Sample Collection SOP

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Implementation plan

This Standard Operating Procedure (SOP) should be followed for all applicable studies that are being set up at the time the SOP is implemented.

For ongoing studies, applicable sections of this SOP should be followed as far as possible after the implementation date. Otherwise, e.g. when the study is approaching the end, the SOP used before this SOP was implemented should be followed to avoid disruption and maintain continuity.

If unsure, the Trial Portfolio Leads and/or Quality Assurance Manager should advise.

Note to User:

It is your responsibility to ensure you are using the latest approved version of this SOP. Please note that versions may be superseded before their planned review date.

THIS IS AN UNCONTROLLED VERSION WHEN PRINTED.

If you are reading this document in printed form, please check that the version number and date match the most recent SOP's details. Current versions of all Bristol Trials Centre (BTC) SOPs and accompanying documents are available on the BTC Teams Quality Assurance channel.

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1. PURPOSE

To produce good quality data, it is important that all samples/reagents are stored and processed in an appropriate and consistent manner, all laboratory procedures and data are reliably recorded, and all equipment is maintained and fit for purpose.

The purpose of this SOP is to describe the BTC procedures to be followed during study set-up, study conduct and study closedown for a research study which involves the storage and/or analysis of biological samples/reagents collected for the purpose of the study. This is to comply with Good Clinical Practice (GCP) for laboratories (Medicines and Healthcare products Regulatory Agency (MHRA) Guidance on the maintenance of regulatory compliance in laboratories that perform the analysis or evaluation of clinical trial samples (July 2009)).

2. SCOPE

This SOP applies to all studies coordinated by BTC with research samples/reagents. It applies to any personnel involved in the development or implementation of laboratory procedures.

The Chief Investigator (CI) must be made aware of this SOP and as a minimum, be signposted to the SOP by BTC.

The SOP is only concerned with GCP for laboratories and does not cover Good Laboratory Practice.

“Research study” (or “study”) refers to health and social care-related research projects (interventional trials or observational studies) involving people, samples and/or data, that are aimed at evaluating a medical, surgical, or behavioural intervention, or studying health related outcomes and/or groups of people defined by a health condition or intervention. It includes Clinical Trials of Investigational Medicinal Products (CTIMPs) or advanced therapy medicinal products or medical devices.

3. DEFINITIONS

For all definitions, common acronyms and abbreviations refer to the BTC-RES-TM-001 Definitions and Acronyms available on the BTC Teams, Quality Assurance channel.

4. RESPONSIBILITIES

Any delegation of responsibilities should be formally agreed by all parties and clearly documented.

4.1. Sponsor(s) or delegate

It is the responsibility of the sponsor(s) (or delegate) to:

- Ensure that laboratories conducting analyses of research samples comply with the principles of GCP;

- Ensure that any relevant approvals (e.g. Research Ethics Committee (REC), Health Research Authority (HRA)) are in place prior to the collection of any research samples;
- Ensure all research samples are appropriately handled, labelled and stored correctly throughout the duration of the study;
- Ensure all research samples are returned, destroyed or transferred to a biobank at the end of the study in line with relevant approvals and consent.

4.2. Chief Investigator (CI) or delegate

It is the responsibility of the CI (or delegate) to:

- Ensure the study protocol accurately describes the type and quantity of samples to be collected during the study and where necessary describes the procedures required to obtain and store the samples;
- Ensure there are appropriate facilities in which to securely store research samples/reagents and where required, a temperature controlled environment;
- Ensure that there is an appropriate process in place to ensure that all equipment and reagents used in the analysis of research samples are fit for purpose and documented accordingly.

4.3. Principal Investigator (PI)

It is the responsibility of the PI to:

- Ensure that tasks performed at local participating sites are delegated appropriately and that local staff at sites are trained in the requirements pertinent to the research samples;
- Ensure that the study protocol and any supporting materials related to the procedures required to obtain, store and transfer the samples are followed at their site.

4.4. Bristol Trials Centre, University of Bristol

It is the responsibility of the BTC to:

- Ensure that appropriate study specific working instructions or laboratory manuals are in place to cover any study specific aspects of the sample collection, labelling, receipt, storage, analysis and transfer (if applicable, e.g. to a tissue bank at the end of study) or destruction of research samples;
- Ensure that the receipt, storage, analysis and destruction or transfer of the research samples are documented in an appropriate manner;
- Ensure that a study specific laboratory site file is set-up (see BTC-TEMP-LAB-002).
- Assist laboratory staff in meeting GCP standards if sample analysis is an endpoint of a study;
- Ensure that there is an appropriate process in place to ensure that appliances used to store temperature sensitive research reagents/samples are monitored appropriately.

4.5. SOP Author(s) or delegate

It is the responsibility of the SOP author(s) (or delegate) to:

- Generate, finalise, and release the SOP;

- Ensure that the SOP remains fit for purpose;
- Ensure that the SOP is reviewed and amended as required;
- Provide relevant training and education materials to ensure that staff are aware of their responsibilities in relation to SOP content and management.

4.6. SOP user

It is the responsibility of the SOP user to:

- Ensure compliance with this document.
- Review procedures during use of the SOP and inform the author of any changes required.
- Undertake training on all aspects of this SOP and record training on the BTC Teams Quality Assurance channel.

5. SPECIFIC PROCEDURES

5.1. Contracts and agreements

Prior to initiation of any laboratory work, there should be a clear agreement that the laboratory has agreed to perform the analysis or evaluation of research samples. See BTC-SOP-TM-001 Study Start-Up for further information on third party contracts.

5.2. Study Initiation

At the start of a new study which involves the collection, receipt, processing, storage or destruction of research samples in a study conducted by the BTC, a study specific laboratory file must be set up (see BTC-TEMP-LAB-002).

All analyses to be completed on samples collected for the study must be agreed and documented in advance. Any subsequent changes to these analyses must be discussed with the study coordination team and documented before implementation. All analyses must comply with the study protocol, ethical approval and participant consent form.

A study specific research sample receipt and storage log (BTC-TEMP-LAB-006) must be generated and maintained throughout the study. BTC-TEMP-LAB-006 may be used as an example sample receipt and storage log.

5.3. Study Specific Work Instructions

Study specific working instructions are not required for any procedures/analysis that are considered to be part of routine clinical care. Any other procedures/analysis should be described in study specific working instructions or the laboratory manual.

These may include:

- Sample transport - this should be considered in cases where samples need to be transported within a certain timeframe or under specific conditions (e.g. on ice or out of sunlight);
- Reporting methods;
- Sample collection and labelling, for example, when blood samples must be taken in a particular order, or at multiple or specific timepoints;
- Aliquot labelling; this should be considered where samples may be stored long term.

Work instructions should include clear criteria to identify breaches which may have an effect on sample/analytical integrity. Before the study begins it should be agreed how and when laboratory staff will report any breaches and who is responsible for recording and reviewing breaches.

6. Sample Labelling, Receipt, Storage and Destruction

6.1. Labelling

The research sample should be taken/collected according to the study working instructions or following the processes described in the study protocol or laboratory manual.

Once the sample has been collected it must be clearly labelled at the earliest opportunity. The label should preferably not obscure the entire sample. Appropriate labels should be used according to the conditions the samples will eventually be stored under (e.g. Cryovial labels should be used for samples being stored at -80°C).

Personal identifiable information (e.g. patient name, date of birth, NHS Trust number etc.) should not be used on any stored samples and if they are, they should be masked at the earliest opportunity.

Personal data may appear on samples that are going to a hospital-run laboratory if sample will be processed immediately, and where the original sample container is not used for long term storage.

In the case of studies where the assessor, laboratory personnel and/or the participant are blinded to the intervention the sample label must not contain any information that could lead to unblinding of the allocation.

All containers used in a study must be clearly labelled, ideally with three identifiers, for example:

- Study ID;
- Date and time sample was taken;
- Sample time point.

It is advisable to also include the study name/acronym, and sample type on the sample label.

Containers used for storing single or multiple samples should be labelled with:

- Name of Principal Investigator;
- Contact name and telephone number of the study co-ordinator;
- Study Acronym and/or an official identifier such as IRAS ID.

Study identifiers are increasingly being incorporated into barcodes. Barcode labels are usually supplied by the laboratory or biobank that will be storing the samples. In some cases pre bar-coded tubes may be supplied which can also be used. Barcode labels are supplied on a roll where each barcode is produced in duplicate; one barcode label should be attached to the sample and the matching label should be attached to the study paperwork. Care should be taken to ensure that the barcode attached to the sample matches that on the participant's study paperwork.

6.2. Sample Transportation

Samples must be transported in a way that maintains their viability and integrity. Transport conditions should be specified in the protocol or study specific working instructions/manual (e.g. blood samples should be transported around the hospital in a sealed container (packed in such a way that leakage cannot occur in transit, labelled in an appropriate regulatory manner) or samples may have to be transported on ice). The University of Bristol guidance on transporting biological material provides further information.

Transportation time and conditions where applicable should be recorded.

Where samples are required to be refrigerated or frozen during transit between sites and/or laboratories, temperature monitoring should be implemented to confirm appropriate conditions are not breached. For CTIMPs this is a legal requirement.

6.3. Receipt of Samples

On receipt of any samples into the laboratories, staff should check that the research sample has arrived as expected. It should be of the correct sample type (e.g. blood or biopsy tissue), correct quantity and the sample should have arrived under the correct transport conditions. If an issue is identified, the study team should be notified and appropriate action should be taken.

Staff should also make sure that the research sample is correctly labelled. If there is a problem with the sample see section 6.6 Dealing with Ambiguous and Unlabelled Samples.

On receipt of samples, the samples should be logged into a study specific research sample receipt and storage log, recording date and time of arrival. (e.g. BTC-TEMP-LAB-006).

6.4. Storage of Samples

Human tissue samples must be stored in a secured facility in secure buildings accessible only to authorised personnel.

The storage conditions for research samples should be specified in the protocol or study specific working instructions/manual. If the research samples have to be moved at any time during the study, the study specific sample receipt and storage log must be updated.

Throughout the duration of the study, the temperature conditions of the storage facility where the research samples are stored should be monitored as described in 9.2 Temperature monitoring of laboratory appliances.

There should be a process in place covering monitoring of the storage facility (e.g. refrigerator or freezer temperatures) and the actions to be taken in the event of a temperature excursion. If a temperature breach occurs the study team should be notified and appropriate action should be taken. The laboratory should make appropriate provision for the storage of samples in the event of a refrigerator or freezer failing. A record of the temperature breach should be documented and kept in the study specific laboratory site file.

6.5. Destruction of Research Samples

According to the Human Tissue Act, any “relevant material" means material, other than gametes, which consists of, or includes human cells. This would include any organs, tissues, whole blood and bodily waste material.

Samples containing “relevant material” may be stored for up to one year after the end of study notification has been submitted to the REC (see BTC-SOP-TM-003 Study Closedown). After this period, samples must only be retained if they are stored in facilities licenced by the Human Tissue Authority or subsequent REC/HRA approvals have been obtained. Sample storage must be in accordance with the study protocol and with respect to what is recorded on the participant consent form. The consent form must be retained for the entire duration the sample is stored.

Guidance and information about what is covered by the Human Tissue Act and regulated by the Human Tissue Authority (HTA) is provided on the HTA website.

Samples that are not covered by the Human Tissue Act, which include serum and plasma, may be retained for further research purposes without holding an HTA license as long as appropriate consent is maintained.

If further research is to be carried out on any research samples, participants will have had to already have consented to their samples being used in further research and REC / HRA approval for the further analysis may also be required.

When samples are destroyed or used for analysis, the study specific sample receipt and storage log must be updated. Samples must be destroyed appropriately, and technical staff will provide advice about the correct procedures to follow.

Samples may also need to be destroyed in cases where a participant withdraws completely from a study or withdraws consent for samples to be held or used for further research.

6.6. Dealing with Ambiguous and Unlabelled Samples

Samples bearing no identification should not be accepted for analysis, and the study team should be informed.

Samples that are incorrectly or inadequately labelled but can be unequivocally identified must be relabelled according to section 6.1 Labelling. If a research sample is incorrectly labelled inform the study team so further training on how to label research samples correctly can be provided.

Samples which are ambiguously labelled should not be analysed until their identity can be confirmed, except for cases where this would compromise the sample results, e.g. due to sample degradation). In these cases samples can be analysed, but results must be quarantined until the sample identity is confirmed.

If a sample is transported incorrectly or there has been any other deviation to the protocol, the sample may need to be destroyed. If the sample can still be used for analysis, it should be retained but actions should be taken to prevent further breaches e.g. re-training of staff transporting sample.

Any breaches affecting sample quality should be reported to the coordinating study team and recorded in the study specific laboratory file and also.

6.7. Preparation of Sample Kits

Where sample kits are prepared 'in house' the expected contents of each kit should be documented. If these are to be sent to participating research sites, the shipment details and number of kits sent should be recorded. A method of tracking sample kits that are delivered and/or returned to sites and expiration dates of kit components should be considered.

7. Sample Analysis

7.1. Method Validation

All analytical methods used in the analysis of research samples should be appropriately validated. This includes assays using manufacturer-validated kits (with the exception of when validation of a method is a study objective).

The validation of methods should ensure that the assay delivers consistent results and is repeatable between users (if necessary). If it is proposed that samples will be frozen prior to analysis, it should be demonstrated and documented that the freeze-thaw cycle has no impact on results. The number of replicates required for analysis should also be determined. Rationale should be provided if samples are to be analysed in less than triplicate.

During validation of analytical methods, the criteria by which an assay is deemed to pass or fail should be determined and documented. For example, an assay may fail if the quality control samples deliver results which are above or below a pre-determined range.

Evidence of assay validation must be documented before study samples are analysed.

7.2. Repeat Analysis

Circumstances where a sample may undergo repeat analysis should be clearly documented, for example, when the assay fails to meet the documented assay acceptance criteria. Repeat analysis must only be done in these circumstances. The rationale for repeating the analysis and the person who authorised the repeat analysis should be clearly documented.

8. Recording Results

8.1. Processing Raw Results

An analysis plan for processing raw data should be documented. Each stage of processing should be risk assessed to ensure data integrity. This should be completed before analysis of samples begins. The following may be considered:

- Secure transfer of raw data – for example, where raw data needs to be transferred from equipment to personal computers for analysis. Care should be taken to ensure files cannot be corrupted. Where possible, transfer should take place using online secured folders (for example, OneDrive or SharePoint). Use of USB sticks should be avoided.
- Standardised analysis of data – in any cases where raw data requires processing (for example, use of a standard curve to convert an optical density to a concentration) an analysis plan should be considered to ensure consistency of processing. Tools to ensure consistency, such as a template excel file with locked formulae may be appropriate.
- Traceability of raw data – secure storage of the raw data file(s), i.e. the initial file produced before any processing, should be considered.

8.2. Results Reporting

Reporting of results should be agreed before samples are analysed. The method and frequency of reporting may be detailed in the study specific work instruction/manual. If data is to be provided directly to the study team (for example, in a spreadsheet) the format of results should be agreed with the study statistician in advance.

Expedited reporting of results which may be clinically significant should be agreed with the Sponsor and investigator in advance.

For blinded studies, care should be taken to ensure the integrity of the blind. If there is any risk of analytical results unblinding the study team, this must be mitigated by establishing an unblinded point of contact for transferring results.

9. Maintenance of Laboratory Equipment and Consumables

9.1. Equipment Maintenance

All equipment should be maintained according to the instruction in the User Manual. There should be an appropriate process to ensure that laboratory equipment is serviced and/or calibrated annually or as required. Documentation of servicing/calibration must be retained.

9.2. Temperature Monitoring of Laboratory Appliances

Appliances such as fridges or freezers used for storage of clinical study samples must be monitored using suitable calibrated equipment to ensure temperature deviations do not impact on integrity of samples stored. Appliances may be monitored by an automated system or manually using paper forms or electronic documents. Proof of calibration should be retained with the monitoring data.

There must be a process in place covering monitoring of refrigerator and freezer temperatures, and the actions to be taken in the event of a temperature excursion.

Similarly, if automated temperature monitoring systems are being used, these will be reviewed as appropriate to ensure that the storage area temperatures have remained within the specified temperature ranges and the checks should be recorded.

9.3. Temperature Deviation

If any of the recorded temperatures are outside the specified temperature ranges, allow sufficient time for temperature to be restored in the affected appliance and re-record temperature.

If a substantial temperature breach occurs (i.e. a breach that could affect the viability of the reagents/samples) the study team must place a note to file in the study specific laboratory site file and then follow any study specific procedures.

SUPPORTING DOCUMENTS

Number	Title
BTC-RES-TM-001	Definitions, Acronyms and Abbreviations Relevant to Research Projects and Management of Research
BTC-TEMP-LAB-002	Lab Site File Contents – Study Specific File
BTC-TEMP-LAB-006	Study Specific Sample Receipt and Storage Log
BTC-SOP-TM-003	Study Closedown SOP

CHANGE HISTORY

Previous version and date	New version and date	Summary of review
NIL	V1.0, 18/06/2024	New document