Site visit inspection report on compliance with HTA minimum standards

King's College London

HTA licensing number 12521

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 May 2016

Summary of inspection findings

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

Although the HTA found that King's College London (the establishment) had met the majority of the HTA standards, five minor shortfalls were found with regard to the Governance and Quality Systems (GQS) and Premises, Facilities and Equipment (PFE) standards. They were in relation to an absence of: (i) governance meetings; (ii) an internal audit system for procedures and records; (iii) consistent reporting and follow up of incidents; (iv) risk assessments; and (v) continuous temperature monitoring of refrigerators, freezers and cryovessels. Advice has been given relating to the Consent, GQS and PFE standards.

Particular examples of 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 (DI), Licence Holder (LH), premises and practices are suitable.

The statutory duties of the DI 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 licenses 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 by King's College London (KCL, the establishment). The establishment's licensing arrangements cover Guy's Campus – the hub site – and the satellite site (Franklin Wilkins Building, FWB, at the Waterloo Campus).

Guy's campus was issued the current HTA licence in October 2008 and was inspected in October 2009. FWB was issued a separate HTA licence in October 2008 and was inspected in January 2009. It became a satellite under this licence in December 2015. The current inspection was a routine site visit of both hub and satellite to assess whether the establishment is continuing to meet the HTA's standards.

The establishment is licensed under the Human Tissue Act 2004 (HT Act) for the storage of relevant material for use for a scheduled purpose. Under the HT Act, relevant material (obtained from living and, occasionally, deceased donors) is being stored for the scheduled purposes of: obtaining scientific or medical information about a living or deceased person which may be relevant to any other person (including a future person); research in connection with disorders, or the functioning, of the human body; education or training relating to human health; and quality assurance.

Samples are obtained from adults, children and foetuses and include both tissue and bodily fluids. Tissue samples include formalin-fixed, paraffin wax-embedded (FFPE) material (blocks and sections on glass slides), isolated cellular preparations (e.g. peripheral blood mononuclear cells, PBMCs), fresh frozen tissue and bodily waste products (e.g. faeces). Bodily fluids include urine, saliva, sputum, whole blood and cerebrospinal fluid.

There are approximately 150,000 samples stored under the licence at the hub and 11,500 samples stored at the satellite.

The hub licence spans several buildings at the Guy's campus. This includes buildings owned by KCL and 'embedded space' within Guy's and St Thomas' NHS Foundation Trust. There are 11 human tissue collections, each managed by a Person Designated (PD). Each collection contains several sample sets, including two Research Tissue Banks (RTBs). Eight collections were inspected. They were:

- The Divisions of: Asthma, Allergy and Lung Biology; Genetics and Molecular Medicine (containing the St John's Institute of Dermatology RTB); Immunology, Infection and Inflammatory Disease (containing the Infectious Diseases RTB); and Transplantation Immunology and Mucosal Biology.
- The Centres of: Molecular and Cellular Biology of Inflammation, and Age-Related Diseases.
- The Diabetes, and Salivary Research Groups.

The satellite is a single building. There are four human tissue collections managed by PDs. All four collections were inspected. They were:

- The Divisions of Analytical and Environmental Sciences, and Diabetes and Nutritional Sciences.
- The Institute of Pharmaceutical Sciences, and the Vascular Biology Group.

Human tissue collections

RTBs. One RTB contains human tissue from patients with cutaneous tumours and the other tissue from patients with infectious diseases. Each RTB is managed by an 'access committee', which reviews all requests for samples. Committee members include the respective PD, senior clinicians and scientists, and lay representatives. The RTBs are accessible to both KCL and UK researchers.

Other sample sets. These include samples previously stored under project-specific NHS REC approval (or those previously stored as part of UKECA-approved clinical trials) where the approval has now expired (65 sample sets at the hub and 15 at the satellite) and samples stored under KCL Ethics Committee approval (30 sample sets). Samples stored under current REC or UKECA approval do not fall under the HTA licence (100 sample sets).

There are no regular governance meetings involving PDs responsible for human tissue collections (*see Shortfall under GQ1*).

Human tissue sources

Samples are obtained from surgical operations within the adjacent Trust, from the diagnostic pathology archives and from healthy volunteers (students and staff) within KCL. There are suitable agreements set up for those samples obtained by collaborators outside KCL.

Consent is sought by KCL or Trust staff, who have received either Good Clinical Practice (GCP) training or consent training provided by the DI, or by staff outside KCL under agreement. The establishment uses RTB- or REC-approved consent forms or those approved by the KCL Ethics Committee and similarly approved participant information sheets.

Sample storage

Tissue is stored under a wide range of conditions: at room temperature, in 4°C refrigerators, in -20°C, -40°C and -80°C freezers, and in liquid nitrogen storage vessels (cryovessels). Each PD is responsible for the storage arrangements of their sample sets.

Storage at the hub. All refrigerators and freezers are linked to a continuous temperature monitoring unit which feeds into a wireless callout system. Temperature excursions outside the set ranges trigger both audible alarms and the callout system and the system is tested regularly. Labels on the freezers indicate steps to be taken if the audible alarms sound but these are out of date (*see Advice item 3*).

There are three liquid nitrogen storage areas. In one of these the cryovessels are linked to the continuous temperature monitoring unit but not in the other two (*see Shortfall under PFE3*). Staff do not carry portable monitors but there are fixed oxygen depletion monitors (*see Advice item 10*).

Storage at the satellite. None of the refrigerators or freezers is linked to a continuous temperature monitoring unit. Temperatures are recorded manually by laboratory staff on a daily basis during the working week. There is an arrangement with the building security staff to patrol the storage areas during week-ends and vacation periods and to notify the relevant staff member if the audible alarms sound (*see Shortfall under PFE3*). Labels on the freezers indicate contact details for staff but these are out of date (*see Advice item 3*).

Governance and record management

Each researcher maintains paper and electronic records for their specific sample sets. Each PD has a record of sample sets within their collection and the DI has a master register of all sample sets, including those under the licence and those currently under REC and UKECA approval.

The DI has created a generic template for standard operating procedures (SOPs) and this is used by all researchers.

The inspection process

The timetable for the site visit inspection was developed after consideration of the establishment's previous inspection reports, compliance update information and reported enquiries. The site visit included a visual inspection of the storage areas and storage facilities. Discussions and interviews were held with key staff and documentation was reviewed. Interviews were held with the DI (Senior Lecturer in Tissue Banking), the (Corporate) LH Contact (CLHC; Director of Research Management) and nine PDs. Several audits of traceability were carried out.

Audits

Audits at the hub. Six audits were carried out. 28 representative samples were selected at random from the -80°C freezers, cryovessels or from room temperature storage, and labelling details were compared to paper and electronic records. The corresponding consent forms and consent training records of those who had sought consent were also examined.

There were two discrepancies noted in one sample set (in the Division of Genetics and Molecular Medicine collection). Paper records for one sample indicated four vials but only three vials were present and electronic records for another sample were missing (*see shortfall under GQ2*).

Audits at the satellite. 12 audits were carried out. 37 representative samples were selected at random from the -20°C, -40°C and -80°C freezers or from room temperature storage.

There was one discrepancy noted in one sample set (in the Institute of Pharmaceutical Sciences collection). The log book for the collection could not be located (*see shortfall under GQ2*).

Inspection findings

The HTA found the DI and the CLH to be suitable in accordance with the requirements of the legislation.

Compliance with HTA standards

Governance and Quality

Standard	Inspection findings	Level of shortfall
GQ1 All aspects of the establishment's work are supported by ratified documented policies and procedures as part of the overall governance process.	In light of the large number of human tissue collections and the complex governance arrangements for managing these, there are no regular governance meetings where PDs and other staff working under the licence can discuss issues relating to HTA-licensed activities. *See Advice item 2.*	**Minor**
GQ2 There is a documented system of quality management and audit.	There is no detailed audit schedule and there is an inconsistent approach to audits. Some PDs have carried out audits on an *ad hoc* basis and others have not audited any of their sample sets. The inspection audit revealed discrepancies in some of the human tissue collections. *See Advice item 4*.	**Minor**
GQ7 There are systems to ensure that all adverse events are investigated promptly.	There is an inconsistent approach to recording and following up incidents. Some PDs have recorded incidents and followed them up with corrective and preventative actions whereas others are not aware of the incident reporting system. *See Advice item 6*.	**Minor**
GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately.	There are health and safety risk assessments but there are no risk assessments covering HTA-licensed activities. *See Advice item 7.*	**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.	The continuous temperature monitoring system does not cover any refrigerators or freezers at the satellite and does not cover two liquid nitrogen storage areas at the hub. The establishment has not risk assessed the current arrangements for monitoring temperatures within these areas out of hours.	**Minor**

Advice

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

No.	Standard	Advice
1.	C1	The DI should ensure that all consent forms containing patient-identifiable information are locked away separately from other paper records.
2.	GQ1	In other establishments, governance meetings cover items such as standardisation of documents, changes to SOPs, audits and their findings, competence and regulatory training, management of incidents, risk assessments, the setting up of agreements with other establishments and updates from the HTA (e.g. e-newsletter items).
3.	GQ1	Several documents are out of date. These include: • The SOP detailing how security staff at the satellite respond to freezer alarms. • The labels on satellite refrigerators and freezers indicating the contact details for staff. • The labels on all refrigerators, freezers and cryovessels indicating steps to be taken if the audible alarms sound. • The form used to record incidents (not reviewed since 2009). • The safety notice for the transport of human tissue samples between college campuses (not reviewed since 2010). The DI should ensure that all SOPs, forms, labels and notices are updated and are included in the establishment's document control system.
4.	GQ2	The DI should develop a formal audit schedule incorporating individual audits within each human tissue collection. PDs and other research staff could contribute to these audits. The types of audit should include horizontal audits, to ensure that SOPs accurately reflect current practices, and vertical traceability audits, from records of consent and receipt to storage, use, distribution or disposal. The DI may also wish to consider including a regular audit against HTA standards as part of the audit schedule.
5.	GQ3	The DI should review and record all staff training to ensure that a systematic approach is taken to the training of staff which assures competence. The DI

		may wish to create a matrix to track training and reassessment as required, as has already been carried out for consent training. The training should include: the familiarity with SOPs and risk assessments, and the reporting process for incidents.
6.	GQ7	The DI should ensure that staff are aware of incidents relating to human tissue. These include: • sample loss • missing or incorrect documentation • security breach • abnormalities in storage temperature readings • sample transport between campuses or to other organisations • inappropriate disposal.
7.	GQ8	The DI should consider the broad risks to human tissue, such as: • sample loss • missing or incorrect documentation • security breach • abnormalities in storage temperature readings • sample transport between campuses or to other organisations • inappropriate disposal.
8.	PFE2	Although PPE is widely used the DI should ensure that staff are provided with specific protective equipment to ensure the safe handling of cryogenic samples.
9.	PFE3	In addition to human tissue, the establishment also stores some animal tissue in separate freezer compartments. The DI should ensure that all refrigerators, freezers and cryovessels containing human tissue are appropriately labelled so that staff are aware of the need to manage these samples in line with the regulatory requirements of the HT Act and to prevent sample mix-ups.
10.	PFE3	The DI should consider whether the use of portable oxygen depletion monitors would further mitigate the risks associated with working in the liquid nitrogen storage areas.

Concluding comments

During the inspection areas of good practice were noted:

- The DI provides consent and regulatory training (including training on the HT Act and the HTA's Codes of Practice) to all PDs and other staff involved in seeking consent. The DI keeps a centralised log of this training and refresher training is provided on a regular basis.
- There is a KCL HTA Management Committee, consisting of all KCL DIs and the CLHC, which meets every six months.
- DI has produced a master register of all sample sets, including those under the licence and those currently under REC and UKECA approval.

- The DI has developed a ‘human tissue application form’ to be completed by all new researchers wishing to store and use human tissue.

There are a number of areas of practice that require improvement, including five minor shortfalls. The HTA has given advice to the DI with respect to the Consent, Governance and Quality Systems, and Premises, Facilities and Equipment standards.

The HTA requires that the DI 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: 09 June 2016

Report returned from DI: 22 June 2016

Final report issued: 14 July 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: 18 May 2018

Appendix 1: HTA standards

The HTA standards applicable to this establishment are shown below. 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 inspection.

   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.