Standard Operating Procedure			**53.002**
The Handling of Poor Quality and Fraud in Clinical Research			
Version	4.0		
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Released by	Julie Brittenden	Signature	Date

1. SOP Category
NHS GG&C Sponsor Governance

2. Staff Category
Research and Innovation (R&I)
- R&I Co-ordinators
- R&I Managers
- R&I Director
- R&I Pharmacy
- R&I Monitors
- R&I Innovation staff
- R&I QA
- R&I Pharmacovigilance
- R&I Research Governance Manager

Clinical Research Facility (CRF)
- CRF Manager

Trial team
- Principal / Chief Investigator

University of Glasgow Research Governance (if appropriate)

3. Scope
This procedure applies to all research sponsored/co-sponsored or hosted by NHS Greater Glasgow and Clyde Board (NHS GG&C) and staff involved in this activity

4. Purpose
The purpose of this SOP is to describe the actions staff members must take if they suspect poor quality and/or fraud in clinical research in order to ensure high standards of quality in clinical research undertaken within NHS Greater Glasgow and Clyde (NHS GG&C)

5. Procedures
5.1. General Principles
Anyone with concerns over the conduct or quality of a clinical study must report these concerns immediately to their line manager or Head of Department who will escalate to one or more of the following:

- Manager of Clinical Research Facility
- Director of NHS R&I
- Senior R&I Manager
- R&I Innovation Lead
- Research Governance Manager NHS R&I
- Lead Clinical Trials Pharmacist NHS R&I
- QA officer/Project Managers CRUK –CTU Glasgow
- University of Glasgow Research Governance (if appropriate)

Suspected non-compliance with GCP and/or the study protocol will be handled according to the SOP on handling non-compliance with Good Clinical Practice (GCP) or the trial protocol, SOP 51.008.

For clinical trials of investigational medicinal products(CTIMP) serious breaches of GCP or the protocol must be reported to the MHRA within 7 days of the sponsor becoming aware of a serious breach. The SOP on Notification of serious breaches of Good Clinical Practice or the trial protocol for clinical trials of investigational medicinal products is to be followed where relevant, SOP 51.009.

For where the issue of research fraud does not relate to a serious breach of GCP FORM 53.002A should be completed and sent to the MHRA within 7 days of the Sponsor becoming aware by the appropriate individual as assigned by the R&I Director or R&I Research Governance Manager. ICH GCP states that although not a legal requirement under section 29A, the MHRA GCP Inspectorate encourages the reporting of all confirmed instances of clinical trial fraud occurring at sites in the UK, which the Sponsor becomes aware of. The reason for this is that, although fraud at one particular trial site may not have a significant impact on scientific value or subject integrity for that particular trial, the MHRA would wish to assess the impact on other trials or subjects/patients at that site.

Following a confirmed case of fraud being reported to the MHRA, appropriate and agreed time frames set out with the MHRA will be followed, this is determined on a case by case basis.

Issues of suspected fraud are highly sensitive. Staff are to handle suspected fraud with great care and will discuss suspicions with as few people as possible and all information should be treated with the highest level of confidentiality. All written material is to be confined to factual observations and must not include opinions and preliminary conclusions.

In exceptional circumstances, where staff deem it is not appropriate to report suspicions through the normal reporting lines, they can make representation directly to the appropriate authorities, e.g. Medicines and Healthcare products Regulatory Agency (MHRA) or appropriate oversight committee, e.g. ethics or any member of the Glasgow Health Science Partnership Regulatory Affairs Group (GHSP RAG).

5.2. Definitions

Poor quality is persistent non compliance with the principles of Good Clinical Practice. Examples of types of poor quality include:

- Missing data. Examples include persistent missing key data in the Case Report Forms (CRFs) for a number of study participants
- Inadequate source documents. Examples include persistent lack of recording of study information in the medical records; persistent errors in documentation of the informed consent process
- Protocol non-compliance. Examples include persistent failure to perform procedures specified in the protocol; persistent inclusion of study participants who fail to comply with eligibility criteria
- GCP non-compliance. Examples include persistent late reporting of serious adverse events; medical decisions being made by non-medical staff (e.g. ECG interpretation, dosing changes); no evidence of study team training or delegation of tasks

Fraud is the deliberate reporting of false or misleading data or the withholding of reportable data. Examples of types of fraud include:

- Fabrication of data. Examples include filling in the CRF, including Diary Card with fictitious information; producing reports (e.g. clinical assessments, lab analyses, X-ray images) when no tests were performed; photocopying data related to one subject to use for another; and creating fictitious subjects.
- Falsification of data. Examples include changing clinical data in the CRF or diary to make a patient eligible for inclusion into the study; to change or intentionally misinterpret data to provide illegitimate results
- Omitted data. Examples include removing subjects from the study for illegitimate reasons; not reporting or disguising adverse events or other clinical data.

5.3. Investigations of quality concerns

5.3.1. Research sponsored or co-sponsored by NHS GG&C

Investigations of poor quality will be conducted through the research governance manager, or the lead clinical trials pharmacist. Updates and outcomes will be reported to the GHSP RAG for oversight and recommendations when necessary. Actions and the offer of support will be given to the investigator to improve the quality. If the actions are not met and the quality does not improve the site or trial may be suspended or closed.

The assessment of an investigator's response to the actions to improve quality depends on the specific circumstances. GHSP RAG will review the case based on the information available that is presented to the group for consideration. If problems persist the study site will be closed down by the NHS R&I Director or an appropriate deputy.

The sponsor is responsible for ensuring that the following actions are taken:

- The investigator's or site's participation in the study is terminated
- The ethics committee is informed
- The MHRA is informed if applicable
- The available data is used to fulfill safety reporting and other requirements of the ethics committees and MHRA if applicable. Additional use of data is decided on a case-by-case basis

A decision of how to deal with patients still participating in the study will be made via the GHSP RAG. Consideration should be given to including the Independent data monitoring committee (if appropriate), the trial steering committee, the ethics committee and, if applicable, the MHRA in the discussions about how to handle these patients. Once a decision has been made, the sponsor will provide the investigator with instructions on how to proceed and will follow-up to ensure that the investigator has taken the required actions.

5.3.2. Externally sponsored Research

If the poor quality issue relates to an externally sponsored trial, or to a research service provided by a vendor, relevant senior management must be notified as per section 5.1. In addition, the trial sponsor, (if not already aware), must be notified of the poor quality immediately, as that sponsor may have responsibility for handling the poor quality. The senior management, in conjunction with the sponsor (where necessary), must determine the appropriate course of action. The GHSP RAG should be notified of the issue, action and outcome.

5.4. Investigations of suspected fraud or misconduct in research

If an individual is suspected of fraud or misconduct, the individual's employer must be notified immediately. If appropriate, the employer's procedures on handling fraud or misconduct should be followed. Suspected misconduct or fraud concerning University of Glasgow employees must be reported to the Vice Principal for Research and Enterprise and handled according to the University's Code of Policy and Procedures for Investigating Allegations of Misconduct in Research.

5.4.1. Research sponsored or co-sponsored by NHS GG&C

Where fraud or misconduct is suspected, the NHS GG&C R&I should be notified immediately. The R&I Director (or delegate if appropriate) will determine the appropriate team to investigate the fraud concerns.

The Procedure for the Investigation of Misconduct in Research (published by the UK Research Integrity Office) may be followed. In this instance, the Named Person for the NHS GG&C is the R&I Director.

Suspicion of fraud which, after the investigation is proven to be groundless will be dealt with as poor quality as described in section 5.2 if the quality of data is unacceptable. If the suspicion of fraud is proven to be groundless and the quality of data is acceptable, no further actions need to be taken.

If the conclusion from the investigation is that fraud is proven, The R&I Director will consult with appropriate individuals to seek their agreement to the planned actions. Those consulted usually include:

- The Chair of the Glasgow Health Science Partnership Delivery Board
- The NHS GG&C Medical Director
- The Head of NHS GG&C Clinical Governance

The R&I Director is responsible for ensuring (if applicable) that the NHS GG&C Fraud Liaison Officer is notified in accordance with NHS GG&C Code of Conduct for Staff.

Examples of appropriate planned actions may include the following:

- The investigator's or site's participation in the study is terminated
- No use is made of any fraudulent data, although the data is retained
- The ethics committee is informed
- The MHRA is informed for clinical trials that come under Medicines for Human Use (Clinical Trials) Regulations 2004 (Statutory Instrument 2004/1031), as amended
- Consider (in agreement with the ethics committee) whether to inform subjects who have completed the study, as well as those who are still participating
- Decide how to manage the treatment of patients still participating in the study
- Review and/or audit the previous studies the investigator has been involved in
- Following notification to the Fraud Liaison Officer, NHS GG&C will take appropriate disciplinary action and/or refer the matter to the appropriate professional body according to NHS GG&C Code of Conduct for Staff, Part 2 Fraud Policy

5.4.2. Externally sponsored research

If the suspected fraud or misconduct relates to an externally sponsored trial, or to a research service provided by a vendor, relevant senior management must be notified as per section 5.1. For research hosted by NHS GG&C, this notification must include the R&I Director. In addition, the trial sponsor, (if not already aware), must be notified immediately, as that sponsor may have responsibility for handling the fraud or misconduct. Senior management, in conjunction with the sponsor (where necessary), must determine the appropriate course of action. The GHSP RAG should be notified of the issue, action and outcome.

6. Referenced documents

- SOP 51.008 – Handling non compliance with Good Clinical Practice (GCP) and/or the trial protocol in clinical research
- SOP 51.009 – Notification of serious breaches of Good Clinical Practice or the trial protocol for clinical trials of investigational medicinal products
- FORM 53.002A – Reporting of fraud in clinical trials of an investigational medicinal product not identified as a serious breach of GCP
- NHS Greater Glasgow & Clyde Code of Conduct for Staff March 2016 (Part 1 The Standards of Business for Staff; Part 2 The Fraud Policy
- University of Glasgow Code of Policy and Procedure for Investigating Allegations of Misconduct in Research 2021
- The Medicines for Human Use (Clinical Trials) Regulations 2004
- Procedure for the Investigation of Misconduct in Research UK research Integrity Office 2008

7. Related documents

None

8. Document History

Version	Date	Description
1.0	14/07/09	Release of Version 1
1.1	04/11/13	Minor administrative and reporting procedures
2.0	15/07/2016	Updated to template v1.4.
3.0	04/01/2019	Temporary change to Author. Governance reporting groups (RAGs) updated to reflect revisions. GU Governance staff added under staff category. "Approver" & "Released by" updated. No changes made to process.
4.0	05/07/2022	Content added to section 5.1 for clarification on issues of fraud not relating to a serious breach. Change to Approver and Author re-instated following temporary change.