Site visit inspection report on compliance with HTA minimum standards

UCL Cancer Institute

HTA licensing number 12055

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**

12-15 August 2014

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 UCL Cancer Institute (the establishment) had met the majority of the HTA standards, major shortfalls were found in relation to the robustness of tissue traceability systems, and documented assessments of risks to stored tissues. Minor shortfalls were also identified in relation to standard operating procedures, auditing of tissue traceability records, and recording of sample disposal.

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 (DI) are set out 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

University College London (UCL) Cancer Institute ('the establishment') is licensed under the Human Tissue Act 2004 ('the HT Act') for the storage of relevant material which has come from a human body for use for a scheduled purpose. The establishment stores a range of tissues and bodily fluids for use for the scheduled purpose of 'research into the disorders, or the functioning, of the human body'. Removal of relevant material from a deceased person for use for a scheduled purpose does not take place under this licence.

The establishment's hub is at the Rockefeller Building, situated in central London, with two satellite sites nearby (The Prostate and Breast Cancer Research Centre, London Research Institute), and a third at Royal National Orthopaedic Hospital and UCL Institute of Orthopaedics, in Stanmore ('RNOH'). RNOH was previously licensed for storage of relevant material for use for a scheduled purpose under another HTA licence (licensing number 12325) from June 2007 until September 2013, after which the licence was revoked and the site became a satellite of this UCL licence. London Research Institute ('LRI') has been a satellite of this UCL licence since April 2013.

Most research collections held under this licence come under the auspices of the Biobank for Studying Health and Disease. This Biobank has NHS Research Ethics Committee (REC) approval as a research tissue bank. Its policies and guidelines provide an overarching framework for the management of research groups and of human tissue collections. Requests to start new research sample collections, and for use of existing samples or data for research, are reviewed by the Biobank Ethical Review Committee (B-ERC).

At each site, most research projects using relevant material have favourable opinion from B-ERC, or another NHS REC. Such material is thus exempt from the HT Act's licensing requirements for the storage of relevant material for use for a scheduled purpose, under the Human Tissue 2004 (Ethical Approval, Exemptions from Licensing and Supply of Information about Transplants) Regulations 2006.

The following takes place under the authority of this HTA licence:

- UCL Cancer Institute (Rockefeller Building) houses a diagnostic tissue archive of paraffin wax embedded tissue blocks and microscope slides primarily from patients who have received treatment at University College London Hospitals. RNOH houses an archive of fresh frozen tissues, tissue blocks and microscope slides, and blood samples from patients who have received treatment at that hospital. Donor consent for storage and use of samples for research is sought at UCLH by clinicians, and at RNOH by research nurses. There are specific patient information leaflets and consent forms for adult donors, and for children and their parents/guardians. Biobank samples are available for use for research by groups within each establishment, and by researchers at other establishments under documented material transfer agreements. The Biobank has National Research Ethics Service (NRES) Research Tissue Bank status.
- The Prostate and Breast Cancer Research Centre houses a small collection of existing holdings, originating from a clinical trial, which is not currently in use for research. This collection will be transferred to other HTA-licensed premises shortly. LRI houses three tissue collections. Two small collections originate from outside of the UK, the third collection, an archive of pathology samples (existing holdings, tissue blocks and microscope slides), was received from another UK organisation. Samples in these collections are used solely by researchers based at LRI, and new samples are not being acquired.

The establishment has been licensed by the HTA since September 2007. This report describes its first, routine, site visit inspection in August 2014. The inspectors interviewed staff involved with licensable activities, reviewed documentation and carried out visual inspections of each tissue storage location. For every collection, tissue traceability was audited. In one audit where a discrepancy in the number of stored blocks was found, an error log was completed and an investigation undertaken by the establishment. The preliminary findings of the investigation are that the blocks were transferred to another HTA-licensed establishment for archiving.

UCL holds other HTA licences under the HT Act (licensing numbers 12120, 12161, 12177, 12198, 12220 and 12272). RNOH has an HTA licence under the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (licensing number 11135). Activities under those licences were not reviewed at this site visit inspection.

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
GQ1 All aspects of the establishment's work are supported by ratified documented policies and procedures as part of the overall governance process.	Several draft and active standard operating procedures (SOPs) at UCL and LRI fail to describe in adequate detail processes being followed, occasionally refer to staff who are no longer working at the establishment, and in some cases contained Wikilinks to other key internal documents which could not be accessed from all locations. Specific examples were discussed with establishment staff during the inspection.. To address this shortfall, all key SOPs will require review and updating. *(Refer to advice item 3)*	**Minor**
GQ2 There is a documented system of quality management and audit.	The establishment carries out a wide range of audits. For example, a random sample of donor consent forms is audited monthly at RNOH, ethically approved projects are audited against a set of criteria based on the HTA's licensing standards, and histopathology archive traceability audits are conducted annually at the hub, with findings circulated to staff. Tissue traceability audits are not, however, currently being performed to a regular schedule for the tissue collections at LRI, and plans for wide-ranging traceability audits of research samples at RNOH remain to be finalised. As noted against standards GQ4 and GQ6, tissue traceability systems across the different collections also need to be strengthened. While audits of every collection held under this licence need not necessarily be of the same format, traceability audits are necessary to reassure the DI on the robustness of tissue tracking systems. *(Refer to advice item 4)*	**Minor**

GQ6 A coding and records system facilitates traceability of bodies, body parts, tissues and cells, ensuring a robust audit trail.	A range of proprietary computer databases and locally created spreadsheets are in use at each site for tracking sample storage locations and release for research. These afford sample traceability, to varying degrees, depending on the tissue collection. Audits performed during the inspection highlighted issues which the establishment needs to address to strengthen tissue traceability. • LRI has a large collection of tissue blocks received from another UK organisation which remains uncatalogued. LRI needs to catalogue this collection fully, otherwise sample traceability cannot be assured; • For another collection at LRI, reference numbers of cryovials used for research are not captured in laboratory records; • At both the hub and RNOH, release of samples from diagnostic archives for use in ethically approved research projects is recorded in an inconsistent manner. At the hub, distribution of samples to groups external to UCL is captured in the biobank database, whereas for samples released to users within UCL the name of the research group is not generally stated in this database. Slide retrieval is usually logged using a paper slip in the slide box. For samples released from RNOH's archive, traceability records in some cases identify by name the research group receiving the samples, whereas in other cases only the name of the receiving establishment is noted. Without greater consistency in recording the research groups which receive samples traceability may be impaired, and possibly lost. Cumulatively, these findings are considered to represent a major shortfall against these licensing standards.	**Major**

GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately.	RNOH has a rigorous documented assessment identifying potential risks to informed consent for donation, sample storage and traceability, which sets out existing control measures and additional steps to be taken to mitigate risks further. However, documented assessments of risks to tissue storage and traceability are not in place for tissue collections at LRI. This is of particular importance as tissues are stored in multiple locations within the building and traceability systems are not wholly robust. In addition, risk assessments for the hub premises have not been reviewed in line with the review dates, contain an inaccurate address and do not consider the two separate storage areas within the Rockefeller Building. Without a more structured approach to the assessment and management of potential risks, the DI cannot assure himself that risk mitigating measures are sufficient.	**Major**

Disposal

Standard	Inspection findings	Level of shortfall
D2 The reasons for disposal and the methods used are carefully documented.	While disposal of research samples is not a routine occurrence, samples could potentially be used to extinction, be misplaced or otherwise become unusable. Whereas proprietary tissue tracking databases used by the establishment have the facility to record such details of sample disposal, other spreadsheets developed locally and used for tissue tracking of some collections do not.	**Minor**

Advice

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

No.	Standard	Advice
1.	C3	At UCLH, consent for donation of tissue samples for research is sought by a wide range of clinical staff. The DI is advised to maintain records to confirm which staff have been assessed as competent to seek patient consent for donation of tissue samples for research. Verification that an individual seeking donor consent is competent to do so could then form a part of the auditing process of consent forms.

2.	GQ1	The DI is advised to supplement his formal governance meetings with Persons Designated with 'virtual meetings', through regular email communications. This will promote sharing of best practice across the sites and, in light of the HTA inspection's findings, enable the DI to be updated on progress with corrective actions at each site.
3.	GQ1	The DI is advised on the following: • to keep hard copies of SOPs describing UCLH's processes for tissue banking, for reference; • to develop a documented policy setting out criteria for accepting into the Biobank tissue samples from ethically approved projects whose ethics approval period has expired; • to append a corrective and preventive action template to the checklist for auditing tissue collections and ethically approved projects, so that any issues which need to be addressed can be recorded and tracked in a structured format; • to amend the LRI SOP for filling liquid nitrogen dewars to reference completion of the associated paper log. The log could also be appended to the SOP, so that it is version controlled.
4.	GQ2	The DI is advised that he may wish to tailor the format, frequency and sample size of traceability audits to each tissue collection. For example, for the discrete collections at LRI where sample acquisition and distribution are not taking place, audits could verify that correct numbers of samples are present in the appropriate storage locations. For diagnostic archives where sample acquisition is ongoing, audits could assess traceability from donor consent, through tissue storage and subsequent use of samples for research and/or disposal.
5.	GQ3	The establishment intends to create appendices to the 'HTA Induction checklist' to specify which SOPs relevant for their laboratory a new starter must read. The HTA considers this good practice. The DI is also advised that if an individual has completed elements of induction training at other sites, he should review documented evidence to confirm such training took place and that it satisfies local requirements.
6.	GQ4	The DI is advised to remind colleagues of the documented procedure for retrieval of tissue blocks and slides from diagnostic archives.
7.	PFE5	Some occasional gaps were seen in daily temperature logs for a sample freezer at RNOH. The HTA understands the SOP and staff responsibilities for recording freezer temperatures are being clarified, and supports these intentions.

Concluding comments

Despite the shortfalls identified, areas of strength were also identified. Staff were very knowledgeable about the activities they were involved in, and communicated this clearly. Procedures for seeking informed donor consent are supported by well written patient information leaflets and consent forms. Discrepancies identified in traceability records are formally captured through an 'error log' process. The auditing of ethically approved projects against criteria resembling the HTA's standards is an area of good practice.

There are a number of areas of practice that require improvement, including two major shortfalls and three minor shortfalls. The HTA has given advice to the Designated Individual with respect to strengthening governance and quality management systems.

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: 3 September 2014

Report returned from DI: 12 September 2014

Final report issued: 13 September 2014

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: 4 December 2014

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.