York and Scarborough Teaching Hospitals NHS Foundation Trust R&D Unit
SOP
R&D/S94

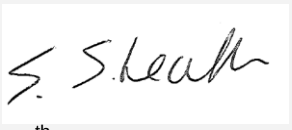
Submitting Research Samples for Laboratory Processing

IT IS THE RESPONSIBILITY OF ALL USERS OF THIS SOP TO ENSURE THAT THE CORRECT VERSION IS BEING USED

All staff should regularly check the R&D Unit's website and/or Q-Pulse for information relating to the implementation of new or revised versions. Staff must ensure that they are adequately trained in the new procedure and must make sure that all copies of superseded versions are promptly withdrawn from use unless notified otherwise by the SOP Controller.

The definitive versions of all R&D Unit SOPs appear online. If you are reading this in printed form check that the version number and date below is the most recent one as shown on the R&D Unit website: https://www.research.yorkhospitals.nhs.uk/sops-and-guidance-/ and/or Q-Pulse

SOP Reference:	R&D/S94
Version Number:	4.0
Author:	Jack Pearce & Megan Worthington
Implementation date of current version:	16th September 2021

Approved by:	Name/Position:	Lydia Harris, Head of R&D
	Signature:	
	Date:	19th August 2021
	Name/Position:	Sarah Sheath, SOP Controller
	Signature:	
	Date:	19th August 2021

This SOP will normally be reviewed at least every 3 years unless changes to the legislation require otherwise

Version History Log

This area should detail the version history for this document. It should detail the key elements of the changes to the versions.

Version	Date Implemented	Details of significant changes
1.0	22nd January 2018	
2.0	8th April 2019	Change of link to R&D website. Update of equipment list
3.0	15th July 2020	Removal of equipment list; information available in R&D/S41. Reference to R&D/T60, R&D/S35 and R&D/F73 added. Reference to R&D/F24 removed; document no longer in use. Shipping considerations have been made more generic instead of specifically applying to the DHL courier service. Minor formatting and grammatical changes. Minor rewording to clarify information and procedures.
4.0	16th September 2021	Addition and removal of areas to bring up to date. Change to Trust name.

Contents

1 Introduction, Background and Purpose

As part of a research study, there may be a requirement to collect research samples. It is the responsibility of the Research and Development (R&D) Laboratory Team (or designated Laboratory personnel) to ensure that these samples are received, processed, stored and shipped in accordance with the study Protocol and Laboratory Manual, Good Clinical practice (GCP) and local Laboratory practices.

Laboratory work performed as part of a clinical research study varies depending on the nature and purpose of the trial. A wide range of activities are carried out which generate data used to monitor research participant safety, assess pharmacokinetic parameters and to measure end points. It generates data that is used directly or indirectly to make decisions related to patient care, and the safety and efficacy of investigational medicinal products (IMP). Consequently, it is of paramount importance that the samples are handled, processed and analysed to acceptable standards so that patient safety is not compromised, and that the data produced is reliable and accurately reported.

Routine inspections are carried out by the Medicines & Healthcare products Regulatory Agency (MHRA), who have responsibility for monitoring Laboratories that perform work in support of clinical trials. All laboratories that support clinical trial delivery are required to implement measures to ensure quality and integrity of the research samples processed, and therefore the data produced. Due diligence should also be exercised to ensure trial participant rights are not compromised.

The purpose of this SOP is to describe the process for receiving, processing, storing and shipping research samples. This SOP should not be used when processing samples via the standard care pathway.

2 Who Should Use This SOP

This SOP should be used by the Trust's R&D Laboratory staff involved in receiving, processing, storing and/or shipping research samples; and Research Teams involved in studies where research samples are sent to the Trust's Laboratories.

3 When this SOP Should Be Used

This SOP should be used when the Trust's Laboratory is involved in receiving, processing, storing and/or shipping research samples.

The Trust's Laboratory may also be involved in developing analytical assays or carrying out evaluations using clinical trial samples. This SOP does not cover performing the analysis or evaluation of human samples collected as part of a clinical trial. Requests for any such work should be considered on trial by trial basis, and appropriate written procedures implemented.

4 Procedure(s)

All study samples that go through the Trust's Laboratory should have a complete chain of custody clearly documented. The procedures below have been put in place to ensure that this is documented.

4.1 Personnel and Training Records

All staff involved in work performed in support of clinical trials should receive GCP training commensurate with their roles and responsibilities. Staff must have an adequate understanding of GCP requirements relating to patient safety, informed consent, confidentiality, integrity and validity of trial data. Periodic GCP refresher training is required following changes to regulations and associated guidance documents, or routinely (every 3 years as a minimum).

Laboratory staff should complete appropriate levels of technical training, prior to participating in work supporting clinical trial research, to ensure that they are competent to perform the techniques required by the Protocol and Laboratory Manual. Roles and responsibilities related to clinical research work for each individual study, should be agreed and documented prior to initiation of the study, with the completion of Training Logs and Study Delegation of Duties Logs.

Each staff member involved in handling clinical trial samples must have an up to date Training File to record all training. A copy of this information must be retained when staff leaves the organisation.

4.2 Sample Receipt and Processing

Sample Receipt

Once collected, the Research Team should bring the research sample(s) directly to the R&D Laboratory Team (or a designated Laboratory staff member) as quickly as possible, or within the agreed time frame, with the correct kits and/or documents. Samples must be transported from the clinical area to the Laboratory in such a way that their integrity and viability remains unaffected (e.g. at the correct temperature and within the correct time period). Research samples should be anonymised at the clinical site before they are received by the laboratory (where applicable).

It is the responsibility of the Research Team to ensure that the R&D Laboratory Team (or designated Laboratory personnel) have been informed in advance, and they are aware of the arrangements made or any agreements in place before the sample is collected. It is best practice for a Research Team member to speak directly to Laboratory personnel, in person or via telephone, to confirm the arrangements on the day of sample collection. The sample(s) must be clearly identifiable as research samples. As a minimum, the following information should be included on the requisition form or in a separate document accompanying the sample(s);

- The name and contact number of the Healthcare Science Associate Practitioner (or a designated staff member) whom the sample is for the attention of
- The clinical trial name
- The name and contact number of the member of staff who dropped the sample off
- The time the sample was left at specimen reception

Upon receipt of the research sample(s) the R&D Laboratory team member (or designated Laboratory staff) should assess sample integrity, and determine whether the correct sample has been received for the specific study and visit (as per the study specific Protocol/Laboratory Manual or laboratory specific instructions/SOPs). Staff should also ensure all documents and labelling have been completed accurately. If samples are not present or labelled correctly, the relevant team must be contacted as soon as possible to notify them of any deviations from the Protocol.

Generally all samples must be labelled with a minimum of 3 identifiable criteria to ensure patient safety. If a sample is not sufficiently labelled then the sample must be rejected constituting a deviation which must be reported to the relevant contacts: the study sponsor, study PI and the responsible Research Nurse and the R&D Quality Assurance via research.governance@york.nhs.uk

The specimen Receipt Log (R&D/F51) must be completed to document the receipt of samples; study specific documents may also need completing. All research samples that are processed by the Trust Laboratory should have a clearly documented chain of custody, to track the movement of each individual sample from arrival to shipment (or disposal), sample(s) must therefore be uniquely identified.

Research Teams are responsible for informing Laboratory personnel in a timely manner if a patient withdraws consent to participate in a research study. This is crucial to ensure that research samples are not processed and/or shipped for analysis without a valid written consent from a patient.

Sample Processing

Research samples must be processed by appropriately trained Laboratory Research Staff (or designated Laboratory staff), in accordance with the clinical trial Protocol, Laboratory Manual, or laboratory specific instructions/SOPs, which will detail specific sample volume, consumables/kits, timelines and conditions for collection, processing, storage and shipping.

Laboratories should not perform any work on clinical trial samples that are not specified in the Protocol. If additional work is requested by the Sponsor or their representative all relevant documentation must be amended prior to the initiation of any additional work. See R&D/S78 for details on processing and implementing amendments within the R&D Laboratory team.

Staff training for each individual study should be documented in the Staff Signature & Training Log (R&D/F73). All lab staff who will be working on the trial must complete the log to indicate thy have read the appropriate training documentation and are competent. It is the responsibility of the HSAP whom is assigned to that care group to ensure all necessary staff have signed on. The Sponsor may require specific aspects of sample processing to be documented (e.g. time sample taken, time received by the laboratory). Any requirement of sample processing will be clearly documented in the Protocol, Laboratory Manual or clinical trial specific instructions/SOPs, and should be appropriately communicated to the research teams. Where deviations occur (such as the red cell layer being disturbed when making plasma aliquots) the R&D Laboratory Team member (or a designated Laboratory staff) **must** take immediate and appropriate action (see section 4.5).

Copies of all requisition forms must be retained within the relevant section of the research laboratory investigatory site file (ISF). In addition, study specific documents may need completing.

All equipment used for research sample processing, must be adequately tested, calibrated and maintained to a standard that will not compromise the integrity of the samples. Records of this must be kept and be available for inspection.

4.3 Sample Storage, Shipping and Destruction (Where Applicable)

Sample Storage

At the outset of each study, it should be established if there is a requirement for samples to be stored (as defined by the Protocol, Laboratory Manual or clinical trial specific instructions/ SOPs), and if required whether there is sufficient capacity for the duration of the clinical trial. Trial-specific procedures detailing specific storage conditions and the actions to be taken following failure of storage units (including information about who should be notified, how and where samples may be transferred to) must be agreed at the outset of each study.

If sample storage is required, the R&D Laboratory Team (or a designated Laboratory staff member) should allocate a suitable storage location.

Sample storage areas must be adequate, and sample storage units (secure laboratories, incubators, freezers and fridges) must be monitored for compliance (temperature monitoring), and maintained and serviced regularly. Temperature and service/maintenance records must be stored safely and available for inspection. Equipment used to monitor temperature must be subject to periodic calibration. It is recommended that clinical trial sample storage areas should be kept separate, clearly labelled, secured, and restricted to relevant personnel.

Sample storage must be documented in the Specimen Location Log (R&D/F32) and where appropriate the Storage Box Sample Location Log (R&D/T60).

Sample Transfer

Every attempt should be made to retain samples in the assigned location, however, if samples are moved from their storage location this must be documented on the Specimen Location Log (R&D/F32). Samples may need to be transported to another location for a number of reasons, including longer-term storage (moving from a -20^{o}C unit to a -80^{o}C unit), equipment maintenance (routine total unit defrost) or unit failure.

All equipment should have a designated calibrated back up equipment in case of unit/power failure. Please see the R&D Laboratory Tutela Temperature Monitoring System (R&D/S41) SOP for full details of storage equipment, monitoring and procedures for managing incidents.

If samples are to be transferred from one storage unit to another, samples must be handled in such a way that their integrity and viability remains unaffected (e.g. at the correct temperature and within the correct time period).

Sample Shipping

During study review and set up, the R&D Laboratory Team should ascertain whether samples will be shipped in batches or on the day of collection, and who the courier will be. It should also be established if the packaging material is provided by the Sponsor or courier. Please see the Laboratory Research Clinical Trial Set-Up (R&D/S35) SOP and Laboratory Research Clinical Trial Set Up Form (R&D/F73) for further information

It is the responsibility of the Research Team and Sponsor to arrange the collection and shipment of samples.

The Research Team must ensure that they provide the R&D Laboratory Team with adequate time to process and store samples, the Research Team should therefore be advised that:

- Samples which are shipped on the day of collection will need to reach the required shipping condition prior to being packaged and shipped (i.e. if a sample is to be shipped frozen, it will require time to freeze before it can be shipped, the amount of time samples take to freeze will vary based on volume and the temperature of the freezer in question).

- Some couriers have a ‘last collection time’, therefore it should be established if samples can be shipped on the next working day if the samples are received too late to meet that shipping time.

- It is usually the Research Teams’ responsibility to order dry ice if samples require frozen transport. Order methods and requirements vary depending on the courier company used.

- If the timing of a patient visit means that there is insufficient time to process samples before the courier cut off times, samples may need to be sent the next day. Please bear in mind that different studies require different preparation times; therefore, it is imperative for Research Teams to liaise with the R&D Laboratory Team (or a designated staff member) to ensure that shipping is

ordered correctly and that there is sufficient time for laboratory staff to process samples prior to the shipping time.

- Considering some Central Laboratories do not accept samples on a weekend, shipping frozen samples on a Friday is not advisable. If in any doubt, please contact the R&D Laboratory Team to discuss.

- Please ensure the required shipping documents are brought to the laboratory with the samples.

Additional considerations;

- Generally, ambient collection must be ordered before 11 am on the day of collection

- Please order dry ice in advance (usually 24 or 48 hours notice prior to shipping)

- Samples must be ready for collection at the start of there collection slot. For example, if shipping is booked between 14:00 and 16:00, the sample must be packaged and ready for collection by 14:00. It should be established whether samples can be shipped on the next working day if the samples are received too late to meet that shipping time.

- As dry ice is packed on a Friday for a Monday delivery, it is not advisable to ship frozen samples on a Monday, due to the risk of sublimation. If there is insufficient dry ice samples could be shipped under inappropriate shipping conditions. It should be established whether samples can be shipped on the next working day, if this is not possible visits should be booked in to ensure appropriate dry ice conditions.

The R&D Laboratory Team (or a designated Laboratory staff) must ensure that each sample shipment is documented in the Specimen Shipping Log (R&D/F62) and where appropriate the Storage Box Sample Location Log (R&D/T60). Shipping receipts must be retained within the relevant section of the laboratory ISF. In addition, study specific documents may need completing.

Sample Destruction

In some cases, samples are not shipped but are instead destroyed. This could be within Protocol, for example some studies require a backup sample to be retained at site, which is then destroyed upon confirmation that the primary sample has been received and analysed by the Central Laboratory. Samples should never be destroyed without written confirmation from the Central Laboratory or study Sponsor. Sample destruction may also be required due to a sample deviation or withdrawal of patient consent. Please see **section 4.5 Documenting Deviations** for further information. If samples are destroyed, this must be documented in a Specimen Destruction Log R&D/F28.

4.4 Data Recording and Retention of Data

All data should be recorded directly, promptly, accurately, and legibly. It should be possible to determine the date on which the sample handling and processing work was performed and the identity of the person who conducted the work.

Any changes to research records should be made so as not to obscure the previous entry. The reason for any changes to the data should be justified and the justification documented. It should be possible to determine who made the change, when the change was made and for what reason.

See R&D/S34 for details relating to document retention and archiving of Laboratory Research Files.

4.5 Quality Assurance and Documenting Deviations

The safety of trial patients takes precedence over any other aspect of the trial. Consequently, prior to the initiation of laboratory work, lines of communication should be established between the Sponsor (or their representative) the Investigator and the Research Team, to ensure that any issues that may impact on patient safety or integrity of research samples/trial data are reported without delay.

Any relevant contact details should be recorded within each Laboratory Study file ensuring they are easily accessible. All research sample deviations must be documented and assessed in the Specimen Deviation Log (R&D/F31) and on the Deviations Quality Assurance Audit spreadsheet (on the X-Drive). Examples of deviations are listed below;

- Equipment failures or temperature excursions that could potentially impact on sample integrity
- Deviations relating to sample receipt – incorrect sample received or in the wrong conditions (e. g. ambient when it should be on wet ice)
- Deviations relating to sample processing – samples processed incorrectly (e. g. centrifuged at the wrong speed or temperature) or outside of the specified timeframe
- Deviations relating to sample shipping – shipped outside of the specified window or under incorrect conditions
- Any deviation from GCP, the Protocol, Laboratory Manual or laboratory specific instructions/SOPs

R&D Laboratory staff (or staff members designated to handle research samples) have the initial responsibility for assessing the impact of any deviation or temperature excursion. This assessment must be documented and the following information should be included in the description of the deviation:

1. A description of the incident, what has happened to the sample(s).
2. The location (including the equipment name) where the deviation/temperature excursion took place (usually only applicable to temperature excursion).

3. The extent and/or duration of the deviation/excursion the research sample(s) were subjected to (usually only applicable to temperature excursions).
4. What has been done about the deviation/what steps have been taken to resolve the deviation
5. An assessment of the impact of the deviation/excursion on the sample(s) integrity if applicable.

This will involve checking any instructions from the Sponsor (study Protocol/ Laboratory Manual or laboratory specific instructions/SOPs). The deviation should be assessed to ascertain if it is a 'Serious Breach'. In the case of handling and processing research samples, a breach is considered serious if it is likely to affect sample integrity, and consequently may have an impact on analysis and results, which may in turn compromise patients' safety or the scientific value of a study.

'Serious Breach' is a particularly significant concept for clinical trials of investigational medicinal products (CTIMPs). This is because there is specific legal obligations to identify and report contained in the UK Clinical Trial Regulations (see Regulation 29A)*:*

Serious Breach is a breach which is likely to effect to a significant degree:
(i) the safety or physical or mental integrity of the research participants; or
(ii) the scientific value of the study.

All suspected serious breaches must be notified to the study Sponsor as soon as possible (and within 24 hours of the breach being identified). A copy of the notification should be sent to the R&D Unit via research.governance@york.nhs.uk and the Research Team. This, and any subsequent resulting correspondence, must be retained in the laboratory research file. In the event of a suspected serious breach the R&D Unit staff will liaise with the reporting individual, to ensure that all necessary actions are taken to ensure that the risk or impact on patient safety or sample and data integrity is assessed following a deviation, and that corrective and preventative measures are implemented.

In cases of any doubt as to whether the breach is to be considered as serious, the study Sponsor should be notified and asked if any further actions are required. The relevant Research Team should be copied into the correspondence. If the study Sponsor deems that the notified breach is serious, the Sponsor's instructions should be followed and the R&D Unit notified via research.governance@york.nhs.uk (within 24 hours of the breach being identified). The R&D Unit staff will liaise with the reporting individual to ensure that all necessary actions are taken.

All deviations (serious and not serious) must be documented. Deviations must be monitored for any patterns of repetition as they may amount to a quality control failure which is reportable as a serious breach. The R&D Laboratory Team are ultimately responsible for retaining oversight of the extent and frequency of all deviations and temperature excursions for research samples and for escalating issues (e.g. quality control issues) to R&D as necessary. All recorded sample receipt, storage and shipment deviations will be filed within the relevant laboratory ISFs; all recorded deviations related to equipment and temperature monitoring will be retained

as per the guidance in the R&D Laboratory Tutela Temperature Monitoring System (R&D/S41) SOP.

At the end of each research study the R&D Laboratory team should ensure the Sponsor has been informed of all laboratory breaches and/or deviations that may have impacted on the study samples for consideration and inclusion in the end of study report. This may be direct from the Lab Research Team or via the Research Team.
The deviations spreadsheet located on the X-drive must be kept up to date with all deviations recorded within it. At the end of each month this sheet is summarised and a small report generated targeting areas to improve if patterns of deviations become visible over time.

Laboratory ISF are to be checked for completeness and audited by a member of the R&D Laboratory team. The Laboratory Investigator Site File (ISF) Audit (R&D/F13) form should be used to guide and document the assessment.

Self-assessment of GCP Compliance in the Laboratory Checklist (R&D/F30) should be completed periodically (annually as a minimum) by the R&D Laboratory team (and designated Laboratory staff) to assess any potential GCP deviations on an individual basis, as well as within the facility so that corrective actions and preventive actions can be taken. The Trust Laboratories also appear on the R&D Research Quality Assurance Audit Schedule, the recorded deviations and breaches will be reviewed upon audit.

4.6 Adverse Incidents

It is a requirement that all Adverse Incidents (AI) within the Trust are reported via the DATIX online system, including adverse incidents that occur in the laboratory.

Where an adverse incident involves any aspect of a research study (this includes research processes, equipment and samples), the reporting individual should check the ‘research’ box on DATIX to ensure that the R&D Unit is appropriately notified.

In cases where a research-related adverse incident is reported and it involves or affects the Trust Laboratory but where the R&D Laboratory Team have not been involved in submitting that report (e.g. where an AI is reported by a member of a research team), then the R&D Unit will ensure that the R&D Laboratory team is notified and involved in any investigation or necessary resulting remedial action.

5 Related SOPs and Documents

R&D/S78 Processing Amendments in the Laboratory Research Team

R&D/S34 Archiving of Laboratory Research Files

R&D/S41 R&D Laboratory Tutela Temperature Monitoring System

R&D/F13 Laboratory Audit Checklist

R&D/F23	Laboratory Amendment Log
R&D/F28	Specimen Destruction Log
R&D/F31	Specimen Deviation Log
R&D/F32	Specimen Location Log
R&D/F51	Specimen Receipt Log
R&D/F62	Specimen Shipping Log
R&D/F72	Staff Signature & Training Log
R&D/F73	Laboratory Research Clinical Trial Set Up Form
R&D/F74	Specimen Incubation Log
R&D/F76	Laboratory Site File Document Reference Log
R&D/T07	Laboratory Site File Contents Page
R&D/T09	Spine Template
R&D/T60	Storage Box Sample Location Log
R&D/F30	Self –assessment of GCP compliance in the laboratory checklist