Site visit inspection report on compliance with HTA minimum 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**

14-16 June 2016

Summary of inspection findings

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

Although the HTA found that Liverpool University (the establishment) had met the majority of the HTA standards, two minor shortfalls were found against the governance and quality standards. The shortfalls related to the lack of comprehensive documentation of policies and procedures and risk assessments. The establishment addressed the shortfall relating to risk assessments before this report was finalised.

Particular examples of strengths and good practice are included in the concluding comments section of the report.

The HTA's regulatory requirements

The HTA must assure itself that the Designated Individual, Licence Holder, premises and practices are suitable.

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.

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. The HTA inspects the establishments it licences against four groups of standards:

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

This is an exception-based report: only those standards that have been assessed as not met are included. Where the HTA determines that a standard is not met, 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 given to the DI.

Reports of HTA inspections carried out from 1 November 2010 are published on the HTA's website.

Background to the establishment and description of inspection activities undertaken

The establishment is licensed under the Human Tissue Act 2004 (HT Act) for storage of relevant material for use for scheduled purposes. The licence covers the University of Liverpool hub site (Central Campus and the University Clinical Departments (UCD) at Royal Liverpool University Hospital) and four satellite sites - Centre for Women's Health Research at Liverpool Women's Hospital, Clinical Sciences Building (third floor) at Aintree University Hospital, Institute of Child Health at Alder Hey Hospital and the Leahurst campus. The licence holder is the University of Liverpool and the corporate licence holder contact is the Pro-Vice-Chancellor for the Faculty of Health & Life Sciences. The Designated Individual (DI) is a Senior Lecturer at the Cancer Research Centre, University of Liverpool.

The licence covers activities relating to nine Research Tissue Banks (RTB) and ten research collections consisting of over 70,000 samples from living and deceased persons. The RTBs have received ethics approvals from NHS recognised research ethics committees (RECs). Ten research collections stored under the licence include existing holdings, collections held following lapse of project-specific NHS REC approvals and collections which have received University (local) ethics approval. Several collections also include samples of DNA, RNA and plasma, which are not considered to be relevant material under the HT Act.

This was the second routine HTA inspection - the previous inspection was undertaken in August 2010. The HTA inspection team took into consideration information provided by the establishment including an up to date list of research collections stored under the licence, the 2015 compliance update and the establishment's 'Quality Manual for the Governance of Storage of Human Material for Research'. The HTA team was also informed that three satellite sites – Aintree University Hospital, Alder Hey Hospital and the Leahurst Campus were not storing any human tissue under the licence at the time of the inspection; these satellite sites were not visited during this inspection.

<u>Governance</u>

Governance arrangements include regular meetings attended by the DI, the Person Designated at each satellite site, Custodians (Biobank Managers) and Human Material Officers (HMOs) at the Faculty of Health and Life Sciences, 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. Regular audits of collections are undertaken by trained staff, including the HMOs, and results of audits are provided to the DI. Since most human tissue is used by groups within the Faculty of Health and Life Sciences, the DI has eight HMOs, one in each of the Research Institutes within this faculty, and one in each of the other faculties.

The DI also attends regular meetings with key members of staff in the Research Support Office of the University of Liverpool, which facilitates sponsorship for healthcare based research undertaken by University staff. The Research Support Office provides administrative support and helps to draft material transfer agreements for research groups as required. The Office also maintains a list of all projects and liaises with HMOs when the REC approval period is about to lapse.

The DI emails all Principal Investigators, not just those known to use human material, on an annual basis to seek information on their tissue collections in order to ensure that information is up to date. The DI provides training on HTA requirements to research staff, which is documented. The DI is in communication with senior members of staff at the various institutes and is currently seeking to ensure that HTA training is included as part of mandatory induction training for new clinical and research staff.

Principal Investigators and/or persons responsible for each collection maintain records of staff training, certificates for good clinical practice 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.

Tissue collections

The HTA team inspected all nine RTBs and five collections at the hub and Liverpool Women's Hospital satellite site. These collections included existing holdings, imported material, tumour tissue, ocular tissue from the deceased, biopsies, surgical tissue, blood, and other biological fluids containing cells. The team inspected the following RTBs– Liverpool Bio-Innovation Hub Biobank, Leukaemia Tissue Bank, Chronic Lymphocytic Leukaemia trials Biobank, Ocular Oncology Biobank, Liverpool Research Eye Bank, Acute Pancreatitis Research Biobank, Chronic Pancreatitis Research Biobank, Pancreas Biomedical Research Unit Control Biobank and the Liverpool Women's Research Tissue Bank.

The HTA team met key members of staff for each of the 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 (as appropriate) and material transfer agreements.

There is secure access to tissues in storage; keys to cupboards, fridges and freezers are only accessible to staff who use the tissues. Contingency arrangements are in place to cover collections stored in -80^{0}C and -140^{0}C freezers in the event of freezer failure. Almost all freezers and fridges are linked to a proprietary temperature monitoring system and there are systems in place to respond if a local alarm is triggered. Freezer alarms are tested and maintained.

Audit trails were undertaken by selecting at least two 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 freezers, fridges and at

room temperature. Paper records and/or electronic records were used to audit traceability. There were no discrepancies.

In the case of RTBs, annual reports to the relevant RECs were reviewed along with participant information leaflets, consent forms, material transfer agreements, records of sample collection, consent training and disposal. Audit trails of randomly selected samples and their storage locations were undertaken. There were no discrepancies.

Inspection findings

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

Compliance with HTA standards

Governance and Quality

Standard	Inspection findings	Level of shortfall
GQ1 All aspects of the establishment's work are supported by ratified documented policies and procedures as part of the overall governance process.	Some collections do not have documented policies and procedures in place which cover all practices. The RTBs have appropriate documentation; however, some of the other collections - including the Liverpool Research Tooth Collection and some projects which are no longer covered by NHS REC approval do not have documented policies and procedures. Please see supporting advice (Advice item 2).	**Minor**
GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately.	Risk assessments which cover regulatory risk and risk to tissues are not undertaken in a systematic manner. Staff responsible for some collections held under the licence do undertake some health and safety risk assessments, but these are not kept up to date. Please see supporting advice, Advice item 8) *Following the inspection, the establishment issued a risk assessment which addressed this shortfall.*	**Minor**

Advice

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

No.	Standard	Advice
1.	C1	The DI is advised to liaise with staff who seek consent for research in order to consider including seeking generic consent for future research. Such consent must then be documented and will help to ensure that the samples are available for use in other research projects.
2.	GQ1	At a minimum, it is expected that most collections will have standard operating procedures (SOPs) covering the following activities: • consent; • collection; • receipt; • labelling; • specimen preparation / preservation; • storage; • relevant transport arrangements; • cleaning and decontamination; • disposal. Collections which hold a variety of material which is released to several research groups may need to cover more areas in their suite of documents. An SOP should be a clear and accurate representation of an existing procedure or process, preferably set out in the format of a stepwise guide. SOPs should be understandable to enable new staff to follow a procedure from beginning to end. They should be detailed enough to ensure uniformity between staff in the performance of a specific function and should be followed by all staff who have been appropriately trained. People undertaking the processes should be involved in developing SOPs to ensure that the written procedures reflect actual practices. Regular review of SOPs will help to prevent incremental departure from written processes with the passing of time and allow establishments to identify improvements. Establishments should introduce a system to record that staff have read and understood SOPs.
3.	GQ1	The DI is advised to formalise the role of the HMOs in order to ensure that they hold regular meetings with staff in the various faculties and institutes and to detail the type of information which must be cascaded to staff. In addition, the DI is advised to consider whether HMOs could be given a role in training new clinical and research staff.
4.	GQ1	All RTBs have suitable governance committees or steering boards. The DI is advised to ensure that all RTBs have documented policies and procedures in place which cover the process of evaluating and approving the transfer of collections or tissues into the RTB.
5.	GQ2	The DI is advised to include audits of all projects which currently have University ethics approval and involve the use of human tissue from staff, students and other volunteers in the overall audit schedule.

6.	GQ3	The DI is advised to consider setting up a research intranet page on the University of Liverpool website and populate the page with resources for use by research groups. Such resources could include templates for consent forms, participant information sheets, risk assessments, audit forms, and material transfer agreements. The DI may also consider including learning tools and links to relevant pages on the Medical Research Council (MRC) website such as the Regulatory Support Centre (http://www.rsclearn.mrc.ac.uk/) which was developed with input from the HTA.
7.	GQ7	There are local systems in place to address adverse incidents. The DI is advised to consider including a discussion of adverse incidents as a standard item in the agenda of meetings held with the HMOs. Such discussions will help to identify common incidents, review corrective actions and help to ensure that effective preventative actions are implemented following incidents.
8.	GQ8	The DI is advised to undertake risk assessments which cover broad risks such as storage of samples for research without consent, security breaches, transport of samples and risks relating to planned changes to premises and practices. The HTA understands that the establishment intends to change the location of some of the tissues and implement new databases to store information and the DI is advised to risk assess these changes in terms of regulatory risks, risks to the data integrity and risks to tissues. The DI is advised to ensure that staff have access to such risk assessments.

Concluding comments

Since the previous inspection, the establishment has improved governance by placing HMOs in each of the Faculties and Research Institutes where human tissue is stored. The HMOs play a crucial role in the management of the licence and cascading information to researchers who work under the licence. They have been trained and are available to provide advice on meeting HTA standards. There are established links between the Research Support Office, the DI and the HMOs. The HMOs attend Regulatory Affairs Committee meetings or Safety Committee meetings as appropriate, held at Research Institute and Faculty level. The DI attends the Faculty of Health and Life Sciences Regulatory Affairs Committee and University Research Governance Committee, which has overarching responsibility for governance of human tissue at the University of Liverpool.

The DI intends to ensure that all induction programmes within the University will include information on the HT Act in order to ensure that new students and staff are aware of the legal requirements under the HT Act. The establishment is looking to implement a research data Information Management system in order to streamline governance of REC approved studies.

The Women's Research Tissue Bank has a comprehensive suite of documents which covers risk management of practices relating to research undertaken at Liverpool Women's Hospital. A robust system of governance is in place at the Liverpool Research Eye Bank, which removes and stores eyes from the deceased. All documentation relating to consent and removal is stored in a bespoke database. Trained staff ('retrievalists') remove eyes at the mortuary, which is licensed in the HTA's post mortem sector. Research co-ordinators have established close links with the bereavement team at Royal Liverpool University Hospital and

are made aware of all deaths. This enables the research co-ordinator to seek consent from relatives of the deceased for the removal and use of eyes for research in a timely manner.

There are a number of areas of practice that require improvement, including two minor shortfalls. The HTA has given advice to the Designated Individual with respect to setting up a research page on the intranet, seeking generic consent for research, providing clarity as to the role and responsibilities of HMOs and extending the scope of internal audits.

The HTA requires that the Designated Individual addresses the shortfall by submitting a completed corrective and preventative action (CAPA) plan 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 shortfall identified during the inspection.

Report sent to DI for factual accuracy: 12 July 2016

Report returned from DI: 26 July 2016

Final report issued: 15 August 2016

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: 14 November 2016

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
• Consent forms comply with the HTA's Code of Practice • Consent forms are in records and are made accessible to those using or releasing relevant material for a scheduled purpose • If the establishment obtains consent, a process is in place for acquiring consent in accordance with the requirements of the HT Act 2004 and the HTA's Codes of Practice • Where applicable, there are agreements with third parties to ensure that consent is obtained in accordance with the requirements of the HT Act 2004 and the HTA's Codes of Practice • Consent procedures have been ethically approved
C2 Information about the consent process is provided and in a variety of formats
• Standard operating procedures (SOPs) detail the procedure for providing information on consent • Agreements with third parties contain appropriate information • Independent interpreters are available when appropriate • Information is available in suitable formats, appropriate to the situation • Consent procedures have been ethically approved
C3 Staff involved in seeking consent receive training and support in the implications and essential requirements of taking consent
• Standard operating procedures (SOPs) detail the consent process • Evidence of suitable training of staff involved in seeking consent • Records demonstrate up-to-date staff training • Competency is assessed and maintained

Governance and quality system standards
GQ1 All aspects of the establishments work are supported by ratified documented policies and procedures as part of the overall governance process
• Policies and procedures are in place, covering all activities related to the storage of relevant material for research in connection with disorders, or the functioning, of the human body • Appropriate risk management systems are in place

- Regular governance meetings are held; for example, health and safety and risk management committees, agendas and minutes
- Complaints system

GQ2 There is a documented system of quality management and audit

- A document control system, covering all documented policies and standard operating procedures (SOPs).
- Schedule of audits
- Change control mechanisms for the implementation of new operational procedures

GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills

- Qualifications of staff and training are recorded, records showing attendance at training
- Orientation and induction programmes
- Documented training programme, (e.g. health and safety, fire, risk management, infection control), including developmental training
- Training and reference manuals
- Staff appraisal / review records and personal development plans are in place

GQ4 There is a systematic and planned approach to the management of records

- Documented procedures for the creation, amendment, retention and destruction of records
- Regular audit of record content to check for completeness, legibility and accuracy
- Back-up / recovery facility in the event of loss of records
- Systems ensure data protection, confidentiality and public disclosure (whistle-blowing)

GQ5 There are documented procedures for distribution of body parts, tissues or cells

- A process is in place to review the release of relevant material to other organisations
- An agreement is in place between the establishment and the organisation to whom relevant material is supplied regarding the tracking and use of material and eventual disposal or return

GQ6 A coding and records system facilitates traceability of bodies, body parts, tissues and cells, ensuring a robust audit trail

- There is an identification system which assigns a unique code to each donation and to each of the products associated with it
- An audit trail is maintained, which includes details of when and where the relevant material was acquired, the consent obtained, the uses to which the material was put, when the material was transferred and to whom

GQ7 There are systems to ensure that all adverse events are investigated promptly
• Corrective and preventive actions are taken where necessary and improvements in practice are made • System to receive and distribute national and local information (e.g. HTA communications)
GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately
• Documented risk assessments for all practices and processes • Risk assessments are reviewed when appropriate • Staff can access risk assessments and are made aware of local hazards at training

Premises, facilities and equipment standards
PFE1 The premises are fit for purpose
• A risk assessment has been carried out of the premises to ensure that they are appropriate for the purpose • Policies in place to review and maintain the safety of staff, authorised visitors and students • The premises have sufficient space for procedures to be carried out safely and efficiently • Policies are in place to ensure that the premises are secure and confidentiality is maintained
PFE 2 Environmental controls are in place to avoid potential contamination
• Documented cleaning and decontamination procedures • Staff are provided with appropriate protective equipment and facilities that minimise risks from contamination • Appropriate health and safety controls are in place
PFE3 There are appropriate facilities for the storage of bodies, body parts, tissues and cells, consumables and records.
• Relevant material, consumables and records are stored in suitable secure environments and precautions are taken to minimise risk of damage, theft or contamination • Contingency plans are in place in case of failure in storage area • Critical storage conditions are monitored and recorded • System to deal with emergencies on 24 hour basis • Records indicating where the material is stored in the premises

PFE 4 Systems are in place to protect the quality and integrity of bodies, body parts, tissues and cells during transport and delivery to a destination
• Documented policies and procedures for the appropriate transport of relevant material, including a risk assessment of transportation • A system is in place to ensure that traceability of relevant material is maintained during transport • Records of transportation and delivery • Records are kept of any agreements with recipients of relevant material • Records are kept of any agreements with courier or transport companies
PFE5 Equipment is appropriate for use, maintained, quality assured, validated and where appropriate monitored
• Records of calibration, validation and maintenance, including any agreements with maintenance companies • Users have access to instructions for equipment and receive training in use and maintenance where appropriate • Staff aware of how to report an equipment problem • Contingency plan for equipment failure

Disposal Standards
D1 There is a clear and sensitive policy for disposing of human organs and tissue
• Documented disposal policy • Policy is made available to the public • Compliance with health and safety recommendations
D2 The reason for disposal and the methods used are carefully documented
• Standard operating procedures (SOPs) for tracking the disposal of relevant material detail the method and reason for disposal • Where applicable, disposal arrangements reflect specified wishes

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.