Site visit inspection report on compliance with HTA minimum standards

Evotec UK Limited

HTA licensing number 12585

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**

29 May 2013

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.

Evotec was found to have met the majority of the HTA's licensing standards; however, two minor shortfalls were identified in relation to monitoring and recording of critical storage conditions (HTA standard PFE3) as well as transport agreements (HTA standard GQ1).

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 first site visit inspection of Evotec UK Limited on 29 May 2013. Evotec UK Limited is a small company that imports hepatocytes which are used in various studies carried out on behalf of pharmaceutical companies in the UK. The hepatocytes are procured from deceased donors. The cells are procured either as single donations or pooled donations, from multiple donors.The hepatocytes are imported from a company based in the

USA, which has Institutional Review Board (IRB) approval and operates to appropriate ethical standards. The company ensures that all tissues procured have valid consent in place. The establishment does not receive the consent forms, but has in place written confirmation from the company that all tissue is ethically sourced with appropriate consent.

The company is responsible for organising the courier and, once the cells arrive at the establishment, the stores department will notify the research groups to collect the cryoshipper containing the cells. Only designated staff members are responsible for receiving the cells and assigning a unique identifier which is used to label the cryovials containing the cells. The cryovials are placed into liquid nitrogen dewers which are located in the research laboratories. The dewars are not connected to temperature loggers to monitor the storage temperature, however there is a written procedure which requires the stores department to re-fill the dewars on a weekly basis. The written procedure does not cover details for checking the minimum level of liquid nitrogen (see minor shortfall against HTA standard PFE3). A human tissue tracking spreadsheet is used to track the unique identifiers of each cryovial, monitor the respective locations as well as track when the cells are used and disposed of. The stores department is also responsible for receiving hepatocytes for disposal which is carried out via a disposal company that collects clinical waste material for incineration.

The inspection comprised a visual tour of storage locations, traceability audits, document review and interviews with key members of staff working under the licence. A template consent form provided by the company was reviewed during the inspection. Traceability audit trails of four tissue samples were conducted. Both forward and reverse audits were carried out, from storage location to the electronic records and then from the electronic records to the storage location. No anomalies were found during the traceability audits and the electronic systems demonstrated accurate record keeping.

Inspection findings

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

Compliance with HTA standards

Governance and Quality Systems

Standard	Inspection findings	Level of shortfall
GQ1 All aspects of the establishments work are supported by ratified documented policies and procedures as part of the overall governance process	The establishment has an agreement with the tissue supplier. The tissue supplier organises the courier and transport to the establishment and provides written confirmation that consent is in place. The agreement lacks details relevant to infectious disease testing of donors that is routinely performed, courier and shipping and return of non-conforming products.	**Minor**

Premises, Facilities and Equipment

Standard	Inspection findings	Level of shortfall
PFE3 There are appropriate facilities for the storage of bodies, body parts, tissues, cells, consumables and records.	The liquid nitrogen dewars that store the hepatocytes are not fitted with a temperature monitoring system. Although there is a procedure in place for the checking and re-filling of the liquid nitrogen dewers by the stores department, there is no system for monitoring or recording the storage temperature nor a system for checking the minimum levels. There is no evidence of a risk assessment relevant to storing hepatocytes without any monitoring of the storage conditions. **See advice and guidance number 3**	**Minor**

Advice

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

No.	Standard	Advice
1.	GQ2	The DI conducts a stock check audit every 12 months to confirm the tissue used and tissue that is still in storage. During these stock checks locations of cryovials are checked. Evidence of the stock check is added onto the human tissue tracking spreadsheet, under the 'stock check' tab. The DI is advised to consider capturing the audit information collected rather than stating that the audit has been carried out. This will provide an evidence trail of the audit findings. The DI is also advised to ensure that all SOPs are reviewed regularly and is advised to assign a review date for all SOPs.

2.	GQ7	Although there is an incident policy in place, the DI is advised to incorporate incidents relevant to loss of human tissue samples, loss of traceability and sample mix up. The tissue tracking worksheet has a tab which allows the reporting of such incidents, however there should also be a documented procedure for reviewing and reporting such incidents.
3.	GQ8	Although the establishment has health and safety as well as biological risk assessments, the DI should consider risks associated with non compliance with HTA standards. Currently the cells are stored within liquid nitrogen dewars that are not subject to maintenance and are not temperature monitored. Therefore the DI is advised to risk assess the current storage practice of cells within dewars, some of which are old and not subject to maintenance. The risk assessment will allow the DI to consider the risks of storage as well as considering mitigating steps to prevent sub-optimum storage of cells.
4.	PFE2	There is no oxygen monitoring system located in the laboratories that contain liquid nitrogen dewers. This would be advised as the laboratories may not provide the necessary ventilation,. The DI is advised to ensure that all staff that have access to or work with liquid nitrogen are working within a safe environment. The DI may wish to consider use of personal alarms or the fitting of an oxygen monitoring system.
5.	PFE5	The DI is advised to assure that the dewars are maintained and function appropriately as some of them are quite old and have not been checked or maintained by any companies. There are informal contingency arrangements for emergency storage with another establishment. The DI should consider formalising these arrangements.

Concluding comments

The DI and establishment staff have a good working relationship with strong communication. The establishment's involvement in human tissue research is still in its infancy, and the systems are currently evolving as the use of human tissue increases. The DI has appropriate oversight but would like to develop quality systems further

A number of examples of good practice were observed during the inspection. The DI ensures that all staff have read the appropriate SOPs and maintains a signature list of all of those who have read them. The DI works closely with staff working with human tissue in the laboratory and maintains oversight of licensable activities. There is appropriate staff training, which is evident through the well maintained and extensive training files for each staff member.

There are a few areas of practice that require improvement, as indicated by the two minor shortfalls in relation to standards PFE3 and GQ1. The HTA has given advice to the

Designated Individual with respect to standards, GQ2, GQ7, GQ8, PFE2 and PFE5. These items of advice relate to audit, SOPs, adverse incident reporting, risk assessments, oxygen monitoring and dewar maintenance.

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.

Report sent to DI for factual accuracy: 20 June 2013

Report returned from DI: 4 July 2013

Final report issued: 4 July 2013

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 and in doing so has taken sufficient action to correct all shortfalls addressed in the Inspection Report.

Date: 30 September 2013

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.