STANDARD OPERATING PROCEDURE FOR IMPLEMENTATION AND MAINTENANCE OF A QUALITY ASSURANCE SYSTEM IN CLINICAL RESEARCH LABORATORIES

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1. PURPOSE

This Standard Operating Procedure (SOP) specifies the requirements for the Quality Management System for University of Dundee (UoD) clinical research laboratories that analyse samples from Clinical Trials of Investigational Medicinal Products (CTIMP) to ensure the purpose and objectives of the Good Clinical Practice (GCP) principles are satisfied. It is considered good practice for all UoD clinical research laboratories to follow this SOP.

2. SCOPE

This SOP applies to members of staff associated with managing and/or analysing samples from CTIMPs sponsored or co-sponsored by the UoD and/or NHS Tayside. It does not include laboratory activities for diagnostic purposes or for the routine clinical care of patients.

3. RESPONSIBILITIES

This SOP is intended for use by research staff (scientific, technical, and clinical) employed in UoD research laboratories who are conducting work in support of Clinical Trials which fall under the Medicines for Human Use (Clinical Trials) Regulations 2004 and subsequent amendments.

By following the information provided in the European Medicines Agency's (EMA) Reflection Paper for laboratories that perform the analysis or evaluation of clinical trial samples (2012), laboratories should be able to maintain quality systems which will comply with GCP.

The following measures should be in place:

- Trained and competent staff.
- SOPs and guidelines.
- A programme of internal audits (processes and facilities) to ensure compliance with GCP for laboratories.

4 PROCEDURE

4.1 Organisation and Personnel

Each laboratory should have a staff organisational chart. The Chief Investigator (CI)/Principal Investigator (PI) will contact a laboratory-designated Analytical Plan Manager (APM) before the start of a new study. The APM will ensure that an Analytical Plan (AP) is completed accordingly (refer to the TASC SOP on APs) and send a copy to the TASC Quality Assurance (QA) Manager for their signature. Any future amendments or deviations to the AP will be documented by laboratory staff. The TASC QA Manager or delegate will audit laboratories for compliance according to the TASC Laboratory Audit Schedule and report to the TASC Laboratory QA Committee.

The TASC Laboratory QA Committee will affect continual improvement through annual review of audit findings, and dissemination of updates to current practice and regulations, to relevant parties.

4.2 Facilities

UoD clinical research laboratories should be of suitable size to ensure segregation of activities and have adequate secure storage areas to permit the orderly retention of materials and equipment.

4.3 SOPs and Guidelines

SOPs and guidelines should include, but not be limited to the following:

- Maintenance, servicing, calibration and use of equipment.
- Validation of equipment, methods and computerised systems.
- Inclusion of adequate Quality Control (QC) functions.

Manuals may be used to supplement procedures written by the laboratory. Consideration should be given to the retention of documents for reconstruction purposes.

4.4 Samples

Informed Consent

The CI/PI must ensure written informed consent has been given by the research participant before analysis of samples. The CI/PI will confirm this on the AP. The lab must be informed if consent for sample processing is withdrawn to ensure that samples in storage are destroyed and no further data is generated. The disposal will be implemented and recorded according to the laboratory's written instructions. Refer to TASC SOPs for Preparation of an Analytical Plan for UoD Laboratories associated with CTIMPs and Management of a Chain of Custody for Samples in Clinical Research.

Sample Identification and Chain of Custody

Samples must not be labelled with patient identifiable information. The laboratory should have a written procedure to deal with this should the situation arise. Also refer to the TASC SOP on Chain of Custody for Samples in Clinical Research.

Sample Storage

Fridge and freezer temperatures must be recorded either manually or electronically. If temperatures go out with the desired range, this must be recorded and appropriate action taken to ensure that the integrity of the stored samples is maintained. Equipment for monitoring temperatures should be subject to periodic calibration and the results documented. Relevant storage stability data must be available if samples are to be stored prior to analysis.

Sample Analysis
Analysis must be carried out in accordance with the laboratory's SOPs and guidelines, and the AP. All deviations required for operational reasons must be documented by the laboratory staff. All data must be recorded as specified in the AP. Repeat analyses should only be undertaken in accordance with clearly defined criteria in accordance with written documentation. It is never acceptable to selectively report data.

4.5 Data Management

Computerised systems used for the capture, processing, reporting and storage of data should be developed, validated and maintained in ways which ensure the validity, integrity and security of the data. Computerised systems must be password protected. It should always be possible to determine the date on which the analysis or evaluation was performed and the identity of the person who conducted the work. Source data must be identifiable, traceable and available.

Manually transcribed data must be checked and signed and dated as such. Automatic transfer and/or analysis of data should be periodically checked and recorded as checked. There should be paper/electronic trails for amendments, deletions and duplications. The data/system should be reliably backed up and the recovery process tested.

Reports
Reports should be provided to the study team. The way in which data will be reported by the laboratory should be documented in the AP. Regardless of how data is reported, it must be accurate, legible and complete. Any amendments or corrections to reports once issued must be signed, dated and the reason documented.

4.6 Equipment, Materials and Reagents

Equipment
Laboratory staff will ensure that equipment is validated, the process whereby documented evidence demonstrates that a system has been developed, implemented, operated and maintained, in a controlled manner. This assures that the system consistently meets its specification and is suitable for its intended purpose. They will also ensure that equipment is cleaned and calibrated according to requirements and records must be kept. Staff must be trained in the use of equipment and this will be recorded in their training records. Faulty or long-term unused equipment will be clearly labelled as out of use.

Materials and Reagents
Laboratory staff will ensure that materials and reagents are labelled, stored at the correct temperatures, kept in secure and suitable storage conditions and used before their expiry dates. Reagents must be identified by title with a record of concentration, date of opening/constitution, and expiry date. Laboratory staff must keep a record of the preparation and dispatch of reagents or sample processing kits that they send to other laboratories.

4.7 Quality Control

Method Validation

Methods must be validated before use with defined acceptance criteria where appropriate. The validation of methods should be documented and, on completion, this documentation should be archived.

Standards and QC Materials

Laboratory staff will analyse and check QC samples at intervals specified in the relevant SOP or instructions. Test sample results will not be reported prior to satisfactory QC results being obtained. QC and calibration data must be recorded.

4.8 Quality Assurance

Laboratory audits, which may be on-site or remote (e.g. MS Teams, email), will be performed by the TASC QA Manager or delegate who must be trained and experienced and independent from the work carried out by the clinical research team and the UoD Laboratory involved. The standard guideline used for laboratory audit is the EMA Reflection Paper (2012). The frequency, duration and content of each audit will vary depending on the history and nature of the work conducted by the laboratory. Serious, non-compliant findings will be reported immediately to the Laboratory Manager or delegate for action. Audit reports will be submitted to the Laboratory Manager or delegate within one week of audit.

The Laboratory Manager or delegate will ensure that the actions identified in the audit report are implemented within a specified timeline. The TASC QA Manager or delegate will either verify that these actions have been implemented so that the report can be closed or allow an extension for justified reasons. Repeated failure to comply within timelines will be reported to the TASC R&D Director. Breaches of GCP, SOPs or study protocols will be reported to the TASC Research Governance team following the TASC SOP on Reporting Breaches in Clinical Research. Summary reports of audit activity will be prepared by the TASC QA Manager for annual review by the TASC Laboratory QA Committee, UoD Research Governance & Policy Sub-Committee and NHS Tayside Care Governance Committee.

4.9 Archiving

Archiving of laboratory data will be carried out according to each individual laboratory's local arrangements.

5 ABBREVIATIONS & DEFINITIONS

AP	Analytical Plan
APM	Analytical Project Manager
CI	Chief Investigator
CTIMP	Clinical Trial of Investigational Medicinal Product
EMA	European Medicines Agency
GCP	Good Clinical Practice
PI	Principal Investigator
QA	Quality Assurance
QC	Quality Control
SOP	Standard Operating Procedure
TASC	Tayside Medical Science Centre
UoD	University of Dundee

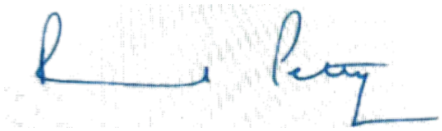
6 ASSOCIATED DOCUMENTS & REFERENCES

European Medicines Agency 28 Feb 2012. Reflection Paper for laboratories that perform the analysis or evaluation of clinical trial samples.

7. DOCUMENT HISTORY

Version Number:	Reviewed By (Job Title)	Effective Date:	Details of editions made:
History of reviewers prior to 2019 is detailed in the archived SOPs			
7	Valerie Godfrey (TASC QA Manager)	26/03/2019	References updated to include EMA Reflection Paper 2012. New TASC SOP format implemented.
8	Valerie Godfrey (TASC QA Manager)	29/01/2021	Section 4.8 updated to include remote audits and annual reporting requirements for UoD and NHS Tayside committees. Date brought forward from March to January to allow upload to new TASC SOP template which shows the new TASC website in the footer. Physical scan converted to electronic pdf as a requirement for upload to new TASC website.
9	Valerie Godfrey (TASC QA Manager)	03/02/2023	Scheduled review, text refreshed and wording in section 4.4 and 4.8 updated.

8. APPROVALS

Sign		Date
APPROVED BY:	Professor Russell Petty, R&D Director, NHS Tayside	
Signature		31st Jan 2023
APPROVED BY:	Dr Valerie Godfrey, TASC QA Manager, Chair of Clinical Research Guidelines Committee	
Signature		26 Jan 2023