Standard Operating Procedure:

Laboratory Facilities

# Purpose:

The purpose of this standard operating procedure (SOP) is to describe procedures which will ensure that equipment within laboratories (and the laboratories themselves) are maintained sufficiently to meet the appropriate standards to allow the handling, processing, receipt, storage or analysis of samples of human biomaterials which contribute to the (primary, secondary and/or exploratory) endpoints of Clinical Trials of Investigational Medicinal Products (CTIMPs) or of human tissue for clinical studies and non-CTIMP trials.

# 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 involved in the analysis of human biomaterials (see Definitions) that contribute to the (primary, secondary and/or exploratory) endpoints of all CTIMPs whether these are sponsored by the UoB or sponsored/co-sponsored by another institution.

See ‘Decision Map’ on page 3 to determine if this SOP is applicable.

# Implementation plan:

This SOP will be implemented in line with this document’s effective date.

# Stakeholders:

* Laboratory academic lead (LAL)
* System administrator

# Background and rationale:

The Human Tissue Authority (HTA) governs the storage of ‘relevant material’ (as defined by the Human Tissue Act) for research and so dictates the standard which must be applied to their management in the laboratory. For the purposes of this SOP, human tissue which falls outside of the licensing requirements of the Human Tissue Act, for example tissue stored for less than 7 days incidental to transport or rendering acellular, will be treated in the same way as that which falls under the licensing requirements (i.e. tissue that will be stored prior to analysis), until such a time as it is either rendered acellular and so no longer considered to be ‘tissue’ or until it leaves the laboratory (see Decision Map below).

The analysis of human biomaterials (see Definitions) which contributes to the endpoints of CTIMPs is regulated by the Medicines and Healthcare products Regulatory Agency (MHRA) and must be conducted to Good Clinical Practice (GCP) in the laboratory standard as described in the [European Medical Agency (EMA) 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).

The samples collected from clinical research need to be stored in well-maintained facilities and analysed using appropriate and well-maintained equipment to ensure the data produced are accurate, reliable and in line with the study or trial protocol.

# 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 that 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.

## Laboratory maintenance

1. **The LAL (or delegate) will follow UoB procedures for waste storage, collection and disposal.**
2. **The LAL (or delegate) will create a housekeeping schedule for laboratories and equipment to be decontaminated appropriately (see** **UoB-CRL-QCD-006 Housekeeping Schedule). This will include:**

* **details of which housekeeping activities must be performed**
* **the planned frequency at which housekeeping activities must be performed**
* **the need to document decontamination.**

1. The LAL (or delegate) will arrange for an adequate degree of separation between activities and storage areas relating to human biomaterials, and their subsequent analyses and other (non-CTIMP trial) activity which may be taking place simultaneously in the same laboratory.

## Refrigerators and freezers

1. **The LAL (or delegate) will arrange for access to refrigerators and freezers used to store human biomaterials to be restricted and this access evidenced.**
2. **The LAL (or delegate) will implement temperature monitoring of refrigerators and freezers used to store human biomaterials or analytical reagents to ensure their temperature remains within defined acceptable parameters (see** **UoB-CRL-QCD-007 Temperature Monitoring):**

* **temperature monitoring records will be traceable to a particular area/equipment**
* **temperature monitoring will take place at a defined frequency**
* **equipment used to monitor temperature should be subject to periodic calibration, this process documented, and the documentation retained (see** **UoB-CRL-QCD-012 Calibration of Thermometers)**
* temperature monitoring will be either continuous (i.e. by a temperature probe and electronic system) or checked manually (see UoB-CRL-QCD-007 Temperature Monitoring) but with the presence of a minimum/maximum thermometer to confirm that appropriate conditions have been maintained between manual checks.

1. **The LAL (or delegate) will develop a documented procedure to be followed in the event of refrigerator or freezer failure (see** **UoB-CRL-QCD-008 Refrigerator or Freezer Failure Management). The procedure will include:**

* **the identification of adequate back-up space to be available in the event of refrigerator or freezer failure**
* **contact details of the person(s) responsible for assessing the impact of a refrigerator or freezer failure**
* **the need for documenting that the laboratory’s procedure has been followed in the event of refrigerator or freezer failure**
* **details of the refrigerator or freezer failure, including by not limited to: details of the failed equipment, when the failure happened, when the equipment was last known to be functioning, the identity of the samples that were affected and when they were moved to the back-up location**
* the need for confirming that an Incident Documentation Record has been completed (see UoB-CRL-SOP-005 Reportable Issues and UoB-CRL-QCD-024 Reportable Issues).

## Equipment maintenance

1. The LAL (or delegate) will confirm that any analytical equipment used in the processing and analysis of human biomaterial samples is fit for its intended use by performing user acceptance testing prior to any analyses (see UoB-CRL-QCD-009 Equipment Fitness for Use and User Acceptance Testing).

* Any tests performed will be by a suitably qualified person.
* The acceptance test criteria and definition of fit for use for each piece of analytical equipment will be defined.
* The planned frequency at which acceptance testing must be performed will be defined.
* Any tests will be documented and archived with the trial documentation (see UoB-CLN-ARC-SOP-001 Archiving).

1. The LAL (or delegate) will create an equipment maintenance schedule that will cover all equipment used in the processing or analysis of human biomaterials (see UoB-CRL-QCD-010 Equipment Maintenance Schedule). The equipment maintenance schedule will include (but not be limited to):

* unique identifiers for each piece of equipment
* calibration frequency that will follow the manufacturer’s recommendations, or in the absence of the manufacturer’s recommendations, will be determined by the LAL (or delegate)
* the need to meet national or international standards of calibration (where appropriate)
* identifying suitably qualified people to perform calibrations (for example, through servicing contracts)
* all maintenance activity will be documented and archived with the trial documentation (see UoB-ARC-SOP-001 Archiving).

1. Where calibration is performed in-house, the LAL (or delegate) will do this as detailed in *UoB-CRL-QCD-011 Calibration of Balances*, *UoB-CRL-QCD-012 Calibration of Thermometers* and *UoB-CRL-QCD-013 Calibration of Single Channel and Multi-channel Pipettes*.
2. Following servicing or maintenance, the LAL (or delegate) will check that analytical equipment remains fit for its intended use by performing user-acceptance testing prior to any analyses of human biomaterial samples (see UoB-CRL-QCD-009 Equipment Fitness for Use and User Acceptance Testing).
3. The LAL (or delegate) will ensure all analysts are trained on each piece of equipment prior to use and ensure that evidence of training and/or competency is retained (see UoB-CRL-SOP-001 Laboratory Set Up and Management, and UoB-CRL-QCD-003 Laboratory Competencies).
4. The LAL (or delegate) will clearly label any equipment that is out of service as such.

## Computerised systems

1. The LAL (or delegate) will site computerised systems in appropriate locations such that environmental conditions do not adversely impact on the systems’ performance.
2. The LAL (or delegate) will identify a person who will act as the administrator for each computer system (see UoB-CRL-QCD-014 Computerised System and User Access Levels). The administrator will:

* control access to computerised systems, and record users and their access levels (see UoB-CRL-QCD-014 Computerised System and User Access Levels)
* perform a periodic (documented) review to ensure that access restrictions remain current and appropriate.

1. The LAL (or delegate) will follow the procedures detailed in UoB-CRL-SOP-004 Laboratory Analysis in regard to the validation of computerised systems.

# List of expected outputs:

* **UoB processes for waste storage, collection and disposal followed.**
* **Housekeeping schedule in place and documented evidence of its implementation (see** **UoB-CRL-QCD-006 Housekeeping Schedule).**
* Adequate degree of separation between areas of storage and analysis of human biomaterial samples and other (non-CTIMP trial) laboratory activity.
* **Restricted access to refrigerators and freezers used to store human biomaterials and access evidenced.**
* **Evidence of appropriate refrigerator and freezer temperature monitoring (see** **UoB-CRL-QCD-007 Temperature Monitoring).**
* **A documented procedure to follow in the event of refrigerator or freezer failure, back-up space identified and evidence of implementation of procedure where necessary (see** **UoB-CRL-QCD-008 Refrigerator or Freezer Failure Management).**
* Evidence of user-acceptance testing performed on equipment used in the processing and analysis of human biomaterials (see UoB-CRL-QCD-009 Equipment Fitness for Use and User Acceptance Testing).
* An equipment maintenance schedule and evidence of equipment maintenance and calibration being performed (see UoB-CRL-QCD-010 Equipment Maintenance Schedule).
* Evidence that equipment is re-assessed for fitness for use following maintenance and calibration (see UoB-CRL-QCD-009 Equipment Fitness for Use and User Acceptance Testing).
* Evidence that analysts are trained on equipment prior to use (see UoB-CRL-SOP-001 Laboratory Set Up and Management and UoB-CRL-QCD-003 Laboratory Competencies).
* Where applicable, out-of-service equipment is labelled as such.
* Computerised systems are sited in appropriate locations such that environmental conditions do not adversely impact on the systems performance.
* Administrators identified for each computer system (see UoB-CRL-QCD-014 Computerised System and User Access Levels).
* Evidence of defined access levels for computerised systems (see UoB-CRL-QCD-014 Computerised System and User Access Levels) and evidence of their periodic review.

# Related documents:

* UoB-ARC-SOP-001 Archiving
* UoB-CRL-QCD-003 Laboratory Competencies
* UoB-CRL-QCD-006 Housekeeping Schedule
* UoB-CRL-QCD-007 Temperature Monitoring
* UoB-CRL-QCD-008 Refrigerator or Freezer Failure Management
* UoB-CRL-QCD-009 Equipment Fitness for Use and User Acceptance Testing
* UoB-CRL-QCD-010 Equipment Maintenance Schedule
* UoB-CRL-QCD-012 Calibration of Thermometers
* UoB-CRL-QCD-011 Calibration of Balances
* UoB-CRL-QCD-013 Calibration of Single channel and Multi-channel Pipettes
* UoB-CRL-QCD-014 Computerised System and User Access Levels
* UoB-CRL-QCD-024 Reportable Issues
* UoB-CRL-SOP-001 Laboratory Set Up and Management
* 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

Note the UoB QMS documents can be found on the [CRCT website](mailto:CRCT%20website). 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>

# Abbreviations and definitions:

| Term | Description |
| --- | --- |
| Calibration | A process undertaken to determine or check the range and accuracy of a piece of equipment. |
| 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. |
| Computerised system validation | The process of documenting that a computer system meets a set of defined system requirements. |
| Decontamination | The removal of microbes or non-biological contaminants. |
| 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 non-CTIMP trials and clinical studies: samples of human tissue obtained for analysis. |
| 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 research; 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 or secondary 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 in which 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. |
| Non-CTIMP | Any clinical trial that is not a CTIMP. See also ‘Clinical trial’. |
| 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. |
| System administrator | A person who is responsible for the upkeep, reliable operation and access control of computer systems. |

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