Site visit inspection report on performance against HTA quality standards
Vertex Pharmaceuticals (Europe) Limited
HTA licensing number 12374

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

17 May 2011

Executive Summary

A site visit inspection of Vertex Pharmaceuticals (Europe) Limited (the establishment) was carried out by the HTA on 17 May 2011.

The establishment was found to meet the majority of the HTA standards across the four areas of: consent; governance and quality; premises, facilities and equipment; and disposal. Some shortfalls were found, particularly in relation to Governance and Quality Systems and Premises Facilities and Equipment. Examples of strengths and good practice are included in the concluding comments section of the report.

The HTA found the Designated Individual (DI), the Licence Holder, the premises and the practices to be suitable in accordance with the requirements of the legislation. The DI is in a more senior position within the establishment than the Licence Holder Contact (LHC), but the HTA noted that the LHC has good links with a member of the establishment's board and so considers the current arrangement to be suitable.

All 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

The establishment forms the UK arm of a global company having offices in the USA, Canada and the UK. The company carries out research relating to the development of pharmaceuticals for treatment of various serious or life threatening diseases in humans.

The licensed activity carried out in the UK is storage of relevant material which has come from a human body for use for a scheduled purpose, in this case research. The establishment does store relevant material in the form of human blood cells and hepatocytes. Blood samples are obtained either from the National Blood Service, or on a voluntary basis from staff, who are provided with information regarding the donation procedure before signing a consent form. The donation itself is made at a local medical practice, with which the establishment has a service level agreement, venepuncture being carried out by a trained phlebotomist after the donor has completed a donor health questionnaire. The donor then delivers the sample to reception at the establishment where it is picked up within a few minutes by a member of the laboratory staff for placement into a storage incubator. Researchers at the establishment are not advised of the identity of the donor, the sample being referred to by the date of collection, as only one donation is carried out per day. Consent forms and donor questionnaires are held by another department at the establishment in order to maintain anonymity. When used, the movement of blood samples through the laboratory is recorded in laboratory workbooks specific to each process, and disposal of the sample is recorded on the donation records. At the time of inspection no blood samples were being stored and in the majority of cases only one blood sample would be stored, another donation being arranged following disposal of the stored sample.

Hepatocytes are imported from Europe, being supplied from the USA. The establishment has copies of the statement of ethics supplied by the company sourcing the cells in the USA together with a certificate confirming consent has obtained. On receipt at the establishment, the hepatocytes are placed into liquid nitrogen storage, and their location is recorded on a storage database, with the hepatocytes from individual donors being referred to by lot number received from the supplying company. When taken from storage, the samples are thawed, used for research and disposed all on the same day and this is recorded in the storage database.

Disposal of cells is as for clinical waste, and the establishment has a contract for incineration by a specialist clinical waste disposal company.

This routine site-visit inspection consisted of a visual inspection of the establishment, during which an audit of stored material was carried out, as detailed below. In addition, a review of governance and quality systems documentation in relation to the licensed activity was carried out. A paperwork review including documented policies and procedures was carried out, along with examination of equipment maintenance and data logs, audits, risk assessments, staff training records and reports relating to untoward incidents. The HTA also carried out interviews with key staff, both as formal interviews and informally as part of the visual inspection.

For the purposes of audit, the hepatocyte database was examined to determine the dates of receipt, confirmation of storage location and date of use and disposal of five samples. Only one sample was still in storage and the location indicated on the database was checked, the sample being found in the indicated storage location within the liquid nitrogen dewar.

No blood samples were being stored on the day of inspection but a review of the records kept in relation to receipt and storage of blood samples was carried out, to determine presence of consent and records of storage, release for use and disposal. No anomalies were found during the audit.

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.

This is an exception-based report: only those standards that have been assessed as not met are included. Where the HTA determines that a licensing standard is not met, the level of the shortfall will be classified as 'Critical', 'Major' or 'Minor' (see Appendix 3: Classification of the level of shortfall).

Unless otherwise advised, the establishment is required to inform the HTA within 14 days of the receipt of the final report of the corrective and preventative actions that will be taken to ensure that the improvements are addressed. A template for this purpose is provided as a separate Word document.

HTA standards not met *(delete as appropriate)*

Governance and Quality

Standard	Inspection findings	Level of shortfall
GQ1 All aspects of the establishment's work are supported by ratified documented policies and procedures as part of the overall governance process.	Many aspects of the establishment's work are supported by documented procedures. However, while staff involved in the licensing activity are aware of the procedures involved in receiving material into storage, releasing samples for use for research and recording the dates of disposal of samples, these have not been formally documented in Standard Operating Procedures.	**Minor**
GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately.	The establishment has carried out and documented risk assessment relating to the processes involvedin the carrying out of research using tissues and cells. However, while it is obvious that risk assessments relating to the receipt, storage and release for use of samples have been made, these have not been formally documented	**Minor**

Advice

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

No.	Standard	Advice
1. GQ	1 GQ8	The DI is advised to ensure that SOPs drafted to support the establishments work are informed by the results of risk assessments of the various activities being carried out.
2.	GQ4	The DI is advised to record the results of the regular audits of records currently carried out.
3.	PFE3	The DI is advised to formally document the weekly check and fill of liquid nitrogen levels in the storage dewars.
4.	PFE5	The DI is advised to document the existing contingency plans covering the failure of the storage incubator or liquid nitrogen dewar and to ensure that the existing standard operating procedure detailing actions to be taken following an incubator out of temperature range alarm is reviewed to clarify how laboratory staff may be called out to deal with any necessary transfer of stored samples to another incubator.
5.	N/A	In the event that the establishment increases the number of blood donations

		received to more than one per day, the DI is advised to consider how a unique identifying number may be allocated to each donation.

Concluding comments

The HTA noted that those involved in carrying out the licensed activity formed part of a small, well trained and motivated team and that there was good communication between all of those involved in carrying out the licensed activity. It was clear that much thought had been applied to obtaining informed consent from staff donating blood and clear steps had been taken to ensure the anonymity of donors. Similarly the DI had obtained information from the company supplying imported hepatocytes to clarify that appropriate consent had been obtained. With regard to the blood samples, the fact that samples will be disposed of after use is covered in the consent information supplied.

Storage of blood samples was in an alarmed incubator, with 24 hour cover and a call out procedure. Ample storage contingency is in place to cover the failure of storage equipment.

The establishment carries out risk assessments for each process involved in the work they carried out and, while some relating to the licensed activity had not been formally documented, it was clear to the HTA that risks had been assessed in setting up policies and procedures.

Minor shortfalls were noted in relation to some documentation but the HTA notes the proactive attitude of the staff involved in the inspection and is confident these will be fully addressed in early course.

Report sent to DI for factual accuracy: 23 May 2011

Report returned from DI: 2 June 2011

Final report issued: 6 June 2011

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.

Date: 18 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
• 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 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 • 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).
- S chedule 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

- D ocumented 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.