in the relevant TMF and Sponsor File (if applicable) and an electronic copy will be filed in the relevant QA and study folder on the ACCORD SharePoint.

5.3.7 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 QA Coordinator, or QA Admin Officer, will add details of all (suspected) serious breaches and the CAPA plan to the Serious Breach Tracker in the QA folder on the ACCORD SharePoint following the SBRC meeting.

5.4.2 The QA Manager, or QA Coordinator 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) and in the relevant QA folder on the ACCORD SharePoint.

5.4.3 The (suspected) serious breach report and all correspondence will be filed in the relevant Trial Master file (TMF) and Sponsor File (if applicable) and an electronic copy

of the (suspected) serious breach report will be filed in the QA and study folder on the ACCORD SharePoint.

5.4.4 Breaches must be considered and included when the study report is written as they may have an impact on the analysis or interpretation of the data.

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). Details of the suspected serious breach will be added to the QA Folder on the ACCORD Sharepoint site. 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 NHSL patients and the organisation.

5.5.2 If called, the SBRC will consist of the NHSL Head of Research Governance, or designee, the QA Manager, or designee, and a Senior Clinical Trials Monitor, or designee. The Principal Investigator (PI), or designee, will be invited to attend.

5.5.3 If unable to attend the meeting, the CAPA plan will be discussed and agreed with the PI.

5.5.4 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), the relevant study file on the R&D shared drive, and in the relevant QA folder on the ACCORD SharePoint.

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

5.5.6 Where the SBRC agree there has been a serious breach of GCP, the QA Manager, or designee, will liaise with the external Sponsor and the ACCORD SMT regarding confirmation of onward reporting i.e. to the MHRA and/or REC. If the external Sponsor

does not report the serious breach to the MHRA/REC, the QA Manager, or designee, will discuss this with the ACCORD SMT and agree next step. Next steps may include;

- Reporting the serious breach to the MHRA and/or REC
- Temporarily halting recruitment in NHSL
- Revoking NHSL R&D management approval for the trial

Actions will be communicated with the external Sponsor.

6 References and Related Documents

- CR003-F01 Suspected Serious Breach Report
- CR010 Management of Protocol and GCP Deviations and Violations
- CR014 Suspected Research Misconduct
- POL003 Data Protection and Confidentiality
- 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

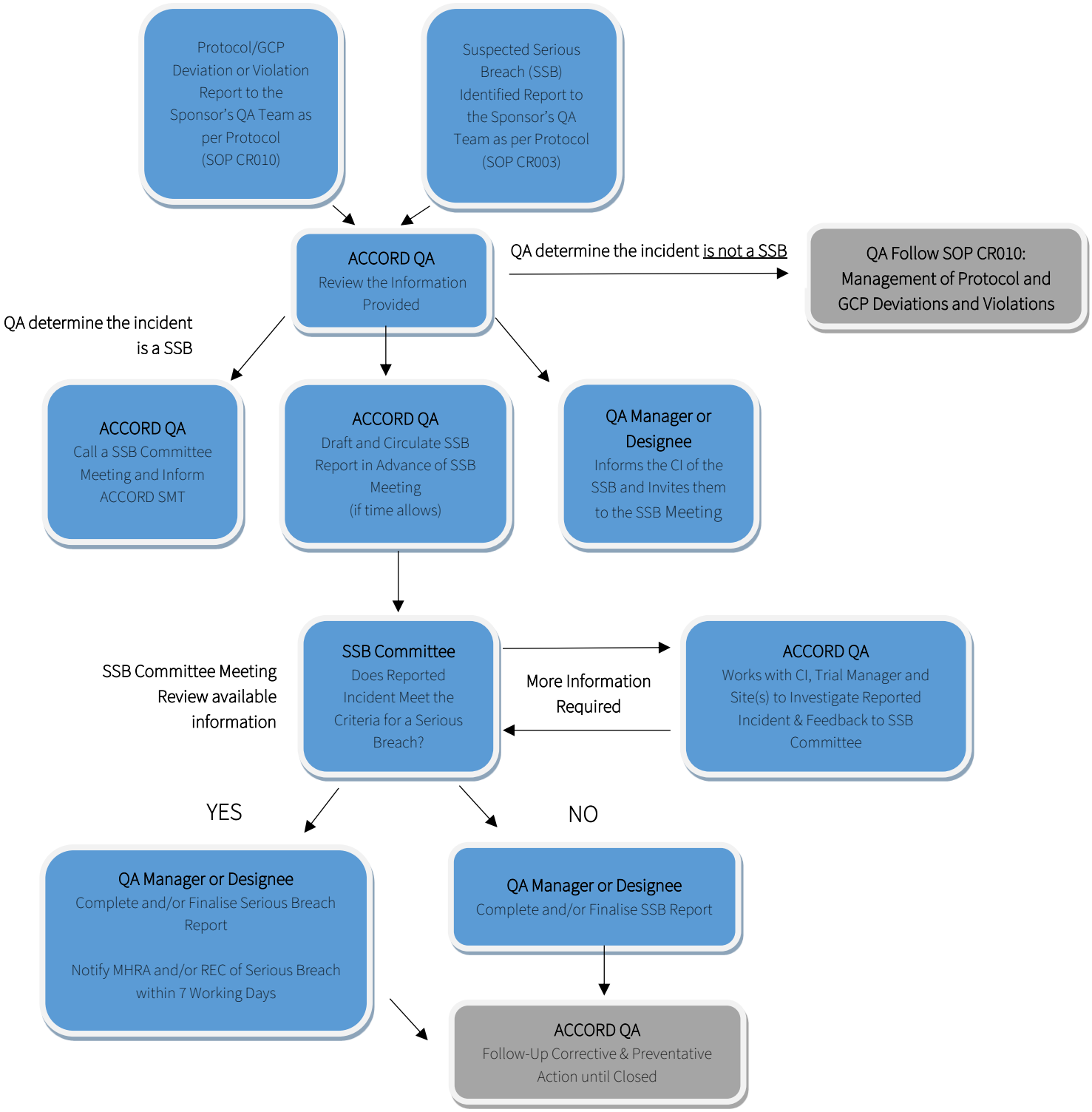
Version Number	Effective Date	Reason for Change
1.0	22 MAR 2011	New SOP
2.0	29 AUG 2016	New title. New SOP template including section 4 on responsibilities. Introduction updated and minor changes to text throughout. The QA Manager, or designee will complete the Suspected Serious Breach Report and report 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).
3.0	30 JUL 2018	Change of author. CR003-F02 document number changed to CR014-F01.
4.0	25 NOV 2022	Change of author. Change to MHRA e-mail address for notification of serious breaches. Reports, notifications and correspondence will be filed on

		the ACCORD SharePoint. Consideration will be given as to whether other MHRA units should be notified (section 5.3.3)
5.0	19 MAY 2023	Change of author. All sections of the SOP have been updated to clarify responsibilities on who will lead on a suspected serious breach and the trial team's involvement in the SSBC meeting. Information added to documented actions around due diligence when an external sponsor has not reported a serious breach to the MHRA. Appendix 1 added. Reference to POL003 added and documentation filing requirements expanded.
6.0	12 MAY 2025	Minor updates made to the text throughout. Addition of requirement to include serious breaches in the final study report at section 5.4 where applicable. Update to CR003-F01 headings.

8 Approvals

Sign	Date
L. Mackenzie AUTHOR: Lorn Mackenzie, QA Manager, NHSL, ACCORD	
Fiona McArdle Fiona McArdle (Apr 25, 2025 06:42 GMT+1) APPROVED: Fiona McArdle, Deputy R&D Director, NHSL, ACCORD	
Heather Charles Heather Charles (Apr 28, 2025 10:48 GMT+1) AUTHORISED: Heather Charles, Head of Research Governance, NHSL, ACCORD	

9 APPENDIX 1: Suspected Serious Breach (SSB) Overview (Locally Sponsored Trials)



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Final Audit Report 2025-04-28

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