Site visit inspection report on compliance with HTA minimum standards

HistologiX Limited

HTA licensing number 12097

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**

23 May 2013

Summary of inspection findings

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

HistologiX Limited was found to have met most of the HTA's licensing standards, however minor shortfalls were identified under standards GQ5, GQ6, GQ7, and PFE4. These shortfalls related to specimen traceability, adverse incident reporting and transportation.

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 describes the first site visit inspection of HistologiX Limited ('the establishment'), a contract research organisation, on the 23 May 2013. HistologiX stores normal and diseased human tissue, which is ordered from a tissue provider for use in research activities that take place at the establishment. The tissue provider is not licensed by the HTA as it is located in Scotland. Tissues are uniquely identified using assigned 'source codes'. The establishment also operates an ethically approved research tissue bank, which receives human tissue in the form of frozen formalin fixed paraffin embedded (FFPE) blocks and slides from the tissue

provider. The research tissue bank material is assigned a unique identifier by the tissue provider, which is also used by the establishment. The research tissue bank material is stored on behalf of the tissue provider and is then transferred to the clients of the tissue provider upon their request. The tissue provider is responsible for organising the courier that is responsible for the collection and transport of the material to the HistologiX Limited.

The establishment stores human tissue in two -80^{0}c freezers that are located in the main laboratory area. The freezers are connected to a CO_2 cylinder which acts as a back up in the event of freezer failure. The freezer temperatures are monitored daily and the temperature logs are maintained by establishment staff. Although the freezers are alarmed, there is no system for out of hours notification should freezer failure occur. Tissue blocks are also stored at room temperature within designated areas in the laboratory. The laboratory staff are not permitted to access the building out of hours due to security policies.

The inspection comprised visual inspections of storage locations, traceability audits, document review and interviews with the Designated Invidual (DI), persons designated (PD) and other key members of staff working under the licence. Traceability audits of five tissue samples in storage were conducted. Both forward and reverse audits were carried out, from storage location to the paper records and then from the paper records to the storage location. Anomalies were noted in two samples. A colon sample located in the freezer was found to be in the wrong location and the paperwork supporting this sample was also incorrect. The records associated with an adrenal sample located in the freezer did not demonstrate that the samples had been used. The donor medical summary was also missing for this sample. There were also inconsistencies associated with unique identifiers associated with multiple blocks that originated from a single piece of tissue.

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
GQ5 There are documented procedures for the distribution of body parts, tissues or cells	The establishment distributes tissue from the ethically approved research tissue bank to clients on behalf of the tissue provider. At the time of the inspection the establishment was unable to produce evidence of agreements either with the tissue provider or clients that stipulate details relating to tissue traceability or tissue disposal after use. The establishment also distributes tissue itself, separate from the RTB work (e.g. to Leicester Bone Bank). Again,there was no agreement or SOP for this.	**Minor**
GQ6 A coding and records system facilitates traceability of bodies, body parts, tissues and cells, ensuring a robust audit trail.	The traceability systems used by the establishment need to be reviewed and improved. I. The systems in their current set up, do not support iden tification of which samples have been used in a particular study. Although this information can be found, it requires searching through individual study records which is time and labour intensive. II. In addition, particular attention should be given to identifying all tissue in storage with a unique identifier including where tissue has been received and sectioned into several blocks. Some of the blocks in storage share the same unique identifier, whereas others have been given a unique code. Currently there is not a consistent approach nor a formal procedure to deal with these cases.	**Minor** **Minor**
GQ7 There are systems to ensure that all adverse events are investigated promptly.	There is no system or formal procedure in place to report or investigate adverse incidents which may relate to loss of tissue, loss of traceability or sample mix up.	**Minor**

Premises, Facilities and Equipment

Standard	Inspection findings	Level of shortfall
PFE4 Systems are in place to protect the quality and integrity of body parts, tissues and cells during transport and delivery to a destination.	The establishment is not directly involved in organising transport of tissues. It is the tissue provider that is responsible for organising the courier to transport tissues to the establishment as well as from the establishment to respective clients. There is no documented procedure for the transfer of tissues to clients and there is also no record of any agreements with the tissue provider that stipulates respective responsibilities of each party relevant to consent, transport and storage requirements.	**Minor**

Advice

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

No.	Standard	Advice
1.	GQ1	The DI is advised to consider introducing HTA compliance into weekly team meetings and should also consider active dissemination of HTA relevant information to members of staff working with human tissue. This will ensure that staff are aware of developments in legislation and areas of change that may affect practice.
2.	GQ2	The GLP Consultant undertakes protocol audits and these also cover aspects of human tissue storage. However, the DI should consider conducting audits internally and ensure that these are documented. The audits should cover aspects related to storage, record keeping and disposal. Corrective and preventative actions should be taken where issues require resolution, and these should be documented
3.	GQ8	Risk assessments surrounding health and safety and human tissue storage are in place. Although there is a good range of risk assessments, the DI is advised to extend the scope of the current risk assessments to include the risks associated with loss of samples and loss of traceability. By extending the scope of the risk assessments this will enable the establishment to consider risks associated with non-conformance to HTA standards.

4.	PFE3	The -80 ^{0}c freezers are backed up by CO_2 cylinders in the event of any failure. The CO_2 cylinders are checked on a weekly basis. There have not been any reported freezer failures and there is an audible alarm. The establishment staff are unable to access the building out of hours in the event of a freezer failure due to premises security. There are informal contingency arrangements with another laboratory based on site, should freezers fail. The DI is advised to formalise these arrangements with the laboratory and update relevant the SOP ('Critical Equipment Failure Procedure SOP') to reflect this. The DI should also consider alternative contingency arrangements, should a power failure affect the whole site.

Concluding comments

The report outlines the first site visit inspection at HistologiX Limited. The establishment is a small contract research organisation with only a few members of staff actively working with human tissue. The DI and establishment staff have good working relationships.

There are a number of areas of practice that require improvement, as indicated by the minor shortfalls relating to specimen traceability, adverse event reporting and transportation. The HTA has also given advice to the Designated Individual with respect to standards relating to governance, audit, risk assessments and storage arrangements.

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.

Report sent to DI for factual accuracy: 17 June 2013

Report returned from DI: 1 July 2013

Final report issued: 1 July 2013

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: 11 October 2013

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.