Site visit inspection report on compliance with HTA minimum standards

Guy's and St Thomas' Research Tissue Bank

HTA licensing number 12121

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 November 2013

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 Guy's and St Thomas' Research Tissue Bank (the establishment) had met the majority of the HTA standards, four minor shortfalls were found with regard to the Consent (C), Governance and Quality Systems (GQS) and Premises, Facilities and Equipment (PFE) standards. The shortfalls were in relation to the consent process, audit and risk assessments of both the premises and the practices. Advice has also been given relating to the GQS standards.

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 (DI), Licence Holder (LH), 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 by Guy's and St Thomas' Research Tissue Bank (RTB; the establishment). This was the first site visit inspection of the establishment since it was issued an HTA licence in September 2007. It was a routine site visit inspection to assess whether the establishment is meeting the HTA's standards.

Governance

The RTB is part of the King's Health Partners (KHP) Integrated Cancer Centre and consists of five tumour tissue biobanks of different tissue types (breast, head and neck, thoracic, upper gastrointestinal tract, prostate). The KHP RTB has NHS Research Ethics Committee (REC) Research Tissue Bank approval to collect, store and issue biological samples and associated clinicopathological data (renewable every five years). All tissue for the KHP RTB is obtained at surgery in the operating theatres at the Guy's (breast, head and neck, thoracic, prostate) or St Thomas' (upper gastrointestinal tract) sites of the Trust. The KHP RTB sits predominantly within premises rented by King's College London (KCL) from the Trust and the KHP RTB staff are either Trust or KCL employees.

The KHP RTB contains approximately 25,000 tissue and blood samples. These include primary tumours, metastatic deposits, premalignant and benign disease, normal tissue and matched whole blood, along with associated patient clinicopathological and demographic data. Tissue samples consist of formalin-fixed, paraffin wax-embedded (FFPE) material,

optimal cutting temperature compound (OCT) fixed samples for frozen sections and fresh frozen material.

The KHP RTB developed from an amalgamation and co-ordination of different clinical specialities, each with its own procedures, over a period of time. The most well established is the breast tissue biobank (started in 1974) and the most recent the prostate tissue biobank (2013). Each tissue biobank has an academic lead, a tissue co-ordinator and an access sub-committee.

Formal ownership of the KHP RTB lies with the Trust, with the Chief Executive as custodian. The KHP RTB Management Committee (including senior clinicians, scientists, independent and patient representatives) organises the governance of the tissue biobank and reports to the Chief Executive via the Trust Risk and Quality Committee.

Now that the five site-specific tissue biobanks have been integrated under a single REC agreement, it will be the aim of the KHP RTB Operational Group to facilitate standardisation of processes and procedures and to share good practices between the individual tissue biobanks. The Operational Group will be chaired by the DI and will include tissue bank academic leads, Quality Managers, senior technical staff and tissue co-ordinators (*see Advice item 3*).

The access sub-committee of each tissue biobank oversees access to tissue and data resources within its specific tissue bank. The committee reviews requests for all material and data, reviews results from pilot and interim studies, and reviews extensions to studies. Each access sub-committee consists of eight members appointed by the Trust and KCL.

The KHP RTB issues an annual report to the REC, as a condition of the NHS REC approval. This report provides details on the number and type of sample accrued and the samples supplied to researchers, as well as a log of reported adverse incidents over the preceding year.

Consent

Informed consent is obtained from each participant for the collection, storage and use of tissue and blood samples and the collection, storage and disclosure of data. Consent is given by the participant in writing and is obtained and witnessed by clinical and non-clinical staff (members of clinical trials teams) who have undertaken approved consent training. The consent is generic and is not limited to specific research projects. There are several additional consent options open to the patient, including consent to the use of the tissue in genetic research and in research involving animals.

Consent is sought from patients who have malignant disease by a member of the clinical trials team prior to the patient's pre-admission assessment. Consent is sought from patients scheduled to undergo surgery for the removal of non-malignant tissue on the day of surgery either by a member of the clinical trials team, a consultant, registrar or senior house officer.

Sample collection and storage

Tissue and whole blood samples are collected from theatres and are taken to the respective pathology unit for processing and fixing. Fresh and fixed material required for tissue biobank storage is removed by the pathologist using a sample which doesn't compromise clinical diagnosis.

All samples are stored under secure conditions. Each whole blood and tissue sample is obtained in duplicate and is stored in separate storage facilities. The breast, thoracic, upper gastrointestinal tract and prostate tissue collections are stored in -80°C freezers on the third floor of the Guy's Tower. Head and neck tissue collections are stored in -80°C freezers and a liquid nitrogen tank on the 28th floor of the Tower. The head and neck collection will move to new premises on the fourth floor of the Tower in 2014.

The freezers and liquid nitrogen container are under data logged, continuous temperature monitoring using internal temperature probes. There is a wireless callout system and callout rota. Storage temperature limits are described in a standard operating procedure and are shown on a work instruction on the freezer doors. Oxygen depletion monitors and backup liquid nitrogen are available.

Contingency freezer storage is available on the 17th floor of the Tower.

Sample distribution

The establishment distributes samples nationally and internationally to research groups using detailed material transfer agreements (MTAs). However, samples sent to local research collaborators within the Trust and KCL are not distributed using this system (*see Advice item 6*).

The site visit inspection included a visual inspection of the laboratories and tissue storage facilities. Meetings were held with the DI (Senior Lecturer/Head of Tissue Banking), the Corporate Licence Holder contact (Professor of Public Health Medicine), the Quality Manager, the Academic Lead - Head and Neck Cancer Tissue Bank, the Advanced Practitioner (Breast Cancer Tissue Biobank) and the Academic Lead - Cancer Tissue Bank Management Committee. A documentation review and audit trail were carried out. Details of the two separate audit trails are provided below; no anomalies were found.

For the head and neck tissue collection, two tissue samples and one blood sample were selected from the freezers and four blocks were chosen from the storage cupboard. The location details were compared to the paper records in the tissue register and the electronic records on the tissue database; no anomalies were found. For the vertical audit, four samples were tracked from consent to receipt, storage and distribution (where appropriate); no anomalies were found.

For the tissue collections on the third floor, the freezer location of a breast, thoracic and prostate tissue sample was each successfully traced to the paper and electronic records. For the vertical audit, three samples were tracked from consent to receipt and storage; no anomalies were found.

Inspection findings

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

Compliance with HTA standards

Consent

Standard	Inspection findings	Level of shortfall
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.	For storage of tissue in the breast collection, confirmation of written consent is required before sample storage. This is reflected in the breast tissue biobank SOP: 'Seeking consent from patients with breast diseases to bank tissue and use clinical data for research purposes' (KHPCBB1001/003). The inspection team noted that, for storage of tissue in the head and neck collection, an assurance from the clinician that consent has been obtained is considered sufficient. This is often, though not always, backed up by a completed consent form. There is a risk that this approach may lead to occasions where tissue could be stored in the collection without patient consent.	**Minor**

Governance and Quality

Standard	Inspection findings	Level of shortfall
GQ2 There is a documented system of quality management and audit.	Staff perform occasional ad hoc sample audits but there is no documented system of audit. *See Advice item 4*.	**Minor**
GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately.	There are risk assessments related to Control of Substances Hazardous to Health (COSHH) risks of laboratory procedures. There are no risk assessments for activities such as consent, sample receipt, transport and storage. *See Advice item 7*.	**Minor**

Premises, Facilities and Equipment

Standard	Inspection findings	Level of shortfall
PFE1 The premises are fit for purpose.	There are no risk assessments of the storage areas, including the proposed storage facility on the fourth floor.	**Minor**

Advice

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

No.	Standard	Advice
1.	N/A	The DI is advised to appoint a person designated (PD) to cover activities in the head and neck tissue biobank.
2.	GQ1	The DI is advised to ensure that SOPs are written and reviewed by separate people. The reviewer should have knowledge of the relevant procedure/process but need not be more senior than the author.
3.	GQ1	The DI is advised to create and formalise meetings of the KHP RTB Operational Group. In other establishments, similar meetings have covered items such as: reportable incidents, changes to SOPs, audits, risk assessments, HTA training, the setting up of agreements and updates from the HTA (e.g. e-newsletter items). Such meetings have the potential to facilitate the standardisation of processes and procedures and the sharing of good practice across all the tissue biobanks.
4.	Principally GQ2 but also relevant to standard GQ4	The DI is advised to devise an audit schedule and divide it into small increments, carried out by different team members. This could include horizontal audits against consent/procurement to ensure that SOPs accurately reflect current practices and vertical tissue traceability audits, from records of receipt to storage, use or disposal. The DI may also wish to consider implementing a regular audit against HTA standards. The results of audit findings (including those performed by other accreditors, e.g. relevant Clinical Pathology Accreditation, CPA, audits) and actions taken should be formally recorded.
5.	GQ3	The DI may wish to consider including the MRC 'Research and Human Tissue Legislation e-learning Module', part of the MRC Data and Tissues Toolkit (both of which were developed with input from the HTA), as part of the staff training programme: http://www.rsclearn.mrc.ac.uk/
6.	GQ5	The DI is advised to consider using MTAs for the distribution of all samples, including those to collaborators on site, to ensure the retention of tissue quality and traceability during transport.
7.	GQ8	A risk assessment template exists in the Quality Manual and could be used to assess the risks posed to human tissue. Once created, the DI is then advised to ensure that all new risk assessments are reviewed regularly, that staff can access such risk assessments and that knowledge of all risk assessments is incorporated into the staff training programme.

Concluding comments

During the site visit inspection of the establishment several areas of strength and good practice were noted:

- The establishment has an excellent process for seeking consent. There is a detailed biobank patient information booklet (covering all five tissue types), a detailed and robust procedure on revoking consent to participate, and a consent training programme.
- There is a detailed staff induction and staff appraisal programme.
- KCL has four HTA research licences. All the relevant DIs have entered into a rolling programme of separate audits of each of the other establishments.
- The DI has contributed to the voluntary accreditation system being developed by the National Cancer Research Institute/Confederation of Cancer Biobanks, and is soon to be inspected under this scheme.
- As a contingency against freezer failure, all samples are duplicated and are stored in freezers in separate fire zones.

There are a number of areas of practice that require improvement and four minor shortfalls have been identified. The HTA has given advice to the DI with respect to governance and quality systems standards. 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: 18 December 2013

Report returned from DI: 3 January 2014

Final report issued: 27 January 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.