The Leeds Teaching Hospitals NHS NHS Trust UNIVERSITY OF LEEDS Standard Operating Procedure	Title	**LTHT / UoL Human Tissue Act (HTA) Standard Operating Procedures applying to the Research Licence** **Audit of HTA relevant material**				
	Scope	**Details of the procedure for audit of HTA relevant material under the LTHT and UoL Human Tissue Authority Research Licence**				
	Version	**V 2.0**	Date issued	**December 2021**	SOP ID	**LRTB SOP M03**
	Planned Review date			2023		

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IMPORTANT NOTE

All non-essential activities related to the collection and storage of human tissues for research were paused in March 2020 due to the Covid-19 pandemic. Essential activities, such as the collection or release of samples for Covid 19 related research or the maintenance of premises or equipment, continued with the appropriate safeguards in place.

The Leeds Teaching Hospitals Trust (LTHT) and the University of Leeds (UoL) are responsible for developing and updating instructions or advice regarding the continuation or resumption of activities within the Trust and University respectively, based on the instructions or advice issued by the relevant public bodies such as the National Institute for Health Protection, the NHS and/or the government. All staff must follow the latest instructions or advice issued by LTHT and/or UoL, depending on the sector within which they work.

The Human Tissue (HT) Act -related activities detailed in this SOP should only be undertaken if:
- they fall within the scope of permissible work according to current LTHT and/or UoL policy;
- the procedures can be adapted to fully observe the current LTHT and/or UoL infection control policy.

The above principles will apply if other exceptional national or local circumstances arise.

Section A LTHT / UoL Standard Operating Procedure

Audit of Research Tissue Banks

1. **Audit by external organisations**
   - **1.1.** All individual research groups working within the Leeds HT Act governance framework will comply with any external audits required by funding bodies or regulatory bodies.
   - **1.2.** If external agencies are involved, a confidentiality agreement will be required, signed by all participating auditors and the UoL or LTHT.
   - **1.3.** No patient identifiable data will be made available to auditors, unless the external organisation is the HT Authority.
   - **1.4.** No patient or sample related paperwork will be removed from the files.
   - **1.5.** Audit reports should remain commercially in confidence.

2. **Independent audits**

2.1. Quarterly audit of patient consent forms co-ordinated by the HTA Manager

2.1.1. Background

2.1.1.1. The Patient Registration System (PRS) is a secure database maintained by LTHT to record the consent of LTHT patients to donate tissues to a research tissue bank for future unspecified research (full details are provided in LRTB SOP IT01 Patient Consent Registration).

2.1.1.2. After the consent for research has been obtained from the patient and checked for accuracy and completeness, the clinical researcher accesses PRS to identify the patient, via an automatic link to the LTHT Patient Administration System (PAS).

2.1.1.3. The PRS creates a unique patient ID and consent-form-specific reference number for each consent form registered for the same patient.

2.1.1.4. The PRS electronically sends the relevant anonymised patient data and consent data including the patient's unique ID and consent reference, across to Medical Achiever, the tissue traceability system maintained by UoL.

2.1.1.5. A research consent form from which all patient identifiable data has been redacted can be printed with the PRS codes to accompany the tissue samples to the research laboratories.

2.1.2. Performance of the audit

2.1.2.1. An access database search is performed to identify the number of consents registered by each research group for the audit period to determine, using a defined algorithm, how many consent forms to audit.

2.1.2.2. The PRS database provides data for each entry:

- **2.1.2.2.1.** Surname
- **2.1.2.2.2.** PRS codes
- **2.1.2.2.3.** Consent date
- **2.1.2.2.4.** Project
- **2.1.2.2.5.** Name of Person Designated (PD)
- **2.1.2.2.6.** Consent taker
- **2.1.2.2.7.** Scan date, the absence of a scan date indicating that no scan has been performed

2.1.2.3. The original, scanned consent form is checked to verify that all required fields are completed correctly.

2.1.2.4. The redacted version of the consent form is reviewed to verify that the patient identifiable data have been removed.

2.1.2.5. The PRS data is compared with the scanned consent form to verify that all dropdown fields (eg consent taker, date of consent) have been selected correctly.

2.1.2.6. The URL link from the PRS to Achiever Medical is followed to review the participant entry which has been created automatically in Achiever to verify the accuracy of the data transferred.

2.1.3. Audit outcomes

2.1.3.1. An excel spreadsheet is sent to each PD, and copied to the DI, to include the following:

2.1.3.1.1. The number of consent entries added to the PRS for the audit period and the number of consent entries audited

2.1.3.1.2. The number of anomalies identified and their nature

2.1.3.1.3. The PRS number of any entries which have no scan data

2.1.3.2. The PDs agree a Corrective and Preventative Actions (CAPA) plan with the HTA manager (and DI if appropriate) and inform the HTA manager when these have been completed.

2.1.3.3. The HTA manager checks that the required actions have been completed and this is recorded in the next quarterly audit.

2.1.3.4. An annual summary is prepared for the HTA management group and is discussed at the next meeting.

2.2. Monthly audit of Achiever records for samples with no apparent active consent

2.2.1. Background

2.2.1.1. When the donor is an LTHT patient, consent is recorded in the PRS (see section 2.1), a donor record is automatically created in Achiever with a participant record linked to the project to which they have consented. A consent form linked to the participant record is automatically populated with the relevant data.

2.2.1.2. When consent has not been recorded in the PRS, Achiever records must be checked using appropriate identifiers to determine whether the donor has a previous record.

2.2.1.3. If there is a donor record, a new participant record can then be created and linked to the new project for which consent has been obtained.

2.2.1.4. If no pre-existing donor record is found, the identifiers entered in 2.2.1.2 are used to create a new donor record and participant record as in 1.2.1.2.

2.2.1.5. The user is then guided through the steps required to enter the consent data, including a description of how the consent has been obtained.

2.2.1.6. The document providing evidence or assurance of consent must be uploaded against the participant record. The evidence can be a redacted consent form if consent has been taken locally from a healthy volunteer for instance. Alternatively, it can be the Tissue Transfer Agreement (TTA), which must be in place before any transfer of samples from an external organisation, as it includes assurance from the external organisation that consent has been obtained according to the HT Act, 2004.

2.2.1.7. Once the above steps have been followed, the status of the consent must be changed to "active" and the samples are linked to the participant record and therefore to consent.

2.2.1.8. Within the project grid, Achiever identifies samples that are not linked to an active consent. This may be because:

2.2.1.8.1. Consent has been withdrawn but the samples have not yet been destroyed.

2.2.1.8.2. Samples have been received from an external organisation and registered in Achiever, but a donor record has not been created, and there is therefore no participant record and linked consent form.

2.2.1.8.3. Samples have been received from an external organisation and rather than a donor record, only a participant record has been created. In this scenario, the consent form is not created automatically.

2.2.2. Performance of the audit

2.2.2.1. The identification of samples with no associated active consent is performed automatically within Achiever for each project on a monthly basis.

2.2.2.2. An email is generated to the responsible officer with a list of sample identifiers for each their projects.

2.2.2.3. The email is copied to the principal investigator of the project and to the HTA Manager.

2.2.2.4. The responsible officer imports the list of samples into an Excel spreadsheet with the following headings:

2.2.2.4.1. Title of the project
2.2.2.4.2. Name of the responsible officer
2.2.2.4.3. Audit date
2.2.2.4.4. Sample ID (enter Not Applicable if no sample have been identified)
2.2.2.4.5. Reason for absence of active consent
2.2.2.4.6. Corrective action planned (or Not Applicable)
2.2.2.4.7. Error rectified (Date completed/No/Not Applicable)
2.2.2.4.8. Preventative Action Planned (Describe or Not Applicable)
2.2.2.4.9. Preventative Measure in Place (Completed on "insert date"/ To be completed by "insert date"/Not Applicable)

2.2.3. Audit outcomes

2.2.3.1. If samples with no active consent have been identified, the responsible officer must identify the cause in each case and complete the corrective actions within five working days.

2.2.3.2. A copy of the updated spreadsheet is sent to the HTA Manager with copy to the Designated Individual (DI). The spreadsheet should include a description of the preventative actions and their status (points 2.2.2.4.8 and 9).

2.2.3.3. The HTA Manager will monitor the progress of the audit and check that all actions have been completed.

2.2.3.4. A copy of the completed spreadsheet should be uploaded against the project.

2.2.3.5. The responsible officer should maintain a master spreadsheet of all audits and their outcomes for a calendar year in order to identify any issues that recur despite the initial preventative measures. This must be shared with the HTA Manager and DI at the end of each 12 month cycle at least, and earlier if a recurrent issue is identified.

3. Internal audits

3.1. Background

3.1.1. The HT Authority code of practice and standards for research require a regular schedule of audit of all licensable activities (see Governance and Quality Systems standards).

3.1.2. Regular audits are required across all activities, and those related to consent, traceability and premises, facilities and equipment must be performed regularly to ideally pre-empt or otherwise quickly correct any potential failures to uphold the fundamental principles of consent or to store the tissue donations safely and in a way that preserves their integrity.

3.1.3. The list of audits described below is not exhaustive. Horizontal audits eg a detailed review of a particular component of the quality management system such as training or equipment maintenance records, should also be performed.

3.2. Audits to comply with HT Authority consent and traceability standards

3.2.1. These audits are fundamental to the Act and involve:

3.2.1.1. Audit 1: Selection of samples from the Achiever records and physical verification that they are in the correct storage location as recorded in Achiever.

3.2.1.2. Audit 2: Selection of locations within the Achiever tissue stores and physical verification that the samples they contain are those recorded in Achiever.

3.2.1.3. Audit 3: Selection of consent forms to then identify the samples that have been donated, including those created by splitting the original donation into subsamples, and trace them to their location.

3.2.1.4. Audits 1 and 2 should be extended to include the verification of consent in at least a subset of cases.

3.2.1.5. As part of 3.2.1.4, the consent form should be checked for completeness. This is particularly important when donors are volunteers or non-LTHT patients, who are therefore not eligible for the PRS and therefore not subject to the quarterly audits detailed in section 2.1

3.2.2. A rolling programme of audit must be established and those responsible for any follow-up actions must be identified and given a timeframe for completion.

3.2.3. To ensure the effectiveness of the audits:

3.2.3.1. The number of cases audited should be proportional to the total number of consents taken and samples

3.2.3.2. The number of cases should be manageable by individual teams so that they can reasonably be performed on a regular basis

3.2.3.3. A balance must also be struck between the numbers of cases audited and the preservation of the integrity of the samples eg the maintenance of the required temperatures for frozen samples in particular.

3.2.3.4. The audit tool available in Achiever Medical should be used to select the samples and locations for audits 1 and 2 to ensure that there is no selection bias. (please refer to the End User Manuals: Sample and Sub-Location auditing).

3.2.3.5. There must be a defined process to select the consent forms for audit 3.

3.2.3.6. Cases should be selected to span the lifetime of the tissue store but a higher percentage of cases should be selected from the more recent entries. This is to identify emerging problems quickly to implement corrective and preventative actions swiftly. Such problems may be, for instance, related to new staff or new procedures. The Achiever audit tool includes a mechanism for doing this.

3.2.3.7. Independent audits are highly desirable, and individual groups should consider a collaborative approach to perform one of the audits for each other, for instance once a year.

3.2.4. The sample to location audit (audit 1) and the location to sample audit (audit 2) should be performed every three months, including the extended pathway to consent verification as in 3.2.1.4;

3.2.5. The audit starting from consent forms, to samples and locations (audit 3) should be performed every six months at least.

3.2.6. The results of the audits should be recorded centrally (eg Achiever) and the reports shared with the Designated Individual and HTA Manager. Audit leads must pay particular attention to any patterns of failure that could indicate a systemic problem.

3.2.7. Records of all audits, including Corrective and Preventive Actions plans and evidence of their successful completion, must be kept as part of site-specific documentation indefinitely and made available for inspection when required.

3.3. Audits related to the Premises, Facilities and Equipment (PFE) standards

3.3.1. The premises must be secure and fit for purpose (standard PFE1)

3.3.1.1. Premises are assessed for this standard at the onset but this should be monitored regularly. For instance, when performing the traceability audits on location, a record should be made to indicate whether the room was locked on arrival as expected and clean.

3.3.2. There must be appropriate facilities for the storage of human tissues (standard PFE2)

3.3.2.1. As part of the traceability audit on location, a record could be made of the room temperature to monitor whether there are fluctuations over time that could put the samples at risk.

3.3.3. Equipment is appropriate for use, maintained and validated and where appropriate, monitored (standard PFE3)

3.3.3.1. Freezer temperatures are monitored with an alarm system in place for failure but a regular review of temperatures to identify a gradual rise could pre-empt a failure.

4. <u>Financial audits of Research Tissue Banks charging for the release of tissues</u>

4.1. Any financial arrangements, such as the operation of a cost recovery model, should be disclosed in the patient information sheet and consent form.

4.2. The development of a cost recovery model requires careful consideration and should be agreed with LTHT, UoL or both, depending on the affiliation of the personnel responsible for the RTB and the location of tissue collection and storage.

4.3. An annual financial audit should be undertaken by the relevant finance department to verify the continued validity of the charging model.

Section B Applicability

1.1 This SOP is relevant to all staff collecting and storing human tissues relevant to the Act. The list of relevant tissues can be found on the Human Tissue Authority website by following the link:
https://www.hta.gov.uk/sites/default/files/migrated_files/List_of_materials_considered_to_be_relevant_material_under_the_Human_Tissue_Act_2004.pdf

1.2 This SOP can also be used as a training tool for new members of staff who have never worked with human tissues before, or who need to follow a new process.

Section C Background

1 Different sample types (blood or other bodily fluids, surgical resections etc) and data are collected from patients and other donors in Leeds for future unspecified research into a wide range of conditions including the investigation of normal cellular functions and their disruption in disease states, whether cancer or non-cancer. The tissue collections resulting from these different research activities are grouped under one research licence granted by the Human Tissue Authority to cover both Leeds Teaching Hospitals NHS Trust and the University of Leeds and referred to as the Leeds Research Tissue Banks. However, not all of these tissues are held within an NHS Research Ethical Committee approved research tissue bank.

2 The Leeds Teaching Hospitals NHS Trust is registered as the Licence Holder with the HT Authority, and the principal licensed site ('the hub') is St James's University Hospital. The University of Leeds main campus and Chapel Allerton Hospital are named satellites on the licence.

3 The research licence **does not** cover all areas within St James's University Hospital, the University of Leeds main campus or Chapel Allerton Hospital, but only named research groups and premises within those sites. There is a formal Leeds HT Act governance structure as described below.

4 The Licence Holder is responsible for appointing a suitable Designated Individual.

5 The DI plays a key role in implementing the requirements of the HT Act as the person under whose supervision the licensed activity is authorised to be carried out. The DI has the primary (legal) responsibility under Section 18 of the HT Act to secure that:

5.1 Suitable practices are used in undertaking the licensed activity;
5.2 Other persons, such as the Persons Designated (PDs), working under the license are suitable and;
5.3 The conditions of the licence are complied with.

6 The Persons Designated are charged with adapting the overarching HT Act related SOPs, including this one, into local SOPs to reflect local conditions and research pathways. They are also responsible for the supervision of staff working to HT Act standards (more detail is available in a separate document "Role of the Person Designated).

7 The organisational chart for the research licence, with details of key personnel responsible for specific HT Act activities, is routinely updated by the HT Act manager and any changes are submitted to the HT Authority.

8 The HT Authority determines the timing and frequency of inspection of an organisation holding a research licence based on a risk assessment. All areas listed in the organisational chart are subject to inspection.

Section D Definitions

The Act	The Human Tissue Act, 2004
DI	Designated Individual as defined by the Human Tissue Authority
HT	The Human Tissue Authority or Act
LTHT	Leeds Teaching Hospitals NHS Trust
PD	Person Designated as defined by the Human Tissue Authority
R&I	Research & Innovation
SOP	Standard Operating Procedure
UoL	University of Leeds

Section E References

Human Tissue Act, 2004

Human tissue Authority, Codes of Practice 2017

Code A: Guiding principles and the fundamental principle of consent
Code E: Research
Code E: Research standards and guidance

Joint Policy for the Storage and Use of Human Tissue – a collaborative document agreed by Leeds Teaching Hospitals NHS Trust

F SOP details and approval process

Author: Patricia Harnden, Designated Individual for the Research Licence

SOP Pages: 9

Version No. of replaced SOP: N/A

Effective date of replaced SOP: N/A

Review date for updated SOP: Biennially from date of approval or review

Review Date: By:

Review Date: By

Review and Approval Process:

	Circulated to	Period of circulation (dates)	Comments received from
Version 1, draft 1	All Persons Designated and key associated staff, HTA Manager, LTHT and UoL Research and Innovation, Medical Achiever leaders	06/12/2021 to 17/01/2021	H. Berry, D. Gibson, A. Morgan, S Myers. Changes to improve clarity accepted in full/
Version 1, draft 2	No further circulations as no substantial changes to draft 1		

Version No of the SOP	Name of DI	Date	Signature
1	Dr Patricia Harnden Designated Individual LTHT/UoL Human Tissue Act	20/12/2021	

Distribution & Storage:

Distribution to

Persons Designated, LTHT/UoL HTA Research Subgroup

Location of Document

Paper: HTA Manager, Risk Management, The Trust Headquarters, St James's University Hospital

Electronic: Research and Innovation website, UoL., http://ris.leeds.ac.uk/info/72/relevant_legislation/107/hta/2