STANDARD OPERATING PROCEDURE FOR MANAGEMENT OF BREACHES OF GCP OR THE STUDY PROTOCOL FOR CLINICAL RESEARCH SPONSORED BY NHS FIFE

SOP NUMBER:	**Fife R&D SOP 50**
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1. PURPOSE

This document describes the procedure in NHS Fife for the management of breaches of Good Clinical Practice (GCP) or the approved clinical research protocol for Clinical Research Sponsored by NHS Fife.

It is the responsibility of all staff using this SOP to ensure they are using the latest version of it. The latest version is available via StaffLink, the R&D section of the NHS Fife website (www.nhsfife.org/research) and EDGE (https://www.edge.nhs.uk). For guidance, contact the R&D Department via fife.randd@nhs.scot.

2. APPLICABILITY

This SOP applies to all individuals associated with and managing **any** clinical research study sponsored by NHS Fife, or co-sponsored by NHS Fife, where NHS Fife is responsible for the management and reporting of breaches.

3. PRINCIPLES

3.1 Protocol and GCP breaches occurring in research studies can be **Serious** or **Non-serious** in nature. Not every deviation from the study protocol represents a **Serious** breach – the majority are technical deviations that do not result in harm to the study subjects or significantly affect the scientific value of the reported results of the study.

A **Serious** breach is defined as a breach that is likely to significantly affect:

- the safety or physical or mental integrity of the subjects of the study.
- the scientific value of the study.

For example:

- Persistent non-compliance with GCP or the protocol that has a significant impact on the integrity of clinical research subjects in the UK or on the scientific value of the study.
- Failure to report adverse events (AEs) or adverse reactions (ARs) in accordance with legislation, such that trial subjects, or the public, are put at significant risk.
- Fraud relating to clinical research records or data.

3.2 The Sponsor, CI, and PI for multi-centre studies, are responsible for providing overall supervision of the study and ensuring it is being conducted in accordance with the principles of GCP and the relevant regulations. They should also ensure that the study team is aware of the definition of a **Serious** breach.

3.3 ***All*** breaches of GCP or study protocol (**Serious** and **Non-serious**) must be documented in the Study Master File (SMF) by the Chief Investigator (CI) or delegate (see Doc Ref 50-01).

3.4 For multicentre studies the Principal Investigator (PI) or delegate must document ***all*** breaches of GCP or study protocol (**Serious** and **Non-serious**) occurring at their site in the Investigator Site File (ISF) using a study specific Breach Log based on Doc Ref 50-01.

3.5 All breaches occurring on studies sponsored by NHS Fife must be reported as soon as possible by the CI or delegate to the R&D Quality & Performance Team (fife.researchquality@nhs.scot) for consideration.

3.6 The UK Policy Framework for Health and Social Care Research requires all research to be run to the principles of GCP and ***serious breaches*** of GCP or the protocol should be reported by the CI to the Research Ethics Committee (REC) that originally granted approval, in accordance with the HRA Standard Operating Procedures for Research Ethics Committees (https://www.hra.nhs.uk/about-us/committees-and-services/res-and-recs/research-ethics-committee-standard-operating-procedures/).

3.7 The CI must also report any breaches to the funder in the time frame determined by the funder, if it is a condition of the funding agreement.

3.8 Following review of all breaches at a RIK Internal Operations Group meeting, if deemed appropriate, the Associate Director RIK, may request that the NHS Fife Quality & Performance Team carry out an audit of specific studies or processes.

4. PROCEDURE

4.1 Recording and Reporting Breaches to the Sponsor

4.1.1 All breaches, both **Serious** and **Non-serious** must be reported to the Sponsor via the Quality & Performance Team (fife.researchquality@nhs.scot).

4.1.2 The CI or delegate must notify the Q&P Team of any potentially Serious Breaches **within 24 hours** of becoming aware of the breach.

4.1.3 In a multi-centre project, the PI or delegate must report breaches to the CI. The PI must notify the CI of any potentially **Serious** breaches **within 24 hours** of becoming aware of the breach.

4.1.4 In multi-centre studies, the PI must report breaches to the CI by completing a Breach Notification Form (Doc Ref: 50-02) and emailing this to the CI and copying in the Quality & Performance Team (fife.researchquality@nhs.scot).

4.1.5 Receipt of the Breach Notification Form must be acknowledged by the Quality & Performance Team via email, copying in the Associate Director RIK.

4.1.6 The Q&P Team must add a '**QA - Sponsored - Breach Report'** Workflow to EDGE, on the same day if possible or on the next working day at least and record the information available to date.

4.2 Assessing Breaches

4.2.1 The CI must assess each breach and identify which principle(s) of GCP, or section(s) of the protocol has been breached and how this may impact on (i) the safety or physical or mental integrity of the study participants, or (ii) the scientific value of the study.

A variety of factors must be considered when carrying out this assessment e.g. the design of the study, the type and extent of the data affected by the breach, the overall contribution of the data to key analysis parameters, the impact of excluding the data from the analysis etc.

The assessment must include a review of any previous breaches to ascertain whether this is likely to be an isolated or systematic incident.

4.2.2 The CI must initiate any Urgent Safety Measures (USMs)* that may be required and advise the R&D Approvals Team if a substantial amendment is required to temporarily halt the study.

Any USM should be communicated immediately to the REC which gave the original favourable opinion, by the CI on behalf of the Sponsor.

4.2.3 Within two working days of receipt of the breach notification, the Q&P Lead in discussion with the CI must ensure the breach workflow has been updated to record the outcome of the CIs assessment of the breach and their opinion as to whether the breach should be deemed **Serious**, **Non-serious** or not a breach, and outline the agreed breach CAPA plan.

4.2.4 The Associate Director RIK must review the outcome of the CIs assessment and sign off the Breach Workflow to confirm their agreement with the assessment and the proposed CAPAs.

4.2.5 If the Associate Director RIK disagrees with the CIs assessment, an independent arbiter will be asked to provide an opinion. An independent arbiter can be the NHS Fife Medical Director or a senior researcher in another Board.

4.3 Follow-up of Breaches

4.3.1 The R&D Quality & Performance Lead must follow up all CAPA until closure.

4.3.2 If the Breach CAPA Plan is not progressing according to agreed timelines, the R&D Quality & Performance Lead must escalate the lack of progress to the Associate Director RIK.

4.3.3 When all CAPA have been addressed, the R&D Quality & Performance Lead must update the Workflow on EDGE and email a copy of the final Breach Workflow to the CI and Associate Director RIK to confirm that the Breach has been closed. A copy of this email must be filed in the Sponsor File and SMF by the Quality & Performance Lead.

4.3.4 For multi-centre studies, a copy of the final Breach Workflow must be emailed by the Quality & Performance Lead to the appropriate PI for filing in the ISF.

4.4 Notification of a Serious Breach to REC

4.4.1 If a breach is confirmed as **Serious**, the CI, on behalf of the Sponsor, must notify the REC that gave the original approval for the study **within 7 calendar days** of the CI becoming aware of the breach.

Any USM should be communicated immediately to the REC.

4.4.2 A Notification of Serious Breach of Good Clinical Practice or Study Protocol to Research Ethics Committee Form (Doc Ref 50-03) should be completed by the CI, and submitted by email to the REC, copying in the Quality & Performance Team and Associate Director RIK.

4.4.3 If the CI or Associate Director RIK determines that the reported event may constitute research fraud or misconduct then R&D SOP49 must be followed.

4.5 Follow-up of Breaches Notified to REC

4.5.1 Once the initial notification has been submitted to the REC, the Quality & Performance Team must continue to review the **Serious** breach to identify any additional pertinent information and highlight this to the CI and Associate Director RIK so that the breach notification to the REC can be updated as appropriate.

4.5.2 If the REC requests any additional information the CI or delegate, on behalf of the Sponsor, will liaise with the relevant study team to obtain the additional documents and will submit them to the REC.

4.5.3 Appropriate corrective and preventative actions must be implemented and any further information on the breach notified to the REC. Any follow up reports should be:

- Clearly identified as a follow-up.
- Identify the unique reference number given by the REC on acknowledgement of the initial report.
- Be sent directly to the person dealing with the initial query (unless otherwise instructed).

4.5.5 If the study has been temporarily halted, the CI will be advised by the Associate Director RIK or delegate of when the study may re-commence. Recommencement may be subject to additional monitoring of the study by the Quality & Performance Team.

4.5.6 Copies of all correspondence relating to the breach will be retained by the R&D Quality & Performance Lead in EDGE.

5. RECORDING BREACHES ON DATIX

All breaches of study protocol and GCP which are deemed to have significantly affected the safety of NHS Fife patients or staff must be reported via DATIX by the CI and followed up in accordance with standard NHS Fife policy.

6. ONGOING REVIEW OF ALL BREACHES

The R&D Quality & Performance Lead (or delegate) will provide regular reports to the RIK Internal Operations Group showing all breaches which have been reported to the Quality & Performance Team. This report will aim to identify any pattern of related breaches that need to be addressed by the RIK Department.

7. ASSOCIATED DOCUMENTS

Doc Ref 50 - 01 - Potential Serious Breach Notification Form – Sponsored Studies.
Doc Ref 50 - 02 - Breach Log
Doc Ref 50 - 03 - Notification of Serious Breach of Good Clinical Practice or Study Protocol to Research Ethics Committee (REC) Form.

8. ABBREVIATIONS

AE	Adverse Event
AR	Adverse Reaction
CAPA	Corrective and Preventative Actions
CI	Chief Investigator
ISF	Investigator Site File
PI	Principal Investigator
REC	Research Ethics Committee
R&D	Research & Development
SOP	Standard Operating Procedure
SMF	Study Master File
USM	Urgent Safety Measure

9. REFERENCES

Standard Operating Procedures for Research Ethics Committees
(Research Ethics Committee – Standard Operating Procedures - Health Research Authority.)

UK Policy Framework for Health and Social Care Research
https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/.

10. DOCUMENT HISTORY

Version Number:	Edited by (job title):	Effective Date:	Details of editions made:
1	Julie Aitken Quality & Performance Lead	24 Jan 2025	New SOP adapted from NHS Fife R&D SOP 22 to create an SOP specifically for Sponsored studies only.

11. APPROVAL

APPROVED BY	Date
Professor Frances Quirk, Associate Director RIK, NHS Fife Signature: 	24 Jan 2025