Site visit inspection report on compliance with HTA licensing standards

University of Exeter

HTA licensing number 12104

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**

11, 12 and 14 July 2017

Summary of inspection findings

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

The University of Exeter (the establishment) was found to have met all HTA standards.

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

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 and description of inspection activities undertaken

This report refers to the activities carried out at the University of Exeter (the establishment) under the HTA licence. The licence covers three premises: St Luke's Campus in Exeter (the hub, for the purposes of HTA licensing), Streatham Campus (the first satellite) in Exeter and Penryn Campus in Truro (the second satellite). This was the second site visit of the establishment since it was granted an HTA licence in June 2007; however, it was the first visit to the satellite sites, which were added in 2013 and 2016. The HTA last inspected the establishment on 12 December 2012. The establishment's research licence covers the storage of relevant material for use for the scheduled purpose of 'research in connection with disorders, or the functioning, of the human body and education or training relating to human health'.

The Designated Individual (DI) is a Senior Lecturer at the University of Exeter Medical School. The Corporate Licence Holder (CLH) is the University of Exeter and the Corporate Licence Holder contact (CLHc) is the University Research Ethics and Governance Manager. Material is stored by approximately 20 Principal Investigators (PIs) / research groups. Each PI or their nominee is appointed as a Person Designated (PD) and all PDs are appointed as either a 'Human Tissue Custodian' or 'Human Tissue Officer', which reflects the amount of activity the individual undertakes under the licence. All PDs are part of the Steering Committee, which meets biannually, to discuss HTA-related matters. If the PD leaves the University, the licensable samples for which they are responsible are either transferred to a different institution, disposed of or transferred internally to the custodianship of another responsible individual. This is overseen by the DI.

The satellite site at Streatham Campus was added to the HTA licence in October 2013. All relevant material at this site is held under projects approved by recognised Research Ethics Committees (RECs) and is therefore exempt from the licensing requirements of the Human Tissue Act 2004 (HT Act). On expiry of these REC-approved projects, the material will be stored under the HTA licence at this site, providing that the donor consented to the on-going storage. The second satellite, at Penryn, was added to the HTA licence in November 2016. This site is not currently storing relevant material under the licence but there is a plan to do so in the near future.

The DI has oversight of all human tissue stored at the establishment across all sites. Before material is stored, researchers are requested to complete an 'Application to Store Human Tissue' form that give details of relevant material which will be held under the licence or under projects approved by recognised RECs. Where tissue is stored under recognised REC approval, the form also includes details of the expiry date of the REC approval. If material is stored under the licence, the DI is able to verify that the researcher who will be seeking consent has been trained and their competency assessed.

Stored samples

The hub site stores relevant material under the HTA licence. This material includes plastinated organs which are imported; a whole skeleton, dry bones and fixed brain slices which are existing holdings; and muscle biopsies, saliva and tissue slide collections. Plasma and urine are stored but have been rendered acellular by a recognised protocol (*American Association of Blood Banks Manual for Plasma Separation*) and are therefore exempt from licensing requirements of the HT Act. These samples are not tracked in the dedicated tissue database. Frozen muscle and saliva samples are held in the Department of Sport and Health Science. The majority of these samples are from healthy donors whose consent has been obtained by trained staff at the establishment. The establishment also obtains samples from The Royal Devon & Exeter Tissue Bank (the Biobank). Three projects, with ethical approval from a recognised REC, are stored at -80°C from this Biobank on the Streatham campus satellite site.

The DI writes all core SOPs relating to human tissue and these are reviewed annually. Research groups must have read the SOPs before a study is set up on the tracked database and this information is captured on the database. Each PI/study group may also create their own bespoke documentation relating to the research projects to capture project-specific details.

Consent

The DI has assurance that relevant material from outside establishments (e.g. commercial companies and the Biobank) has been sourced with appropriate consent via the material transfer agreements that are in place.

Volunteer donors for the Sports and Health Sciences and Department of Psychology studies are recruited via posters displayed on campus and by word of mouth. The consent process for these studies is undertaken by trained staff. These studies have been given ethical approval from the relevant University of Exeter College Research Ethics Committee and are held under the HTA licence. The DI provides internal training on informed consent and on the HT Act, and all researchers and staff working with human tissue are required to attend. Samples are destroyed on the completion of the studies. All participant information sheets and consent forms are approved by the relevant College Research University Ethics Committee and consent forms are audited as part of the annual audit cycle undertaken by the DI.

Receipt and labelling

Most relevant material samples from studies are recorded in a central database. Each sample is assigned a unique identification (ID) code immediately after collection or on receipt by the establishment (see *Advice*, item 1). Sample IDs are linked to the consent form and these consent forms are stored within individual study files which are held securely by each research team. Some legacy samples are tracked using spreadsheets maintained on the establishment's server, which is backed-up regularly.

Storage

Hub site

The establishment stores human tissue in five -80°C freezers that are located in a secure, dedicated freezer storage area. The freezers are connected to an power supply which provides back-up emergency power in the case of supply failure. There is also a separate, monitored emergency -80°C back-up freezer facility located within the Medical School. The Technical Services Manager monitors freezer temperatures for trends by taking a daily snapshot of 24 hour temperature readings. There is a remote call-out system to alert

establishment staff of any temperature excursions from the expected range or a failure in the power supply (see *Advice*, item 2). Annual preventative maintenance is performed. Two collections are held at room temperature: one collection of faeces within the freezer storage area and a tissue slide collection held within the adjacent laboratory. There are three collections of human material stored at room temperature which are existing holdings and are stored under the licence: a collection of tissue sections on slides, one whole skeleton and a collection of dry bones/ fixed brain slices which are securely stored within the Medical School.

There is also human material associated with three projects stored at -80°C and three projects storing tissue slides held at room temperature that are under approval from a recognised REC. These samples do not fall under the licence and are managed by individual PIs. The samples are not required to be recorded on the in-house tracking system; however, the DI has ensured that a robust tracking system and audit will be in place. All samples not being held under the authority of the HTA licence are audited by researchers although these results are not communicated to the DI.

Streatham Campus (first satellite)
All projects storing relevant material at this site have approval from recognised RECs (three projects) or are from the Biobank (three projects). These are stored in one dedicated -80°C freezer which has a similar monitoring system to that at the hub site, with a call-out system. There is a back-up carbon dioxide cylinder in place to maintain the required temperature in the event of a power failure. There is also one recently donated sample stored at 4°C in a secure fridge within the Physics laboratory. These samples are audited by researchers (see *Advice*, item 3).

Penryn Campus (second satellite)
The establishment is not yet storing relevant material at this site but will commence storage in the near future. The PD in place (Human Tissue Officer) is the Technical Services Manager who also sits on the Steering Committee. Tissue will be stored at -80°C on these premises with a similar monitoring system to the hub (see *Advice,* item 9). There are plans for the PD to undertake quarterly audits on the stored human tissue and, in addition, the DI plans to undertake annual audits. There are technological links in place between the hub and satellites.

Description of inspection activities undertaken

The timetable for the inspection visit of the hub and satellites was developed after consideration of the previous inspection report, changes in the licence, compliance update information and communications with the HTA since the last inspection. The inspection included a visual inspection of the site (sample reception and storage areas), discussions with the DI, the University Research Ethics and Governance Manager, the Technical Services Manager, a senior lecturer and a doctoral student. Audits of traceability were also carried out.

Traceability audits from storage location to database, and from sample identifier to the relevant consent forms, were performed on 16 saliva and muscle biopsies stored at -80°C, two faecal samples and four tissue slides stored at room temperature. An audit was also performed on two plastinated samples, a whole skeleton and five dry bone specimens. No anomalies were identified during any of the audits.

Inspection findings

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

Compliance with HTA standards

All applicable HTA standards have been assessed as fully met.

Advice

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

No.	Standard	Advice
1.	GQ1(a)	To further strengthen sample traceability, the DI is advised to ensure the procedures for assigning a unique ID code and recording the details of samples on the tissue database are captured within the protocol SOP03/UoE/HTA: Receipt and Storage of Human Tissue V5).
2.	GQ1(a)	Currently, plasma and urine are rendered acellular prior to storage using a recognised protocol and, as such, this material is not relevant material under the HT Act. The DI is advised to include details of this protocol in the following procedural documents to assure herself that all researchers are using an appropriate procedure to render plasma and urine acellular: - SOP04_Blood Sample Separation V5 - SOP05_Centrifugation of Blood Samples V5.
3.	GQ2(a)	Researchers indicated that samples stored with approval from recognised RECs are being stored in accordance with the project participant's consent. The DI is advised to continue with the good practice of monitoring, through audit, the expiry dates of these projects so that she is aware when samples will be required to be stored under the HTA licence.
4.	GQ2(a)	The projects with approval from RECs are not currently audited by the DI. The DI is advised to review IRAS/HRA forms to ensure that storage of samples under the licence on expiry of the REC-approved project is in line with terms of consent given for further storage.
5.	GQ6(a)	There are documented risk assessments for most practices and processes requiring compliance with the HT Act and the HTA's Codes of Practice. The DI is advised to add inappropriate disposal of samples and withdrawal of consent to the documented risk assessments of all practices and procedures connected with licensed activities.
6.	T1(c)	Although full traceability was demonstrated, one minor discrepancy was found in the transfer records of the legacy database whereby samples which had been transferred to another researcher outside of the establishment had no details of their destination recorded in the database. The DI is advised to ensure the destination field on the legacy database is incorporated into future audits to provide an ongoing assurance of accuracy and completeness.

7.	PFE1(c)	Cleaning and decontamination procedures are performed regularly and recorded on a checklist within the freezer storage area. An updated version, to include the cleaning of filters and de-icing of the freezers, has been created and is contained within the suite of the establishment's documents; however, it had not yet been put into use. The DI is advised to implement this checklist across all of the establishment's sites so that she can assure herself that the freezers are being appropriately and consistently maintained by establishment staff.
8.	PFE2(c)	The tissue storage alarm system is regularly tested to ensure that the call-out function is working correctly and that the nominated duty staff receive SMS or text alerts. The DI is advised to consider undertaking periodic unannounced checks to verify that the nominated staff respond appropriately to the alarms and would be available to attend the site if an alarm is triggered.
9.	PFE2(c)	The storage facility consists of a number of -80°C freezers and the ambient room temperature in this area is maintained by air conditioning units. The DI is advised to consider placing a probe to monitor room temperature in this area which can be connected to the existing monitoring system. This would help to detect any failure in the air conditioning system so that corrective action/s can be taken. This will help to reduce the risk of the ambient room temperature rising in the event of an air conditioning failure, which may cause difficulty for the freezers in maintaining an appropriate storage temperature.
10.	PFE2(c)	The designated -80°C freezer which will store relevant material at the Penryn satellite site is currently attached to the alarm call-out system in the event of storage failure. The daily temperature is not currently monitored. The DI is advised to consider fitting a temperature-monitoring probe to the freezer or ensure daily temperatures are recorded manually on the commencement of storage of samples under the licence. This will ensure that critical storage conditions are monitored.

Concluding comments

During the inspection, several areas of good practice were noted:

- The DI ensures that no study can be set up with samples recorded on the tissue database and subsequently stored without the researcher accessing and reading all overarching human tissue SOPs. This is information captured on the dedicated database.

- An 'Application to Store Human Tissue' form is completed for all samples, whether stored under the HTA licence or as part of an approved study from a recognized REC. This helps to assure the DI that she is made aware of all projects which store human tissue.

- SharePoint has recently been introduced to the University and all information and SOPs are held within the Human Tissue Folder. This helps to assure the DI that all staff and students have access to up-to-date human tissue information and training.

- The Technical Services Manager reviews the daily temperature plots from the monitoring system of the freezers which helps to identify a potential failure of the storage facility before it occurs.

The HTA has assessed the establishment as suitable to be licensed for the activities specified

Report sent to DI for factual accuracy: 11 August 2017

Report returned from DI: 18 August 2017

Final report issued: 29 August 2017

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.