

**Site visit inspection report on performance against HTA quality standards
Astex Therapeutics Ltd
HTA licensing number 12122**

**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**

25 May 2011

Executive Summary

A site-visit inspection of Astex Therapeutics Ltd (the establishment) was carried out by the HTA on 25 May 2011.

The establishment was found to meet all of the HTA standards across the four areas of: consent (C); governance and quality systems (GQS); premises, facilities and equipment (PFE); and disposal (D). No shortfalls were found in relation to these standards. Examples of strengths and robust practice are included in the concluding comments section of the report.

The HTA found the Designated Individual, the Licence Holder (Astex Therapeutics Ltd), the premises and the practices to be suitable in accordance with the requirements of the legislation.

All reports of HTA site-visit inspections carried out from 1 November 2010 are published on the HTA's website.

Background to the establishment and description of inspection activities undertaken

This report refers to the activities carried out by Astex Therapeutics Ltd (the establishment). This was the first site-visit inspection of the establishment by the HTA.

Astex Therapeutics Ltd is a drug discovery company with several compounds either in, or about to enter, clinical development in the specialities of oncology and virology.

The establishment stores approximately 1500 samples of relevant material from living donors. These include frozen samples (whole blood, peripheral blood mononuclear cell, PBMC, pellets), blocks (skin biopsies, tumour tissue, bone marrow biopsies) and slides (tumour, skin, and bone marrow biopsies, fine needle aspirates).

All samples are taken at UK and US clinical sites as part of clinical trials. Some of these trials are ongoing and have received ethical approval from an ethics committee recognised by the United Kingdom Ethics Committees Authority (UKECA). Storage of these samples is exempt from HTA licensing. Other samples are being stored from clinical trials that have now been completed. Storage of these samples falls under the HTA licence. Samples are also being stored as part of trials ethically approved outside the UK (e.g. USA). Storage of these samples also falls under the licence. Two commercially sourced human skin samples are also stored for use in pre-clinical compound characterisation. These also fall under the licence.

During the site-visit inspection, the inspectors met with staff carrying out licensable activities, inspected the storage areas and reviewed documentation.

A vertical traceability audit of material stored under the licence was carried out. Two PBMC samples in the -80°C freezer and three blocks of skin biopsy and tumour tissue were chosen. All stored material was fully traceable.

Meeting the HTA's licensing standards

The HTA developed its licensing standards with input from its stakeholders, in order to ensure the safe and ethical use of human tissue. The HTA expects licensed establishments to meet these standards.

All applicable HTA standards are met

Advice

Below are matters which the HTA advises the DI to consider.

No.	Standard	Advice
1.	GQ1	The DI may wish to consider setting up meetings with other DIs working in the sector, to share information and experience with them and their Persons Designated (PDs). This may help facilitate learning and understanding of staff at this establishment as well as being a forum for the establishment to discuss its good practices.
2.	GQ3	The DI may wish to consider using the MRC Research and Human Tissue Legislation E-learning Module, part of the MRC Data and Tissues Toolkit, when developing training for staff: http://www.rsclearn.mrc.ac.uk/ The module and the toolkit were developed with input from the HTA.
3.	GQ4	The DI is advised to record the number of slides stored from each block on their database and in the records folder.
4.	GQ8	There is a documented Standard Operating Procedure (SOP) for freezer failure and a risk assessment has been carried out but has not been documented. The DI is advised to document the risk assessment for freezer failure.
5.	PFE3	The contingency for failure in the storage area is to temporarily transfer all frozen samples to an unlicensed establishment on the Science Park. The DI is advised to put an agreement in place with a licensed establishment for longer term (>7 day) contingency storage.

Concluding comments

Overall, the HTA is satisfied that the practices undertaken under the licence are suitable. In addition, the HTA observed several strengths and areas of good practice, including:

- A comprehensive and well-developed Good Clinical Practice (GCP) compliance training programme, including consent training, for staff at each clinical site. This is undertaken by an external consulting company.
- A detailed and extensive Quality Management System, including a comprehensive 'Translational Biology Quality Manual'.
- A comprehensive SOP on adverse events (AEs), including examples of such AEs.
- The observation that all procedures involving sample receipt, storage, release from quarantine (if samples arrive with no documented consent or are mislabelled) are double-checked by two authorised personnel.
- The observation that all staff involved in the licensable activities function well together as a team under the DI.

Overall the HTA is satisfied that the premises are suitable. They are well maintained, are monitored, and are fit-for-purpose.

Report sent to DI for factual accuracy: 10 June 2011

Report returned from DI: 17 June 2011

Final report issued: 14 July 2011

Appendix 1: HTA inspection process

The Human Tissue Authority regulates the removal, storage, and use of human bodies, body parts, organs and tissue for activities such as research, transplantation, and education and training. The legal requirements for establishments which carry out such activities are set out in the Human Tissue Act 2004 and The Human Tissue Act 2004 (Ethical Approval, Exceptions from Licensing and Supply of Information about Transplants) Regulations 2006.

We license establishments in England, Wales and Northern Ireland that carry out these activities, and inspect them to make sure legal requirements are met.

Inspections

We use the term 'inspection' to describe when we:

- visit an establishment to meet with staff, view premises and facilities, and review policies and procedures (a site-visit inspection); or
- assess written information we have requested from an establishment (a desk-based assessment / inspection).

We carry out inspections to assess if the Designated Individual (DI) is suitable to supervise the activity covered by the licence, as it is their responsibility to ensure that:

- other staff working under the licence are suitable;
- suitable practices are used when carrying out the activity; and
- the conditions of the licence are met.

We also need to be satisfied that the licence applicant or holder, the establishment's premises, and the practices relating to licensed activities, are suitable.

To help us reach our decisions, we have developed standards under four headings: Consent; Governance and Quality; Premises, Facilities and Equipment; and Disposal.

After every site visit inspection, we write a report documenting our findings. Where we find a particular standard is not fully met, we will describe the level of the shortfall as 'Critical', 'Major' or 'Minor'. In most cases, it will be the responsibility of the DI to seek the HTA's agreement on how they will address the identified shortfalls. More information about the classification of shortfalls can be found in Appendix 3.

The majority of our site-visit inspections are announced. If we have concerns about an establishment, we can also undertake an unannounced site visit inspection.

You can find reports for site visit inspections which took place after 1 November 2010 on our website.

Appendix 2: HTA standards

Standards which are not applicable to this establishment have been highlighted.

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
<ul style="list-style-type: none">• 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
<ul style="list-style-type: none">• 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
<ul style="list-style-type: none">• 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
<ul style="list-style-type: none">• Policies and procedures in place 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

<ul style="list-style-type: none"> • Regular governance meetings are held; for example, health and safety and risk management committees, agendas and minutes • Complaints system
<p>GQ2 There is a documented system of quality management and audit</p>
<ul style="list-style-type: none"> • 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
<p>GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills</p>
<ul style="list-style-type: none"> • 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
<p>GQ4 There is a systematic and planned approach to the management of records</p>
<ul style="list-style-type: none"> • 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)
<p>GQ5 There are documented procedures for distribution of body parts, tissues or cells</p>
<ul style="list-style-type: none"> • 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
<p>GQ6 A coding and records system facilitates traceability of bodies, body parts, tissues and cells, ensuring a robust audit trail</p>
<ul style="list-style-type: none"> • 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
<ul style="list-style-type: none"> • 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
<ul style="list-style-type: none"> • 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
<ul style="list-style-type: none"> • 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
<ul style="list-style-type: none"> • 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.
<ul style="list-style-type: none"> • 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 3: 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. There are varying levels of 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.

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.

Follow up actions

A template corrective and preventative action plan is available as a separate Word document. 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.