SOP number	**51.029**	Version	**4.0**
Title	**Writing Study Specific Laboratory Manuals for Research Sponsored by NHSGGC or Co-Sponsored by NHSGGC and the University of Glasgow**		

Prepared by Signature	Lynsey Gillespie Date
Approved by Signature	Samantha Carmichael Date
Released by Signature	Julie Brittenden Date

SOP category	51 NHSGGC Sponsor R&I

Staff category

Staff Category	**R**	**A**	**C**	**I**
Lead Pharmacist Clinical Trials/R&I		X		
Project Managers	X			
Chief Investigator	X			
R&I Sponsor Research Co-Ordinators	X			
Innovation contracts manager	X			
Biorepository Manager			X	
Laboratory Quality Managers			X	
University of Glasgow Head of Research Regulation and Compliance			X	
Senior R&I Managers				X

1. Scope

This procedure applies to research Sponsored by NHS Greater Glasgow & Clyde (NHSGGC) or Co-Sponsored by NHSGGC and the University of Glasgow (GU). Project Managers staff category includes Project Managers from NHSGGC Project Management Unit, Glasgow Oncology Clinical Trials Unit, University of Glasgow and Glasgow Clinical Trials Unit.

2. Purpose

The analysis of samples collected from participants in clinical research forms a key part of the clinical research process. It is a requirement for all NHS and non-NHS laboratories that perform work in support of clinical research to implement appropriate measures to assure the quality and integrity of the data they produce and to exercise due diligence to ensure that the research participants rights are not compromised. In order to meet this requirement a Study Specific Laboratory Manual (Form 51.029A) is required for all NHSGGC Sponsored and Co-Sponsored research which include standard tests, with specific requirements or non-standard, research tests or central laboratory functions – category 2 & 3 tests as defined in SOP 51.028.

The Study Specific Laboratory Manual must ***only include work that is covered by the research study or clinical trial protocol***. It should contain sufficient detail to allow reconstruction of techniques for non-standard, research tests undertaken on research samples. The SOPs and processes in operation within the laboratory for processing and analysis of the research samples must be followed and referenced. A study may require more than one Laboratory Manual depending on the number of NHSGGC as well as non-NHSGGC laboratories involved and/or type of laboratory activities specified within the protocol.

3. Procedures

The analysis or evaluation of clinical research samples in accordance with the study specific manual should be overseen by a named individual(s) who assumes responsibility for the conduct of the work. Laboratory Management should ensure that laboratory personnel are appropriately trained and qualified to perform the roles and responsibilities assigned to them and that the Assistant General Manager has reviewed and agreed the laboratory has the necessary resources to conduct the research.

The Study Specific Laboratory Manual should be written by the Chief Investigator (CI) or delegate in conjunction with the named individual(s) performing the analysis. The process will be co-ordinated by the Project Manager or the CI in the absence of a PM. The manual requires to be approved by the CI, Sponsor representative and relevant Laboratory Quality Manager. The Study Specific Laboratory Manual should be filed in the Laboratory Master Research File for the relevant NHSGGC lab (Form 56.002L).

Appropriate laboratory costs will be identified by the Research Co-Ordinator at the grant application stage as per SOP 51.010 and approved as per SOP 52.007 “Authorisation for NHS resource use in R&D submission”.

3.1. Categorisation of Laboratory Tests

Prior to study commencement each laboratory test detailed within the study protocol should be classified according to the following criteria and this should be filed in the laboratory section of the Sponsor Trial Master File (TMF), per SOP 51.028 and Form 51.028A and the Laboratory Master Research File, as per SOP 56.002 and Form 56.002L:

Category 1: Standard test i.e. validated and in use in clinical practice within NHS
Category 2: Standard test, with specific requirements or
Category 3: Non-standard test, research tests

Category 2 and 3 tests require the production of a Study Specific Laboratory Manual and the categorisation of all lab tests must be detailed within it.

3.2. Safety

The Study Specific Laboratory Manual must detail the communication plan to be followed with the CI to ensure that any issues that may impact on study participant’s safety are reported to them without delay. This must include the reporting of out of range results and significant deviations from the protocol or the Study Specific Laboratory Manual. If there are no potential safety issues, this should be stated in the Manual.

3.3. Consent

The Study Specific Laboratory Manual must detail how the study team or Project Manager will notify the laboratory of a patient being recruited. It must also detail any actions to be implemented by lab staff if notified by the study team or PM that a participant has withdrawn consent. Some laboratories may require copies of consent forms, e.g. pathology in order to release archived or other tissue samples. This must be detailed in the Study Specific Laboratory Manual.

3.4. Sample handling, labelling, receipt, storage and chain of custody

Sample handling & chain of custody:

- The Study Specific Laboratory Manual may cross-refer to the processes for sample handling and transport to the Laboratory which are detailed in SOP 51.030.
- The Study Specific Laboratory Manual must detail the receipting process for the laboratory staff. It must also detail any handling processes for the samples to be undertaken by the laboratory staff at the point of receipt or thereafter.
- The Study Specific Laboratory Manual must detail processes for entering the samples into a LIM (Laboratory Information Management) System or how the samples will be tracked within the laboratory.
- The Study Specific Laboratory Manual must detail processes in relation to any movement of the samples in and out of the laboratory after initial receipt.

Sample labelling:

- The Study Specific Laboratory Manual must detail the labelling process which was undertaken by the participating site. The research study or clinical trial sample must be labelled in such a way as to allow their unequivocal identification at all times in the analysis or evaluation process. This may necessitate the use of different or additional labels.
- In exceptional circumstances, such as those in which the laboratory need to access tissue which is already stored as part of routine clinical care such as pathology archive or take additional samples from a pathological specimen that would normally be sent to that laboratory it may be necessary to include patient identifiable details so that the consent form can be cross-checked.
- The Study Specific Laboratory Manual must detail how the laboratory staff will use these labels and if processes are required to cross reference the applied labels with processes and labelling requirements of the laboratory procedures. The processes of entering labelling details into the LIM System or tracking process must be detailed.

Sample Receipt:

Standard details to be included in the Study Specific Laboratory Manual are:

- All samples used in eligibility criteria, primary, secondary or safety end-point analysis to be assessed on arrival to check their physical integrity. If samples have been compromised in transit the Project Manager must be promptly notified. The date and time of receipt must be recorded.
- On receipt, laboratory staff must ensure that all samples are accounted for. If samples are poorly labelled, missing or if unexpected samples are receipted the Project Manager should be contacted to investigate and resolve the issue.
- Unexpected samples must not be analysed until their origin is confirmed.
- Samples and associated documentation being received at a NHSGGC Laboratory undertaking central laboratory functions from participating sites ***should not contain any patient identifiable details***. The PM must be notified if patient identifiable details are included.

Sample storage conditions:

- The Study Specific Laboratory Manual must detail the processes of checking the storage conditions of the samples during transit to the laboratory and the processes of dealing with samples that may have experienced out of range conditions, e.g. temperature excursion, at the time of receipt.
- The Study Specific Laboratory Manual must detail the storage conditions and process of monitoring the conditions, e.g. temperature monitoring within the laboratory.
- Processes to evidence the monitoring of the samples must be detailed as well as how any actions taken in the event of any excursions from the specified ranges are reported to the PM, documented and retained.

3.5. Blinding

The Study Specific Laboratory Manual must detail any processes in place to maintain the blind if required. Standard details to be included are:

- Point of contact to receive unblinded data/reports from the laboratory.

3.6. Equipment

The Study Specific Laboratory Manual must detail equipment required to undertake the specified analyses. If new equipment is required to be purchased for the study the Study Specific Laboratory Manual must detail the processes for purchase, commissioning, maintenance and how the equipment is added to the laboratory equipment inventory. This may be in accordance with the laboratory's standard practice.

3.7. Method Validation

The Study Specific Laboratory Manual must detail the validation processes to be undertaken for the specified analyses. Standard Details to be included are:

a) The process for validating the methods for category 3 tests.

For all category 3 tests where a commercially sourced kit is used, the detail of the validation and comprehensive testing should be within this section.

Where a fully validated commercial kit is used, often referred to as ready to use, an insert or document will be provided from the manufacturer detailing the validation checks that the kits has been subjected to. This should include an acceptable range of values, confirmation of reproducibility, and limits of variation. These details should be provided in this section or link to the information.

Where the commercial kit has not been previously validated, all validation testing will need to be performed before any trial samples are tested. These tests should determine reproducibility, accuracy, acceptable range of values, and if any, which control samples are required. The details of these tests should be provided in this section.

a) Definitions of acceptance criteria.
b) Definitions of suitability tests and quality control samples.
c) Definition of limits of inter-and intra-assay variation and accuracy.

Inter and intra assay variation is required to be performed during the run of tests where more than 1 kit is used, regardless of whether the kit is fully validated or not.

3.8. Data recording

The Study Specific Laboratory Manual must detail the processes for recording data generated within the laboratories. Standard details to be included are:

- All data must be recorded directly, promptly, accurately and legibly.
- The data and identity of the person conducting the work should be recorded.
- A quality control procedure must be in place to ensure that all data are accurate and complete.
- An audit process for tracking if data are modified or corrected.

3.9. Reporting

The Study Specific Laboratory Manual must detail the manner in which the laboratory data will be reported. The format, number and frequency of reports to be generated should also be included, e.g., the results of a clinical analysis may be supplied as electronic source data, printouts from the analytical equipment used to perform the tests, or a report which contains data and interpretation of results.

3.10. Data transfer

The Study Specific Laboratory Manual must detail the processes of data transfer from the laboratory to the data-management centre, e.g. when analyses may be carried out in a central function requiring that batches of data have been held and require transfer. Data may be sent to the Clinical Trial Units, Data Centre Provider or research team (for non-CTIMPs) as hard paper copy or electronically. If data is manually entered onto a worksheet or electronic case report form then the process of auditing this must be defined, e.g., a predefined random proportion of values will be audited or requirements for a 100% check of entries.

With the exception of pathology, studies which use Telepath to record Category 2 or 3 tests, must ensure that results are downloaded every 28 calendar days or earlier to ensure a complete audit trail is available.

3.11. Computerised Systems

The Study Specific Laboratory Manual must detail all computerised systems used for the capture, processing, reporting and storage of data. The processes of development, validation and maintenance of these systems must be detailed. These processes must ensure the validity, integrity and security of the data. Any access that laboratory teams require to the electronic case report must be detailed along with how that access is given.

3.12. Retention of Trial Data

The Study Specific Laboratory Manual must detail the processes of retention of trial data. Standard detail to be included:

- Study specific documents to be retained in accordance with the requirements of GCP and national legislation and archived in accordance with the Sponsor archive standard operating procedures [SOP 51.024 or SOP 51.025].
- Non study-specific documents to be retained in accordance with the laboratory policies.

3.13. Retention and destruction of research samples

The Study Specific Laboratory Manual must detail the processes to be applied to samples at the end of the study and must be in accordance with the Human Tissue Act 2004. These will be dependent on the approved detail within the protocol and as defined in the ethical application. The processes may include storage, retention, or destruction. The duration must be detailed in the Study Specific Laboratory Manual. The expectation is that Category 2 samples will be destroyed in accordance with the Laboratory standard operating procedures, unless otherwise stated.

3.14. Non-compliances and Potential Serious Breaches in GCP

The Study Specific Laboratory Manual must detail the processes to be followed when incidents occur that are considered to be a non-compliance with GCP and/or potential serious breaches in GCP. Definitions of such incidents may require to be included in the Study Specific Laboratory Manual.

3.15. Protocol Amendments

The Study Specific Laboratory Manual must detail the processes to be followed when protocol amendments have been made. The Research Co-Ordinator will capture any impact of the protocol amendment on the Laboratory manual as part of completing Form 51.021C (Sponsor review of amendment checklist). This must include how the Sponsor will risk assess the impact to the Study Specific Laboratory Manual and ensure updates to it are distributed and implemented accordingly.

4. Referenced documents

- SOP 56.002 – Project Management Trial Set-up
- Form 56.002L – Laboratory Master Research File
- SOP 51.028 – NHS Laboratory Samples for Research Sponsored by NHSGGC or co-sponsored by NHSGGC and University of Glasgow or hosted by NHSGGC
- SOP 51.010 - Preparation and Review of Grant Applications and Costs
- Form 51.021C - Sponsor review of amendment checklist
- Form 51.028A – Categorising Lab Tests
- Form 51.029A – Laboratory Manual Template Central Lab
- SOP 51.030 – Writing Sample Handling Manuals for Sites Participating in Research Sponsored by NHSGGC or co-sponsored by NHSGGC and University of Glasgow
- SOP 52.007 – Authorisation for NHS resource use in R & D Submission
- SOP 51.024 – Archiving Essential Documents from Clinical Research – Process for a Sponsored Clinical Trial of an Investigational Medicinal Product (CTIMP)
- SOP 51.025 – Archiving Essential Documents from Clinical Research – Process for a Sponsored Non CTIMP

5. Related documents

- EMA Reflection paper for laboratories that perform the analysis or evaluation of clinical trial samples (2012)
- MHRA Good Clinical Practice Guide, Chapter 13 (2012)

6. Document history

Version	Date	Description
1.0	24/05/18	First release
2.0	02/11/2018	Glasgow University PMs added CRUK PMs added Glasgow CTU (RCB) PMs added Clarifications in processes added
3.0	25/01/2024	Update to SOP template v2.0 Addition of RACI matrix Minor formatting /updates Change of author / approver Update to include all research projects and not just CTIMPs
4.0	03/05/2024	Further clarifications