SOP number	**51.008**	Version	**5.0**
Title	**Handling Non-Compliance with Good Clinical Practice (GCP) and/or the trial protocol in clinical research Sponsored, Co-Sponsored or Hosted by NHS Greater Glasgow and Clyde**		

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Released by Signature	Jesse Dawson Date

SOP category	NHS GG&C Sponsor R&I

Staff category

Staff Category	**R**	**A**	**C**	**I**
R&I Research Governance Manager		X		
R&I Lead Pharmacist Clinical Trials	X			
All R&I Staff	X			
Chief Investigator	X			
Project Managers	X			
Clinical Trials Unit (GO-CTU) Glasgow staff	X			
Beatson CRF Head of Trial Co-ordination	X			
Beatson QA Lead	X			
Principal Investigators				X

1. Scope

This SOP applies to all staff engaged in clinical research Sponsored, Co-Sponsored or hosted by NHS Greater Glasgow and Clyde. Principal Investigators may be provided with this SOP for their information, however, it is the responsibility of the CI, Project Managers, Monitors, QA staff and representatives from CRFs to ensure the content of this SOP is included within training provided to Principal Investigators.

2. Purpose

The purpose of this SOP is to describe the process of reporting, documenting and handling Non-Compliances in clinical research Sponsored by NHSGGC, Co-Sponsored by NHSGGC and The University of Glasgow, or hosted by NHSGGC. The process is separated into NHSGGC Sponsored / Co-Sponsored CTIMPs, CIMDs, Non- CTIMPs and Hosted research.

3. Procedures

3.1. Definitions

Non-Compliance is defined as "An act, item or result which does not comply with the Protocol, Standard Operating Procedures, ICH GCP or Regulatory requirements". A Non-Compliance may also be as a result of Poor Quality or Fraud in Clinical research as defined in SOP 53.002. Non-Compliances that result from unintended deviations from the Protocol are referred to as Protocol Deviations and follow their own specific process. For NHSGGC, Sponsored/Co-Sponsored CTIMPs/CIMDs Protocol Deviations are managed through Trial Management Groups, and for NHSGGC Sponsored/Co-Sponsored non-CTIMPs by the Research Teams. However, Category 3 or above require escalation to Sponsor. For all Hosted Research Protocol Deviations are managed by the external Sponsor. All Protocol Deviations are Non-Compliances but not all Non-Compliances are Protocol Deviations.

A comprehensive guide on the different types of Non-Compliance and how they fit together is available in Guideline 51.008C.

A Non-Compliance may meet the definition of a serious breach of GCP and if this is identified SOP 51.009 will be followed.

3.2. Identifying and Reporting Non-Compliances

All R&I staff and those involved in clinical research must identify and report Non-Compliances. Anyone connected to the research—such as Sponsors, Site staff, Vendors, Laboratories, R&I Departments, or Data Centres—can identify these issues. When a Non-Compliance is detected, it must be documented, reported, and escalated, if necessary, immediately upon discovery. Protocol Deviations are recorded using the forms listed in Section 3.5, and escalated Non-Compliances are reported to the Research Governance Manager and/or R&I Lead Pharmacist Clinical Trials.

Concerns about compliance with GCP, regulations, Sponsor requirements, research processes, or study conduct should be raised with the Research Governance Manager or R&I Lead Pharmacist Clinical Trials.

3.3. Categorising a Non-Compliance and Protocol Deviations

There are a wide variety of issues which can be identified as a Non-Compliance, each of these issues can be categorised using the criteria detailed below. If there is dubiety over which category a Non-Compliance falls into, err on the side of caution and identify as the higher category, escalate and this will be reviewed and the categorisation confirmed or changed by the Research Governance Manager or R&I Lead Clinical Trials Pharmacist and/or monitors. If the Non-Compliance relates to hosted research then the categorisation/severity will be discussed with the Sponsor.

Category 1	Issues of Non-Compliance of an administrative or technical nature are detected that do not compromise patient safety and/or the integrity of the data.
Category 2	Issues are detected that could affect the conduct of the study but do not constitute a potential serious breach of GCP or the protocol. Category 2 may include issues that have a minor impact. It is important to record Category 2 issues as a reasonable volume of the same issue can lead to a Category 3 issue.
Category 3	Issues are detected that may have an impact on patient safety and/or integrity of the data. This may include potential serious breaches of GCP and/or the trial protocol.
Category 4	Issues are detected that have a significant/critical and/or immediate impact on patient safety and/or integrity of the data. This may include life threatening patient safety issues and potential serious breaches of GCP and/or the trial protocol.

3.4. Escalated Non-Compliances

Non-Compliances relating to research system/process failures, failures to comply with GCP, Regulations, Sponsor SOPs, eligibility; pharmacovigilance processes or GDPR issues, etc. suspected to be categorised as **3 or 4 must be escalated** to the Research Governance Manager and/or R&I Lead Pharmacist Clinical Trials. A Sponsor representative may be contacted in the first instance and this must then be escalated to the Research Governance Manager and/or R&I Lead Pharmacist Clinical Trials as appropriate. This can be achieved in person, through e-mail or telephone call, but may require follow up of relevant information. This is applicable for all trials Sponsored, Co-Sponsored or Hosted by NHSGGC and includes the Glasgow CRF, Beatson CRF and GO CTU along with all other departments undertaking trial activity.

Note: Ownership for matters related to IMP or Laboratories will be assigned to the R&I Lead Pharmacist, Clinical Trials. All other matters will be managed by the Research Governance Manager. Category 1 or 2 non-compliances concerning IMP may be discussed with the Sponsor Pharmacist and/or the Sponsor Pharmacy Technician for the relevant trial.

For laboratory-based issues classified as Category 1 or 2, discussions may involve the R&I Coordinator, Project Manager, and R&I Lead Pharmacist, Clinical Trials, as appropriate.

Non-compliance discussions may occur anytime with the Research Governance Manager or R&I Lead Pharmacist Clinical Trials, and with the R&I Director during leave. Immediate escalation is required for suspected Category 3 or 4 Non-Compliances, or those meeting listed criteria, before completing a Protocol Deviation form if applicable.

3.4.1. Logging and Numbering Of Escalated Non-Compliances

Each year, an excel file is created to act as a log of all escalated Non-Compliances, this is stored on the common drive and maintained by the Research Governance Manager and the R&I Lead Pharmacist Clinical Trials. All non-compliances captured on this log will be transcribed into Q-Pulse and given a unique ID number generated by the system. Each record will make reference to the ID held on the excel log and vice versa for cross referencing and this will be maintained and updated either by the owner of the non-compliance (excel log) and the QA team (Q-pulse), details of managing Non-Compliances in Q-Pulse can be found in Guideline 51.008A..

All escalated suspected Category 3 & 4 Non-Compliances will be recorded on the Non-Compliance log and given a unique number starting with the year and order the Non-Compliance was logged (e.g. 202501 refers to non-compliances occurring in the year 2025 and 01 referring to the first one logged). If the issue is re-classified at a lower category this will be documented on the Non-Compliance log.

Audit trails will be retained on an NHS server by the Research Governance Manager and/or R&I Lead Pharmacist Clinical Trials when managing each non-compliance.

The root cause and Corrective and Preventative Actions (CAPA) will be established by the Research Governance Manager, R&I Lead Pharmacist Clinical Trials and or monitor as appropriate. It is the responsibility of all involved in any **Escalated** Non-Compliance to respond in a timely manner to any questions asked and to keep the R&I Lead Pharmacist Clinical Trials, Research Governance Manager and or monitor up to date on progress of completion.

3.4.2. Non-Compliances Related to GDPR

Non-Compliances that arise in all types of research both Hosted and Sponsored relating to the sharing of unconsented personal data will be reported to the NHS Research Governance Manager or a member of the Governance team. GDPR issues must also be reported to Information Governance within the NHS and when appropriate logged on DATIX. When a large number of unconsented data is shared with a third party it is important to understand that Information Governance may not consider this a breach of GDPR as contracts may be in place with the third party thus minimising the sharing of data to one organisation. However, from an MHRA reporting perspective this may be considered a Serious Breach of GCP (SOP 51.009) as a system failure has led to personal data that has not been consented for by the participants being shared with a third party. For non-CTIMPs this may be considered a breach of GCP also.

3.5. Protocol Deviations in Sponsored and Co-Sponsored Trials

3.5.1. Protocol Deviations within CTIMPS

Protocol Deviations are unintended departures from approved research protocols, identified retrospectively. Deliberate deviations are considered protocol waivers and are not permitted**. Such waivers deliberately breach Regulation 29 of SI 2004/1031, which requires clinical trials to follow the Protocol.**

Specific Guidance on Protocol Deviations is available in Guideline 51.008B, this details how to classify and manage Protocol Deviations.

Category 1 or 2 Deviations must be reported to the Project Manager, Trial Monitor, or Sponsor representatives and logged on Form 51.008C by the site team. The PI signs the log, which is reviewed quarterly by the CI and Monitor to confirm correct categorisation and detect any misclassified serious deviations.

Category 3 or 4 Deviations involving key data (e.g. consent, eligibility, pharmacovigilance, endpoints) must be escalated to the Research Governance Manager or R&I Lead Clinical Trials Pharmacist. These are reported using Form 51.008A (signed by PI), followed by Form 51.008B for CAPA tracking and root cause analysis.

Non-engagement by sites in completing forms or CAPA should first be escalated to the CI. If unresolved, it must be reported to the Research Governance Manager or R&I Lead Pharmacist, who will intervene and determine if further escalation (e.g. file note, local governance, GHSPRAG, MHRA) is required.

Compliance Monitoring: The Sponsor and CI request that the data centre provide compliance data to the CI, TMGs, and, when appropriate, oversight committees such as TSC, IDMC, or safety review boards. Sponsor and Co-Sponsor agreements and contracts play a crucial role in delineating responsibilities, oversight processes, and compliance expectations during clinical trials. These documents ensure that all parties are aligned regarding data governance, protocol adherence, and the evaluation of trial deviations.

The CI and statistician are responsible for evaluating the impact of deviations on trial safety and outcomes. This review may take place at the TMGs and the minutes act as evidence it has taken place.

In some instances Protocol Deviations may be captured on the e-CRF. This process will be defined within the protocol and or the trial risk assessment.

3.5.2. Protocol Deviations within Non-CTIMPs

Form 51.008D will be supplied by the R&I Co-Ordinator to the CI and will be completed and held within the site file. It is the responsibility of the CI to maintain this form, keep a record of all categories of Protocol Deviations and to regularly review for trends. Protocol Deviations suspected of being category 3 or 4 will be reported to the Research Governance Manager or R&I Lead Pharmacist Clinical Trials. The monitor will provide all identified by both routes to the TMG.

3.5.3. Protocol Deviations Highlighted by GO-CTU Glasgow

For NHSGGC-Sponsored or Co-Sponsored trials co-ordinated by GO-CTU Glasgow, their Protocol Deviation management process applies. GO-CTU Glasgow staff will manage Category 1 and 2 logs, oversee site logs, and complete deviation forms. Suspected Category 3 or 4 deviations must be escalated immediately to the Sponsor representative, Research Governance Manager, and R&I Lead Pharmacist Clinical Trials before completing local Protocol Deviation forms. All deviation categories (1-4) will be routinely shared with the trial statistician and CI for trend review.

For trials managed by the GO CTU Glasgow, all other sections and forms related to this SOP will be adhered to.

3.6. Non-Compliance Relating to Medical Devices

For trials involving a non-CE marked Medical Device, any Protocol Deviations and Non-Compliances that are suspected to be category 3 or 4 must be reported to the Research Governance Manager or R&I Lead Pharmacist Clinical Trials.

Protocol Deviations in trials with non-CE marked medical devices must be reported to the MHRA. For Category 3 or 4 deviations, Appendix A shows the required form; the latest version is available on the MHRA website. The Project Manager and CI are responsible for submitting these reports. CAPA and root cause management will be handled by the Research Governance Manager or R&I Lead Pharmacist Clinical Trials, as with other Protocol Deviations.

3.7. Non-Compliances That Arise Within the Glasgow or Beatson CRF (Hosted Research)

If research services from the GCRF or Beatson CRF result in Non-Compliance/Protocol Deviations the CRF involved must report it to the external Sponsor as specified in the contract or service agreement. The issue is also escalated to the RGM or R&I Lead Clinical Trial Pharmacists for CAPA oversight and may be discussed at the relevant CRF GCP Compliance Committee.

3.8. Reporting

3.8.1. Reporting to Ethics and MHRA

Non-Compliances that result in a Serious Breach of GCP or the Protocol, will be reported to the MHRA (CTIMPS only) and Ethics by the Research Governance Manager or R&I Lead Pharmacist Clinical Trials, as appropriate in accordance to SOP 51.009. For research that is defined as a non- CTIMP only Ethics will be notified.

3.8.2. Reporting to Glasgow Health Science Partnership Regulatory Approval Group (GHSP RAG) and Glasgow Health Science Partnership Delivery Board.

The Research Governance Manager will provide a report on the status of all escalated Non-Compliances to GHSP RAG members during GHSP RAG meetings. The Chair of GHSP RAG is responsible for reporting Non-Compliances to the GHSP Delivery Board as needed.

3.8.3. Reporting Research Non-Compliances to Local Clinical Governance

Non-Compliances that result in potential patient safety issues that take place within NHSGGC will be reported through the NHSGGC Clinical Governance reporting system, DATIX. It is the responsibility of the trial team to report the incident on DATIX. NHSGGC Site errors and “near misses” leading to Non-Compliance issues must be reported on DATIX by the appropriate department. The Research Governance Manager or R&I Lead Pharmacist Clinical Trials will inform the Investigator/trial team if the incident needs to be reported on DATIX, if it has not already been recorded, or reported through their local clinical governance system/process if external to NHSGGC.

Examples of Non-Compliances that should be reported on DATIX (or equivalent) include, patient consenting to multiple trials with trial Investigators and Sponsors unaware of other trial; wrong dose of IMP given which leads to potential patient safety issue; patients on trials who are ineligible for the trial (do not meet inclusion/exclusion criteria) and data protection non-compliance issues.

Serious Adverse Events (SAEs) and Suspected Unexpected Serious Adverse Reactions (SUSARS) may be reported through DATIX (or equivalent) in addition to being reported via the Pharmacovigilance Reporting system which is a regulatory requirement. These are not considered a Non-Compliance as such unless the SAE or SUSAR resulted from a breach of GCP or a breach of the protocol.

3.8.4. Reporting of Non-Compliances Through NHS Governance Groups

The progress of the completion of a CAPA and the establishment of the root cause for the Non-Compliances will also be discussed at the CTIMP oversight groups to ensure issues are shared between trial groups and R&I staff

The R&I Director may also share Non-Compliances at NHSGGC Clinical Governance Group.

3.9. Publication

The CI, statistician, and Trial Management Team are tasked with verifying that Non-Compliances and Protocol Deviations are taken into account during report and publication analyses. The CI is also responsible for documenting this consideration in the Trial Master File.

3.10. Temporary Halt or Early Termination of Clinical Trial

In certain circumstances, e.g. following a series of Non-Compliances deemed to be of a serious nature it may be required to temporarily halt or terminate early a CTIMP, this process is defined in SOP 53.003.

3.11. Collaborators, Vendors, Central Units, Central Laboratories and Data Management Centres

R&I should confirm that third parties have adequate systems in place through contracts to ensure relevant training and /or SOPS in these organisations covers reporting of Non-Compliances and Protocol Deviations.

4. Referenced documents

- Form 51.008A - Protocol Deviation Reporting Form
- Form 51.008B - Protocol Deviation Reporting Form (part 2)
- Form 51.008C – Non- Compliance Protocol Deviation Log
- Form 51.008D - Non- CTIMP PROTOCOL DEVIATION and Non-compliance LOG
- GUI 51.008A – Managing Non-Compliance in Q-Pulse
- GUI 51.008B – Protocol Deviations Guidance
- GUI 51.008C- Guidance on Types of Non-Compliance and Associated Documentation
- The Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 2004/1031)
- SOP 53.002 – The handling of poor quality and fraud in clinical research
- SOP 53.003 – Temporary halt or early termination of clinical trials of investigational medicinal products
- SOP 51.009 – Notification of serious breaches of Good Clinical Practice or the trial protocol for clinical trials of investigational medicinal products.

5. Related documents

- Form 51.004A – Risk Assessment Tool
- SOP 53.001 – Notification of urgent safety measures for clinical trials of investigational medicinal products.

6. Document history

Version	Date	Description
1.0	14/07/2009	Release of Version 1
2.0	06/11/2013	Section 4.1.1 who to report GCP issues Section 4.2 The grading is not done by GBRAG but by Governance Manager and reported to GBRAG Section 4.2.2 The Handling of the issues is dealt with by Governance Manager and SOP needs to reflect this Addition of form 51.008 A
2.1	19/01/2015	Section 2 and 3 addition of research investigator Section 5 clarification of procedures Section 5.1.2 clarification of reporting procedures and storage of forms Section 5.2 clarification of sponsor procedures Section 5.2.1 new section Explanation of issues numbering
3.0	14/07/2016	Renumbered and change of author Section 5 amended to clarify process and include process flow chart Amendment of FORM 51.008A Addition of FORM 51.008 B
3.1	20/12/2018	More defined process for handing and categorizing protocol deviations
4.0	19/04/2022	Restructure and review of whole document and introduction of use of Q-Pulse. Updated to include publication and responsibility of statisticians. Updated to include protocol deviation recording process implemented under process development during COVID 19 pandemic
5.0	23/09/2025	Separation of sponsored CTIMPS, non-CTIMPS and medical devices, addition of logs for non-CTIMPS and medical devices

Appendix A – Example of Protocol deviation reporting form for devices – for reporting to the MHRA. For most recent form visit Clinical investigations guidance - GOV.UK

Protocol Deviation Number	Site #	Pt. Number	Major/ Minor	Justification	Deviation Type	Visit Affected	Description of the Protocol Deviation	Deviation Date	Corrective and Preventative Action	Deviation Status - open /closed	Additional relevant info