Site visit inspection report on compliance with HTA licensing standards

Loughborough University

HTA licensing number 12577

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**

10 and 11 July 2018

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 Loughborough University had met the majority of the HTA's standards, two major and six minor shortfalls were identified against the Consent, Governance and quality systems, Traceability and Premises, facilities and equipment standards.

There has been noteable expansion in both the departments storing relevant material and in the number of samples held under the establishment's licence. There has also been a change in Designated Individual since the last HTA site visit inspection.

Particular examples of strengths and 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

Loughborough University (the establishment) is an academic institution undertaking research into a variety of health related conditions. The HTA licence covers the storage of relevant material for use for a scheduled purpose by three independent research groups (School of Sports Exerise and Health Sciences, Centre for Biological Engineering and Department of Chemistry). Each of the research groups has an assigned Person Designated (PD) under the licence who reports to the DI on matters relating to licensable activities. Individual research projects that have recognised research ethics committee (REC) approval are excepted from the licensing requirements of the Human Tissue Act 2004 (HT Act). However, tissue collections associated with these research projects are subject to licensing by the HTA if they continue to be stored after the REC approval has expired. At the establishment, all new research projects must be approved by the university's Ethics Approvals (Human Participants) Sub-Committee prior to commencing. Upon receipt, samples are assigned an unique identifier generated by an electronic laboratory management system (LIMS) database. This system is used by all groups across the university and administrated by the Regulatory Compliance Officer. Consent is generally sought by individuals from each research study group. Consent training is provided in-house by the Regulatory Compliance Officer. Material is also received or transferred from or to other research institutes under material transfer agreements (MTAs).

The establishment has been licensed by the HTA since February 2011. This report describes the second, routine, site visit inspection of this establishment. The timetable for the site visit inspection was developed in consideration of the establishment's licence application, compliance update information and pre-inspection discussions with the DI.

Description of inspection activities undertaken

The site visit inspection included a visual inspection of the storage areas, a review of documentation and meetings with establishment staff. An audit of traceability records, including paper-based and electronic databases, and storage locations was conducted for each of the tissue collections and the anatomical bone collection (see *Advice,* item 5) held under the HTA licence. All samples reviewed during the audit were chosen at random by the inspection team. Anomalies were found in traceability records for collections held in the School of Sports, Exercise and Health Sciences (SSEHS); and the Centre for Biological Engineering. (see shortfall against T1(c)). Consent documentation and training of staff involved in seeking consent, were also reviewed for samples identified during the traceability audits (see shortfalls against C1(a) and C2(b)).

The inspection team conducted round table interviews with the PDs, the Regulatory Compliance Officer and the individual department Quality Managers. A separate round table interview was also conducted with a consent seeker and consent trainer. The DI and Safety

Officer attended all round table interviews and were present with the inspection team throughought the inspection process.

A summary of each of the individual research groups is described below:

School of Sports, Exercise and Health Sciences (SSEHS):

This department holds the majority of the relevant material that is stored under the licence. Material is stored between the National Centre for Sport and Exercise Medicine and the adjacent Clyde Williams building. Some of the material is held under current, recognised REC approval and is therefore excepted from the licensing requirements of the HT Act. The department holds approximately 65,000 samples, all from the living. Samples are predominanently stored frozen at -80ºC. Consent is sought by individuals from each research study, the training for which is provided by the Regulatory Compliance Officer in house.
A collection of human bones, including 3 whole skeletons, is held within this department for the scheduled purpose of education or training relating to human health.

Department of Chemistry:

A total of approximately 600 samples, all from the living, are held within this department and are frozen at -80ºC. The majority of samples are imported and are held under current recognised REC approval and are therefore excepted from the licensing requirements of the HT Act.

Centre for Biological Engineering (CBE):

A total of 45 samples from both the living and deceased are held within this department and are stored at both -80ºC and in vapour phase liquid nitrogen storage. All samples are either purchased from commercial suppliers, imported or obtained from other research institutes under the authority of material transfer agreements (MTAs). Consent is therefore not sought by the researchers themselves but by a third party.

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

Consent

Standard	Inspection findings	Level of shortfall
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.	SSEHS and Department of Chemistry – Internal proceedures with regards to the recording of consent are not being followed. A number of consent forms were completed with ticks rather than the donor who is giving consent initialling as requested on the form. In addition, both options for retention of tissue for future research or retention for only the specific project had been completed in several examples reviewed. By completing both options, it makes the wishes of the person giving consent unclear and poses a risk that tissue may be used outside of the scope of the given consent.	**Minor**
b) Records demonstrate up-to-date staff training.	Department of Chemistry – During the audit of consent records, evidence of an untrained researcher seeking consent for the collection of relevant material from study participants was seen.	**Major**

Governance and Quality

Standard	Inspection findings	Level of shortfall
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.	The University Biological Safety Policy, dated December 2008 and used by multiple departments at the establishment, is out of date and requires reviewing and, if appropriate, updating. Department of Chemistry – The department lacked a number of SOPs relating to the licensable activity taking place. These include but are not limited to the receipt, transfer and collection of samples.	**Minor**

	The SOP CMHTA-QUALSOP-02 does not stipulate that consent training must be completed via SSEHS prior to seeking consent and collection of samples from study participants. SSEHS – The induction training programme for new starters has a review date of August 2017. This induction programme should be reviewed and updated as required.	**Minor**
GQ2 There is a documented system of audit		
a) There is a documented schedule of audits covering licensable activities.	SSEHS and Department of Chemistry – Currently, there is no schedule of audits of the licensable activities being undertaken. Audit findings should be recorded and corrective and preventative actions identified and actioned in order to help assure the DI that the establishment's procedures remain appropriate and comply with regulatory requirements.	**Minor**
GQ5 There are systems to ensure that all adverse events are investigated promptly		
a) Staff are instructed in how to use incident reporting systems.	SSEHS – The SOP SSEHS-AI-038 refers to reporting of incidents to the HTA. However, this SOP describes the process of incident reporting for establishments licensed under different legislation, the Human Tissue (Quality and Safety for Human Application) Regulations 2007. Reporting of adverse events to the HTA from establishments licensed in the research sector is not mandatory though establishments are encouraged to discuss any relevant concerns with us. The establishment's incident reporting SOP should be updated to instruct staff how to use the in-house incident reporting procedures.	**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.	The establishment's risk assesments are mainly related to Health and Safety matters rather than identifying the potential risks posed to the donors and tissues in consideration of undertaking the licensed activity. Risk assessments which are not present include but are not limited to: • retention of tissue without appropriate and valid consent, • loss of traceability, • or the inappropriate or inaccurate consent seeking processes leading to a donor being mis-informed.	**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		
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.	SSEHS – During the sample traceability audits that were undertaken, it was identified that the physical sample storage locations did not match those recorded on the electronic database. In addition, samples which had been recorded as disposed, were found to still be in storage. This poses a risk of inadvertent retention of material. Human bone specimens were labelled using a combination of colored dots, however the colour yellow was used as part of this labelling system which was difficult to see and may lead to a risk of misidentification. In addition, the establishment's inventory of bone specimens did not always reflect the labelling system used, for example, there was a case where the inventory stated 3.5 specimens but the physical specimens were labelled 1 to 4. CBE – Some examples of samples in -80^{o}C freezer where they had been stored with other samples collectively within a bag were found.	**Major**

	The unique identifier given by the establishment's LIMS database had been added to the storage bag meaning that each sample tube within the bag was not labelled with a unique sample identifier. Samples stored in liquid nitrogen were not labelled with the establishment's LIMS unique identifier and identifiers found on the samples themselves, were not recorded on the database.This results in it not being possible to link the samples to the LIMS database's location records.	

Premises, Facilities and Equipment

Standard	Inspection findings	Level of shortfall
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.	The establishment's freezers are not covered by maintentance contracts. The temperatures of -80^{o}C freezers are not monitored regularly or reviewed for trends. Temperature monitoring alarm systems, where fitted, that alert establishment staff to deviations from the expected temperature range are not tested to assure staff that they continue to function as expected. CBE – Liquid nitrogen tanks storing relevant material have no temperature monitoring system that is linked to an alarm which whould alert staff to a deviation from the expected temperature range. Although liquid nitrogen levels are monitored manually on a regular basis, there has been no validation exercise to assure the DI that a defined liquid nitrogen level is sufficient to maintain the required temperature for a certain period of time.	**Minor**

Advice

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

No.	Standard	Advice
1.	C2(a)	The current consent training programme covers only the HT Act's consent requirements for material obtained from the living. The DI is advised to include information regarding the consent requirements for obtaining tissue from the deceased, to help assure the DI that staff have an awareness of the appropriate requirements.
2.	GQ4(c)	The document HTALSC/QM 005 University HTA Licence Compliance Quality Manual does not refer to the University's Freedom of Information and public disclosure policies. The DI is advised to update this document to include a reference to the University's policy documents which refer to the systems employed.
3.	T2(a)	In terms of disposal, the HTA recognises that what is sensitive and what is feasible at local level needs to be taken into account. As set out in the HTA's code of practice relating to research, the DI is advised that it is good practice for human tissue to be bagged separately from clinical or other laboratory waste. The DI is advised to bring this to the attention of all staff working with relevant human material.
4.	PFE2(b)	The establishment has a dedicated -80^{o}C freezer room which houses a number of freezers. The room is air-conditioned to help mitigate the effect of the heat produced by the operation of the freezers. The DI is advised to consider installing a temperature monitoring system for the room itself so that a failure of the room's cooling system may be detected early. Any such failure could be addressed before the temperature rose significantly and posed a potential risk to the correct operation of the freezers.
5.	PFE4(b)	Currently, human bone specimens, including the full skeletons, are stored in a locked cupboard with other general equipment and supplies. The DI is advised to consider storing the human bones separately from equipment which may help to reduce unescessary handling and disturbance of the specimens when retrieving equipment. This separate storage may also help to preserve the dignity of the deceased.
6.	N/A	It was noted that human bone specimens had residual adhesive on them from when they had been used for teaching and demonstration purposes. Following their use, the DI is advised to ensure that residual adhesive is removed in order to help preserve the integrity of the specimens.

Concluding comments

A number of examples of good practice were observed during this second routine site visit inspection of Loughborough University, including:

- Implementation of a finance safety check - ordering of biological goods or arrangements for the transport of biological material, results in an alert notice being sent from the finance department to the Safety Officer, who is in turn able to assure

themselves that relevant checks and authorisations to work with human tissue have been undertaken.

- In CBE, ordering of any human material must be done via the PD and Departmental Quality Manager. Again, this helps to assure the DI that the PDs maintain oversight of any proposed work using human relevant material within the department.
- In SSEHS, participants returning for further involvement in various studies requiring multiple repeat visits, are asked to complete a repeat visit form. This form records a confirmation that the participants are content to continue their participation in the study and for their material to be stored and used for research.
- When participants are non English speaking or are visually impaired, the department provides information sheets in an accessible format to ensure fully informed consent can be obtained.

The Designated Individual oversees multiple users of human tissue which is supported by the PDs located in each of the groups. The DI has implemented regular HTA governance meetings with the PDs to assist the DI in maintainingtheir oversight of the licensable activities being undertaken at the establishment and to share good working practices between the various research groups. The DI delivers part of the in house HTA training offered to all researchers using relevant material, allowing those conducting licensable activities to be aware of who the DI is within the establishment. A good level of interaction and communication between the DI and those carrying out licensed activities was observed during the inspection.

There are a number of areas of practice that require improvement, including two major and six 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: 10 August 2018

Report returned from DI: 23 August 2018

Final report issued: 30 August 2018

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 February 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.