



## **Site visit inspection report on compliance with HTA minimum standards**

**Oxford BioDynamics Ltd**

**HTA licensing number 12571**

**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**

**11 December 2014**

### **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 BioDynamics 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), Premises, Facilities and Equipment (PFE), and Disposal (D) 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 BioDynamics Ltd (the establishment), based in central Oxford.

Oxford BioDynamics was founded in 2007. It has developed a proprietary biomarker set of tests based on gene expression, non-coding RNA and epigenetics. The tests are sensitive enough to identify very low copy numbers of abnormally expressed genes in small samples of cells. The test is non invasive and produces results in less than four hours.

The technology has been applied to the screening, early detection, monitoring and prognosis in oncological, inflammatory, metabolic, cardiovascular and neurodegenerative conditions. The company employs approximately 20 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: research in connection with disorders, or the functioning, of the human body ('research'); and, quality assurance. The predominant scheduled purpose is research. This was the first site visit inspection of the establishment since it was issued an HTA licence in August 2010. It was a routine inspection, to assess whether the establishment is continuing to meet the HTA's standards.

The establishment stores approximately 2000 normal and diseased human tissue samples and body fluids. Specimens are obtained from living and deceased donors. Tissue samples include formalin-fixed, paraffin wax-embedded (FFPE) material (both blocks and slides),

optimal cutting temperature (OCT) compound-mounted samples for frozen sections, tissue slices, isolated cellular preparations (e.g. peripheral blood mononuclear cells) and fresh frozen tissue. Body fluids include plasma and whole blood.

#### Tissue sources: Consent and ethical approval

Relevant material is supplied to Oxford BioDynamics Ltd from sources both within and outside the UK. Suppliers of blood and tissue samples include commercial organisations, NHS Trusts, private hospitals, universities and Research Tissue Banks (RTBs). Each supplier is required to give assurance that informed donor consent has been sought and ethical approval has been obtained (see *Advice item 3*). Suppliers are responsible for transport of material to the establishment.

The establishment is not responsible for seeking consent itself.

#### Sample storage

Samples received into the establishment are logged onto a tracking 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.

FFPE material is stored in a dedicated -20°C freezer and frozen tissue and fluid samples in a dedicated -80°C freezer, which is backed up by a liquid carbon dioxide tank.

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

Emergency backup freezers are available in the event of storage failure.

#### Sample transport and distribution

The establishment occasionally distributes tissue samples back to the supplying source under a Material Transfer Agreement (MTA).

#### Electronic management of human tissue usage within Oxford BioDynamics Ltd

Samples are logged into the database with key data and information on their location in the freezers. Samples are given a unique code and, if fluid aliquots are made or tissue blocks are divided into separate slides, these are given their own separate, unique code. The database is continually updated as samples are used, depleted, destroyed or returned to suppliers. Only two 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 (Director of Science and Innovation); the (Corporate) LH Contact (CLHC; Director and Chief Scientific Officer); and, the Persons Designate (PDs: Director of Manufacturing and Quality Manager; Chief Operating Officer and Project Manager).

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

Three samples, selected at random from cryoboxes in the -80°C freezer, were chosen and the location details were compared to the database; no anomalies were found.

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	A training presentation has been created which comprehensively covers the regulatory requirements underlying consent, storage and use of human tissue. This is currently given to selected staff members. The DI is advised to extend this training to all staff involved with human tissue, including new staff at induction, to further increase regulatory awareness.
2.	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: <a href="http://www.rsclearn.mrc.ac.uk/">http://www.rsclearn.mrc.ac.uk/</a>
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 (MTA) is then drawn up with each organisation using these criteria as the supplier's responsibilities. The DI may wish to consider adopting a similar approach.
4.	PFE3	The DI is advised to ensure that all freezers which contain human tissue are labelled to indicate this, so that staff are aware of the necessity to maintain the quality, safety and security of such material.
5.	D1	The DI may wish to consider using regular disposal of batched human tissue specimens (for example, on a monthly basis) to ensure that these are disposed separately from other clinical waste.

### Concluding comments

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

- The establishment's governance meetings have a HTA standing agenda item and have excellent oversight of follow-up actions, e.g. audit findings and incident management.

- An audit against the HTA standards is performed on a six-monthly basis.
- Staff training involves shadowing experienced personnel and all staff must be fully competent in their area before working unsupervised.
- The unique sample coding system extends to individual slides made from specific blocks and individual aliquots made from primary fluid samples.
- The establishment has a strong culture of reporting concerns, near misses and internal audits. Follow-up corrective and preventative action plans are well documented and have a clear audit trail through the governance system.

The HTA has given advice to the DI with respect to the Governance and Quality Systems, Premises, Facilities and Equipment, and Disposal standards.

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

**Report sent to DI for factual accuracy: 13 January 2015**

**Report returned from DI: 14 January 2015**

**Final report issued: 16 February 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
<b>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</b>
<ul style="list-style-type: none"><li>• Consent forms comply with the HTA's Code of Practice</li><li>• Consent forms are in records and are made accessible to those using or releasing relevant material for a scheduled purpose</li><li>• 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</li><li>• 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</li><li>• Consent procedures have been ethically approved</li></ul>
<b>C2 Information about the consent process is provided and in a variety of formats</b>
<ul style="list-style-type: none"><li>• Standard operating procedures (SOPs) detail the procedure for providing information on consent</li><li>• Agreements with third parties contain appropriate information</li><li>• Independent interpreters are available when appropriate</li><li>• Information is available in suitable formats, appropriate to the situation</li><li>• Consent procedures have been ethically approved</li></ul>
<b>C3 Staff involved in seeking consent receive training and support in the implications and essential requirements of taking consent</b>
<ul style="list-style-type: none"><li>• Standard operating procedures (SOPs) detail the consent process</li><li>• Evidence of suitable training of staff involved in seeking consent</li><li>• Records demonstrate up-to-date staff training</li><li>• Competency is assessed and maintained</li></ul>
Governance and quality system standards
<b>GQ1 All aspects of the establishments work are supported by ratified documented policies and procedures as part of the overall governance process</b>
<ul style="list-style-type: none"><li>• 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</li><li>• Appropriate risk management systems are in place</li><li>• Regular governance meetings are held; for example, health and safety and risk management</li></ul>

<p>committees, agendas and minutes</p> <ul style="list-style-type: none"> <li>• Complaints system</li> </ul>
<b>GQ2 There is a documented system of quality management and audit</b>
<ul style="list-style-type: none"> <li>• A document control system, covering all documented policies and standard operating procedures (SOPs).</li> <li>• Schedule of audits</li> <li>• Change control mechanisms for the implementation of new operational procedures</li> </ul>
<b>GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills</b>
<ul style="list-style-type: none"> <li>• Qualifications of staff and training are recorded, records showing attendance at training</li> <li>• Orientation and induction programmes</li> <li>• Documented training programme, (e.g. health and safety, fire, risk management, infection control), including developmental training</li> <li>• Training and reference manuals</li> <li>• Staff appraisal / review records and personal development plans are in place</li> </ul>
<b>GQ4 There is a systematic and planned approach to the management of records</b>
<ul style="list-style-type: none"> <li>• Documented procedures for the creation, amendment, retention and destruction of records</li> <li>• Regular audit of record content to check for completeness, legibility and accuracy</li> <li>• Back-up / recovery facility in the event of loss of records</li> <li>• Systems ensure data protection, confidentiality and public disclosure (whistle-blowing)</li> </ul>
<b>GQ5 There are documented procedures for distribution of body parts, tissues or cells</b>
<ul style="list-style-type: none"> <li>• A process is in place to review the release of relevant material to other organisations</li> <li>• 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</li> </ul>
<b>GQ6 A coding and records system facilitates traceability of bodies, body parts, tissues and cells, ensuring a robust audit trail</b>
<ul style="list-style-type: none"> <li>• There is an identification system which assigns a unique code to each donation and to each of the products associated with it</li> <li>• 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</li> </ul>

**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.