York Foundation Trust R&D Unit
SOP
R&D/S94

Processing Laboratory Research Samples

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 Staff must ensure that they are adequately trained in the new procedure and must make sure that all copies of superseded versions are promptly withdrawn from use unless notified otherwise by the SOP Controller.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: www.northyorksresearch.nhs.uk/sops.html and/or Q-Pulse

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	Date:	18th January 2018
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	Signature:	Signed copy held by R&D Unit
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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	

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 Laboratory Research Team (or designated Laboratory staff) 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. It comprises of a wide range of activities which generate data used to monitor research participant safety, assess pharmacokinetic parameters and to measure end points. It generates data that are 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.

The Medicines & Healthcare products Regulatory Agency (MHRA) has responsibility for monitoring Laboratories that perform work in support of clinical trials, and they carry out routine inspections. There is a requirement for all Laboratories that support delivery of clinical trials to implement appropriate measures to assure the quality and integrity of the research samples they process and the data that they produce; and to exercise due diligence to ensure that the 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 Trust's Research 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 doesn't 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 & training records

All staff involved in work performed in support of clinical trials should receive GCP training commensurate with their roles and responsibilities; and 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).

In addition, laboratory personnel should carry out an appropriate level of technical training prior to their participation in work supporting clinical 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 (Training Logs & Study Delegation of Duties Logs should be completed).

A record of training must be maintained for each staff member involved in handling clinical trial samples, kept up to date and documented in a Training File. Copy of this information must be retained when staff leaves the organisation.

4.2 Sample Receipt and Processing

Sample Receipt

As soon as possible after a research sample has been collected, the Research Team should bring the samples directly to the Laboratory Research Team (or a designated Laboratory staff member) 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).

Samples may be left at Laboratory Medicine Specimen Reception; however this should be avoided where possible as it may cause delays in processing samples which may require special storage or immediate processing. If samples are left at specimen reception the Research Team **must** ensure that the Laboratory Research Team (or a designated Laboratory staff) is aware of this by speaking directly to a member of the team and clearly identifying it as a research specific sample. Please include the following information on the sample requisition form:

- The name and contact number of the 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 samples the Laboratory Research staff (or a designated Laboratory staff) should assess sample integrity and whether they have received the correct samples for the study and the correct study visit (as per the study specific Protocol/Laboratory Manual or Laboratory specific instructions/SOPs); and whether 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.

Specimen Checklist (R&D/F24) must be completed to confirm the correct samples have been received in accordance with the Protocol/Manual or Lab Specific Instructions. The specimen Receipt Log (R&D/F51) must be completed to document the receipt of the samples. In addition, study specific documents may need completing. All research samples that are processed by the Trust's Laboratory should have a clearly documented chain of custody allowing tracking the movement of each sample from arrival to shipment or disposal (each sample must be uniquely identified).

Research Teams are responsible for informing the Laboratory staff in a timely manner if patient consent to participate in a research study is withdrawn for any of the research participants. 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 as per the clinical trial Protocol, Laboratory Manual or Laboratory specific instructions/SOPs (this includes the specific sample volume, tubes/kits, timelines & conditions for collection, processing, storage and shipping) by appropriately trained Laboratory Research staff (or a designated Laboratory staff member). Laboratories should not perform any work on clinical trial samples that is not specified in the clinical trial 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 & implementing amendments within Laboratory research.

Staff training for each individual study should be documented in the Staff Signature & Training Log (R&D/F73). 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. Specimen Checklist (R&D/F24) must be completed to confirm samples have been processed in accordance with the Protocol, Laboratory Manual or clinical trial specific instructions/ SOPs. Where deviations occur (such as the red cell layer being disturbed when making plasma aliquots) the Laboratory Research Team (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 File. 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 & 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 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 and how and where samples may be transferred to (back up facility) must also be agreed at the outset of each study.

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

Sample storage areas must be adequate, and sample storage units (incubator or 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 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 be transported to another location for a number of reasons, including equipment maintenance (6 monthly defrost) or unit failure.

All equipment should have a designated calibrated back up equipment in case of unit/power failure. Please see the summary of the equipment below:

Equipment	Storage Condition	Location
York Hospital		
ALPHA	-80°C Freezer	HPLC Laboratory S2.9
BRAVO	-80°C Freezer	R&D Laboratory
CHARLIE	-20°C Freezer	Balance Room S2.4
FOXTROT	-80°C Freezer	R&D Laboratory
GOLF	-20°C and Refrigerator	R&D Laboratory
MIKE	Refrigerator	HPLC Laboratory S2.9
Scarborough Hospital		
T01221	-70°C Freezer	Portable cabin
To be confirmed	Back up -70°C Freezer	To be confirmed
T00983	-40°C Chest Freezer	Portable cabin
T00980	-20°C Freezer	Specimen Reception

T01228	-20°C Freezer	Portable cabin
T01008	Refrigerator	Specimen Reception
T01287	Refrigerator	Specimen Reception

Samples must be transferred from one storage area to another storage unit 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 Laboratory Research 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.

It is the responsibility of the Research Team/Sponsor to arrange the collection/shipment of samples. **The Research Team must ensure that they provide the Laboratory Research Team with adequate time to process and store samples therefore the Research Team should 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 be 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 the research teams' responsibility to order dry ice if samples require frozen transport. Order methods and requirements vary depending on that courier company used.

- If the timing of a patient visit means that there 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 Laboratory Research 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.

- Shipping frozen samples on a Friday is not advisable, as some central laboratories do not accept samples on a weekend. Again, if in any doubt, please contact the Laboratory Team to discuss.

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

Additional considerations for DHL at York Hospital:

- Please order ambient collection before 11am on the day of collection.
- Please order dry ice in advance (before 11am, 24 or 48 hours prior to shipping depending on the shipping instructions).
- Collection time is always **2pm**
- Shipping frozen samples on a Monday is not advisable as the dry ice is packed on the Friday and shipped to site on the Monday; therefore, there is a risk of the dry ice subliming. If there is insufficient dry ice left samples could be shipped under inappropriate shipping conditions. 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.

The Lab Research Team (or a designated Laboratory staff) must ensure that each sample shipment is documented in the Specimen Shipping Log (R&D/F62) and the Specimen Checklist (R&D/F24). Shipping receipts must be retained within the relevant section of the research Laboratory File. In addition, study specific documents may need completing.

Sample Destruction

In some cases samples are not shipped but instead destroyed. This could be within protocol, for example, in some cases a backup sample is retained at site and then destroyed once confirmation that the sample have been received and analysed by the central laboratory. Samples should never be destroyed without a written confirmation form 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 & 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 with the sponsor, or their representative, and with the

investigators, to ensure that any issues that may impact on patient safety or integrity of research samples or trail data are reported without delay.

The relevant contact details should be recorded within each Laboratory Study file and easily accessible. All research sample deviations (including temperature excursions which could potentially impact on sample integrity/equipment failures, sample receipt, processing and shipping deviations, or deviations from GCP or study procedures) must be documented and assessed on the Specimen Deviation Log (R&D/F31).
Laboratory research staff (or a staff member 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. The location (including the equipment name) where the deviation/temperature excursion took place (usually only applicable to temperature excursion).
2. The extent and/or duration of the deviation/excursion the research sample(s) were subjected to (usually only applicable to temperature excursion).
3. What has been done about the deviation/what steps have been taken to resolve the deviation
4. 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 Lab Specific Instructions/SOPs) and it must include an assessment as to whether the breach is deemed to be 'serious' or not **,** and it should be signed by the individual making the assessment.
'Serious Breach' is a particularly significant concept for clinical trials of investigational medicinal products (CTIMPs). This is because there are specific
legal obligations to identify and report them 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.

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 scientific value of a study.

All suspected serious breaches must be notified to the study sponsor as soon as possible (and within 24h of the breach being identified). Copy of the notification should be sent to 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, sponsor's instructions should be followed and R&D Unit notified via research.governance@york.nhs.uk (within 24h 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. These 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 Laboratory Research 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 research files; all recorded deviations related to equipment and temperature monitoring will be kept in the Laboratory Equipment File for clear oversight of their extent/frequency. At the end of each research study the lab research team should ensure that all laboratory breaches and/or deviations that may have impacted on the study samples are notified to the Sponsor for consideration and inclusion in the end of study report. This may be direct from the lab research staff or via the research team.

In addition:

- Laboratory Research Files will be regularly checked for completeness by a member of the Laboratory Research Team. The Laboratory Audit Checklist (R&D/F13) should be used to make and document the assessment;

- Self- assessment of GCP Compliance in the Laboratory Checklist (R&D/F30) should be completed on periodic basis (annually as a minimum) by Laboratory Research staff (and designated Laboratory staff) at both sites (York & Scarborough Hospital) to assess for any potential GCP deviations on individual basis, as well as within the facility so that corrective & preventive actions can be taken;

- The Trust Laboratories also appear on the R&D Research Quality Assurance Audit Schedule, and 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 and this includes 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.

Where a research-related adverse incident is reported that involves or affects the Trust Laboratory but where the lab research 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 lab research 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/F13	Laboratory Audit Checklist
R&D/F23	Laboratory Amendment Log
R&D/F24	Specimen Checklist
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/F30	Self –assessment of GCP compliance in the laboratory checklist