Site visit inspection report on compliance with HTA minimum standards

Keele University

HTA licensing number 12349

Licensed under the Human Tissue Act 2004 for the

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

19 & 20 October 2016

Summary of inspection findings

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

Although the HTA found that Keele University (the establishment) had met the majority of the HTA's licensing standards, two shortfalls were identified in relation to the Governance and Quality systems (GQ) and Premises, Facilities and Equipment (PFE) standards. The shortfalls were identified in relation to sample traceability and freezer monitoring. Advice has also been given on a wide range of matters.

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

This report refers to the activities carried out at two locations in Keele University (the establishment); the Guy Hilton Research Centre (the hub, for the purposes of HTA licensing) and Keele University (the satellite). The establishment is licensed in the HTA's research sector for the storage of relevant material for a scheduled purpose under the Human Tissue Act 2004 (HT Act). The establishment has been licensed since 2007 and was last inspected in October 2009. This inspection was the second routine site visit inspection.

The DI is the Director for the Institute for Science and Technology in Medicine (ISTM) and is a Professor of Stem Cell Biology. The Corporate Licence Holder is Keele University and the Corporate Licence Holder contact is the Pro-Vice Chancellor (Research and Enterprise). There are three Persons Designated (PD) under the licence; two at the hub and one at the satellite.

At both the hub and satellite sites, all research projects are subject to review by the University's research ethics committee. An initial review is done through the University's Independent Peer Review system (IPR). During this process projects involving human tissue are identified. 'Human Tissue Officers' are then notified and a spreadsheet, the HTA Log, is completed. All projects, including those in the application stage, are recorded on this log. This

allows the Human Tissue Officers to maintain oversight of all current and upcoming projects. University ethical approval cannot be granted without first being subjected to IPR.

Samples come from a number of sources, including the local hospital, commercial companies and healthy volunteers (staff and students). Patients involved in research projects are recruited in the local hospital and their consent is sought by clinicians. Researchers obtaining material from commercial sources ensure consent was ethically sought prior to receiving tissue, and evidence of this was seen during the inspection. Material is not routinely sourced from outside of the UK; however, in the case of one project, tissue was received from the USA. Evidence of material transfer agreements, as well as confirmation that consent had been obtained in accordance with the HT Act and patient information documentation were reviewed during the inspection. For all projects, the Human Tissue Officers will check that valid consent has been sought and that there is an agreement in place between the establishment and the supplier of the samples. All members of staff involved in seeking consent have received consent training as part of their mandatory induction, and evidence of this was seen during the inspection.

All samples held under the licence are recorded on the HTA Log. Human Tissue Officers hold a centralised copy of the HTA Log and each researcher holds their own local copy, updating the centralised version every two months (see Advice, item 6). The HTA Log details the types of tissue, the name of the responsible researcher, whether consent records have been reviewed, disposal information as well as the end date of projects with NHS REC approval.

At the time of the inspection, new mandatory training had recently been implemented for all students and staff working with relevant material. The training pertains to the HT Act, consent requirements and the HTA's Codes of Practice (see Advice, item 5).

Audits are performed by the Human Tissue Officers on a quarterly basis in the hub and satellite (see Advice, item 3). The 'ISTM Human Tissue Committee' convenes, annually, to discuss issues pertaining to the HTA licence.

The inspection of the hub and satellite comprised: a round-table discussion about consent, governance and quality systems and disposal, with all members of staff working under the licence; a visual inspection of the areas where human tissue is stored; interviews with a Senior Lecturer in Medicine and Neuroscience, the Research Institute Manager (Institute for Science and Technology in Medicine, Guy Hilton Building) (PD), a Lecturer in Human Biology, a Lecturer in Biosciences (Human Tissue Officer and PD for the hub premises), a Professor of Neuroscience (PD), a Lecturer in Biosciences (Human Tissue Officer for the satellite premises), the Designated Individual (DI), and; a review of governance documentation.

In addition, traceability audits were carried out using 12 samples at the hub premises (stored at -20°C, -80°C and liquid nitrogen) and six samples (stored at -80°C and liquid nitrogen) at the satellite premises. Samples were identified from their storage locations and traced to the HTA Log, and identified from the HTA Log to their storage location. A number of anomalies were found (see shortfall identified against HTA standard PFE3).

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
GQ6 A coding and records system facilitates traceability of bodies, body parts, tissues and cells, ensuring a robust audit trail.	Audits of stored samples at both the hub and satellite sites identified inconsistencies in how samples are labelled. A number of samples were found to be missing a unique identifier; some were not recorded consistently on the HTA Log; a number of samples had illegible labels and, of the 18 samples that were audited; one sample could not be located. Following the inspection, and after checking the paper records which were not available at the time of inspection, the establishment confirmed that the HTA Log had not been updated to show the sample had been disposed of. The training available to staff does not specify the information that should be recorded on the sample tube, leading to inconsistencies. Documented procedures are in place but the results of the audits done by the inspection team indicated that these are not being followed.	**Minor**

Premises, Facilities and Equipment

Standard	Inspection findings	Level of shortfall
PFE3 There are appropriate facilities for the storage of bodies, body parts, tissues, cells, consumables and records.	At both sites, relevant material is stored in a number of -20°C freezers, -80°C freezers and liquid nitrogen dewars. At the hub, the use of an unlocked room means that all staff with access to the laboratories can access all freezers. This increases the risk of samples being misplaced or being incorrectly used. At both sites, temperatures are monitored on a weekly basis; however, the data is not reviewed for trends. In addition, freezers are not linked to a remote call-out system. The liquid nitrogen dewars are not linked to a remote call-out system either but a weekly rota ensures liquid nitrogen levels are maintained. Staff are reliant on audible alarms to herald deviations in temperatures. However, this system requires strengthening as the alarm sounded during the inspection of the hub and staff did not respond. At the hub site, there are no formalised procedures in place for monitoring the temperatures out of hours. Instead, checks are done on an ad hoc basis, when staff are present. At the satellite site, -80°C freezers are checked at night by security staff and, at the weekends, by research staff who need to access the laboratories; however, this process has not been formalised or documented. The schedule for defrosting is not adequate to prevent a build-up of ice in -20°C freezers. During the inspection it was noted that a -20°C freezer was being held shut with autoclave tape due to a build-up of ice. In consideration of the cumulative impact of the problems identified against this standard, the HTA determines the level of shortfall to be 'Major'.	**Major**

Advice

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

No.	Standard	Advice
1.	C1	Consent for some projects involving patients in the local hospital is sought by clinicians. One of the Human Tissue Officers also seeks consent for their own studies. Consent forms for these projects were examined during the inspection and did not provide adequate detail about how consent can be withdrawn from projects. The DI is advised to ensure consent forms are updated to include information about how a participant may withdraw from the study, as well as contact details and who to contact if they wish to withdraw.
2.	GQ1	At the time of inspection, the ISTM Human Tissue Committee had not been convened for a number of years; however, the committee is due to reconvene in December 2016. The DI is advised to regularly hold and document the meetings. The meetings provide staff working under the licence with a scheduled opportunity to formally discuss issues or upcoming changes.
3.	GQ2	Audits are performed on a quarterly basis. At present, findings are shared only with the groups at the individual sites. The DI is advised to share findings with all groups on both sites working under the licence to encourage cross-communication and to share learning.
4.	GQ2	During the audits conducted by the inspection team, sample legibility was identified as an area of weakness. At present, the audit schedule does not include sample legibility, and the DI is advised to update the audit schedule to include regular checks of samples. Samples which are not clearly labelled increase the risk of incorrect samples being used, or inadvertently being disposed of.
5.	GQ3	HTA training has recently been developed and implemented, with the future aim of training all students and staff. However, some weaknesses identified during the inspection could be improved using this training. The DI is advised to expand the scope of the training to include sample labelling, completion of the HTA Log and sample storage. This should improve consistency by ensuring that all staff are trained to the same level and are using the same system for recording samples.
6.	GQ4	The HTA Log is a valuable tool for recording the samples held under the licence. At present, each researcher is adapting the log to suit their own laboratory needs, making it difficult to readily locate samples during an audit. The DI is advised to review the format of the HTA Log, creating a master copy with defined, non-editable column headings which facilitate the recording of consistent sample information.
7.	GQ4	While contingency storage is available at both the hub and satellite sites, their locations, and the processes for accessing them, are not clearly identified in relevant documents. The DI is advised to ensure documents reflect the procedure for transferring samples to contingency storage in the event of a freezer failure.
8.	GQ8	All establishments should identify the risks inherent in the key activities and procedures should be developed in consideration of, and to mitigate, these potential risks where appropriate. DIs should also assess the risks associated with licensed activities. Documented risk assessments should include an

		evaluation of the level of the risk and, where appropriate, the mitigating actions identified and the level of residual risk remaining. Risk assessments should include the risks relating to the premises, practices and procedures connected with licensed activities. A range of risk assessments are described in the HTA-31: Risk Assessment for Human Tissue Projects but the DI is advised to consider the following additional areas: • security arrangements; • sample mix-up due to inappropriate labelling; • damage affecting the quality of human tissue for use in research; Risk assessments should be reviewed periodically (typically, every 1-3 years) and the actions to mitigate risks updated as necessary. Risk assessments should also be reviewed following an incident. By documenting risk assessments, staff are made aware of identified risks, which helps to prevent risks materialising and informs the development of procedures and relevant documentation.
9.	PFE5	While the freezers are routinely subject to portable appliance testing (PAT), there are no regular maintenance agreements for the freezers. The DI is advised to ensure that freezers are maintained in accordance with recommendations from the manufacturers.
10.	PFE5	During the inspection, it was noted that there were no oxygen depletion monitors in use where numerous liquid nitrogen dewars are stored. HTA inspectors were informed that University Health and Safety personnel had confirmed that there was sufficient airflow in the room and that monitors were not required. Given that there are 16 liquid nitrogen dewars in the room, the DI is advised to request documented confirmation of this risk assessment.
11.	D2	Disposal of research samples is recorded for all material using the HTA Log; however, this is not completed in a consistent manner by researchers – for example, the method and date of disposal should consistently be recorded. The DI is advised to consider providing training on completion of the log as well as regularly auditing the disposal records to ensure researchers are completing the records consistently.
12.	N/A	As the Human Tissue Officer at the satellite site is responsible for the governance of the site, including writing and reviewing SOPs and performing regular audits, we recommend that they are added to the licence as a PD.

Concluding comments

During the inspection, a number of areas of good practice were noted, including using the IPR process to highlight any projects using human tissue. Once a project has been flagged as using, or potentially using, human tissue, 'Human Tissue Officers' are notified and the HTA Log is updated accordingly. The Human Tissue Officers maintain a log of the potential projects, providing them with in an in-depth oversight of human tissue in use across the University.

There are a number of areas of practice that require improvement, including one major and one minor shortfall. The HTA has also given advice to the Designated Individual on a wide range of matters, including: consent documentation, governance, audit, staff training,

contingency storage arrangements, risk assessments, freezer monitoring and improving the consistency of records.

The HTA requires that the Designated Individual addresses the shortfalls 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 shortfalls identified during the inspection.

Report sent to DI for factual accuracy: 15 November 2016

Report returned from DI: 29 November 2016

Final report issued: 05 December 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: 12 June 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
• 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.