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**

15 September 2016

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 the majority of the HTA's licensing standards; however, a minor shortfall was identified under standard GQ8, relating to risk assessments.

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 second site visit inspection of HistologiX Limited ('the establishment'), a contract research organisation. The establishment stores normal and diseased human tissue (from the living and deceased) with consent for research, which is ordered from a tissue provider for use in research activities that take place at the establishment. The tissue provider has provided written assurance to the establishment that all tissue provided for research has been consented for this purpose. The tissue provider may also occasionally provide the establishment with a copy of an anonymised consent form along with the tissue sample, however this is not consistent practice (Advice, item 1).

The tissue provider is not licensed by the HTA as it is located outside of England, Wales and Northern Ireland. Tissue is uniquely identified using assigned 'source codes' which are assigned once the tissue arrives at the establishment. The establishment also stores human tissue on behalf of the tissue provider, which is then transferred to their clients by the establishment upon their request. The tissue which is stored on behalf of the tissue provider is not assigned a source code by the establishment; however, it contains a unique identifier assigned by the tissue provider. The establishment uses a paper system to record traceability of all tissue being stored in the freezers. The tissue provider organises a courier, which has responsibility for the collection and transport of the material to the establishment, as well as the transport from the establishment to the client.

The establishment stores human tissue in three -80^{0}c freezers that are located in the main laboratory area. Two freezers are dedicated to tissue stored for the establishment's research activities and the other is dedicated to tissue that is stored on behalf of the tissue provider. The freezers are connected to a CO_2 cylinder, which is regularly weighed, and 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, a formal risk assessment has not been carried out which takes into consideration the risks of freezer failure taking place during this period (minor shortfall, GQ8). 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 of a visual inspection of storage locations, traceability audits, document review and interviews with the Designated Individual (DI), Histology Manager, Histology Technician and Immunohistochemistry Manager working under the licence. As the current Histology Manager was leaving the establishment, the person taking on this job role was interviewed.

Forward and reverse tissue traceability audits were carried out and samples, including bone marrow, breast tissue, ureter and parathyroid gland, were identified from the paper records and traced to their respective locations. Although no discrepancies were identified, advice has been given in respect of labelling of the bags (Advice, item 5).

A paper audit exercise was carried out which followed the receipt of three whole kidneys by the establishment from the tissue provider and the subsequent dispatch of one of the kidneys to another establishment for their use in research. All paper records were fully traceable and no discrepancies were found. A further audit was carried out which focussed on a study. A lung block was identified in the paper records and was traced to its storage location. No discrepancies were identified.

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
GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately	Although the establishment has in place health and safety risk assessments, the following areas of risk have not been considered: I) all the risks associated with the licensed activity of storage of human tissue for research (see Advice, item 7); II) the arrangements for release, dispatch and transport of human tissue to clients on behalf of the tissue provider; III) the absence of an out of hours alarm system to notify staff of freezer failures during this period as well as lack of access to the building out of hours.	Minor

Advice

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

No.	Standard	Advice
1.	C1	Currently, consent forms are not always provided to the establishment with the tissue samples and on other occasions they are. Although, the tissue provider has provided written confirmation that tissue with consent is supplied to the establishment, the DI may wish to consider adopting a more consistent approach.
2.	GQ1	Although there have not been any reported complaints the DI is advised to implement a system to manage complaints.
3.	GQ2	Audits are regularly performed by a Quality Assurance team, which include a review of processes relating to receipt and storage of human tissue samples. To strengthen audit processes further, the DI may wish to consider developing an internal audit schedule which includes audits undertaken by staff. In addition, the DI may also wish to consider using

		staff working within Immunohistochemistry and Histology, to audit one another's areas.
4.	GQ4	The DI is advised that all corrections to records should be initialled and dated, and not completely erased. This is important to ensure that records remain auditable.
5.	GQ6	The DI is advised to consider reviewing the suitability of the ink used to label the bags containing the tissue samples stored in the freezer as it was noted that, on some bags, the information was no longer visible as it had rubbed off over time. Whilst this did not present a loss of traceability as the samples contained within the bags are labelled, the DI is advised to consider improving the external labelling.
6.	GQ7	Procedure SOP/IHC/006 provides information about reporting incidents relating to human tissue. Whilst the procedure is detailed, the DI is advised to review and include additional incidents from the list below: • receiving and/or storing specimens without appropriate consent documentation; • storing or using human tissue after consent withdrawal; • storage failure or other damage affecting human tissue quality for useful research; • loss of human tissue; • sample mix-up or loss of traceability; • transport of specimens to and from the establishment; • security arrangements; • incorrect disposal. This illustrative information will give staff a better understanding of the types of incidents involving human tissue that must be reported and investigated.
7.	GQ8	All establishments should identify the risks inherent in the key activities, and procedures should be developed in consideration of and to mitigate these potential risks where appropriate. Establishments may tend to focus risk assessments on health and safety issues which, in themselves, are not sufficient to meet our standards. DIs should also assess the risks associated with licensed activities. Documented risk assessments should include an evaluation of the level of the risk and, where appropriate, the mitigating actions identified and the level of residual risk remaining.

		Risk assessments should include the risks relating to the premises, practices and procedures connected with licensed activities, including: • receiving and/or storing specimens without appropriate consent documentation; • storing or using human tissue after consent withdrawal; • storage failure or other damage affecting human tissue quality for useful research; • loss of human tissue; • sample mix-up or loss of traceability; • transport of specimens to and from the establishment; • security arrangements; • incorrect disposal Risk assessments should be reviewed periodically (typically, every 1-3 years) and the actions to mitigate risks updated as necessary. Risk assessments should also be reviewed following an incident. By documenting risk assessments, staff are made aware of identified risks, which helps to prevent risks materialising and informs the development of procedures and relevant documentation.
8.	PFE3	The DI is advised to formally document the manual challenge of the critical storage area alarm call-out system to ensure it is functioning correctly and that critical storage failures will not go unnoticed.
9.	PFE3	The DI may wish to consider installing an electronic temperature monitoring system to enable the critical storage conditions to be monitored continuously. This will reduce the risk of critical storage failure going unnoticed.
10.	PFE3	Although there is a disaster recovery procedure (SOP/ADM/031) in place which includes information about on site contingency, the DI is advised to also consider off site contingency arrangements with other HTA-licensed establishments. This should provide the assurance that, should the on-site contingency arrangments fail, there are suitable arrangements to transfer human tissue samples elsewhere.
11.	D2	Procedure SOP/ICH/008 is about human tissue disposal. The DI may wish to update this procedure to include information on how this material is bagged, when it is collected for incineration and by whom.

Concluding comments

The establishment has worked hard since the last site visit inspection in 2013 to meet the HTA standards and the DI has a good oversight of staff working with human tissue.

Some areas of good practice were noted during the inspection which includes the:

- monitoring of the CO_2 back up cylinders;
- chain of custody document for all tissue samples;
- disaster recovery procedure provides information on the length of time the CO_2 back up cylinders will support the freezers.
- approach taken to ensuring that both Histology and Immunohistochemistry staff are trained in each other's procedures.

There are a number of areas of practice that require improvement, including a minor shortfall against standard GQ8. The HTA has also given advice to the Designated Individual with respect to, consent, complaints, audits, records management, traceability, incidents, risk assessments, temperature monitoring/contingency and disposal.

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: 13 October 2016

Report returned from DI: 8 November 2016

Final report issued: 9 November 2016

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.