

SOP-QA-25 V6

Title: Deviations and Breaches

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GRAMPIAN CLINICAL RESEARCH OFFICE



Document History

Version	Description of update	Date Effective
4	Change of author Responsibilities and process updated, and insertion of Introduction at 3	30-11-21
5	Updated text to adhere to informed consent process at 3.3 Delegate added at 4.18	21-03-24
6	Reference to MDCIs not being covered by this SOP at 1.2, 1.3 and 3.5 Reference to protocol waivers at 3.2 Clarification on trial office teams at 4.1	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 Deviations and 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 deviations and breaches to Sponsor and funder (if required).
Principal Investigator (PI)/Delegate	Identifying, logging, and reviewing deviations and breaches at their site. Reporting deviations and breaches to CI or delegate.
Sponsor	Review, assess, and manage deviations and breaches.

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Research Governance Manager (RGM)/ Delegate	Review and assess deviations & breaches. Notify CSOG of escalating breaches/ areas of concern in CTIMPs. Liaise with CSOG and CI.
Research Governance Team (RGT)	Review and notify RGM/QAM of breaches. Notify CSOG of escalating breaches/ areas of concern in non-CTIMPs. Liaise with CSOG (as required) and CI on reporting requirements and close out of breaches. Collate and report to CTFG when required.
Quality Assurance Manager (QAM)/Delegate Clinical Trial Monitors	Review and assess deviations & breaches Review log of deviations to identify trends and notify RGT/ QAM of areas of concern.

3. Introduction

- 3.1 The study team should not deviate from, or make changes to, the study documents (including protocol) without prior review of an amendment, and documented approval/favourable opinion from the Sponsor/Research Ethics Committee (REC), the Competent Authority (if applicable) and R&D (if applicable), **except** where necessary to eliminate an immediate hazard(s) to study participants (see SOP-QA-42 Urgent Safety Measures).
- 3.2  A Protocol Waiver occurs when researchers prospectively agree and intentionally implement a change from the study protocol (or Study Investigation Plan) without prior approval of an amendment. **Protocol Waivers are not permitted.** Suspected or actual waivers shall be managed as breaches. Unavoidable changes, unintentional changes identified retrospectively, and prospective changes implemented to offset an immediate hazard to a participant, are not considered protocol waivers.
- 3.3 A departure from the approved study documentation or from Good Clinical Practice (GCP) must be identified and recorded as a deviation or a breach (definitions and examples are provided below).
- 3.4 A Deviation is any change, divergence, or departure from the study design, procedures defined in the protocol, research project documentation, SOPs, confidentiality and data protection or GCP that does not significantly affect a subject's rights, safety, or well-being, or study outcomes.

Examples of a deviation include:



- Visit date outside the study visit window.
- Missed or incomplete study procedure (eg lab test).
- Missed or incomplete study evaluation (eg exam).
- Non-conformances identified during a monitoring visit.

A Breach is a deviation that may potentially significantly impact the completeness, accuracy, and/or reliability of the study data or that may significantly affect a subject's rights, safety, or well-being.


Examples of a Breach include:

- Failure to obtain informed consent, adhere to defined informed consent process
- Delivery of study intervention to participants that do not meet the inclusion/exclusion criteria
- Undertaking a trial procedure not approved by REC, Licensing Authority or NHS R&D (unless for immediate safety reasons)

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- Failure to report adverse events, serious adverse events or SUSARs in accordance with requirements, such that trial participants, or the public, are put at significant risk or risk of harm
- Investigational Medicinal Product(s) dispensing, labelling or dosing error.

3.5  Where the CI/ delegate is unsure if a deviation is a breach they **must** contact Sponsor (pharmaco@abdn.ac.uk) for advice without delay, ideally **within 24 hours** (requirement for CTIMPs) of becoming aware of the event.

4. Procedure

4.1 A Deviation or Breach may occur at any site or central facility (eg trial office (including statistics, programming, health economics and qualitative), laboratory or pharmacy) and may be identified by Sponsor or by CI/research team.

Reporting and Management of Deviations


4.2 Once identified, deviations shall be recorded by the CI, PI or delegate on the **Log of Deviations** (TMP-QA-93).


4.3 The CI, PI, or delegate, will detail on the deviation log:

- Site name
- Incident Number
- Date deviation identified (added to log)
- Date deviation occurred
- Participant ID
- Description of deviation
- Corrected action (immediate action taken when the deviation was discovered to correct/ document the deviation)
- Preventive action (action taken to prevent re-occurrence of this deviation in the future, including root cause analysis)

4.4 Once the incident has been resolved and no further action is required the CI, PI, or delegate, shall sign and date the deviation log to confirm the incident has been closed.

4.5 A copy of the deviation log shall be filed in the Investigator Site File (ISF) and/or Trial Master File (TMF).

4.6  The deviation log shall be sent to the Sponsor **quarterly** by email (pharmaco@abdn.ac.uk), unless otherwise agreed by Sponsor (and detailed in the protocol).

4.7  If no deviations are reported during the quarter, the CI, PI, or designee will inform the Sponsor via email to pharmaco@abdn.ac.uk.



4.8 A new deviation log shall be started at the beginning of each reporting period, continuing the event number sequence from the previous deviation log.

4.9 Sponsor shall acknowledge receipt by email.

4.10 The clinical trial monitors will review the deviation log for:




- trends
- deviations that should have been reported as breaches and raise any concerns to RGM/QAM who will communicate with the study team and may request that a deviation is reported as a breach (see section 4.13 – 4.24).

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- 4.11 The clinical trial monitor and Sponsor representative shall sign the deviation log and return a copy to the study team.
- 4.12 Copies of these documents will be retained in the TMF and/or Sponsor File, together with any communication regarding resolution of corrective/preventive action.


Reporting and Management of Breaches

- 4.13 If a deviation is considered to meet the definition of a breach, a **Breach Report form** (eg TMP-QA-20) shall be completed and reported to the Research Governance Team by email to pharmaco@abdn.ac.uk. The PI or delegate shall also record the breach on the **Log of Breaches and Urgent Safety Measures form** (TMP-QA-51) and provide with breach report form.
- 4.14 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, ideally **within 24 hours** (requirement for CTIMPs/) of becoming aware of the event.
- 4.15  If the breach is suspected as being a serious breach this **shall** be reported to Sponsor **within 24 hours**.
- 4.16 The breach report form shall include information on:
- Date of incident
 - Site where breach occurred
 - Date breach reported to trial staff
 - Details of person reporting breach
 - Details of breach
 - CAPA
- 4.17 The Research Governance Team shall acknowledge receipt by email.
- 4.18 The RGM/delegate shall review and make an assessment on seriousness, in liaison with the Quality Assurance Manager (QAM)/delegate.
- 4.19 If deemed a Non-Serious Breach the RGT will notify the CI, or delegate, of the assessment.
- 4.20 The RGT shall liaise with the CI, or delegate, to implement any outstanding CAPA, as required, prior to close out.
- 4.21 If suspected and/or categorised as a **Serious Breach** the Suspected Serious Breach procedure (SOP-QA- 43) shall be followed.
- 4.22  It should be noted that repeated Non-Serious Breaches which become systematic, or impact multiple participants, may be regarded as a Serious Breach.
- 4.23 All correspondence relating to the Breach shall be filed in the TMF.
- 4.24 Non-Serious Breaches shall be referred by the RGM to the Clinical Trials Facilitation Group (CTFG) for review and confirmation at each meeting.
- 4.25  The CTFG may, upon review, upgrade a Non-Serious Breach to a Serious Breach. In this instance the RGM/RGT shall notify the CI or delegate of this outcome and the Suspected Serious Breaches procedure (see SOP-QA- 43 Suspected Serious Breach).

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5. Management (Deviation and breaches)

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



6. Abbreviations

CAPA	Corrective and Preventive Action/Correction, 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
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

7. Related documentation and references

SOP-QA- 42	Urgent Safety Measures
SOP-QA- 43	Suspected Serious Breach
TMP-QA-20	Breach reporting form
TMP-QA-51	Log of Breaches and Urgent Safety Measures
TMP-QA-93	Log of Deviations

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