SOP-QA-43 V2

Title: Suspected Serious Breaches

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Document History

Version	Description of update	Date Effective
1	New SOP	30-11-21
2	Removal of reference to MDCIs throughout Delegates and review by Sponsor Physician as required added -5.3 & 5.6 Changed 'RGM to 'RGT' – 5.8 & 5.12	19-12-24

1. Scope

1.1 This SOP applies to all researchers and Sponsor staff participating in interventional research projects sponsored or co-sponsored by University of Aberdeen (UoA) and/or NHS Grampian (NHSG).

1.2 Interventional research projects include Clinical Trials of Investigational Medicinal Product (CTIMP) and other interventional studies (eg surgical studies, , non CTIMP drug studies and any other projects deemed to be 'interventional' by the Sponsor). Medical Device Clinical Investigations (MDCI) are not covered in this SOP.

1.3 For other non-interventional projects (not listed in 1.2) and MDCIs sponsored or co-sponsored by University of Aberdeen (UoA) and/or NHS Grampian (NHSG), where the process for reporting Breaches is not clearly defined in the protocol, contact Sponsor for advice (pharmaco@abdn.ac.uk).

1.4 For research projects which are sponsored externally to the UoA or NHSG, local researchers and support staff should refer to the respective Sponsor's procedure and any timelines for handling Deviations and Breaches.

2. Responsibilities

Chief Investigator (CI)/delegate	Reporting breaches to Sponsor, REC and funder (if required).
Principal Investigator (PI)	Reporting breaches to CI or delegate
Research Governance Manager (RGM)/ Delegate	Review and assess breaches. Notify MHRA and CSOG of Serious Breaches in CTIMP. Liaise with CI on reporting requirements.
Research Governance Team (RGT)	Review and notify RGM/QAM of breaches. Notify CSOG of serious breaches in non-CTIMPs. Liaise with CSOG (as required), REC and CI on reporting requirements and close out of breaches. Collate and report to CSOG when required.

Quality Assurance Manager (QAM)/ Delegate Sponsor	Review and assess breaches Report Serious Breaches in CTIMP to MHRA and REC.

3. Introduction

3.1 It is a statutory requirement to report serious breaches of the clinical study protocol or Good Clinical Practice (GCP) to the REC and/or MHRA.

In CTIMPs Regulation 29A of SI 2004/1031 (as amended) defines a serious breach as a breach which is likely to effect to a significant degree:

- the safety or physical or mental integrity of the subjects of the trial; or
- the scientific value of the trial

For studies sponsored by University of Aberdeen and/or NHS Grampian this definition is used for CTIMP and other interventional studies (eg surgical studies, non-drug studies and other projects deemed to be 'interventional' by Sponsor).

Serious breach example scenarios can be found in the MHRA Guidance for Notification of Serious Breaches of GCP or the Trial protocol (The impact of SI 2006/1928 (publishing.service.gov.uk)).

4. Reporting Timelines

4.1 The CI, must ensure that potentially Serious Breaches of the research protocol and/or the principles of GCP are reported to the Sponsor **within 24 hours** of being identified. In a multi-site project, if such a breach has occurred at a remote investigational site, the Principal Investigator (PI) shall report the Breach to the CI, and the CI to Sponsor within 24 hours.

4.2 The Sponsor is responsible for reporting Serious Breaches in CTIMPs to the MHRA **within 7 calendar days** of the Serious Breach being notified to Sponsor.

4.3 For all research projects, the CI is responsible for reporting Serious Breaches to the relevant Research Ethics Committee (REC) within **7 calendar days** of the Breach being confirmed as serious.

5. Procedure

5.1 A Deviation or Breach may be identified by Sponsor or by CI/research team.

5.2 Breaches shall be recorded on the **Log of Breaches and Urgent Safety Measures** (TMP-QA-51) and Breaches reported using the **Breach Report form** (eg TMP-QA-20) to the Research Governance Team via pharmaco@abdn.ac.uk, unless previously agreed with Sponsor. The Research Governance Team shall acknowledge receipt.

5.3 The RGM (or delegate) shall review and make an assessment on seriousness, in liaison with the Quality Assurance Manager (QAM) (or delegate) and, where required, a Sponsor Physician.

5.4 If assessed as a **Serious Breach** the RGT will notify the CI of the assessment. The RGT shall set up a **Breach Assessment Team** to discuss the Breach in conjunction with the CI and necessary staff (see 5.6).

5.5 If a Breach is assessed as Serious the Sponsor may suspend the project until all necessary corrections and CAPA have been implemented.

Sponsor assessment and further investigation of a Breach

5.6 Where required, the RGM (or delegate), in liaison with the Quality Assurance Manager (or delegate), shall facilitate a systematic evaluation of the issue with a **Breach Assessment Team** comprising; the CI, PI (when available), lead physicians for the Sponsor(s), and key members of the research team (eg Trial Manager), as appropriate. The Breach Assessment Team shall involve experts from within the Sponsor organisation(s) or external parties as required. In some cases, the Breach Assessment Team may request further investigation is carried out before an assessment can be made.

The assessment made by the Breach Assessment Team shall:

- Confirm whether the Breach is a Serious Breach or not.
- Identify which section of GCP or the approved protocol has been breached.
- Identify how the Breach impacts on trial participants and/or the scientific integrity of the research.

5.7 The Breach Assessment Team shall work with the CI to identify the extent of the Breach and make a Corrective and Preventative action (CAPA) plan. The Breach Assessment Team shall agree who needs to be notified of the Breach and any follow up actions required. In addition, all records of assessments of potential Serious Breaches shall be retained in the Sponsor files and TMF, including those not confirmed serious by the assessment team.

Notification of a Serious Breach to the relevant parties

5.8 For CTIMPs the RGT shall notify the MHRA of a serious breach using the **Notification of Serious Breach template** provided within the MHRA Serious Breach guidance (current version available on the MHRA website) http://www.gov.uk/good-clinical-practice-for-clinical-trials#report-a-serious-breach
Copies of all Serious Breach Notifications shall be filed in the relevant TMF and the Sponsor files.

5.9 For all studies the CI shall forward the Breach Report form (eg TMP-QA-20) and, in a CTIMP the Notification of Serious Breach template, to the REC that provided the favourable opinion for the study, and the local NHS R&D departments for the sites where the Serious Breach occurred, copying in pharmaco@abdn.ac.uk.

5.10 For all studies the CI shall inform the Project Management Group (PMG) and, where applicable, the relevant Trial Steering Committee (TSC) and/or Data Monitoring Committee (DMC) of the Serious Breach. In certain situations, only limited details of the Breach may be reported to the committees in order to maintain trial blinding.

5.11 The RGM shall report all Serious Breaches to the Clinical Studies Oversight Group (CSOG) at its next meeting, or an extraordinary meeting may be called for this purpose.

CTIMPs: providing follow-up reports to the relevant parties

5.12 The RGT is responsible for follow-up notifications to relevant authorities.

5.13 The MHRA may request additional information (eg current protocol, SOPs, corrective action plan). The CI/PI, or delegated individual, shall provide all requested documents to the RGT, to be forwarded on to MHRA on behalf of the Sponsor.

5.14 The Sponsor shall keep the Breach under review in order to close out the agreed correction and CAPA, identify any additional information and forward follow-up reports to the MHRA, REC and local NHS R&D office(s), until the Breach is formally closed by the MHRA.

5.15 The RGT will notify the CI when the breach has been formally closed out.

6. Management (Deviation and breaches)

6.1 The CI of the research project is responsible for ensuring mechanisms are in place to monitor research activity and identify any deviations and breaches within the study or principles of GCP. The CI may share this responsibility with other members of the research team, or a steering committee. Any such arrangements which are in place shall be documented in the Trial Master File.

6.2 A log of Deviations (TMP-QA-93) and a log of Breaches and Urgent Safety Measures (TMP-QA-51) shall be available in the TMF and completed as necessary by the CI, PI, or delegate.

6.3 All correspondence relating to the Breach shall be filed in the TMF.

4. Abbreviations

CAPA	Corrective and Preventive Action
CI	Chief Investigator
CSOG	Clinical Studies Operational Group
CTFG	Clinical Trials Facilitation Group
CTIMP	Clinical Trial of an Investigational Medicinal Product
GCP	Good Clinical Practice
MDCI	Medical Device Clinical Investigations
NHSG	NHS Grampian
PI	Principal Investigator
QAM	Quality Assurance Manager
R&D	Research and Development
REC	Research Ethics Committee
RGM	Research Governance Manager
RGT	Research Governance Team
TMF	Trial Master File
UoA	University of Aberdeen

5. Related documentation and references

SOP-QA- 42	Urgent Safety Measures
SOP-QA- 25	Deviations and Breaches
TMP-QA-20	Breach reporting form
TMP-QA-51	Log of Breaches and Urgent Safety Measures
TMP-QA-93	Log of Deviations