The Leeds Teaching Hospitals NHS Trust UNIVERSITY OF LEEDS **S**tandard **O**perating **P**rocedure	Title	**LTHT / UoL Human Tissue Act (HTA) Standard Operating Procedures applying to the Research Licence** **Transfer of Tissues within and between Organisations**				
	Scope	**Details of the procedure for transferring tissues covered by the LTHT and UoL Human Tissue Authority Research Licence within and between organisations**				
	Version	**V 4.0**	Date issued	**2021**	SOP ID	**LRTB SOP M07**
	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 HTA-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

Transfer of tissues within and between organisations

1. Status of the tissues relative to the Human Tissue (HT) Act, 2004

1.1 Researchers must determine whether the proposed transfer of tissues falls within the Leeds HT Act governance framework by following the algorithm and accompanying explanatory notes provided in the appendix.

1.2 In summary, there are three circumstances when the requirement to comply with the HT Act governance framework **does not** apply:

1.2.1 The tissues are not relevant to the HT Act (please see the explanatory notes in the appendix for more detail and links to the HT Authority website).

1.2.2 The study has been given project/study specific approval by an NHS Research Ethics Committee (REC), which confers an exemption to the requirements of the HT Act during the period of REC approval (normally five years). This is the case even when the tissues would be otherwise classified as relevant eg cellular.

1.2.3 Leeds is collecting relevant material on behalf of an external organisation, who will store the material in their HT Authority licenced premises for future unspecified research **AND** the samples will be transferred from Leeds within no more than seven days. If the seven day grace period for sample batching purposes cannot be respected, collection must cease and the group must contact the Designated Individual (DI) for Research to agree a mechanism for storage in licensed premises.

1.3 The circumstances when researchers are required to operate within the HT governance framework are:

1.3.1 There is no NHS REC project/study specific approval in place and Leeds researchers are proposing to receive relevant material from an external organisation. Examples includes obtaining tissues from a commercial tissue bank. Leeds researchers may also transfer tissues to another HT Authority licenced establishment, or to an organisation abroad, providing appropriate measures and safeguards are in place (see section 3).

1.3.2 A Leeds research group has applied to an NHS REC for Research Tissue Bank (RTB) status and receives and stores samples collected by external organisations for future unspecified research, for instance in the context of a national or international trial.

1.3.3 A Leeds RTB has additional approval from the NHS REC to release tissues to internal or external researchers under the equivalent of NHS REC project/study specific approval, granting a temporary exemption to the requirements of the Act. Although the tissues may then be stored and used in unlicensed premises within Leeds or by an external organisation, the tissues were collected under the Leeds HT Act governance framework and must be managed accordingly at the end of the approval period. All Leeds RTBs are covered by the Leeds research licence with the approval and support of the Designated Individual (DI), who must appoint a Person Designated (PD) to ensure that the bank complies with the HT Act compliance requirements.

2 Transfer of tissues within the Leeds HT governance framework

2.1 All tissue transfers must be the subject of a standard Tissue Transfer Agreement (TTA), available on the University of Leeds Research and Innovation website. Those taking responsibility for the management or storage of the tissues at local research level must be identified.

2.2 Prior to the completion of the TTA, tissue transfer proposals must be reviewed by an appropriate ethical committee on submission of a study protocol.

2.3 The ethical review may be performed by an NHS REC, the Governing Board of NHS REC approved RTB who has been given permission by the NHS REC to confer the equivalent of project/study specific approval or, in the case of studies involving healthy volunteers for instance, the University's Ethical Committee.

2.4 The protocol must include the purpose for which the tissues can be used and the templates of the information sheets and consent form used to obtain donor permission for the use of the tissues in research. This allows the committee to check whether the proposed research is within the scope of the consent and whether donors have agreed to the transfer of their tissues to another organisation.

2.5 It must also include details of the numbers and types of tissues, their form (eg fixed or frozen material) and the types of clinical data that may accompany the samples.

2.6 All samples and data must be sent or received in an anonymised form that does not allow donor identification, although the supplying organisation may retain a link between samples and donors in a secure environment in keeping with the Data Protection Act, 2018.

2.7 During the course of the research, there may be findings of potential clinical relevance to the donor. A mechanism for the feedback of any such results must be detailed within the protocol.

2.8 The date of transfer of the samples must be agreed and a suitable courier or method of internal transfer identified, which will depend on the form of the samples eg formalin fixed or fresh frozen.

2.9 A sample transfer list, giving details of the tissue type, a unique coded identifier and the number of samples must be forwarded by the supplier to the recipient, who must provide written confirmation of the safe receipt of the samples promptly after their delivery.

2.10 An agreement must be reached on the fate of any unused, relevant material at the end of the study period. If the material that remains is insufficient to be useful for further studies, or the integrity of the tissues has been compromised, disposal may be the only option. This should be done in accordance with the HT Authority traceability standards for disposal.

2.11 All the above documentation must be retained for a period of five years after return or disposal of the last sample in the study and made available during the HT Authority inspection process.

2.12 It is mandatory to record the transfer of HTA relevant samples and their origin or destination within Medical Achiever. All relevant, non-exempt, samples must be stored in the licensed premises listed with the HT Authority under the Leeds research licence.

2.13 All of the above points are covered in detail in the relevant TTA and explanatory notes.

3 The import or export of relevant material

3.1 According to the HT Act, "import" means import to England, Wales or Northern Ireland from another country (including Scotland) and "export" means export from England, Wales or Northern Ireland to another country (including Scotland).

3.2 Before importing or exporting tissues, researchers must familiarise themselves with the relevant section in HT Authority Code of Practice for Research (code E, paragraphs 98-114).

3.3 In addition to the requirements in section 2, a local protocol must be in place to demonstrate and document that comparable material cannot be sourced from England, Wales or Northern Ireland or is for a particular purpose that justifies import. The case of need for importing may include accessibility, quality, timeliness of supply, risk of infection, quality of service, cost effectiveness or scientific or research need.

3.4 Documented evidence of how consent was obtained and the confidentiality of donors safeguarded should be retained, as well as evidence that the material has been sourced in a manner consistent with the legal and ethical framework of England, Wales and Northern Ireland.

3.5 All documentation listed in 3.3 and 3.4 must be made available for HT Authority inspection purposes and retained by both recipient and supplier for a period of five years after return or disposal of the last sample in the study.

3.6 All imports and exports of human tissues must normally be declared to HM Revenue and Customs.

4 Transfer of relevant material that is not exempt from the requirements of the HT Act

4.1 This applies when human tissues that are relevant to the HT Act, 2004 are transferred from an establishment licenced by the HT Authority (the Supplier) to another licenced establishment (the Recipient) and no exemptions apply.

4.2 Specifically:

4.2.1 There is no NHS REC project/study specific approval in place, for instance when the donors are healthy volunteers or the tissues are imported;

4.2.2 A Leeds RTB is storing relevant material collected by external organisations for future unspecified research, for instance in the context of a national or international clinical trial. A specific Leeds RTB must be cited as the storage facility in the ethics submissions for the trial. A copy of the ethical submission and approval must be kept by the relevant Person Designated (PD).

4.2.3 The tissues are transferred from one Leeds RTB to another.

4.3 There is no need for a TTA if tissues are transferred internally between licenced premises in Leeds that are within the same unit or department, under the supervision of the same PD.

4.4 All of the provisions detailed in sections 2 and 3 apply.

4.5 The relevant TTA is Document A: Tissue Transfer Agreement involving human tissues for the scheduled purpose of research when the requirements of the Human Tissue Act, 2004 apply. It is available on the UoL Research and Innovation Service website, together with the algorithm

that allows researchers to determine whether they have to operate within the Leeds HT Act governance framework (appendix).

4.6 The TTA (document A) should be completed in conjunction with the explanatory notes, appended to the end of the TTA.

5 Release of tissues by an NHS REC approved Leeds RTB

5.1 Any group wishing to apply to an NHS REC for RTB status must first obtain the approval of the DI and agree to adhere to the Leeds HT Act governance framework, including all the policies and procedures developed to ensure compliance with the Act.

5.2 One of the benefits of obtaining RTB status is the opportunity to set up an RTB Governing Board in order to review applications for tissue samples either from Leeds as part of internal collaborations or from external collaborators or independent researchers.

5.3 As part of the submission to an NHS REC for RTB status, it is possible, and best practice, to obtain permission from the REC for the RTB Governing Board to confer the equivalent of NHS REC project/study specific approval after review of the study protocol, thereby streamlining the process and maximising the use of the tissues.

5.4 The RTB management committee must keep a register of all applications and approvals, which must be given an RTB-specific, unique identifier (ethical approval reference).

5.5 Researchers may first apply to an NHS REC for project/study specific approval before applying to an NHS REC approved RTB for tissues, for instance if the project/study requires a range and number of samples that would not be available within a single RTB. The Leeds RTB Governing Board may then accept the recommendation of the NHS REC and streamline its own review process, but must verify that the proposed study is within the scope of donor consent.

5.6 If project/study specific approval has been granted by an NHS REC or the equivalent conferred by the NHS REC approved RTB, the tissues are exempt from the requirements of the Act for the period of approval, and therefore can be held in unlicenced premises within the Leeds Teaching Hospitals or University of Leeds or transferred to an organisation that does not hold a HT Authority licence.

5.7 The exemption from the requirements of the Act is in place until the end of the approval period for the specific project/study. Researchers may apply for an extension to the approval period or submit a new application for the use of the same tissues for a different project, as in 5.3 or 5.5. If the application is submitted before the end of the original approval period, the exemption remains in place until the ethical review is completed.

5.8 At the end of the approval period, and if there is no further application for NHS REC or RTB equivalent project/study specific approval, or if the application was unsuccessful, any remaining, relevant material will be subject to the requirements of the Act.

5.9 The RTB management committee must devise a system to trigger an alert that the end of the approval period is approaching.

5.10 The alert system must be sufficiently robust to ensure that it is not dependent on a specific member of staff but linked to a job role (eg RTB manager), so that taking the required actions is not affected by changes in personnel.

5.11 Prior to the end of the approval period, a plan must be in place to ensure that any remaining, relevant material is managed in an HT Act compliant manner.

5.12 The provisions in sections 2 and 3 (export only) apply.

5.13 When tissues are released to researchers, the TTA Document B: Tissue transfer agreement for human tissues transferred by a Research Tissue Bank, available on the UoL Research and Innovation Service website, together with the algorithm that allows researchers to determine whether they have to operate within the Leeds HT Act governance framework (appendix).

5.14 The RTB-specific, unique ethical approval reference must be entered in the TTA (see 5.4) and the NHS REC reference (see 5.6) if applicable.

5.15 The TTA (document B) should be completed in conjunction with the explanatory notes, appended to the TTA.

Section B Applicability

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

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.

3 This SOP has been written to formally establish a consistent procedure for transferring human tissues to or from research groups in Leeds covered by the Research Licence for LTHT/UoL granted by the Human Tissue Authority.

4 The main aim of this SOP is to ensure that relevant staff, by referencing this document, can easily follow the process of sending tissues to or receiving tissues from external organisations, including other academic institutions or industry, in the context of sponsored academic or clinic national and international research.

5 This SOP does not cover collaborations with industry established on a commercial basis.

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 LTHT and the UoL 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 LTHT is registered as the Licence Holder with the HT Authority, and the principal licensed site ('the hub') is St James's University Hospital. The UoL 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 UoL 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

Previous Author: Patricia Harnden

Reviewer: Patricia Harnden, Designated Individual for the Research Licence

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Version , draft 1	All Persons Designated and key associated staff, HTA Manager, LTHT and UoL Research and Innovation, Medical Achiever leaders	14/09/2021 to 27/09/2021	Tim Brend Debby Gibson Sarah Myers Major: Include when TTAs do or do not apply to internal transfers
Version , draft 2	As above	06/10/2021 to 20/10/2021	None

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4.0	Dr Patricia Harnden Designated Individual LTHT/UoL Human Tissue Act	24/10/2021	

Distribution & Storage:

Distribution to

Persons Designated, LTHT/UoL HTA Research Licence, HTA Research Subgroup

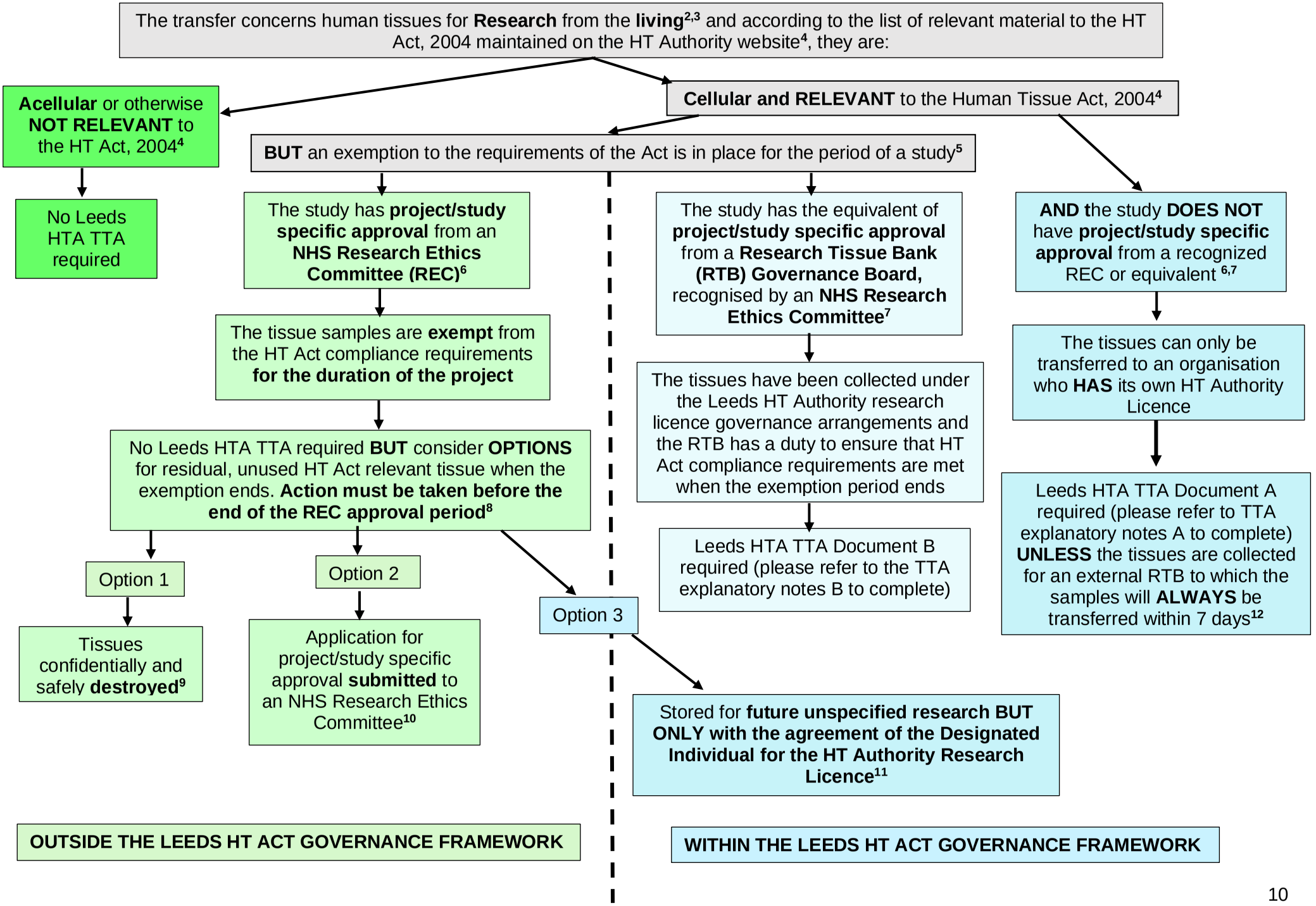
Location of Document

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

Electronic: Research and Innovation website, UoL

Appendix: TTA algorithm

DOES MY PROPOSED TRANSFER OF HUMAN TISSUES FALL WITHIN THE LEEDS HUMAN TISSUE ((HT) AUTHORITY RESEARCH LICENCE GOVERNANCE FRAMEWORK[1] AND ASSOCIATED TISSUE TRANSFER AGREEMENTS (TTAs)?



NOTES

[1] The Leeds HT Authority research licence covers specific research groups and locations within both the Leeds Teaching Hospitals NHS Trust and the University of Leeds. The Designated Individual (DI) for Research has the primary legal responsibility to ensure the proper conduct of the activities carried out under the licence under Section 18 of the HT Act. The HT Authority sets the standards that apply to consent, the governance and quality management systems, tissue traceability and the suitability of premises, facilities and equipment for the storage of tissues. The DI must appoint a Person Designated (PD) for each group. The PDs are responsible for assisting the DI in developing and implementing the required procedures to ensure compliance in their local area. The PDs and locations for which they are responsible are registered with the HT Authority under the Leeds licence and are subject to their inspection process.

[2] The HT Authority grants different types of licences depending on the activity undertaken. The licences held in Leeds are those for:
- the **Human Application** sector: procuring, testing, processing, storing, distributing and/or importing and exporting tissues intended for patient treatment including advanced therapy medicinal products;
- the **Organ Donation or Transplantation** sector;
- the **Anatomy** sector (body donation);
- and the **Post Mortem** sector: removing relevant material from the **deceased,** including for research purposes.

[3] Collecting tissues from the deceased in Leeds must always be performed under the authority of the DI for the Post-Mortem licence. However, researchers in Leeds may **receive** tissues from the deceased from **external organisations** under the authority of the DI for the Research licence.

[4] The fundamental concept of relevant material is that if a sample is known to contain even a single cell that has come from a human body, then the sample should be classified as relevant material. However, there are exceptions, such as cell cultures that have divided outside the body. The list of relevant material can be found at https://www.hta.gov.uk/policies/list-materials-considered-be-%E2%80%98relevant-material%E2%80%99-under-human-tissue-act-2004.

[5] Tissues that would otherwise be HT Act relevant can be exempt from the requirements of the HT Act if project/study specific approval for the collection and use of the tissues has been obtained by a recognized Research Ethics Committee. The exemption only applies for the period of approval, normally five years.
There is an additional very temporary exemption, which applies to tissues collected in Leeds on behalf of an external organization with its own licence. However, this situation must be actively monitored to ensure that the condition of the exemption (tissues retained in unlicenced premises in Leeds for 7 days at most prior to shipment) is always met (see note 12).

6 Only NHS Research Ethics Committees (RECs) or equivalent (see note 7) can confer this exemption. The ethical committees of other organisations, such as universities, cannot.

[7] In order to obtain NHS REC approval, RTBs are required to set up a Governance Board to oversee the workings of the bank and to review submissions from researchers for access to tissue samples. Additionally, the RTB may obtain approval from the REC to allow this Governance Board to conduct its own ethical approval process and confer project/study specific approval equivalent to that of the NHS REC itself.

[8] Unused HT Act relevant tissues left at the end of the specific project are subject to the requirements of the HT Act **immediately** on the date the NHS REC approval is no longer valid. One of the three options to ensure compliance with the Act must therefore be actioned before this date.

[9] Destruction of the tissues must be performed in accordance with the procedures for the disposal of human tissues developed by either the Trust or the University, depending on the location or affiliation of the research group.

[10] The exemption remains in place during the NHS REC review process but the application must be submitted before the expiry date of the initial approval. A plan to revert to option 1 or 3 should be in place in case the submission is not given a favourable opinion.

[11] If the likelihood of residual HT Act relevant tissues is high, the option to store tissues for future unspecified research should be considered during the project development as donors should be informed and consulted as part of the consent process. The option would only be appropriate if there is a high likelihood that the tissues will be used, and a mechanism is in place for access by researchers. It is not appropriate to store tissues with no plan to allow their use. Discussions with the DI need to take place as early as possible as tissues would have to be transferred to a research group working within the Leeds HTA Research Licence Governance Structure to take responsibility for the management of the tissues (see note 1). There is a cost associated with the storage of tissues and the performance of the recurrent activities required to maintain and demonstrate compliance with the Act and any transfer requires the agreement of the PD for that group.

[12] Tissues may be collected from donors in Leeds for an external RTB under the licence of another organization, for instance in the context of a multicentre clinical trial or a national collection of rare diseases. The HT Authority recognizes that samples may be batched to reduce the costs of shipment. It therefore allows for samples to be held in unlicenced premises for a short period, no more than seven days, before they are transferred to the licenced RTB. Governance processes must be in place in Leeds to ensure that this deadline is respected. A risk assessment must be performed. A contingency plan to mitigate risk must be agreed with the DI for the tissues to be held within the Leeds HT Authority governance framework in licenced premises.