Site visit inspection report on compliance with HTA minimum standards

Antitope Limited

HTA licensing number 12627

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**

9 December 2015

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.

Antitope Limited was found to have met all the HTA standards.

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 Antitope Limited (the establishment). The establishment has been licensed by the HTA since February 2015 for storage of relevant material for use in research. The establishment is involved in developing technologies for immunogenicity assessment and protein engineering and works collaboratively with the pharmaceutical industry.

The establishment receive blood and buffy coat samples for which consent for storage and use for research has been obtained, including for genetic studies. The samples are provided through collaboration with third party providers located in the UK and in Europe. To maintain donor anonymity, the establishment does not receive copies of consent forms but has in place an agreement with the tissue provider that states the consent arrangements (see advice item, 1).

Samples are delivered by courier to the establishment's Stores Department and then collected by a member of the laboratory team who will check that the packaging is intact and undamaged. The establishment stipulates that samples must be received within 24 hours to ensure samples remain viable. Samples received after 24 hours will be discarded immediately. The establishment receives samples which have been screened for evidence of HIV, Hepatitis B virus and Hepatitis C virus infection by the tissue provider. Some suppliers

provide samples to the establishment before the results are available. In these circumstances, once the results are available and if found to be positive, the sample will be discarded immediately.

Once the samples are received into the laboratory, they are assigned a unique identifier which is generated by the electronic traceability database. The processing team will complete a 'batch set up record' document for all samples processed, which contains; the unique identifier of each vial, the number of vials, the cell viability of each sample and the storage location of each vial. The samples will then be placed in a -80^{0}C freezer for up to 96 hours for the samples to be subjected to controlled rate freezing, before being placed into vapour phase liquid nitrogen tanks for long term storage.

Critical storage conditions are continuously monitored using an electronic software system. If the temperature goes outside of normal parameters, an audible alarm will sound. The electronic software system will also alert members of staff if there is a temperature fluctuation both during and out of hours. In the event that the freezer or vapour tanks fail, the establishment has a contingency arrangement for samples to be transferred to another HTA licensed establishment.

The inspection included: a visual inspection of the sample processing laboratory and storage areas; a document review, and; interviews with key members of staff, including the Quality and Compliance Manager, the Vice President Biology, the Corporate Licence Holder contact (CLHc), a Research Scientist and the Designated Individual (DI).

Both forward and reverse traceability audits were carried out. Samples were identified by reviewing the batch set up record to obtain the unique identifiers for each sample and the numbers of vials in storage. The electronic traceability database was accessed to check the locations of the vials against their physical location. A total of 52 vials were audited. No discrepancies were identified. A reverse audit was carried out to confirm if two empty storage locations was also reflected in the electronic traceability database. No discrepancies were identified.

Inspection findings

The HTA found the Licence Holder to be suitable in accordance with the requirements of the legislation.

Compliance with HTA standards

All applicable HTA standards have been assessed as fully met.

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

No.	Standard	Advice
1.	C1	The establishment receives tissue from two providers. An agreement with one of the tissue providers sets out the consent arrangements for the use of samples in research as well as the responsibility of the third party tissue provider to maintain a register of donor consent. The DI is strongly advised to formalise all arrangements for receiving samples for research use to provide assurance that only material that has been consented to for research use will be supplied.
2.	GQ1/D1	The DI is advised to review the SOP 0136 to include more comprehensive information in regards to the traceability steps to be followed for the disposal of human tissue. In its current format SOP 0136, does not provide much detail about how the electronic traceability system must be updated; nor does it provide clarity on how to capture the date and method of disposal.
3.	GQ6/D2	The establishment has moved away from using spreadsheets to record traceability to using a database system. Whenever an amendment is made to the database, for example; removal or movement of vials, this is recorded in the history function of the system. Whilst there is an audit trail to demonstrate that a sample was removed for disposal on a particular date, the DI should consider whether an extra field can be added to allow the date a particular sample was removed for disposal to be recorded. In addition, although disposal does not take place on site and is organised by a department who collect the clinical waste on a daily basis, as good practice, the DI should also consider adding a field which describes the method of disposal used.
4.	GQ8	There are three items of advice: 1. There is a comprehensive range of risk assessments concerning human tissue licensable activities and health and safety. The DI should consider re-drafting the current template to include a risk matrix system. This would enable the levels of risks and the likelihood of an incident occurring to be defined clearly. 2. Furthermore, the DI is advised to re-visit the risk assessment, 'failure of the cryostore'.The risk assessment refers to the transfer of samples to another licensed establishment as a control measure. However, the risk assessment does not take into consideration whether the 'emergency' dewars which are co-located with the vapour tanks can be used in the event of critical storage failure. 3. Currently there are approximately over 24,000 human tissue samples being stored in two vapour tanks. The DI is advised to risk assess the existing storage capacity in light of the growing demands for sample storage.
5.	PFE3	The DI should consider placing signage on the freezer which provides the alarm set point temperatures. In the event that the alarm system fails, this information would serve as a reminder to researchers either passing by or accessing the freezer.
6.	PFE4	Samples are delivered by courier to the establishment. As the samples need to be received within 24 hours to maintain sample viability and in light of a recent occasion where the courier failed to transport the samples within the correct

		timeframes, the DI should consider formalising the arrangements with the courier.

Concluding comments

The establishment staff have worked hard to achieve a high standard of compliance with the HTA standards. A number of areas of good practice were seen during the inspection:

- Thorough follow up of actions following audits and CAPAs, as well as regular internal and external audits;
- The use of two operators to mitigate the risk of errors occurring during processing of tissue, as well as storing samples;
- Traceability systems also apply to the freezing containers use to store human tissue for controlled-rate freezing;
- A disaster recovery plan is in place with a licensed establishment for contingency purposes;
- A 'Code of Practice' for use of the cryostore is in place and available for researchers to read when accessing the room;
- Induction training is made available to all staff, including MRC training, which staff should achieve a pass mark of 70%. Furthermore all technical staff handling human tissue samples are shadowed and observed before they are sign off as competent;
- The use of trend analysis which focuses on vial errors, critical storage temperatures and contamination of cells is undertaken regularly.

The HTA has given advice to the Designated Individual on a range of issues to make further improvements.

Report sent to DI for factual accuracy: 6 January 2016

Report returned from DI: 20 January 2016 (with comments)

Final report issued: 26 January 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.