Standard Operating Procedure:

Sample Management

# Purpose:

The purpose of this standard operating procedure (SOP) is to describe procedures which will ensure that human biomaterial management within laboratories (either for clinical trials or for clinical studies) is set up and managed correctly to meet the appropriate standard ensuring that patient safety is not compromised, that data is reliable and accurately reported, and in accordance with applicable law, and with established policies at the University of Birmingham (UoB).

# Scope:

The SOP is applicable to all UoB staff involved in the analysis of human biomaterials (see Definitions) for clinical trials of investigational medicinal products (CTIMPs) whether these are sponsored by the UoB or sponsored/co-sponsored by another institution.

The SOP is applicable to 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.

See ‘Decision Map’ on page 3 below 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)

# 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 that must be applied to their management in the laboratory. For the purposes of this SOP, human tissue that 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 is 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 standards 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).

Samples collected as part of clinical research need to be managed appropriately to maintain their integrity and ensure that any analytical analyses produce results that are accurate, reliable and in line with the study protocol. Careful consideration needs to be given to the complete sample-management process, from collection, including receipt, processing, storage and analysis, and including any transfer steps.

# 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.

## Preparation and distribution of clinical sample kits (where applicable)

Some laboratories or departments may prepare and dispatch clinical sample kits to sites. Where this is the case the points listed below will be followed.

1. The LAL (or delegate) in liaison with the chief investigator (CI) will set up robust processes to ensure sites order sample kits in a timely fashion.
2. The LAL (or delegate) will arrange for a designated area for the preparation of clinical sample kits (and the storage of components thereof), which will be large enough to allow an adequate degree of separation between this and other activities.
3. The LAL (or delegate) will develop a monitoring schedule for areas where clinical-sample-kit components are stored to confirm their integrity is maintained (see UoB-CRL-QCD-006 Housekeeping Schedule).

* This will include, for example, monitoring the temperatures of any refrigerators or freezers used to store clinical-sample-kit components (see UoB-CRL-QCD-007 Temperature Monitoring)*.*

1. The LAL (or delegate) will create a ‘sample kit preparation and dispatch record’ (see for an example UoB-CRL-QCD-015 Clinical Sample Kits), this will include:

* the components to include in a clinical sample kit
* documented quality checks to perform, for example
* reviewing expiry dates of components
* confirming the correct components are present in the clinical sample kit
* the need to document who prepared the clinical sample kits.

1. The LAL (or delegate) will make appropriate provisions for the resupply of clinical kits at short notice, for example, if a component is found to be faulty or is recalled by the supplier.

* Consider assigning a stock level ‘trigger number’ to each clinical kit component which, if reached, would instigate more of the component to be ordered.

1. If it becomes necessary to source a product from a different supplier, the LAL (no delegation allowed) will assess the need for cross validation of the product.

## Consent

1. **The** **LAL (or delegate) in liaison with the CI (if UoB sponsored) or sponsor (if externally sponsored) will establish a process for laboratory staff to confirm that full and appropriate consent was obtained for any given sample.**

* **Where samples are moved under the ethical approval of another trial/study, consider filing a blank copy of all relevant versions of the patient information sheet and consent form under which the samples were originally collected in the laboratory master file along with details of the original REC number.**

1. **The LAL (or delegate) will agree a communication plan for confirmation of consent with the trial team at trial set up. This will include:**

* **how the laboratory will be informed of consent being obtained**
* **who the laboratory should contact for any queries regarding consent**
* **the need to file the communication plan in the ‘Consent’ section of the Laboratory Master File (LMF) (see** **UoB-CRL-QCD-001 Setting Up a Laboratory Master File).**

1. **The LAL (or delegate) will set up a process to capture confirmation of consent in the laboratory.**

* **This will include how laboratory staff will document their review, e.g. on a worksheet.**

1. **The LAL (or delegate) will ensure that contact details are completed in the Key Contacts form (see** **UoB-CRL-QCD-005 Key Contacts) to allow the LAL (or delegate) to address any issues of consent with the originating site in a timely manner.**
2. **The LAL (or delegate) will develop a documented procedure for participant withdrawal from the trial, where the participant wishes for their samples and/or data to be removed (see** **UoB-CRL-QCD-016 Managing Withdrawal of Consent in the Laboratory). The procedure will include the points listed below.**

* **A clear description of lines of communication between the laboratory, the sites responsible for enrolling participants and the CI (if UoB sponsored) or Sponsor (if externally sponsored).**
* **The laboratory specific processes to be followed when a participant withdraws their consent, including:**
* **how the laboratory will be informed of consent being withdrawn**
* **how samples should be destroyed, for example via a clinical waste route**
* **where analytical data will be stored and who has access.**
* **A clear description of how the removal (and destruction) of samples and/or data will be documented and whether confirmation of removal (and destruction) must be sent to site and/or coordinating centre.**
* **The need to store the procedure for participant withdrawal in the ‘Consent’ section of the laboratory master file (LMF) (see** **UoB-CRL-QCD-001 Setting up a Laboratory Master File).**

## Sample receipt into the laboratory

1. **The LAL (or delegate) will set up processes for samples to be transported to the laboratory in such a way as to preserve their integrity and viability (see** **UoB-CRL-QCD-017 Sample Transport) which will include, but will not be limited to:**

* **sample information, including type of sample and quantity**
* **transport information, including type of transport, time in transit, dispatch and destination addresses**
* **measures to ensure sample integrity, including temperature monitoring and packaging requirements.**
* **the transport of samples will meet all biological safety requirements, see the** [**University of Birmingham Biological Safety webpage**](https://intranet.birmingham.ac.uk/hr/wellbeing/worksafe/biological/index.aspx) **or contact your local shipping advisor.**

1. **The LAL (or delegate) will ensure that a material transfer agreement (MTA) is in place for incoming samples. The LAL (or delegate) will work with the** [**UoB Contracts Team**](https://intranet.birmingham.ac.uk/finance/rss/contracts/index.aspx) **to set up an MTA for outgoing samples.**
2. **The LAL (or delegate) will develop a sample receipt form to be used when receiving samples into the laboratory (see** **UoB-CRL-QCD-*018 Sample Receipt, Labelling, Tracking and Storage*). The aspects listed below will be included.**

* **The need to record details of the samples, including type, identification and originating site.**
* **Checking the physical integrity of the sample.**
* **Where samples require temperature-controlled transport, checking that these conditions were maintained.**
* **Ensuring that all samples are accounted for.**
* **Confirming that no patient identifiers are present on the sample (unless this is in compliance with the protocol and explicit consent has been obtained for this).**
* **Confirmation that samples have been accepted into the laboratory or whether the process for damaged, unexpected or mislabelled samples was followed (see** **UoB-CRL-QCD-019 Processing of Damaged, Unexpected or Mislabelled Samples).**
* **Confirmation of samples’ receipt with the sender of the samples to ensure complete sample traceability.**
* **The need to document that the above steps have been followed.**
* **Documented checks of the use of sample receipt forms will occur.**

1. **The LAL (or delegate) will create a documented procedure for the processing of damaged, unexpected or incorrectly labelled samples (see UoB-CRL-QCD-019 Processing of Damaged, Unexpected or Mislabelled samples). The aspects listed below will be included.**

* **The need to store, but not analyse, samples until confirmation of sample ID is received.**
* **Action to be taken in the event that the sample ID cannot be confirmed.**
* **Action to be taken in the event that damaged samples may pose a biological safety risk.**
* **Who should be contacted in the event of receiving damaged, unexpected or incorrectly labelled samples.**
* **In the event that a delay in analysis would compromise the viability of the sample, it will be processed as per standard work instructions but the results quarantined until the identity of the sample is confirmed. If the sample cannot be identified the results should not be reported.**
* **Who will authorise closure of the incident.**
* **The need to document the steps followed for each incorrectly labelled sample received.**

1. The LAL (or delegate) will ensure that where samples from blinded trials are handled by the laboratory, processes are in place to prevent inadvertent compromise of the blind (see UoB-RND-SOP-001 Randomisation and Blinding and UoB-CRL-SOP-001 Laboratory Set Up and Management for further information).

## Sample traceability and storage

1. **The LAL (or delegate) will create a sample management plan (see UoB-CRL-QCD-018 Sample Receipt, Labelling, Tracking and Storage) that will include (but not be limited to):**

* **sample labelling**
* **sample storage (see** **UoB-CRL-SOP-002 Laboratory Facilities)**
* **tracking of all samples and their derivatives through receipt into the laboratory, storage, analysis, transfer out of laboratory, and/or destruction**
* **periodic documented checks of the tracking system, for example, a vertical sample audit, whereby a sample is traced from its arrival into the laboratory through any processing to analysis or storage.**

# List of expected outputs:

* Information relating to the contents, destination and quantity of clinical sample kits appropriately shared with recruiting sites (see UoB-CRL-QCD-015 Clinical Sample Kits), if applicable.
* Designated area for the preparation of clinical sample kits.
* Monitoring schedule for clinical sample kit preparation and storage areas and evidence of its use (see UoB-CRL-QCD-006 Housekeeping Scheduleand UoB-CRL-QCD-007 Temperature Monitoring).
* A clinical sample kit preparation and dispatch record and evidence of its use (see UoB-CRL-QCD-015 Clinical Sample Kits), if applicable.
* Evidence that components of clinical kits can be re-supplied at short notice, if applicable.
* **A process for laboratory staff to confirm appropriate consent was obtained for each sample and evidence of its implementation.**
* **A documented procedure for withdrawal of consent (see UoB-CRL-QCD-016 Managing Withdrawal of Consent in the Laboratory) and evidence of its implementation, where applicable.**
* **Evidence that samples are transported to the laboratory correctly (see UoB-CRL-QCD-017 Sample Transport).**
* **Use of a sample receipt form (that includes all the quality checks listed in ‘Procedure’) when samples are received into the laboratory (see UoB-CRL-QCD-018 Sample Receipt, Labelling, Tracking and Storage).**
* **A documented procedure for the processing of damaged, unexpected or incorrectly labelled samples (see UoB-CRL-QCD-019 Processing of Damaged, Unexpected or Mislabelled Samples) and evidence of its implementation, where applicable.**
* **A tracking system to allow sample traceability (see UoB-CRL-QCD-018 Sample Receipt, Labelling, Tracking and Storage) and evidence of its implementation.**

# Related documents:

* UoB-CRL-QCD-001 Setting Up a Laboratory Master File
* UoB-CRL-QCD-005 Key Contacts
* UoB-CRL-QCD-006 Housekeeping Schedule
* UoB-CRL-QCD-007 Temperature Monitoring
* UoB-CRL-QCD-015 Clinical Sample Kits
* UoB-CRL-QCD-016 Managing Withdrawal of Consent in the Laboratory
* UoB-CRL-QCD-017 Sample Transport
* UoB-CRL-QCD-018 Sample Receipt, Labelling, Tracking and Storage
* UoB-CRL-QCD-019 Processing of Damaged, Unexpected or Mislabelled Samples
* UoB-CRL-SOP-001 Laboratory Set Up and Management
* UoB-CRL-SOP-002 Laboratory Facilities
* 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

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>
* UoB Contracts Team: <https://intranet.birmingham.ac.uk/finance/rss/contracts/index.aspx>
* UoB Biological Safety: <https://intranet.birmingham.ac.uk/hr/wellbeing/worksafe/biological/index.aspx>

# Abbreviations and definitions:

| Term | Description |
| --- | --- |
| 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 participants) 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 sample kit | The necessary components required to collect clinical samples prior to their analysis or evaluation in a laboratory. |
| 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 | 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 clinical trials: 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: 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 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 master file (LMF) | 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 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. |

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