Site visit inspection report on compliance with HTA minimum standards

Horizon Discovery Limited

HTA licensing number 12638

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 July 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.

Although Horizon Discovery Limited (the establishment) was found to have met majority of the HTA standards, one minor shortfall was identified against standard PFE3 in relation to documented monitoring of critical storage conditions.

The establishment was provided with advice and guidance about areas that could be improved further. 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 licenses against four groups of standards:

- consent
- governance and quality systems
- premises facilities and equipment
- disposal.

This is an exception-based report: only those standards that have been assessed as not met are included. Where the HTA determines that a standard is not met, the level of the shortfall is classified as 'Critical', 'Major' or 'Minor' (see Appendix 2: Classification of the level of shortfall). Where HTA standards are fully met, but the HTA has identified an area of practice that could be further improved, advice is given to the DI.

Reports of HTA inspections carried out from 1 November 2010 are published on the HTA's website.

Background to the establishment and description of inspection activities undertaken

This report describes the first site visit inspection of Horizon Discovery Limited (the establishment), which has been licensed for the storage of relevant material for a scheduled purpose since October 2015. The establishment is involved in the development of drug screening assays and cell lines, and stores small quantities of Peripheral blood Mononuclear cells (PBMCs), Mesenchymal Progenitor Cells (MPCs), Primary Human CD3 T Cells (CD3) and immunohistochemistry slides, which are purchased from third party suppliers and used for specific research studies. It also procures small quantity of human tissue from an HTA-licensed establishment, which supplies leucocyte cones from platelet donors. However, these are used immediately on arrival and are therefore not subject to licensing for storage under the HT Act.

All suppliers are approved by the establishment before tissue can be purchased; new suppliers are required to complete an evaluation form, which prompts them to provide confirmation that the tissue supplied meets the consent requirements of the Human Tissue Act 2004 (HT Act). Once a researcher completes a project request form, the Lead Scientist for each tissue type requested completes a comprehensive risk assessment. The project request form is also reviewed by the Designated Individual (DI) who provides approval for research involving human tissue.

Tissue is received by the 'Goods In' team, who alert the Lead Scientist to undertake integrity checks before the tissue can be placed in storage. A quarantine system is in place for managing non-conforming tissue samples. All tissue samples are assigned a unique identifier (SNB number) by the establishment's traceability database, which also generates a barcode label for each sample.

At the time of inspection there was no tissue being stored at -80C, although the establishment has the facilities for refrigerated storage. The PBMCs are stored in a liquid nitrogen tank alongside cell lines (not relevant material under the HT Act 2004). There is a dial-out system,

which notifies staff if there is a temperature excursion, both during and out of hours; however, staff do not monitor and record the temperatures for the liquid nitrogen tank (*minor shortfall, PFE3*). Furthermore, establishment staff are not currently testing alarms (advice and guidance, item 6). The room, where the liquid nitrogen tank is located, has an oxygen alarm and lone working in this area is not permitted at any time.

The inspection comprised a visual inspection of the areas where human tissue is stored, interviews with a Lead Scientist (person designate), Director of Facilities and Corporate Operation (person designate), Shipping Team Leader, Designated Individual (DI) and the Corporate Licence Holder Contact (CLHc) and a review of governance documentation.

In addition, traceability audits were carried out using four tissue samples (including PBMCs, MPC and CD3) stored in liquid nitrogen and 16 immunohistochemistry slides. A forward traceability audit was carried out, with samples identified from their storage location and traced to the relevant documentation and electronic database. A reverse traceability audit was carried out, with samples identified from the sample traceability database, relevant paperwork and traced through to respective storage locations. No discrepancies were found.

Although the leucocyte cones are not stored under the licence as they are used immediately on arrival, for thoroughness the electronic and paper records relating to two cones received by the establishment were reviewed along with the researcher's project request form. No discrepancies were noted.

Inspection findings

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

Compliance with HTA standards

Premises Facilities and Equipment

Standard	Inspection findings	Level of shortfall
PFE3 There are appropriate facilities for the storage of bodies, body parts, tissues and cells, consumables and records.	Although there is an auto-dial out system which notifies staff if there is a temperature excursion and staff informally check the liquid nitrogen tank temperatures, there is no formal process for checking and recording the temperatures on a daily basis. Regular temperature monitoring may help reduce the likelihood of a failure going unnoticed. *This shortfall was addressed before the report was finalized.*	**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 review sub sections, 5.4.8 and 5.4.10 of BP-00-01-11 (HTA-Codes of Practice). Both sub-sections refer to regulatory requirements under the Q&S Regulations 2007, in relation to the retention of traceability and raw data records as well as reporting of Serious Adverse Events and Reactions to the HTA. These requirements are not applicable to establishments licensed under the HT Act 2004.
2.	GQ2	The DI is advised to put in place an audit schedule which includes an audit of compliance against HTA standards and encompasses the entire process; from consent, transport, storage, use and disposal of human tissue samples.
3.	GQ4	Researchers storing and using human tissue have access to the traceability database. It was noted during the traceability audit that there is some variability in how researchers use the system, particularly in relation to the way in which records are edited and managed. The DI may wish to consider standardising the approach that researchers use to ensure that the database is used in a consistent manner.
4.	GQ6	The DI is advised that tissue blocks and slides are regarded as relevant material and should also be recorded on the traceability database. The 15 slides that were reviewed during the audit trail were fully traceable against the paperwork, but had not been added to the traceability database.
5.	GQ7	The DI is advised to set out the types of incidents that would need to be reported and investigated in the incident procedure. Incidents may include, but are not limited to: • 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 information enables staff to have a better understanding of the types of incidents involving human tissue that must be reported and investigated.
6.	GQ8	Although there are risk assessments in place to manage health and safety risks as well as risks associated with licensable activities, the DI is advised that documented risk assessments should include an evaluation of the level of risk and, where appropriate, the mitigating actions identified and the level of residual risk remaining. Furthermore, the DI is advised to review the information in the risk mitigation column to ensure it accurately reflects the steps taken to reduce the risk.
7.	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 critical storage failures will not go unnoticed.

8.	PFE3	The liquid nitrogen tank stores cells lines and human tissue and is currently approximately 80% capacity. There is a contingency plan in place with another HTA-licensed establishment in the event that the liquid nitrogen tank fails; however, this arrangement only accommodates the cell lines at present, and not human tissue. The DI is advised to consider contingency arrangements for the human tissue stored in the liquid nitrogen tank, should the tank fail or reach capacity.
9.	D2	The 'Human Tissue Disposal' Procedure (BP-04-13-04) is concise and provides a step-by-step method for organising disposal; however, the DI is advised to review the procedure and set out in more detail how human tissue is bagged, who is responsible for its collection and the disposal method used for human tissue.

Concluding comments

The establishment has worked hard to achieve a high level of compliance with the HTA's licensing standards and is keen to develop its understanding of HTA requirements. The DI has a good oversight of activities being undertaken and works cohesively with all staff working with human tissue. A number of areas of good practice were seen during the inspection:

- An evaluation form is used to review whether suppliers meet consent requirements under the HT Act 2004.
- The DI has had proactive involvement in auditing systems and processes to review whether these would be suitable for handling tissue blocks. Although the establishment does not store tissue blocks at present, a documented audit using a 'dummy tissue block' (i.e. containing wax only) was carried out to identify areas for improvement before tissue blocks are purchased, stored and used for research.
- A risk assessment of each tissue type is carried out before tissue can be purchased.
  The DI provides HTA training to all staff who will work under the licence, as well as providing refresher training on a yearly basis.

There are some areas of practice that require improvement, including one minor shortfall against, PFE3. The HTA has given advice to the Designated Individual on a range of matters relating to standards GQ1, GQ2. GQ4, GQ6, GQ7, GQ8, PFE3 and D2, to make further improvements.

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: 12 August 2016

Report returned from DI: 23 August 2016 (with comments)

Final report issued: 30 August 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

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.