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 and licensable activities**			
	Scope	**Details of the procedure for audit of HTA relevant material and licensable activities under the LTHT and UoL Human Tissue Authority Research Licence**			
	Version	**V 3.0**	Date issued	**January 2023**	SOP ID	**LRTB SOP M03**
	Planned Review date			January 2025		

CONTENTS

Important Notice		page 01
Section A	Standard Operating Procedure	page 02
Section B	Applicability	page 07
Section C	Background	page 07
Section D	Definitions	page 08
Section E	References	page 08
Section F	SOP detail and approval process	page 09

Section A LTHT / UoL Standard Operating Procedure

Audit of Research Tissue Banks / HTA tissue holdings

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.** No patient identifiable data will be made available to auditors, unless the external organisation is the HT Authority
   - **1.3.** No patient or sample related paperwork will be removed from the files
   - **1.4.** In principle audit reports should remain commercially in confidence

2. **Independent audits**
   - **2.1. Quarterly audit of patient consent forms in the Patient Registration System (PRS) co-ordinated by the HTA Manager**

     2.1.1. Background

     2.1.1.1 For full background information about PRS, refer to LRTB SOP IT01 - 'LTHT Patient Consent Registration via the Patient Registration System (PRS)'.

     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:
     - Surname
     - PRS codes
     - Consent date
     - Project
     - Name of Person Designated (PD)
     - Consent taker
     - 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:
     - The number of consent entries added to the PRS for the audit period and the number of consent entries audited
     - The number of anomalies identified and their nature
     - 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.

2.1.3.5. The HTA manager will present the annual audit report findings for discussion at the research sub group meetings.

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

2.2.1. Background

2.2.1.1. For full background information about Achiever, refer to LRTB SOP IT02 - 'Managing Human Tissue Samples in Achiever Medical'.

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

- Consent has been withdrawn but the samples have not yet been destroyed.
- 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.
- 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 of their projects.

2.2.2.3. The email is copied to the Chief Investigator and the Oversight Officer (PD) of the project.

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

- Title of the project
- Name of the responsible officer
- Name of the Chief Investigator
- Name of the PD
- Audit date
- Sample ID (enter Not Applicable if no sample have been identified)
- Reason for absence of active consent
- Corrective action planned (or Not Applicable)
- Error rectified (Date completed/No/Not Applicable)
- Preventative Action Planned (Describe or Not Applicable)
- 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. 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.

2.2.3.2. At the end of each 12 month cycle the spreadsheet should be archived and must be made available for inspection when required.

2.2.3.3. PDs must add results of audits to their 6 monthly assurance report for Research Licence sub group

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 (PFE) 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.

3.1.4. To ensure the effectiveness of the audits, audit leads must pay particular attention to any patterns of failure that could indicate a systemic problem.

3.2. Audits to comply with HT Authority Consent, Traceability and Premises, Facilities & Equipment (PFE) standards

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

3.2.1.1. **Audit 1 – Sample to Location Audit**: Random selection of samples and physical verification that they are in the correct storage location as recorded. Achiever users must use the Sample to Location auditing function within the project.

3.2.1.2. **Audit 2 – Location to Sample Audit**: Random selection of locations within the tissue storage records and physical verification that the samples they contain correspond with those recorded. Achiever users must use the Location to Sample auditing function with a different storage location being chosen each time.

3.2.1.2.1. The PFE standards will also be audited.

3.2.1.3. **Audit 3 – Consent to Sample Audit**: 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.

3.2.1.4.1. 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

NB: The auditing functions within Achiever Medical select samples and locations for audits 1 and 2 ensuring that there is no selection bias. Instructions can be found in the Achiever End User Manual: Sample and Sub-Location auditing.

3.2.2. A rolling programme of audit must be followed as shown in the table below. A higher proportion of recent cases are selected to identify emerging problems quickly and enable corrective and preventative actions to be implemented swiftly.

Audit type	Frequency		Number Audited	Sample Selection	No of Consents Audited
	RTB / HTA Tissue Holdings actively collecting / receiving samples	RTB / HTA Tissue Holdings not actively collecting / receiving samples	(whichever is lower)		
Audit 1	3 monthly	6 monthly	10% or 20	75% within last 12 months of active collection 25% before this period	2
Audit 2	3 monthly	6 monthly	10% or 20	Randomly selected throughout storage location	2
Audit 3	6 monthly	Annually	2	1 = consent taken within last 6 months of active collection 1 = randomly selected	2

3.2.2.1. **Audit 1 – Sample to Location Audit**

- Within Achiever use the Sample to Location auditing function on the Audit navigation menu within the Project record (if samples are not tracked within Achiever an alternative method must be set up to randomly identify samples).
- Enter a title for the audit using the format 'Project ID/Year/Calendar Year Quarter' eg: PR000xxx 2022 Q1.
- Set the start date as the date of the earliest sample banked.
- Set the end date as the audit date.
- Select the number of samples as in the table in 3.2.2 as a minimum.
- Leave the 'Exclude checked out samples' box unticked so that these are included,
- Use the audit bands to select samples within the date range as shown in the table above.
- Validate Bands and Allocate Samples.
- After the samples have been allocated the sample list can be exported to Excel and saved or printed.
- Check the selected samples within the physical storage locations. Check that each sample is within the expected location and is labelled appropriately.
- Check the consent for 2 of the selected samples.
- Update the Audit Link details.
- If any samples failed, update the fail reason. Investigate and then update the resolution.
- Complete the internal traceability audit report form LRTB-FRM-M03-F1.
- Identify any corrective or preventative actions and enter the details on LRTB-FRM-M03-F1 including the person responsible and a due date for completion. Update the form when these have been completed.
- Enter a result/outcome for the Achiever audit and mark it as completed.
- Send a copy of LRTB-FRM-M03-F1 to the Designated Individual and the HTA Manager.

3.2.2.2 Audit 2 – Location to Sample Audit

- Select a storage location containing HTA relevant samples.
- Within Achiever use the Location to Sample auditing function on the Audit navigation menu within the relevant Storage Location record (if samples are not tracked within Achiever an alternative method must be set up to randomly identify places).
- Enter a title for the audit using the format 'Storage location name/Year/Calendar Year Quarter' eg: Freezer xx 2022 Q1.
- Select the number of places as shown in the table in 3.2.2 as a minimum.
- Validate and allocate places.
- The places and sample numbers can be exported to Excel and saved or printed from the Audit Links navigation menu within the Audit window.
- Check the condition of the storage location and the room and complete the details on internal traceability audit report form LRTB-FRM-M03-F2
- Check the selected places within the storage location and note whether the expected sample is found. The audit may also select locations that are expected to be empty.
- Check the consent for 2 of the selected samples.
- Update the Audit Link details.
- If any places failed, update the fail reason. Investigate and then update the resolution.
- Complete the rest of LRTB-FRM-M03-F2.
- Identify any corrective or preventative actions and enter the details on LRTB-FRM-M03-F2 including the person responsible and a due date for completion. Update the form when these have been completed.
- Enter a result/outcome for the Achiever audit and mark it as completed.
- Send a copy of LRTB-FRM-M03-F2 to the Designated Individual and the HTA Manager.

3.2.2.3 Audit 3 – Consent to Sample Audit

- Two consents should be selected as detailed within the table in 3.2.2.
- Check the consent forms for completeness.
- Identify all donated samples including sample splits and trace them to their location.
- A sample list can be generated within Achiever by searching for the Participant within the Project. For consents logged within PRS, the PRS ID is the Participant Study Ref within Achiever.
- When viewing the Samples navigation menu within the Participant window, all samples for that participant will be shown, including split samples, released samples and depleted samples.
- This sample list can be exported to Excel and saved or printed.
- Confirm the presence of the samples within the listed storage location(s) or confirm that complete records are present if the samples have been released or depleted.
- Complete internal traceability audit report form LRTB-FRM-M03-F3.
- Keep a record of the sample list and the findings.
- Identify any corrective or preventative actions and enter the details on LRTB-FRM-M03-F3 including the person responsible and a due date for completion. Update the form when these have been completed.
- Send a copy of LRTB-FRM-M03-F3 to the Designated Individual and the HTA Manager.

3.3 Audits on all Research HTA Standards

3.3.2 An audit encompassing all of the Research HTA Standards must be completed annually by each Research Tissue Bank/HTA tissue holding.

3.3.3 The audit must be completed before the first week in July each year.

3.3.4 Complete the audit using the Internal Research HTA Standards Audit Report Form LRTB-FRM-M03-F4.

3.3.5 Identify any Corrective or Preventative Actions and enter the details on LRTB-FRM-M03-F4 including the person responsible and a due date for completion. Update the form when these have been completed.

3.3.6 Send a copy of LRTB-FRM-M03-F4 to the Designated Individual and the HTA Manager by the first week in July each year.

3.4 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.

3.5 Audit reports will be discussed within the regular research sub group meetings. This will be a forum to share good practice and highlight areas of learning.

Section B Applicability

This SOP is relevant to all staff collecting and storing human tissues relevant to the HT Act, under the Authority of the HTA Research Licence no 12352.

Section C Background

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. Not all of these tissues are held within an NHS Research Ethical Committee approved research tissue bank.
The aim of this SOP is to ensure that all groups follow the same structure for carrying out audits of HTA relevant material and licensable activities.

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.

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.

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

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:

Suitable practices are used in undertaking the licensed activity;

- Other persons, such as the Persons Designated (PDs), working under the license are suitable and;
- The conditions of the licence are complied with.

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").

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.

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

Section F SOP details and approval process

Author: Patricia Harnden, Designated Individual for the Research Licence

SOP Pages: 9

Version No. of replaced SOP: 2

Effective date of replaced SOP: 27/1/23

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 3, draft 1	Jo Brown, Designated Individual, HTA Manager, Medical Achiever leaders, Person's Designated	3/11/22 - 11/1/23	C Skinner J Brown D Gibson G Langton T Brend J Scragg A Morgan H Berry A Jones C McKinley
Version 3, draft 2 & 3	Jo Brown, Clare Skinner, Debby Gibson & paper for Sub group 18/1/23	12/1/23 - 18/1/23	Discussed at sub group

Version No of the SOP	Name of DI	Date	Signature
3	Mrs Clare Skinner Designated Individual LTHT/UoL Human Tissue Act	27/1/23	

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