

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

### **Fisher BioServices**

**HTA licensing number 11074**

#### **Licensed for the**

- **storage, distribution and import/export of human tissues and cells for human application under the Human Tissue (Quality and Safety for Human Application) Regulations 2007**
- **storage of relevant material which has come from a human body for use for a scheduled purpose other than transplantation under the Human Tissue Act 2004**

**11 February 2014**

#### **Summary of inspection findings**

Fisher BioServices (the establishment) was selected to receive a themed inspection. The themes selected for 2013/14 include quality management, contingency planning and risk management.

The establishment was found to have met all HTA standards relating to each theme.

In addition, the HTA reviewed the establishment's response to previous inspection findings including matters offered as advice and guidance. As the result of the establishment's proactive approach to the inspection process the scope of inspection extended beyond the planned themes and included review of compliance with HTA standards applicable to equipment validation, maintenance and tracking. The establishment was found to have met these HTA Standards. The inspection also provided an opportunity to discuss the establishment's plans for potential expansion within the existing site.

The HTA previously found the Designated Individual and the Licence Holder, to be suitable in accordance with the requirements of the legislation. Their continued suitability was verified during this inspection.

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.

However, a themed inspection may be carried out on establishments which have been found previously to represent a lower risk. Themes target Standards which the HTA has identified as common shortfalls across the human application sector in 2011. The themes selected for 2012/13 are outlined in the table below.

Themes	HTA Standards
<b>Quality management</b>	
Standard operating procedures for licensed activity	GQ1(b)
Document control system	GQ1(d)
Quality Management System – continuous and systematic improvement	GQ2(a)-(c)
Internal audit system for licensable activities	
<b>Contingency Planning</b>	
Plan to ensure records of traceability are maintained for 10 or 30 years as required.	GQ4(m)
<b>Risk Management</b>	
Procedures for the identification, reporting, investigation and recording of adverse events and reactions	GQ7
Risk assessments	GQ8
Traceability	GQ6

In addition to the Standards listed above, the HTA will follow-up on any other issues that have arisen since the establishment's last inspection.

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.

### Licensable activities carried out by the establishment

'E' = Establishment is licensed to carry out this activity.

'E\*' = Establishment is licensed to carry out this activity but is not currently carrying it out.

Tissue type	Procurement	Processing	Testing	Storage	Distribution	Import	Export
PBSC				E	E	E*	E*
Umbilical Cord Blood				E	E	E*	E*
Umbilical Cord Tissue				E	E	E*	E*
Other Blood Cells				E	E	E*	E*

### Background to the establishment and description of inspection activities undertaken

The establishment is licensed for the storage, distribution, import and export of human tissues and cells for human application under the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (the Regulations). The establishment is also licensed for the storage of relevant material which has come from a human body for use for a scheduled purpose, namely research, under the Human Tissue Act 2004 (HT Act). Relevant material under the HT Act and tissues and cells under the Regulations are stored at the establishment under controlled conditions in accordance with client agreements.

The establishment is licensed by the Medicines and Healthcare Products Regulatory Agency (MHRA) as it is involved with the storage, release, distribution, import and export of a range of investigational medicinal products for use in clinical trials. This may include advanced therapy medicinal products. As a further aspect of its support of clinical studies, the establishment also undertakes the assembly and distribution of sample kits in accordance with trial protocols. The establishment is also licensed by the Human Fertilisation and Embryology Authority (HFEA) as it has formal agreements with a number of HFEA-licensed establishments for the storage of human reproductive cells in the event of contingency storage requirements. The establishment is ISO accredited having had its most recent site visit assessment in February 2014.

The establishment has been licensed by the Human Tissue Authority since 2006 and this routine inspection was the fourth site visit. The timetable for the site visit was developed following consideration of previous inspection reports and pre-inspection discussion with the Designated Individual (DI). The timetable addressed the HTA standards identified under the components of the themed inspection and comprised a visual inspection of the premises, review of the establishment's documentation and discussion with members of staff conducting licensable activities.

The scope of inspection included a traceability audit which comprised review of a client specific project plan documenting the history of licensable activities, requests for return of stored tissue / cells and the tracking of these tissue / cells from original receipt through storage and subsequent distribution back to the client. The audit trail was complete and accurate. No anomalies or discrepancies were identified.

Advice is offered to the DI regarding the provision of a formal link to any deviations or non-conformances within the establishment's 'status change form' (please refer to advice item 2).

### Inspection findings

The HTA found the Designated Individual and the Licence Holder 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.	GQ1 (b)	The establishment has recently had to return a consignment of tissue / cells to a client. On selection from ultra-cold storage, the packaging was observed to be damaged. Steps were taken to safeguard the tissues / cells, whilst still providing them back to the client. In response to this event the standard operating procedure (SOP) for dealing with damage to packaging has been updated. The DI is advised to progress with the issue of the updated SOP detailing steps to be taken in the event of discovery of damaged primary and / or secondary packaging of tissues / cells in storage. In accordance with the establishment's document control and training procedures, the process of SOP revision and issue will include formal training of members of staff in the revised procedure and the reasons for revision.
2.	GQ1 (b) (h) & (i)	As part of the traceability audit it was noted that the 'status change form' which logs the issue of tissue / cells to the client does not flag the need to cross reference any deviation or non-conformance report relating to the tissue / cells. The DI is advised to update the relevant form to include a prompt to check for any reference to deviation or non-conformance.
3.	PFE5 (a)	The visual inspection of the facilities included review of the status of an empty storage vessel. Whilst a status label was applied during the course of inspection, the DI is advised to remind the facility operations team of the need to maintain status labelling of vessels at all times, in accordance with the establishment's

		procedure.
4.	Licensing	The DI is advised to utilise the HTA role of 'Person Designated' to reflect responsibilities relating to governance and quality that are undertaken by members of staff at the establishment, for example the Quality Team Leader. <i>NB immediately following the inspection, the DI confirmed the Quality Team Leader as a Person Designated under the licence.</i>

### Concluding comments

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 has been in post from the start of licensing by the HTA and demonstrates a good working knowledge and understanding of HTA requirements. The DI has a key role in relation to quality management and regulatory compliance and is the principal point of contact for activities licensed by the HTA and other regulators. The Quality Management System is well developed in that it has been designed to meet a single set of quality standards and procedures that apply to the requirements of the HTA, MHRA, HFEA and ISO.

There are a number of good systems in place. These include but are not limited to:

- use of a workplace organisation programme to measure performance and drive continuous improvement;
- use of a proprietary system for the recording of internal audit findings and the tracking and closure of actions resulting from audits;
- a well-considered incident response plan, which includes mapped out actions to be taken in the periods immediately following an incident;
- an extension to risk assessment and risk management strategy through identification of 'critical quality attributes' applicable to licensable activities and incorporation of 'failure mode effects analysis' techniques as part of the risk assessment process.

The HTA has given advice to the Designated Individual where the HTA identified opportunities for improvement to existing systems and procedures.

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

**Report sent to DI for factual accuracy: 11 March 2014**

**Report returned from DI: No comments from the DI on factual accuracy**

**Final report issued: 11 April 2014**

## 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.

### Human Tissue (Quality and Safety for Human Application) Regulations 2007 Standards

#### Consent

Standard
C1 Consent is obtained in accordance with the requirements of the HT Act 2004, the Human Tissue (Quality and Safety for Human Application) Regulations 2007 and as set out in the HTA's Codes of Practice.
a) Standard not applicable.
b) Standard not applicable.
c) Standard not applicable.
d) Standard not applicable.
e) Standard not applicable.
C2 Information about the consent process is provided and in a variety of formats.
a) Standard not applicable.
b) Standard not applicable.
c) Standard not applicable.
d) Standard not applicable.
C3 Staff involved in seeking consent receive training and support in the implications and essential requirements of taking consent.
a) Standard not applicable.
b) Standard not applicable.

#### Governance and Quality

Standard
GQ1 All aspects of the establishment's work are supported by ratified documented policies and procedures as part of the overall governance process.
a) There is an organisational chart clearly defining the lines of accountability and reporting relationships.
b) There are procedures for all licensable activities that ensure integrity of tissue and / or cells and minimise the risk of contamination.

c) There are regular governance meetings, for example health and safety, risk management and clinical governance committees, which are recorded by agendas and minutes.
d) There is a document control system to ensure that changes to documents are reviewed, approved, dated and documented by an authorised person and only current documents are in use.
e) Standard not applicable..
f) Standard not applicable.
g) There are procedures to ensure that an authorised person verifies that tissues and / or cells received by the establishment meet required specifications.
h) There are procedures for the management and quarantine of non-conforming consignments or those with incomplete test results, to ensure no risk of cross contamination.
i) There are procedures to ensure tissues and / or cells are not released from quarantine until verification has been completed and recorded.
j) There are procedures detailing the critical materials and reagents used and where applicable, materials and reagents meet the standards laid down by the European directives on medical devices and in vitro diagnostic medical devices.
k) There is a procedure for handling returned products.
l) There are procedures to ensure that in the event of termination of activities for whatever reason, stored tissues and / or cells are transferred to another licensed establishment or establishments.
m) Standard not applicable.
n) The establishment ensures imports from non EEA states meet the standards of quality and safety set out in Directions 003/2010.
o) There is a complaints system in place.
p) There are written agreements with third parties whenever an activity takes place that has the potential to influence the quality and safety of human tissues and / or cells.
q) There is a record of agreements established with third parties.
r) Third party agreements specify the responsibilities of the third party and meet the requirements set out in Directions 003/2010.
s) Third party agreements specify that the third party will inform the establishment in the event of a serious adverse reaction or event.
t) There are procedures for the re-provision of service in an emergency.
<b>GQ2 There is a documented system of quality management and audit.</b>
a) There is a quality management system which ensures continuous and systematic improvement.
b) There is an internal audit system for all licensable activities.
c) An audit is conducted in an independent manner at least every two years to verify compliance with protocols and HTA standards, and any findings and corrective actions are documented.

d) Processes affecting the quality and safety of tissues and / or cells are validated and undergo regular evaluation to ensure they continue to achieve the intended results.
<b>GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills.</b>
a) There are clearly documented job descriptions for all staff.
b) There are orientation and induction programmes for new staff.
c) There are continuous professional development (CPD) plans for staff and attendance at training is recorded.
d) There is annual documented mandatory training (e.g. health and safety and fire).
e) Personnel are trained in all tasks relevant to their work and their competence is recorded.
f) There is a documented training programme that ensures that staff have adequate knowledge of the scientific and ethical principles relevant to their work, and the regulatory context.
g) There is a documented training programme that ensures that staff understand the organisational structure and the quality systems used within the establishment.
h) There is a system of staff appraisal.
i) Where appropriate, staff are registered with a professional or statutory body.
j) There are training and reference manuals available.
k) The establishment is sufficiently staffed to carry out its activities.
<b>GQ4 There is a systematic and planned approach to the management of records.</b>
a) There are procedures for the creation, identification, maintenance, access, amendment, retention and destruction of records.
b) There is a system for the regular audit of records and their content to check for completeness, legibility and accuracy and to resolve any discrepancies found.
c) Written records are legible and indelible. Records kept in other formats such as computerised records are stored on a validated system.
<b>d) There is a system for back-up / recovery in the event of loss of computerised records.</b>
e) The establishment keeps a register of the types and quantities of tissues and / or cells that are procured, tested, preserved, processed, stored and distributed or otherwise disposed of, and on the origin and destination of tissues and cells intended for human application.
f) Standard not applicable.
g) There is a system to ensure records are secure and that donor confidentiality is maintained in accordance with Directions 003/2010.
h) Raw data which are critical to the safety and quality of tissues and cells are kept for 10 years after the use, expiry date or disposal of tissues and / or cells.
i) The minimum data to ensure traceability from donor to recipient as required by Directions 003/2010

are kept for 30 years after the use, expiry or disposal of tissues and / or cells.
j) Standard not applicable..
k) There are documented agreements with end users to ensure they record and store the data required by Directions 003/2010.
l) The establishment records the acceptance or rejection of tissue and / or cells that it receives and in the case of rejection why this rejection occurred.
m) In the event of termination of activities of the establishment a contingency plan to ensure records of traceability are maintained for 10 or 30 years as required.
<b>GQ5 There are documented procedures for donor selection and exclusion, including donor criteria.</b>
a) Standard not applicable.
b) Standard not applicable.
c) Standard not applicable.
d) Standard not applicable.
e) Standard not applicable.
f) Standard not applicable.
<b>GQ6 A coding and records system facilitates traceability of tissues and / or cells, ensuring a robust audit trail.</b>
a) There is a donor identification system which assigns a unique code to each donation and to each of the products associated with it.
b) An audit trail is maintained, which includes details of when the tissues and / or cells were acquired and from where, the uses to which the tissues and / or cells were put, when the tissues and / or cells were transferred elsewhere and to whom.
c) The establishment has procedures to ensure that tissues and / or cells imported, procured, processed, stored, distributed and exported are traceable from donor to recipient and vice versa.
<b>GQ7 There are systems to ensure that all adverse events, reactions and/or incidents are investigated promptly.</b>
a) There are procedures for the identification, reporting, investigation and recording of adverse events and reactions, including documentation of any corrective or preventative actions.
b) There is a system to receive and distribute national and local information (e.g. HTA regulatory alerts) and notify the HTA and other establishments as necessary of serious adverse events or reactions.
c) The responsibilities of personnel investigating adverse events and reactions are clearly defined.
d) There are procedures to identify and decide the fate of tissues and / or cells affected by an adverse event, reaction or deviation from the required quality and safety standards.
e) In the event of a recall, there are personnel authorised within the establishment to assess the need for a recall and if appropriate initiate and coordinate a recall.

f) There is an effective, documented recall procedure which includes a description of responsibilities and actions to be taken in the event of a recall including notification of the HTA and pre-defined times in which actions must be taken.
g) Establishments distributing tissue and / or cells provide information to end users on how to report a serious adverse event or reaction and have agreements with them specifying that they will report these events or reactions.
h) Establishments distributing tissues and / or cells have systems to receive notifications of serious adverse events and reactions from end users and notify the HTA.
GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately.
a) There are documented risk assessments for all practices and processes.
b) Risk assessments are reviewed regularly, as a minimum annually or when any changes are made that may affect the quality and safety of tissues and cells.
c) Staff can access risk assessments and are made aware of local hazards at training.
d) Standard not applicable.

#### **Premises, Facilities and Equipment**

<b>Standard</b>
PFE1 The premises are fit for purpose.
a) A risk assessment has been carried out of the premises to ensure that they are fit for purpose.
b) There are procedures to review and maintain the safety of staff, visitors and patients.
c) The premises have sufficient space for procedures to be carried out safely and efficiently.
d) Standard not applicable.
e) There are procedures to ensure that the premises are secure and confidentiality is maintained.
f) There is access to a nominated, registered medical practitioner and / or a scientific advisor to provide advice and oversee the establishment's medical and scientific activities.
PFE2 Environmental controls are in place to avoid potential contamination.
a) Tissues and / or cells stored in quarantine are stored separately from tissue and / or cells that have been released from quarantine.
b) Standard not applicable.
c) There are procedures for cleaning and decontamination.
d) Staff are provided with appropriate protective clothing and equipment that minimise the risk of contamination of tissue and / or cells and the risk of infection to themselves.

<b>PFE3 There are appropriate facilities for the storage of tissues and / or cells, consumables and records.</b>
a) Tissues, cells, consumables and records are stored in secure environments and precautions are taken to minimise risk of damage, theft or contamination.
b) There are systems to deal with emergencies on a 24 hour basis.
c) Tissues and / or cells are stored in controlled, monitored and recorded conditions that maintain tissue and / or cell integrity.
d) There is a documented, specified maximum storage period for tissues and / or cells.
<b>PFE4 Systems are in place to protect the quality and integrity of tissues and / or cells during transport and delivery to its destination.</b>
a) There is a system to ensure tissue and / or cells are not distributed until they meet the standards laid down by Directions 003/2010.
b) There are procedures for the transport of tissues and / or cells which reflect identified risks associated with transport.
c) There is a system to ensure that traceability of tissues and / or cells is maintained during transport.
d) Records are kept of transportation and delivery.
e) Tissues and / or cells are packaged and transported in a manner and under conditions that minimise the risk of contamination and ensure their safety and quality.
f) There are third party agreements with courier or transport companies to ensure that any specific transport conditions required are maintained.
g) Critical transport conditions required to maintain the properties of tissue and / or cells are defined and documented.
h) Packaging and containers used for transportation are validated to ensure they are fit for purpose.
i) Primary packaging containing tissues and / or cells is labelled with the information required by Directions.
j) Shipping packaging containing tissues and / or cells is labelled with the information required by Directions.
<b>PFE5 Equipment is appropriate for use, maintained, quality assured, validated and where appropriate monitored.</b>
a) Critical equipment and technical devices are identified, validated, regularly inspected and records are maintained.
b) Critical equipment is maintained and serviced in accordance with the manufacturer's instructions.
c) Equipment affecting critical processes and storage parameters is identified and monitored to detect malfunctions and defects and procedures are in place to take any corrective actions.
d) New and repaired equipment is validated before use and this is documented.
e) There are documented agreements with maintenance companies.

f) Cleaning, disinfection and sanitation of critical equipment is performed regularly and this is recorded.
g) Standard not applicable.
h) Users have access to instructions for equipment and receive training in the use of equipment and maintenance where appropriate.
i) Staff are aware of how to report an equipment problem.
j) For each critical process, the materials, equipment and personnel are identified and documented.
k) There are contingency plans for equipment failure.

**Disposal**

<b>Standard</b>
<b>D1 There is a clear and sensitive policy for disposing of tissues and / or cells.</b>
a) The disposal policy complies with HTA's Codes of Practice.
b) The disposal procedure complies with Health and Safety recommendations.
c) There is a documented procedure on disposal which ensures that there is no cross contamination.
<b>D2 The reasons for disposal and the methods used are carefully documented.</b>
a) There is a procedure for tracking the disposal of tissue and / or cells that details the method and reason for disposal.
b) Disposal arrangements reflect (where applicable) the consent given for disposal.

## Appendix 2: Classification of the level of shortfall (HA)

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 direct risk of causing harm to a recipient patient or to a living donor,

*Or*

A number of 'major' shortfalls, none of which is critical on its own, but viewed cumulatively represent a systemic failure and therefore are considered 'critical'.

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.

A shortfall in the carrying out of licensable activities which poses an indirect risk to the safety of a donor or a recipient

*or*

A shortfall in the establishment's quality and safety procedures which poses an indirect risk to the safety of a donor or a recipient;

*or*

A shortfall which indicates a major deviation from the **Human Tissue (Quality and Safety for Human Application) Regulations 2007** or the **HTA Directions**;

*or*

A shortfall which indicates a failure to carry out satisfactory procedures for the release of tissues and cells or a failure on the part of the designated individual to fulfil his or her legal duties;

*or*

A combination of several 'minor' shortfalls, none of which is major on its own, but which, viewed cumulatively, could constitute a major shortfall by adversely affecting the quality and safety of the tissues and cells.

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 and, which can be addressed by further development by the establishment.

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 review or at the time of the next 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.