Standard Operating Procedure:

Laboratory Set-up and Management

# Purpose:

This standard operating procedure (SOP) describes the processes involved in setting up and managing a laboratory to meet the appropriate standard. For clinical trials of investigational medicinal products (CTIMPs), the laboratories will be set up and managed in accordance with Good Clinical Practice (GCP) in the laboratory. For clinical studies and non-CTIMP trials that involve the handling, processing, receipt, storage or analysis of samples of human tissue, laboratories will be set up and managed in accordance with the Human Tissue Act. See ‘Decision Map’ on page 3 to determine which standard is applicable.

# Scope:

The SOP is applicable to University of Birmingham (UoB) staff involved in the handling, processing, receipt, storage or analysis of samples of human tissue (see Definitions) for clinical studies and non-CTIMP trials.

The SOP is also applicable to all UoB staff and laboratories performing analyses that contribute to the (primary, secondary and exploratory) endpoints of CTIMPs, whether these trials are sponsored by the UoB or sponsored/co-sponsored by another institution.

# Implementation plan:

For clinical trials (to include primary, secondary and exploratory endpoints of CTIMPs and non-CTIMPs) this SOP will be implemented within 3 months of the effective date. For clinical studies this SOP will be implemented within 6 months of the effective date.

# Stakeholders:

Note that where the UoB takes on the sponsor’s responsibility, the UoB will delegate the majority of these duties to the Chief Investigator (CI) who may delegate these duties further to their trials team(s).

* CI (for the purposes of this SOP this term will include the UoB lead where the CI is not employed by UoB)
* Laboratory academic lead (LAL)
* Clinical Research Compliance Team (CRCT)

# Background and rationale:

The analysis or evaluation of samples collected from subjects participating in clinical research forms a key part of the clinical research process. The purpose of this SOP is to describe procedures which will ensure that laboratories which analyse or evaluate human biomaterial (either for clinical trials or for clinical studies) are set up and managed to the appropriate laboratory standard in accordance with applicable law, established policies at the UoB and for CTIMPs the accepted principles of GCP; to ensure that patient safety is not compromised and data is reliable and accurately reported.

For CTIMPs, where the laboratory analysis is limited to exploratory endpoint(s) only, it is recommended to consider during the trial’s design phase whether the exploratory analyses could be completed as a stand-alone clinical study with its own study protocol and ethical approval.

The laboratory set-up can only fully start after clarifying what is expected to be analysed. This includes the number of samples, types of samples, types of analyses, duration of the research, visit schedule in which samples are collected, etc. This information may be captured in communications between the laboratory team and the clinical research management team, and will ultimately be captured in the research protocol.

At the UoB the quality assurance (QA) role described in the [European Medical Agency - Reflection paper for laboratories that perform the analyses or evaluation of clinical trial samples (PDF - 136 KB)](http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2012/05/WC500127124.pdf) for CTIMPs will be undertaken by the Clinical Research Compliance Team (CRCT).

# Procedure:

Follow the Decision Map to determine the requirements within this SOP for your research.

## Decision Map



See ‘Abbreviations and definitions’ below for more information on relevant material.

Processes described below which apply to ALL laboratories receiving and managing human tissue for clinical research are in BOLD text.

Additional processes applying to laboratories required to be compliant with GCP standards are written in NON-BOLD text.

## Roles and responsibilities

1. **The CI (or delegate) will co-opt a laboratory academic lead (LAL) who will lead the laboratory team and the laboratory-based research and in turn will be responsible for maintaining the appropriate laboratory standard (i.e. GCP in the Laboratory or Human Tissue standard) as listed in the UoB Quality Management System Clinical Research in the Laboratory (CRL) SOPs.**
2. **The LAL (no delegation allowed) may assign roles and duties to other members of the laboratory team, for example:**

* **‘analytical manager’ who will be responsible for assay validation**
* **analyst(s) who will be responsible for performing assays.**

1. **Where necessary, the LAL (no delegation allowed) may assign multiple roles to one individual.**
2. The LAL (or delegate) will document all roles and duties as detailed in UoB-CRL-QCD-002 Laboratory Roles and Duties.
3. It is expected that as part of the set-up the LAL (or delegate) will liaise with the CRCT ([crct@contacts.bham.ac.uk](mailto:crct@contacts.bham.ac.uk)) in their role as UoB QA representative, prior to any trial samples being received by the laboratory.

## Training and competency

1. **The LAL (or delegate) will take on the responsibilities of the ‘Manager’ as described in** **UoB-TRN-SOP-001 Training, to ensure that all laboratory personnel are trained and competent to perform in their assigned roles** **(see** **UoB-CRL-QCD-003 Laboratory Competencies).**
2. The LAL (or delegate) will develop and document an internal process for assessing competency of all trial-specific assays or evaluations, including both ‘Competent to perform’ and ‘Competent to train’ assessments (see UoB-CRL-QCD-003 Laboratory Competencies).

* ‘Competent to perform’ statements will be signed by a person who is ‘Competent to train’.
* ‘Competent to train’ statements will be signed by the LAL (or delegate).
* Competency statement may cover experience gained in previous roles.

## Contracts

1. The LAL (or delegate) will work with the [UoB Contracts Team](https://intranet.birmingham.ac.uk/finance/Financial-Services/Research-Support-Group/Contracts/index.aspx) when drafting, agreeing, reviewing or revising a ‘Sample Analysis for Clinical Trials Contract’ between the laboratory and sponsor (where the laboratory is not part of the sponsor’s organisation). Ensuring the Sample Analysis for Clinical Trials Contract (see also UoB-CRL-QCD-004 Laboratory Contracts and Agreements Checklist):

* Meets all of the regulatory requirements, including but not limited to:
* The European Medical Agency - [Reflection paper for laboratories that perform the analyses or evaluation of clinical trial samples (PDF - 136 KB)](https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/reflection-paper-laboratories-perform-analysis-evaluation-clinical-trial-samples_en.pdf)
* [The Human Tissue Act (2004)](http://www.legislation.gov.uk/ukpga/2004/30/contents)
* For CTIMPs, the [Medicines for Human Use (Clinical Trials) Regulations 2004 and amendments](http://www.legislation.gov.uk/uksi/2004/1031/contents/made)
* The principles of GCP.
* Does not conflict with the requirements of the protocol or any analytical plans.
* Contains sufficient detail of the analysis the laboratory will perform, if not sufficiently detailed in the protocol.
* Describes how and when the laboratory will be reporting to the sponsor.
* Details who will be responsible for the archiving of laboratory trial documentation and source data at trial closure (see UoB-ARC-SOP-001 Archiving).

1. **Where clinical trial samples are to be shipped from/ to the UoB to/from another institution, the LAL (or delegate) will work with the UoB Contracts Team when drafting, agreeing, reviewing or revising Material Transfer Agreements (MTAs). MTAs will be in place before clinical trial samples are shipped from or to the university, unless terms have been covered by another contract (e.g. Sample Analysis for Clinical Trials contract).**
2. The LAL (or delegate) will ensure a documented agreement is in place between the CI and the laboratory, where the laboratory is part of the sponsor’s organisation, and will ensure the agreement meets all the requirements listed above for a Sample Analysis for Clinical Trials Contract.
3. The LAL (or delegate), in liaison with the UoB Contracts team, will ensure any contracts relating to sub-contracting (where the laboratory is sub-contracting analysis of clinical trial samples to a non-UoB laboratory) stipulates which QMS will be followed.

* If the sub-contracted laboratory will be following a non-UoB QMS, the LAL (or delegate) will, in liaison with CRCT, perform documented checks to ensure that it aligns with the UoB QMS.

1. The LAL (or delegate) will ensure that all contracts and agreements are signed and in place before the laboratory receives any samples for analysis.
2. The LAL (or delegate) will implement a contract or agreement between the laboratory and any companies that provide services linked to the analysis or evaluation of clinical trial samples; for example, equipment maintenance or servicing contracts. Contracts will stipulate the nature of the service.
3. **The LAL (or delegate) will ensure that where the** [**Human Biomaterials Resource Centre (HBRC)**](mailto:hbrc-tissuebank@contacts.bham.ac.uk) **is used to source, store or process human biomaterial samples on behalf of the clinical research project the HBRC is contacted at the project set-up phase and a contract is set up to stipulate the nature of the service prior to receiving the first sample.**

* **Where the HBRC is to be used for hosting or histology services only, the number, type and storage temperature of samples, inflow and outflow expectations, funders details and copies of applicable study documents will be required to set up the contract.**
* **Or, where the HBRC is to be used to obtain samples for the research project an application form will need to be completed, which can be obtained by contacting the** [**HBRC**](https://www.birmingham.ac.uk/facilities/hbrc/contact/index.aspx) **directly.**

## External laboratories

1. Where external laboratories (i.e. non-UoB laboratories) will be used to process or analyse clinical trial samples the CI (or delegate) will assess the ability of the external laboratory to perform the work to the correct standard (see UoB-CLN-SOP-006 External Laboratory Set-up and Oversight (currently under development) for further information.

## Sub-contracting laboratory analysis

1. The LAL (or delegate) will assess the ability of the sub-contractor to perform the work to the correct standard; see UoB-CPR-SOP-001 Compliance Review for further information.

* Particular attention will be paid to staff training and competency and the validation and approval of computerised systems.

It is expected that the process will be documented (see UoB-CRL-QCD-004 Laboratory Contracts and Agreements Checklist).

1. The LAL (or delegate) will inform the sponsor (if externally sponsored) or CI (if UoB-sponsored) in advance if sample analysis is to be sub-contracted to another laboratory.

## Clinical trial protocol

1. The LAL (or delegate) will ensure that, as a minimum, the relevant sections of the current and approved protocol are made available to the laboratory team. Under most circumstances it is expected that the LAL (or delegate) ensures that the whole protocol is available.
2. The LAL (or delegate) will retain a copy of all superseded versions of the protocol, clearly labelled as such to avoid confusion.
3. The LAL (or delegate) will establish lines of communication between the sponsor (if externally sponsored) or CI (if internally sponsored) (or delegate) to ensure that:

* the sponsor/CI (or delegate) is able to update the LAL (or delegate) when amendments are made to the protocol
* the LAL (or delegate) can confirm with the sponsor/CI (or delegate) that they hold the current version of the protocol
* these lines of communication will be documented (see UoB-CRL-QCD-005 Key Contacts).

## Requests for additional work

1. If extra work is requested by the sponsor (where externally sponsored) or the CI (where internally sponsored) the LAL (or delegate) will first confirm with the sponsor/CI that:

* all trial documents and ethical approval have been updated (where required)
* the additional work does not conflict with the protocol
* the additional work does not compromise the informed consent given by the participants
* contracts/service level agreements are updated where necessary, in collaboration with the [UoB Contracts Team](https://intranet.birmingham.ac.uk/finance/rss/contracts/index.aspx)
* sufficient resource/costings are available to perform the additional analyses/evaluations.

## Blinding/unblinding

1. Where laboratories analyse samples from blinded trials the LAL (or delegate) will ensure processes are in place to prevent the blind being inadvertently compromised (see UoB-RND-SOP-001 Randomisation and Blinding).
2. Where analytical laboratories are required to unblind samples for analysis purposes, the (LAL) (or delegate) will ensure a documented procedure is in place detailing:

* how data will be communicated in a blinded manner and to whom it can be communicated
* the storage of information that allows samples to be unblinded
* the re-blinding of samples.

## Laboratory master file

1. **The LAL (or delegate) will create a laboratory master file as detailed in** **UoB-CRL-QCD-001 Setting Up a Laboratory Master File, which will include documented processes to cover all key areas of activity in the laboratory to underpin the quality and integrity of the data generated. This will include appropriate review, approval and version control of all documents.**

* **The laboratory master file will be archived (see** **UoB-ARC-SOP-001 Archiving) alongside all source data and data reported to allow the reconstruction of the trial and to provide evidence of compliance.**

# List of expected outputs:

* **Evidence of laboratory duties defined and documented, including the identification of the laboratory academic lead** **(see** **UoB-CRL-QCD-002 Laboratory Roles and Duties).**
* **Training** and competency **definitions and records** (see UoB-CRL-QCD-003 Laboratory Competencies).
* **Evidence of all required contracts and agreements to be in** **place** (see UoB-CRL-QCD-004 Laboratory Contracts and Agreements Checklist).
* Evidence of assessments where sub-contracting of laboratory analysis (where required, see UoB-CRL-QCD-004 Laboratory Contracts and Agreements Checklist and UoB-CPR-SOP-001 Compliance Review).
* Evidence that the sponsor (if externally sponsored) or CI (if UoB-sponsored) has been notified if laboratory analysis has been sub-contracted to another laboratory.
* A copy of the current and approved protocol (or relevant sections) and all superseded versions available for the laboratory team (see *UoB-CRL-QCD-005 Key Contacts*).
* Evidence of documented lines of communication established to ensure laboratory has up-to-date version of protocol (or relevant sections of the protocol) (see *UoB-CRL-QCD-005 Key Contacts*).
* Evidence of processes to prevent inadvertent unblinding of samples and data, where applicable (see UoB-RND-SOP-001 Randomisation and Blinding).
* **A laboratory master file** **(see** **UoB-CRL-QCD-001 Setting Up a Laboratory Master File).**

# Related documents:

* UoB-ARC-SOP-001 Archiving
* UoB-CPR-SOP-001 Compliance Review
* UoB-CRL-QCD-001 Setting up a Laboratory Master File
* UoB-CRL-QCD-002 Laboratory Roles and Duties
* UoB-CRL-QCD-003 Laboratory Competencies
* UoB-CRL-QCD-004 Laboratory Contracts and Agreements Checklist
* UoB-CRL-QCD-005 Key Contacts
* UoB-CRL-SOP-002 Laboratory Facilities
* UoB-CRL-SOP-003 Sample Management
* UoB-CRL-SOP-004 Laboratory Analysis
* UoB-CRL-SOP-005 Reportable Issues
* UoB-CRL-SOP-006 External Laboratory Set-up and Oversight
* UoB-RND-SOP-001 Randomisation and Blinding
* UoB-TRN-SOP-001 Training

Note the UoB QMS documents can be found on the [CRCT website](https://www.birmingham.ac.uk/research/activity/mds/mds-rkto/governance/index.aspx). Internal work instructions can be obtained from the CRCT ([crct@contacts.bham.ac.uk](mailto:crct@contacts.bham.ac.uk)) and/or from the RGT ([researchgovernance@contacts.bham.ac.uk](mailto:researchgovernance@contacts.bham.ac.uk)).

# References and frameworks:

* Reflection paper for laboratories that perform the analyses or evaluation of clinical trial samples (2012), European Medical Agency: [www.ema.europa.eu/docs/en\_GB/document\_library/Regulatory\_and\_procedural\_guideline/2012/05/WC500127124.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2012/05/WC500127124.pdf)
* The Human Tissue Act (2004): <http://www.legislation.gov.uk/ukpga/2004/30/contents>
* The Medicines for Human Use (Clinical Trials) Regulations 2004 and amendments: <http://www.legislation.gov.uk/uksi/2004/1031/contents/made>
* UoB Contracts team: <https://intranet.birmingham.ac.uk/finance/rss/contracts/index.aspx>

# Abbreviations and definitions:

| Term | Description |
| --- | --- |
| Analyst | The person(s) that perform the analysis or evaluation of clinical trial samples. |
| Analytical manager | A named individual who oversees the analysis or evaluation of clinical trial samples and takes responsibility for the conduct and reporting of the work. |
| Analytical plan | This is a written plan that will include the purpose of the analysis and the methodology that will be used to perform the analysis. Also described as a “work instruction” or “analytical protocol” in the *Reflection paper for laboratories that perform the analyses or evaluation of clinical trial samples (2012), European Medical Agency*. It is expected that this role will be assigned to the principal investigator of the laboratory and that they will in turn delegate some of the responsibilities to other members of the laboratory’s team. |
| Blinding | Blinding is the process that keeps one or more parties involved in a clinical research project (for example, the sponsor, the investigator team, and/or the participant) unaware of what treatment arm participants have been randomised to. In relation to an investigational medicinal product, blinding is the deliberate disguising of the identity of the product in accordance with the instructions of the sponsor. |
| Clinical study | Any health related research study on humans. This includes:   * study administering questionnaires/interviews for quantitative analysis, or using mixed quantitative/qualitative methodology * study involving qualitative methods only * study limited to working with human tissue samples (or other human biological samples) and data (specific project only) * study limited to working with data (specific project only). |
| Clinical trial | For clinical trials of an investigational medicinal product(s):  Any investigation in human participants intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of one or more investigational medicinal product(s), and/or to identify any adverse reactions to one or more investigational medicinal product(s) and/or to study absorption, distribution, metabolism and excretion of one or more investigational medicinal product(s) with the object of ascertaining its (their) safety and/or efficacy. See also ‘clinical trial of an investigational medicinal product (CTIMP)’.  For all other clinical trials:  Prospective biomedical research on human participants that is conducted to allow safety (or more specifically, information about adverse drug reactions and adverse effects of other treatments) and efficacy data to be collected for health interventions. Examples include devices, surgery and radiotherapy trials. |
| Clinical trial of an investigational medicinal product (CTIMP) | Any investigation in human participants intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of one or more investigational medicinal product(s), and/or to identify any adverse reactions to one or more investigational medicinal product(s) and/or to study absorption, distribution, metabolism and excretion of one or more investigational medicinal product(s) with the object of ascertaining its (their) safety and/or efficacy. |
| Human biomaterial | For CTIMPs: samples taken from a human being to be analysed for the purposes of that clinical trial. This may include both HTA ‘relevant’ and ‘non-relevant’ material.  For clinical studies and non-CTIMP trials: samples of human tissue obtained for analysis. |
| Human Biomaterials Resource Centre (HBRC) | An ethically approved, HTA-licensed human sample biorepository at the University of Birmingham offering sample collection, processing, storage and analytical service. |
| Human tissue | Any and all constituent part/s of the human body formed by cells. |
| Laboratory | A facility that conducts manipulation, analysis or evaluation of samples collected as part of a clinical trial; such analysis or evaluation may include the generation of pharmacokinetic or pharmacodynamic data, safety data, primary efficacy data, histopathology data or data used to support any other stated primary, secondary and exploratory end point. |
| Laboratory academic lead (LAL) | Referred to as ‘Laboratory Manager’ and ‘Analytical Manager’ in the *Reflection paper for laboratories that perform the analyses or evaluation of clinical trial samples (2012), European Medical Agency*.  The individual(s) having the authority and formal responsibility for the organisation and functioning of a laboratory where work that forms part of a clinical trial is conducted.  It is expected that this role will be assigned to the principal investigator of the laboratory and that they will in turn delegate some of the duties to other members of the laboratory’s team. |
| Laboratory manual | A document containing work instructions/assay plan to ensure trial-specific sample analyses are GCP compliant. |
| Laboratory master file | A file containing evidence and documentation to demonstrate compliance with the applicable standard in the laboratory (i.e. human tissue standard or GCP in the laboratory) (see UoB-CRL-QCD-001 Setting Up a Laboratory Master File). |
| Non-CTIMP | Any clinical trial which is not a CTIMP. See also ‘Clinical trial’. |
| Randomisation | The process of assigning participants to treatment or control groups using an element of chance to determine the assignments in order to reduce bias. |
| Relevant material | As defined by the Human Tissue Act: material, other than gametes, which consists of or includes human cells, does not include embryos outside the human body, or hair and nail from the body of a living person. |
| Unblinding | The disclosure of the identity of blinded intervention/treatment. |

See also the [Glossary of Terms](https://www.birmingham.ac.uk/research/activity/mds/mds-rkto/governance/Glossary-of-Terms.aspx).