Site visit inspection report on compliance with HTA licensing standards

University of Liverpool

HTA licensing number 12020

Licensed under the Human Tissue Act 2004 for the

- **storage of relevant material which has come from a human body for use for a scheduled purpose**

19 – 21 March 2019

Summary of inspection findings

The HTA found the Designated Individual (DI) and the Licence Holder (LH) to be suitable in accordance with the requirements of the legislation.

Although the HTA found that the University of Liverpool had met the majority of the HTA's standards, one major shortfall was found against the premises, facilities and equipment standard. This was in relation to monitoring of conditions in a liquid nitrogen storage area. Seven minor shortfalls were found against governance and quality, traceability and premises, facilities and equipment standards.

The HTA's regulatory requirements

Prior to the grant of a licence, the HTA must assure itself that the Designated Individual is a suitable person to supervise the activity authorised by the licence and that the premises are suitable for the activity.

The statutory duties of the Designated Individual are set down in Section 18 of the Human Tissue Act 2004. They are to secure that:

- the other persons to whom the licence applies are suitable persons to participate in the carrying-on of the licensed activity;
- suitable practices are used in the course of carrying on that activity; and
- the conditions of the licence are complied with.

Its programme of site visit inspections to assess compliance with HTA licensing standards is one of the assurance mechanisms used by the HTA.

The HTA developed its licensing standards with input from its stakeholders. They are designed to ensure the safe and ethical use of human tissue and the dignified and respectful treatment of the deceased. They are grouped under four headings:

- consent
- governance and quality systems
- traceability
- premises facilities and equipment.

This is an exception-based report: only those standards that have been assessed as not met are included. Where the HTA determines that there has been a shortfall against a standard, the level of the shortfall is classified as 'Critical', 'Major' or 'Minor' (see Appendix 2: Classification of the level of shortfall). Where HTA standards are fully met, but the HTA has identified an area of practice that could be further improved, advice is provided.

HTA inspection reports are published on the HTA's website.

Background to the establishment

The establishment is licensed under the Human Tissue Act 2004 (HT Act) for the storage of relevant material for use for scheduled purposes. The licence covers the University of Liverpool (UoL) hub site (Central Campus and the University Clinical Departments (UCD) at Royal Liverpool University Hospital) and four satellite sites. These are the Centre for Women's Health Research at Liverpool Women's Hospital, the Clinical Sciences Building at Aintree University Hospital, the Institute of Child Health at Alder Hey Hospital and the Leahurst campus.

The establishment has been licensed since 2010 and was last inspected in 2016. The establishment stores human samples for use for the scheduled purpose of 'research in connection with disorders, or the functioning, of the human body'. The licence covers activities relating to 12 Research Tissue Banks (RTBs) which store approximately 89,000 samples. The RTBs have received broad ethical approvals from recognised (NHS) research ethics committees (RECs). The establishment also stores samples of relevant material for use for specific research projects which have received approval from a recognised REC, thereby exempting storage of these samples from the HT Act's licensing requirements. Approximately 732,000 samples are held in such research collections, from living and deceased persons. The establishment's systems relating to the storage and use of this material were not assessed as part of this inspection.

The Corporate Licence Holder (CLH) is the University of Liverpool and the CLH contact is the executive Pro-Vice-Chancellor for the Faculty of Health & Life Sciences. The Designated Individual (DI) is a Senior Lecturer in the Department of Molecular and Clinical Cancer Medicine, University of Liverpool.

<u>Research collections</u>

Since the last inspection, there has been an increase in the number of RTBs, from 10 to 12. The RTBs are: the Liverpool Bio-Innovation Hub (LBIH) Biobank; Ocular Oncology Biobank; the University of Liverpool Research Eye Bank; Acute Pancreatitis Research Biobank; Chronic Pancreatitis Research Biobank; Pancreas Biomedical Research Unit (PBRU) Pancreatic Diseases Control Biobank; ESPAC T (European study group for pancreatic cancer); CLL Trials; Liverpool Blood Diseases Biobank; Peripheral T cell Lymphoma (PTCL) Biobank; Liverpool Musculoskeletal Biobank (LMB) and the Women's Research Tissue Bank (WRTB). The University of Liverpool Research Eye Bank has not collected or released samples since June 2016.

Storage of other tissue collections under the licence for use in research are from projects with expired ethical approval from a recognised REC, projects with local REC (e.g. healthy volunteers) or tissue that is imported. Some of these are legacy collections, which are

archived and are no longer being added to but are available for use for research. A number of these samples are ‘existing holdings’, held prior to the HT Act coming into force on 1 September 2006, and are therefore exempt from the HT Act’s consent requirements.

The DI has oversight of all human material stored at the establishment through an annual review of human material holdings. The DI obtains bi-annual reports of newly sponsored human material studies from research and development (R&D) managers at the establishment’s NHS partners and live reports of newly approved studies utilising human material sponsored by the University. In addition, an annual review of research holdings of human material identifies sponsorship, NHS REC and UoL Ethics approvals and end dates. The University’s Research Support Office is responsible for maintaining oversight of REC approval. However, it is the responsibility of the researcher to ensure that, where approval expires or samples are stored outside the terms of the approval, the relevant material is declared annually as being stored under the licence.

Governance arrangements include a quarterly meeting of the Human Material Oversight Committee between the DI, the central PD, University legal, ethical and research governance representatives and representative Human Material Officers (HMOs) at the Faculty of Health and Life Sciences, the Faculty of Science and Engineering and the Faculty of Humanities and Social Sciences. The HMOs provide advice to researchers on meeting HTA standards, and follow-up on studies where the approval period by the recognised REC is nearing completion, in order to determine when the storage of any remaining material has to be covered by the HTA licence. Best practice and quality issues such as audit findings, quality incidents and the review of overarching policies and documentation are discussed at these meetings. The DI also attends regular meetings with key members of staff within the University Research Support Office and the Research Governance Committee, which oversee all aspects of research governance. In addition, quarterly (or more frequently when required) meetings are held between the DI, the central PD and all the PDs and HMOs from across the University and satellite sites. The HMOs provide advice to researchers on meeting HTA standards, and follow-up on studies where the approval period by the recognised REC is nearing completion, in order to determine when the storage of any remaining material has to be covered by the HTA licence.

Regular audits of collections held in the RTBs are undertaken by trained staff, including the HMOs, and results of audits are provided to the DI. At the time of inspection, there was no evidence of audits being undertaken by groups holding the tissue collections. The DI provides documented training on HTA requirements to research staff and ensures that HTA training is included as part of mandatory induction training for new clinical and research staff and is repeated every three years if the researcher is actively using human material.

Biobank managers, chief investigators and/or persons responsible for each collection maintain records of staff training, evidence of training in handling human material, certificates

for Good Clinical Practice (GCP) and/or local consent training, standard operating procedures (SOPs), material transfer agreements, ethics approval documents (as appropriate), risk assessments and paper records of traceability. Traceability records for the larger collections are maintained using computer databases, which are backed up.

Each group is responsible for maintaining traceability records for their sample collections. The establishment's procedures require that all samples stored under the licence are assigned a unique identification number or name, which is used to track sample receipt, storage, use, distribution and disposal. Each group uses their own databases and procedures to record sample traceability. Where samples are disposed of, this is by incineration and each group keeps records of disposal.

Description of inspection activities undertaken

The HTA team inspected all 12 RTBs and 15 tissue collections at the hub and at three satellite sites. These collections included existing holdings, imported material, tumour tissue, ocular tissue from the deceased, biopsies, surgical tissue, blood, and other biological fluids containing cells. There is no relevant material currently being stored at the Leahurst campus and this site was not visited during this inspection.

The HTA team met key members of staff for each of the RTBs/tissue collections and reviewed relevant records; consent forms, records of consent training provided to staff, information provided to donors, arrangements for access to samples, storage conditions and monitoring of those conditions and records of disposal. During the inspection, the team reviewed SOPs, ethical approvals from the relevant RECs and material transfer agreements. Traceability audits were undertaken on 135 samples by selecting at least three samples from each collection and tracing those samples and related documentation from consent (as appropriate) through to receipt, storage location and disposal. Audits also included a reverse of this process for samples selected in storage. The samples selected were stored in liquid nitrogen, freezers, fridges and at room temperature. Paper records and/or electronic records were used to audit traceability.

Inspection findings

The HTA found the Licence Holder and the Designated Individual to be suitable in accordance with the requirements of the legislation.

Compliance with HTA standards

Governance and Quality

Standard	Inspection findings	Level of shortfall
GQ2 There is a documented system of audit		
a) There is a documented schedule of audits covering licensable activities.	There was no evidence of audits undertaken for the tissue collections held under the licence after expiry of the relevant REC approvals. Audits against HTA standards have recently been completed for all RTBs. However, at the time of inspection, there were no documented schedules of future audits for the LMB and PBRU biobanks.	**Minor**
GQ6 Risk assessments of the establishment's practices and processes are completed regularly, recorded and monitored		
a) There are documented risk assessments for all practices and processes requiring compliance with the HT Act and the HTA's Codes of Practice.	A number of groups working under the licence do not have risk assessments relating to compliance with the HT Act and HTA's Codes of Practice. Although the requirements to perform risk assessments related to risks to human tissue are stated in the Human Material Quality Manual, not all RTB or tissue collections could provide evidence of this, for example, LIBH and WRTB.	**Minor**

Traceability

Standard	Inspection findings	Level of shortfall
T1 A coding and records system facilitates the traceability of bodies and human tissue, ensuring a robust audit trail		

a) There is an identification system which assigns a unique code to each donation and to each of the products associated with it.	Not all samples have unique identifiers. For several sample collections, identical portions of a larger sample are labelled with the same identification code. The establishment maintains traceability of these samples by recording the number of portions of the original sample. However, some databases did not clearly record the number of portions remaining and the fate of the used (or disposed of) portions.	**Minor**
b) A register of donated material, and the associated products where relevant, is maintained.	The traceability records for one tissue collection lacked detail, such as individual identifiers, for tissue stored at -80ºC and 20ºC.	**Minor**
c) An audit trail is maintained, which includes details of: when and where the bodies or tissue were acquired and received; the consent obtained; all sample storage locations; the uses to which any material was put; when and where the material was transferred, and to whom.	The sample traceability processes for some research groups are not sufficiently robust and some groups had difficulty demonstrating full traceability of samples during the HTA audit. Traceability audits were performed on 135 samples. Discrepancies in traceability were identified and include: - Two samples recorded on the database could not be located in storage for two tissue collections. - Several samples in storage could not be traced back to the consent form due to the incorrect recording of the date on the database for one tissue collection. - Several samples in storage were not recorded on the database for one tissue collection. - One sample in storage was not recorded on the database and could not be traced to transport records for one tissue collection.	**Minor**
T2 Bodies and human tissue are disposed of in an appropriate manner		
b) The date, reason for disposal and the method used are documented.	One tissue collection could not evidence records of disposal during the inspection ,.	**Minor**

Premises, Facilities and Equipment

Standard	Inspection findings	Level of shortfall
PFE1 The premises are secure and fit for purpose		
b) Arrangements are in place to ensure that the premises are secure and confidentiality is maintained.	At the time of the inspection, one tissue collection held at room temperature was stored in an unlabelled, unlocked unit with access by unauthorised staff and researchers.	**Minor**
PFE2 There are appropriate facilities for the storage of bodies and human tissue		
c) Storage conditions are monitored, recorded and acted on when required.	At the time of inspection, there was no evidence of monitoring of liquid nitrogen levels or temperatures within the liquid nitrogen storage tank. The liquid nitrogen storage area does not have oxygen monitoring to alert staff to low levels of oxygen in the event of accidental leakage of liquid nitrogen. This poses a significant health and safety risk to researchers and staff, particularly when lone working. These risks have not been formally assessed and documented.	**Major**

Advice

The HTA advises the DI to consider the following to further improve practices:

No.	Standard	Advice
1.	C1(a)	Several tissue collections previously held under REC approval are being stored with no consent for further research. These collections are not being used for a scheduled purpose. The DI is advised to review the scope of the donor consent for these historical projects and determine whether tissue should continue to be stored or not.
2.	C1(b)	The DI is advised to ensure all consent forms are reviewed regularly to assess that they continue to be fit for current purpose/s. Consent forms for two RTBs were dated 2104 and 2015 respectively (LBIH and WRTB).
3.	GQ2(a)	The DI is advised that consent forms are audited for completeness as some discrepancies were noted in the recording of the version number of the donor information sheet and completion of consent form tick boxes by the donor.
4.	T1(c)	The DI is advised to consider labelling all storage units to indicate that they contain human tissue samples stored under the licence and with the storage

		identification number. This may help to ensure that sample traceability records accurately reflect storage location.
5.	PFE1(c)	At the time of inspection, some freezer storage units showed significant build-up of frost. Freezers are cleaned and decontaminated on an 'ad hoc' basis. The DI is advised to ensure all groups implement and adhere to a cleaning and decontamination schedule.
6.	PFE2(c)	During the audit of samples held at one tissue collection storage facility, it was noted that the ambient temperature of the room containing the storage freezers was elevated. This may pose a risk to the efficient operation of the sample storage freezers. The DI is advised to monitor and keep the temperature of the room under review to assure herself that the operation of the freezers is not compromised by an elevated ambient room temperature.
7.	PFE2(c)	The establishment's freezers are monitored and alarms are activated if temperatures deviate from their expected ranges. Establishment staff are alerted to alarms by an automated dial-out system or through a 24-hour monitoring organisation. In the event of an alarm triggering, establishment staff are contacted sequentially using an emergency call-out list. The DI is advised that all alarm or remote call–out challenge testing for all temperature controlled storage is performed periodically and documented to ensure the alarm or alert system is functioning as expected.
8.	PFE3(c)	The DI is advised to review temperature records for trends in excursions or drifting that may help to identify potential future freezer breakdown before it happens. This is particularly relevant when storage units are no longer under maintenance contracts.

Concluding comments

There are a number of areas of practice that require improvement, including one major shortfall and seven minor shortfalls.

The HTA requires the Designated Individual to submit a completed corrective and preventative action (CAPA) plan setting out how the shortfalls will be addressed, within 14 days of receipt of the final report (refer to Appendix 2 for recommended timeframes within which to complete actions). The HTA will then inform the establishment of the evidence required to demonstrate that the actions agreed in the plan have been completed.

The HTA has assessed the establishment as suitable to be licensed for the activities specified subject to corrective and preventative actions being implemented to meet the shortfalls identified during the inspection.

Report sent to DI for factual accuracy: 24 April 2019

Report returned from DI: 7 May 2019

Final report issued: 28 May 2019

Completion of corrective and preventative actions (CAPA) plan

Based on information provided, the HTA is satisfied that the establishment has completed the agreed actions in the CAPA plan and in doing so has taken sufficient action to correct all shortfalls addressed in the Inspection Report.

Date: 25 September 2019

Appendix 1: HTA standards

The HTA standards applicable to this establishment are shown below; those not assessed during the inspection are shown in grey text. Individual standards which are not applicable to this establishment have been excluded.

Consent standards
C1 Consent is obtained in accordance with the requirements of the Human Tissue Act 2004 (HT Act) and as set out in the code of practice
a) Consent procedures are documented and these, along with any associated documents, comply with the HT Act and the HTA's Codes of Practice.
b) Consent forms are available to those using or releasing relevant material for a scheduled purpose.
c) Where applicable, there are agreements with other parties to ensure that consent is obtained in accordance with the requirements of the HT Act and the HTA's Codes of Practice.
d) Written information is provided to those from whom consent is sought, which reflects the requirements of the HT Act and the HTA's Codes of Practice.
e) Language translations are available when appropriate.
f) Information is available in formats appropriate to the situation.
C2 Staff involved in seeking consent receive training and support in the essential requirements of taking consent
a) There is suitable training and support of staff involved in seeking consent, which addresses the requirements of the HT Act and the HTA's Codes of Practice.
b) Records demonstrate up-to-date staff training.
c) Competency is assessed and maintained.

Governance and quality system standards
GQ1 All aspects of the establishments work are governed by documented policies and procedures as part of the overall governance process
a) Ratified, documented and up-to-date policies and procedures are in place, covering all licensable activities.
b) There is a document control system.
c) There are change control mechanisms for the implementation of new operational procedures.
d) Matters relating to HTA-licensed activities are discussed at regular governance meetings, involving establishment staff.
e) There is a system for managing complaints.
GQ2 There is a documented system of audit
a) There is a documented schedule of audits covering licensable activities.
b) Audit findings include who is responsible for follow-up actions and the timeframes for completing these.

GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills
a) Qualifications of staff and all training are recorded, records showing attendance at training.
b) There are documented induction training programmes for new staff.
c) Training provisions include those for visiting staff.
d) Staff have appraisals and personal development plans.
GQ4 There is a systematic and planned approach to the management of records
a) There are suitable systems for the creation, review, amendment, retention and destruction of records.
b) There are provisions for back-up / recovery in the event of loss of records.
c) Systems ensure data protection, confidentiality and public disclosure (whistleblowing).
GQ5 There are systems to ensure that all adverse events are investigated promptly
a) Staff are instructed in how to use incident reporting systems.
b) Effective corrective and preventive actions are taken where necessary and improvements in practice are made.
GQ6 Risk assessments of the establishment's practices and processes are completed regularly, recorded and monitored
a) There are documented risk assessments for all practices and processes requiring compliance with the HT Act and the HTA's Codes of Practice.
b) Risk assessments are reviewed regularly.
c) Staff can access risk assessments and are made aware of risks during training.

Traceability standards
T1 A coding and records system facilitates the traceability of bodies and human tissue, ensuring a robust audit trail
a) There is an identification system which assigns a unique code to each donation and to each of the products associated with it.
b) A register of donated material, and the associated products where relevant, is maintained.
c) An audit trail is maintained, which includes details of: when and where the bodies or tissue were acquired and received; the consent obtained; all sample storage locations; the uses to which any material was put; when and where the material was transferred, and to whom.
d) A system is in place to ensure that traceability of relevant material is maintained during transport.
e) Records of transportation and delivery are kept.
f) Records of any agreements with courier or transport companies are kept.
g) Records of any agreements with recipients of relevant material are kept.

T2 Bodies and human tissue are disposed of in an appropriate manner
a) Disposal is carried out in accordance with the HTA's Codes of Practice.
b) The date, reason for disposal and the method used are documented.

Premises, facilities and equipment standards
PFE1 The premises are secure and fit for purpose
a) An assessment of the premises has been carried out to ensure that they are appropriate for the purpose.
b) Arrangements are in place to ensure that the premises are secure and confidentiality is maintained.
c) There are documented cleaning and decontamination procedures.
PFE2 There are appropriate facilities for the storage of bodies and human tissue
a) There is sufficient storage capacity.
b) Where relevant, storage arrangements ensure the dignity of the deceased.
c) Storage conditions are monitored, recorded and acted on when required.
d) There are documented contingency plans in place in case of failure in storage area.
PFE3 Equipment is appropriate for use, maintained, validated and where appropriate monitored
a) Equipment is subject to recommended calibration, validation, maintenance, monitoring, and records are kept.
b) Users have access to instructions for equipment and are aware of how to report an equipment problem.
c) Staff are provided with suitable personal protective equipment.

Appendix 2: Classification of the level of shortfall

Where the HTA determines that a licensing standard is not met, the improvements required will be stated and the level of the shortfall will be classified as 'Critical', 'Major' or 'Minor'. Where the HTA is not presented with evidence that an establishment meets the requirements of an expected standard, it works on the premise that a lack of evidence indicates a shortfall.

The action an establishment will be required to make following the identification of a shortfall is based on the HTA's assessment of risk of harm and/or a breach of the HT Act or associated Directions.

1. **Critical shortfall:**

   A shortfall which poses a significant risk to human safety and/or dignity or is a breach of the Human Tissue Act 2004 (HT Act) or associated Directions

   or

   A combination of several major shortfalls, none of which is critical on its own, but which together could constitute a critical shortfall and should be explained and reported as such.

   A critical shortfall may result in one or more of the following:

   (1) A notice of proposal being issued to revoke the licence

   (2) Some or all of the licensable activity at the establishment ceasing with immediate effect until a corrective action plan is developed, agreed by the HTA and implemented.

   (3) A notice of suspension of licensable activities

   (4) Additional conditions being proposed

   (5) Directions being issued requiring specific action to be taken straightaway

2. **Major shortfall:**

   A non-critical shortfall that:

   - poses a risk to human safety and/or dignity, or
   - indicates a failure to carry out satisfactory procedures, or
   - indicates a breach of the relevant CoPs, the HT Act and other relevant professional and statutory guidelines, or
   - has the potential to become a critical shortfall unless addressed

   or

   A combination of several minor shortfalls, none of which is major on its own, but which, together, could constitute a major shortfall and should be explained and reported as such.

   In response to a major shortfall, an establishment is expected to implement corrective and preventative actions within 1-2 months of the issue of the final inspection report. Major shortfalls pose a higher level of risk and therefore a shorter deadline is given, compared to minor shortfalls, to ensure the level of risk is reduced in an appropriate timeframe.

3. **Minor shortfall:**

   A shortfall which cannot be classified as either critical or major, but which indicates a departure from expected standards.

This category of shortfall requires the development of a corrective action plan, the results of which will usually be assessed by the HTA either by desk based or site visit.

In response to a minor shortfall, an establishment is expected to implement corrective and preventative actions within 3-4 months of the issue of the final inspection report.

Follow up actions

A template corrective and preventative action plan will be sent as a separate Word document with both the draft and final inspection report. You must complete this template and return it to the HTA within 14 days of the issue of the final report.

Based on the level of the shortfall, the HTA will consider the most suitable type of follow-up of the completion of the corrective and preventative action plan. This may include a combination of

- a follow-up site-visit inspection
- a request for information that shows completion of actions
- monitoring of the action plan completion
- follow up at next desk-based or site-visit inspection.

After an assessment of your proposed action plan you will be notified of the follow-up approach the HTA will take.