Site visit inspection report on compliance with HTA minimum standards

Oxford Gene Technology (Operations) Ltd

HTA licensing number 12586

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**

4 February 2015

Summary of inspection findings

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

Oxford Gene Technology (Operations) Ltd (the establishment) was found to have met all of the HTA standards. Advice has been given relating to the Governance and Quality Systems (GQS) standards.

Particular examples of 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 (DI), Licence Holder (LH), premises and practices are suitable.

The statutory duties of the DI 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 refers to the activities carried out by Oxford Gene Technology (Operations) Ltd (OGT; the establishment). The establishment's licensing arrangements cover the Southern Centre (the hub site; based at Oxford Industrial Park, Yarnton) and the Institute of Advanced Technology (the satellite site; based at Begbroke Science Park). The hub and satellite both have separate nominated Persons Designate (PD) who report to the DI.

OGT was founded in 1995. The company specialises in the detection and interpretation of chromosomal and molecular genetic abnormalities in various diseases, including abnormalities in developmental delay, cancer, heart disease, type 1 diabetes and muscular dystrophy. The company is also involved in reproductive health research - improving the chances of successful in-vitro fertilisation. OGT employs approximately 60 staff.

The establishment is licensed by the HTA under the Human Tissue Act 2004 for the storage of relevant material for use for scheduled purposes. The scheduled purposes applicable to this licence are: obtaining scientific or medical information about a living or deceased person which may be relevant to any other person (including a future person); and, research in connection with disorders, or the functioning, of the human body ('research'). This was the first site visit inspection of the establishment since it was issued an HTA licence in September 2011. It was a routine inspection, to assess whether the establishment is continuing to meet the HTA's standards.

The establishment has previously stored relevant material (whole blood samples) for research projects. At the present time, 250 normal and diseased fresh frozen imported faecal

samples, obtained from living donors, are stored for research purposes. All other human samples are not considered to be relevant material (double-spun plasma, lysed cellular preparations and isolated DNA and RNA).

Tissue sources

Samples are supplied to OGT from sources both within and outside the UK. Suppliers include commercial organisations, NHS Trusts, universities and Research Tissue Banks.

The establishment relies on suppliers to provide assurance that informed donor consent has been given for each sample and that ethical approval has been obtained (*see Advice item 3*).

Suppliers are also responsible for transport of material to the establishment.

Sample storage

Samples received into the establishment are logged into Laboratory Information Management System (LIMS) database. There is an integrity check of the samples themselves and of the temperature of the shipment packaging. Samples should be supplied with diagnostic and de-identified donor information. Non-conforming samples are quarantined separately in a -80°C freezer until the information is received.

There are several laboratories and storage facilities on both sites. At the present time, relevant material is stored in a dedicated -80°C freezer at the hub site.

All freezers and refrigerators are linked to a data-logged, continuous temperature monitoring facility which feeds into a call-out system. Excursions outside the set ranges trigger both audible alarms and the call-out system. Power failure to the storage facilities also triggers the alarms and the call-out system. The system is tested regularly.

Emergency back-up freezers are available in the event of storage failure.

Electronic management of human tissue usage within OGT

Samples are given a unique code and are logged into the LIMS database with key data and information on their location in the freezer. The database is updated as samples are used, depleted or destroyed. Only three members of staff can amend the database to ensure the integrity of the data. The database is backed up regularly on the main servers.

The inspection process

The timetable for the site visit inspection was developed after consideration of the establishment's licence application, compliance update information and discussions with the DI. The site visit inspection included a visual inspection of the storage areas and storage facilities for tissue and records.

Meetings were held with staff working under the licence. They were: the DI (Executive Vice-President, Biomarker Discovery); the PDs [(i) Quality Manager, Biological Safety Officer, HTA Co-ordinator; (ii) Research and Development Director - Cancer and Infection, Deputy Biological Safety Officer]; and, a Principal Investigator (PI; Head of Service Operations).

A documentation review and horizontal and vertical audits were carried out. Details of the two separate audits are provided below.

Four samples, selected at random from cryoboxes and sample bags in the -80°C freezer, were chosen and the location details were compared to the database; one anomaly was found. On exploration this was an incorrect date transposition and did not impact on the ability to locate the sample.

Identifiers from three samples, selected at random on the electronic database, were used to identify the samples stored in the -80°C freezer. All samples were located correctly in the recorded storage location.

Inspection findings

The HTA found the DI and the (Corporate) LH (CLH) 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.	GQ3	The DI may wish to consider including the MRC 'Research and Human Tissue Legislation e-learning Module', part of the MRC Data and Tissues Toolkit (both of which were developed with input from the HTA), as part of the staff training programme: http://www.rsclearn.mrc.ac.uk/
2.	GQ3	The DI is advised to include staff familiarity with the Quality Management system, including all standard operating procedures and generic risk assessments, as part of the staff training programme.
3.	GQ5	Other licensed establishments have set up a register of 'approved suppliers'. Each potential supplier is sent a 'due diligence form', asking for details of governance structure, ethical approval, ethical warranties, informed consent forms, consent warranties and regulatory compliance (where appropriate). A Material Transfer Agreement, using the establishment's own template, could then be drawn up with each organisation using these criteria as the supplier's responsibilities. The DI may wish to consider adopting such an approach.

Concluding comments

During the site visit inspection of the establishment several areas of good practice were noted:

- There are two lines of reporting for the Quality Manager, thus ensuring autonomy.
- The establishment has both an HTA committee (meeting every six months) and a biological safety committee (meeting every month). These committees have excellent oversight of all follow-up actions involving human tissue, e.g. audit findings and non-conformance/incident management. There is a central register of adverse events, monitored by the Quality Manager.
- The establishment has a good management system for all projects involving human tissue. They are risk assessed before submission to and authorisation by the HTA committee.
- The establishment has organised independent audits of the premises, processes, samples and records using separate external auditors.
- The review period for risk assessments varies according to the severity of the risk.

The HTA has given advice to the DI with respect to the Governance and Quality Systems standards.

The HTA has assessed the establishment as suitable to be licensed for the activities

specified.

Report sent to DI for factual accuracy: 27 February 2015

Report returned from DI: 4 March 2015

Final report issued: 31 March 2015

Appendix 1: HTA standards

The HTA standards applicable to this establishment are shown below. Individual standards which are not applicable to this establishment highlighted as grey text.

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 inspection.

   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.