



Site visit inspection report on compliance with HTA licensing standards

University of Sheffield

HTA licensing number 12182

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**

21 & 22 March 2019

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.

Although the HTA found that University of Sheffield had met the majority of the HTA's standards, one major shortfall and seven minor shortfalls were found against the Consent, Governance and quality systems, Traceability and Premises, facilities and equipment 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

This report refers to licensable activities carried out at University of Sheffield (the establishment). The establishment is licensed for the storage of relevant material that has come from a human body for use for a scheduled purpose, under the Human Tissue Act 2004 (HT Act). Human samples are stored for use for the scheduled purpose of 'research in connection with disorders, or functioning, of the human body'. The establishment has been licensed since October 2007 and this was their second routine site-visit inspection.

The establishment stores relevant material in five separate research tissue banks (RTBs) that have broad ethical approval from recognised research ethics committees (RECs) and one histopathology collection that functions as a RTB but is not ethically approved. One of the RTBs holds samples from the deceased; all other samples held in these collections are from the living. The Corporate Licence Holder for the establishment was Sheffield Teaching Hospitals NHS Foundation Trust; however, they are now in a transition of moving all research tissue banks under the governance of the University of Sheffield, as all staff working with human tissue are university employees.

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 REC approval are excepted from the licensing requirements of the 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 (see *Advice*, item 6).

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

- Sheffield Brain Research Tissue Bank (REC reference: 19/SS/0029) which contains -80°C frozen brain and spinal cord tissue, formalin fixed brain tissue and tissue blocks and slides stored at room temperature. This collection has around 70,000 samples.
- The Cardiovascular Research Tissue Bank (REC reference: 18/YH/0441) contains over 30,000 blood and urine samples frozen at -80°C samples.
- The Ophthalmology Research Tissue Bank (REC reference 15/NW/0239) contains over 1000 samples of tumour tissue and whole blood with samples being stored in liquid nitrogen, -80°C and tissue blocks at room temperature.
- The Lung Research Tissue Bank (REC reference: 15/NW/0657) contains around 1000 samples of lung tissue, stored in -80°C freezers.
- The Musculoskeletal Research Tissue Bank (REC reference: 15/SC/0132) contains over 67,000 samples of whole blood and urine stored at -80°C.
- The Histopathology Tissue Bank is a collection of existing holdings containing surplus diagnostic tissue samples. They include brain, breast, lymph and colorectal samples.

Each RTB assigns their own unique identifier to each sample stored in the biorepository. The biorepository uses a CloudLIMS electronic database for the management of samples in storage. Samples are stored in four different locations on the main site: the cryostore which has four liquid nitrogen storage tanks, the biorepository freezer store with -80°C freezers, the brain bank for formalin fixed tissue and a handling and storage area for samples stored at room temperature. All locations have swipe card and/or key lock access and only authorised personnel, working directly under the licence, have permission to access these samples.

Freezers are fitted with automated alarms that are triggered by deviations from the set acceptable temperature ranges. If temperatures go out of range, an external monitoring service alerts relevant members of staff by phone, 24 hours-a-day. The alarm system is tested (see shortfall against PFE2(c)). All freezers are subject to annual servicing (see *Advice*, item 8). The establishment has contingency arrangements for all temperature-controlled storage.

Consent is generally sought by individuals from each of the research groups. Designated persons are responsible for consent seeking and they receive training in consent and refresher training (see *Advice*, item 2). In some cases, clinicians and nursing staff are responsible for consenting patients (see shortfall against C2(a)). Consent is sought using either project-specific or broad consent forms that reflect the requirements of the Human Tissue Act 2004 and the HTA's Codes of Practice. All potential donors are given information sheets (see *Advice*, item 1).

Overarching governance documents cover all main activities being carried out under the licence (see shortfall against GQ1(a)). Each RTB has their own documentation relating to specific processes being carried out. Some of the collections use different databases and methods to facilitate the traceability of material (see shortfall against T1(c)). For some of the RTBs material is distributed to other research institutes (see shortfall against T1(f)) under material transfer agreements (MTAs).

Description of inspection activities undertaken

The inspection team conducted roundtable interviews with the PDs and relevant staff working under the licence. The site visit inspection included a visual inspection of the storage areas, and a review of documentation. An audit of traceability records, including paper-based and electronic databases, and storage locations was conducted for each of the tissue collections held under the HTA licence. Storage records including the movement of samples into and out of the biorepository were also reviewed. Audits of the following, randomly selected collections were conducted:

- Five samples from the Ophthalmology RTB
- Six samples from the Brain RTB
- Three samples from the Histopathology Collection
- Three samples from the Musculoskeletal RTB
- Three samples from the Cardiovascular RTB
- Three samples from the Lung RTB

Minor anomalies were found in traceability for collections held in the Cardiovascular and Musculoskeletal RTBs, where sample location did not match the exact recorded storage location; however, these samples were located. For the samples selected from the Histopathology Collection, two could not be located and one was in the incorrect position within the storage box (see shortfall against GQ2(a)). Consent documentation and training of staff involved in seeking consent, were also reviewed for samples identified during the traceability (see shortfall against C2(a)).

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

Consent

Standard	Inspection findings	Level of shortfall
C2 Staff involved in seeking consent receive training and support in the essential requirements of taking consent		
<p>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.</p>	<p>Internal procedures 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 initialing as requested on the form. In some case there were no ticks or initials against any of the consent boxes; not completing these sections 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.</p> <p>During the roundtable discussions, it became clear that for some of the RTBs, clinicians and nurses who had not received any consent training specific to the requirements of the HTA Act and HTA Codes of Practice had been seeking consent.</p>	Major

GQ1 All aspects of the establishments work are governed by documented policies and procedures as part of the overall governance process		
<p>a) Ratified, documented and up-to-date policies and procedures are in place, covering all licensable activities.</p>	<p>Previous Trust SOPs used by the establishment and referred to in the University of Sheffield Quality Manual, are out of date and require reviewing to ensure the procedures are accurate. The following SOPs are relevant to the licence and should be brought under the governance of the university:</p> <ul style="list-style-type: none"> - SOP C120 - The Use of Human Tissue in Research - SOP C116 Material Transfer Agreements for the Transfer of Human Tissue - SOP A106 Informed Consent - SOP C127 Human Tissue Audits 	Minor

GQ2 There is a documented system of audit		
a) There is a documented schedule of audits covering licensable activities.	<p>There is a schedule of audits of the licensable activities being undertaken; however, it is clear that internal traceability audits are not being routinely undertaken by all of the individual Research Tissue Banks.</p> <p>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.</p>	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.	<p>The establishment's risk assessments are mainly related to Health and Safety matters rather than identifying the potential risks to the tissues in consideration of undertaking the licensed activities.</p> <p>Areas of risk which are not covered include but are not limited to:</p> <ul style="list-style-type: none"> - Loss of human tissue - Inconsistent or suboptimal consent seeking processes leading to problems with consent - Storing or using human tissue after consent withdrawal - Sample mix-up or loss of traceability - Transport of samples to and from the establishment. 	Minor

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.	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. This poses a risk that incorrect samples could be used by researchers and highlights the need for the establishment to be conducting regular traceability audits.	Minor
f) Records of any agreements with courier or transport companies are kept.	The establishment occasionally sends material to other establishments and uses the same courier; however, there is no formal agreement with the courier for the transportation of these samples of relevant material.	Minor

PFE1 The premises are secure and fit for purpose		
c) There are documented cleaning and decontamination procedures.	Currently all cleaning is performed on a 'when required' basis. The establishment does have cleaning records but these are not currently being completed. There is also no cleaning schedule.	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.	<p>Not all storage conditions are currently being monitored, increasing the likelihood that temperature excursions will go undetected.</p> <p>The alarm call-out system is not routinely challenge tested or documented, to ensure that the dial-out system, which notifies staff, is functioning properly.</p> <p>The temperature records are also not being monitored for trends in temperature deviations over time, alerting staff to potential issues, which could require corrective or preventative action/s.</p>	Minor

Advice

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

No.	Standard	Advice
1.	C1(d)	Some of the participant information sheets did not explain the process by which participants can withdraw consent or provide the required contact details for them to do so. The DI is advised to review all participant information sheets to ensure contact details for withdrawal of consent information is available to the donor.
2.	C2(a)	A number of consent forms across a variety of studies were completed with ticks or not completed at all, rather than the donor's initials as requested on the form. The DI is advised that completion of consent forms should be included in the competency assessment audits for the consent taking procedure. A policy should be developed to detail how to deal with issues surrounding consent if forms are not filled out correctly.
3.	GQ1(c)	Currently changes to SOPs and policies are sent to staff by email. However, there is no mechanism in place for staff to acknowledge they have received, read and understood the updated procedures. The DI is advised to implement a system for staff to acknowledge they have received, read and understood the revised SOP/policy.
4.	GQ2(a)	The DI is advised to include vertical audits of records and samples (for example, from sample through to consent documentation) within the audit schedule. Records should be audited regularly to ensure completeness, accuracy and legibility. Audits should ideally include horizontal audits by staff involved in the processes, to ensure that SOPs accurately reflect actual practices across the tissue banks and to identify areas for improvement.
5.	GQ5(a)	Roundtable discussions highlighted that staff are not always aware of how to report incidents with regards to the tissue. The DI is advised to strengthen training in this area so staff are fully aware of the process.
6.	T1(a)	The DI is continuing with the process of adding all sample information for each of the tissue banks to the CloudLIMS system. With the collections growing, a streamlined approach to sample management, such as a unified database, may help reduce the risks associated with loss of traceability. Furthermore, the DI may wish to consider a harmonised approach to sample management between the samples held under the licence and the samples stored for REC-approved projects. This may help with a smoother transition for samples moving under the licence when REC approvals expire.
7.	T2(b)	Disposal records are held by the individual RTBs. DI is advised to consider whether, as all tissue from the RTB's will be housed within the Biorepository, all sample and disposal information should be recorded in the CloudLims system. This should record, date, reason for disposal and method of disposal. The Biorepository should have full sample traceability recorded from point of receipt to disposal.
8.	PFE3(c)	The DI is advised to ensure internal cleaning and maintenance of the -80 freezers takes place regularly. The establishment can devise their own schedule and form to complete, to capture every time maintenance checks are performed.

9.	N/A	During the audit of material, it was noted that historical collections were being stored. These collections were reported to not be of use for any current or identified future research. The DI is therefore advised to continue with his review of the existing holdings and determine if it is appropriate to continue to store the relevant material or dispose of sensitively. If a decision is made to keep the collection, the DI is advised to fully audit the material in storage to ensure appropriate traceability.
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Concluding comments

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

- The establishment has a policy where any human material that needs to be transferred to another HTA-licensed establishment must be completed through the PD for the relevant tissue banks. This practice helps to assure the DI that the PDs maintain oversight of any proposed work using relevant human material.
- The establishment has their own HTA committee. All RTB PDs attend these meetings and the DI is the Chair. Any issues relating to the university's use of tissue with regards to the HTA licence is discussed.
- The establishment has a process whereby any new or existing tissue collections being transferred to the Biorepository are temporarily quarantined, until the legitimacy of storage for future use is demonstrated. The Sheffield Biorepository Management Committee must be satisfied that samples have been collected ethically and that any previous REC approval or donor consent does not preclude the storage of samples for future research.

The Designated Individual oversees multiple tissue banks of human tissue, 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 maintaining oversight of the licensable activities being undertaken at the establishment and to share good working practices between the various research groups. 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 one major shortfalls 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: 8th April 2019

Report returned from DI: 10th April 2019

Final report issued: 30th April 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
<p>a) Consent procedures are documented and these, along with any associated documents, comply with the HT Act and the HTA's Codes of Practice.</p> <p>b) Consent forms are available to those using or releasing relevant material for a scheduled purpose.</p> <p>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.</p> <p>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.</p> <p>e) Language translations are available when appropriate.</p> <p>f) Information is available in formats appropriate to the situation.</p>
C2 Staff involved in seeking consent receive training and support in the essential requirements of taking consent
<p>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.</p> <p>b) Records demonstrate up-to-date staff training.</p> <p>c) Competency is assessed and maintained.</p>
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
<p>a) Ratified, documented and up-to-date policies and procedures are in place, covering all licensable activities.</p> <p>b) There is a document control system.</p> <p>c) There are change control mechanisms for the implementation of new operational procedures.</p> <p>d) Matters relating to HTA-licensed activities are discussed at regular governance meetings, involving establishment staff.</p> <p>e) There is a system for managing complaints.</p>
GQ2 There is a documented system of audit
<p>a) There is a documented schedule of audits covering licensable activities.</p> <p>b) Audit findings include who is responsible for follow-up actions and the timeframes for completing these.</p>

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.