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

SOP NUMBER:	**Fife R&D SOP 22**
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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 studies Hosted 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 members of staff associated with and managing **any** clinical research study conducted in NHS Fife.

3. PRINCIPLES

3.1 Any departure from the following may be considered a breach:

- the Protocol
- the Principles of Good Clinical Practice (GCP)
- Written procedures (such as SOPs)
- Regulatory requirements
- Confidentiality and Data Protection legislation and policies

3.2 Breaches can be ***Serious*** or ***Non-serious*** in nature. 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. Breaches of this type, while they must be documented, are not serious breaches or reportable.

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 or on the scientific value of the study.
- Failure to control or to account for Investigational Medicinal Products (IMPs) such that trial subjects are put at significant risk or the scientific value of the trial is compromised.

- 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.

3.3 If a potentially ***Serious*** breach is identified by the research team, it must be reported to the study Sponsor contact by the PI or delegate **within 24 hours** of the breach being identified.

3.4 All breaches (***Serious*** and N***on-serious***) must be documented in the Investigator Site File (ISF) by the Principal Investigator (PI) or delegate.

4. PROCEDURE

4.1 Reporting and Recording Breaches

4.1.1 The PI or delegate must follow the Protocol or the Sponsor's own instructions for reporting breaches to the Sponsor.

4.1.2 All potentially ***Serious*** breaches must also be reported by the PI or delegate to the R&D Quality & Performance Team via fife.researchquality@nhs.scot.

4.1.3 The R&D Quality & Performance Team must acknowledge receipt of the breach notification within 2 working days of receipt and add a ***'QA – Breach Report – Hosted'*** workflow to the project record on EDGE.

4.1.4 The R&D Quality & Performance Team must immediately inform the Associate Director RIK, Lead R&D Research Nurse, and Clinical Trials Pharmacy Team (where the breach relates to IMP management).

4.1.5 The PI or delegate must update the workflow on EDGE to record the outcome of the Sponsor's assessment of the breach and any CAPA plan, as soon as this is confirmed.

4.1.6 The PI, R&D Quality & Performance Lead, Associate Director RIK, Lead R&D Research Nurse and Clinical Trials Pharmacist (where the breach relates to IMP management) must review the details of the potential ***Serious*** breach and advise the local research team if there is a need to initiate any Urgent Safety Measures (USMs).

4.1.7 If after discussion with the local research team and the Lead R&D Research Nurse, the R&D Quality & Performance Team assess that a breach does not warrant the completion of a Breach Workflow, a Workflow must still be added to record the reason(s) for this assessment and the Workflow abandoned. If the study Sponsor subsequently assesses the breach as ***Serious***, the breach workflow must be restored and completed.

4.1.8 In situations where there may be disagreement between the PI, external Sponsor and NHS Fife RIK Department over the assessment of a breach as ***Serious*** or ***Non Serious***, the NHS Fife RIK Department will exercise due diligence and give consideration as to whether it has a responsibility to report directly to the REC or

Regulatory Authorities. This decision will be made by the Associate Director RIK (or delegate) and documented in the ISF.

4.2 Follow-up of Potentially Serious Breaches

4.2.1 All reported potentially serious breaches must be reviewed by the next RIK Internal Operations Group to assess if any additional RIK Department CAPA are required, in addition to those requested by the Sponsor for a particular study. The outcome of this assessment must be documented in the workflow by the R&D Quality & Performance Lead.

4.2.2 All CAPA must be followed up until closure. 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 Lead R&D Research Nurse and Associate Director RIK.

4.2.3 A copy of any completed study specific reporting forms and all associated correspondence must be filed by the PI or delegate within the ISF.

4.2.4 Copies of all RIK Department internal correspondence relating to the breach will be uploaded by the R&D Quality & Performance Lead to the project record on 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 PI or delegate. These will be followed up in accordance with standard NHS Fife policy.

6. ONGOING REVIEW OF ALL POTENTIALLY SERIOUS BREACHES

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

7. 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
USM	Urgent Safety Measure

8. DOCUMENT HISTORY

Version Number:	Edited by (job title):	Effective Date:	Details of editions made:
1	Julie Aitken R&D Trials Facilitator	02 Feb 2015	New *(Adapted from TASC SOP 24, version 1 and TASC SOP 25, Version 7)*
2	Julie Aitken R&D Trials Facilitator	08 Jab 2018	Rewritten for clarity and to reflect current practice.
3	Julie Aitken R&D Quality & Performance Lead	14 Sept 2020	Amended for consistency with R&D SOP template. Procedure updated to reflect current practice. Contact details for R&D Department updated throughout. New associated documents Doc Ref 22-04, 22-05 and 22-06 added. Text refreshed throughout for clarity.
4	Julie Aitken R&D Quality & Performance Lead	24 Jan 2025	Reference to NHS Fife sponsored studies removed as this SOP has been revised to cover NHS Fife hosted research only. All associated documents withdrawn as breaches are now recorded and tracked in EDGE. Process for adding and completing an EDGE workflow outlined. Process for review of potentially Serious breaches by the RIK Internal Operations Group outlined.

9. APPROVAL

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