Site visit inspection report on compliance with HTA minimum standards

Biovault Scientific Ltd

HTA licensing number 11063

Licensed for the

- **procurement, processing, testing, 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; and**

- **storage of relevant material which has come from a human body for use for a scheduled purpose**

23-24 April 2014

Summary of inspection findings

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

Although the HTA found that Biovault Scientific Ltd (the establishment) had met the majority of the HTA standards, four shortfalls were found in relation to Governance and Quality Systems, and Premises, Facilities and Equipment. These relate to the validation of procedures used for the processing of umbilical cord tissue; the approach taken by the establishment to independent audits and the carrying out of non-viable particulate monitoring during tissue processing; and the steps taken to ensure that imported tissues meet standards of quality and safety equivalent to those outlined in Directions 003/2010.

Prior to completion of the inspection, the DI provided evidence that provisional arrangements had been made with another HTA-licensed establishment for reciprocal audits to be completed against HTA standards on a bi-annual basis. The HTA considers the shortfall against standard GQ2c to have been met.

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.

Licensable activities carried out by the establishment

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

'TPA' = Third party agreement; the establishment is licensed for this activity but another establishment (unlicensed) carries out the activity on their behalf.

Tissue type	Procurement	Processing	Testing	Storage	Distribution	Import	Export
Bone				**E**	**E**	**E**	
Tendons				**E**	**E**	**E**	
Cartilage				**E**	**E**	**E**	
Demineralised bone matrix				**E**	**E**		
Acellular bone chips				**E**	**E**		
PBSCs		**E**		**E**	**E**		
Bone marrow		**E**		**E**	**E**	**E**	

DLIs		**E**		**E**	**E**		
Umbilical cord blood	**TPA**	**E**	**TPA**	**E**	**E**	**E**	**E**
Umbilical cord tissue	**TPA**	**E**	**TPA**	**E**	**E**	**E**	**E**

Background to the establishment and description of inspection activities undertaken

This report refers to the activities carried out by Biovault Scientific Ltd. The establishment, which is based on the Plymouth International Medical & Technology Park, is licensed for the procurement, processing, testing, storage, distribution and import/export of human tissues and cells under the Human Tissue (Quality and Safety for Human Application) Regulations 2007. It is also licensed for the storage of relevant material which has come from a human body for use for a scheduled purpose under the Human Tissue Act 2004.

Biovault Scientific Ltd offers a range of tissue banking services and facilities to both the public and private sectors. Tissues and cells, such as umbilical cord blood and tissue, are procured by third parties under the terms of appropriate agreements using kits supplied by the establishment. Other relevant material, such as PBSCs, BM and DLIs, are procured by other HTA-licensed establishments under the terms of service level agreements and sent to Biovault for processing. Processing of tissues and cells takes place within a dedicated cleanroom facility comprising of two Grade B cleanrooms, each containing microbiological safety cabinets capable of providing a Grade A environment. The facility includes primary and secondary change rooms and dedicated support and analytical rooms. All critical, open processing takes place within the microbiological safety cabinets during which environmental monitoring in the form of settle plates and finger dab plates is performed. Non-viable particulate monitoring is performed on a proportion of samples received into the facility (see below). Plates and samples for microbiological testing are incubated and analysed in-house, or are sent away for analysis as appropriate. In the case of volume-reduced umbilical cord blood, samples are additionally processed in a closed cell separation system. Blood samples taken for donor serology testing are sent to one of two CPA-accredited laboratories in the UK for analysis under the terms of appropriate third party agreements.

Although the majority of tissues and cells are processed by the establishment's core staff, PBSCs, BM and DLIs procured at the neighbouring Derriford Hospital are processed by Biomedical Scientists from that organisation under the terms of appropriate agreements. Staff from Derriford Hospital who process tissues and cells in Biovault's cleanroom facility do so according to well-defined procedures and only after completion of appropriate training. Honorary contracts are also given to Derriford staff to help ensure there is appropriate oversight of this work.

For all tissues and cells requiring ultra-low temperature storage, samples meeting the establishment's acceptance criteria are held for long term, vapour-phase storage in dedicated liquid nitrogen tanks situated on site. The storage facility includes provision for separate storage of samples requiring long-term quarantine storage.

The establishment also imports and stores tendons and bone products for distribution to end users. At the time of the inspection, the majority of these samples were imported from tissue banks in the USA, each of which is registered with the US Food and Drug Administration (FDA) for the processing, packaging, storage, labelling and distribution of Human Cells, Tissues, and Cellular and Tissue-based Products (HCT/P's).

The establishment has been licensed by the HTA since March 2014 under its current name. Prior to this, the establishment was licensed under the name 'Biovault Ltd' and, as such, had been licensed by the HTA since July 2006. The establishment's current licence encompasses the activities carried out by Biovault Technical Ltd and UK Processing and Storage Services, both of which are wholly-owned subsidiaries of Biovault Scientific Ltd. This report describes the establishment's fourth routine site visit inspection which took place on 23-24 April 2014. The inspection included interviews with key members of staff working under the licence, including the Business Development and Processing Facility Director, who is also the Designated Individual, the Quality Co-ordinator, the Process Manager and Work Place Trainer, and a Laboratory Technician. A review of documentation relevant to the establishment's activities and a visual inspection of the premises where licensable activities are carried out were also conducted as part of the inspection.

An audit of two samples held in storage was performed. Storage locations were cross-checked with appropriate records to ensure that traceability was maintained. No discrepancies were found. The records associated with a further 12 samples, representative of the range of relevant material procured, processed and stored by the establishment, were also reviewed.

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

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

Governance and Quality

Standard	Inspection findings	Level of shortfall
GQ1 All aspects of the establishment's work are supported by ratified documented policies and procedures as part of the overall governance process.		
n) The establishment ensures imports from non-EEA states meet the standards of quality and safety set out in Directions 003/2010.	Although the establishment has Service Level Agreements (SLAs) in place with each of its overseas tissue suppliers, these do not contain adequate provision for ensuring that imported material will meet the quality and safety standards set out in Directions 003/2010. Further measures that would help ensure this, such as the carrying out of appropriate audits, although planned, have yet to be completed.	**Minor**
GQ2 There is a documented system of quality management and audit.		
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.	Although the establishment has set out and implemented a clearly defined schedule of audits in relation to their licensable activities, independent audits conducted since the last inspection have focused on assessing compliance with the terms of SLAs rather than assessing compliance with the establishment's own protocols and HTA standards. **Prior to completion of the inspection, the DI provided evidence that provisional arrangements had been made with another HTA-licensed establishment for reciprocal audits to be completed against HTA standards on a bi-annual basis. The HTA considers this shortfall to have been met.**	**Minor**

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.	Although Biovault has well-defined procedures for the processing of umbilical cord tissue (UCT) that have been derived from published methodologies, the validation work that has been completed by the establishment to date is not sufficient to demonstrate that the procedures being followed do not render the samples clinically ineffective or unsafe. As the UCT is being stored under the authority of the establishment's human application licence, Biovault Scientific Ltd must be able to demonstrate that the processing methodologies being employed satisfy this requirement, as set out in paragraph 128 of the HTA's Guide to Quality and Safety Assurance for Human Tissues and Cells for Patient Treatment which forms the Annex to Directions 003/2010.	**Major**

Premises, Facilities and Equipment

Standard	Inspection findings	Level of shortfall
PFE2 Environmental controls are in place to avoid potential contamination.		
b) Where processing of tissues and / or cells involves exposure to the environment, it occurs in an appropriate, monitored environment as required by Directions 003/2010.	Although the establishment carries out regular non-viable particle monitoring during the processing of tissues and cells, at the time of the inspection this form of environmental monitoring was not being performed throughout critical processing for all samples.	**Minor**

Advice

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

No.	Standard	Advice
1.	C1a	The DI is advised to update the establishment's standard operating procedure (SOP) on the taking of consent to include the information contained within the organisation's 'Collection, Processing and Storage Reference Guide' which sets out the information that should be provided to all potential clients. The DI is also advised to consider whether other control measures, such as the use of a prescribed script or a consent checklist, could be implemented to help ensure that information crucial to the obtaining of informed consent is always provided.

2.	C1a	Although consent forms set out the limitations of the UCT banking service being offered, the information contained on the establishment's website implies that stems cells will be stored as part of the UCT service. However, these claims are not substantiated by the establishment's current validation work. The DI is therefore advised to review the information contained in the establishment's wider promotional material to ensure that it is consistent with the service being offered.
3.	GQ1p	The DI is advised to review the wording of agreements with third parties to ensure that company names are accurate and that abbreviations are clearly defined. The DI is also advised to ensure that references to HTA Directions within such documents are up to date.
4.	GQ4k and GQ7g	The DI is advised to update the wording of end user agreements to include specific reference to "serious adverse events and reactions" rather than "unscheduled events" as is currently the case. The DI is also advised to include clear guidance on the retention of records relating to traceability within such documents to help ensure compliance with Directions 003/2010.
5.	GQ4m	The DI is advised to review the group's contingency plans to ensure that there is adequate provision for the transfer of records to other HTA-licensed premises in the event that the establishment should terminate its licensed activities.
6.	GQ5b	The DI is advised to review and update the establishment's procedures and its agreements with third parties to ensure that they accurately reflect the donor testing requirements set out in Directions 003/2010. In particular, the DI should ensure that samples taken for donor serology testing are collected within the mandatory window for the tissue type in question and that this is reflected in relevant documentation. Although the establishment has recently updated a number of agreements in this regard, a small number of documents still include reference to inaccurate donor testing requirements.
7.	GQ8a	The establishment has a wide range of well-documented risk assessments covering activities such as the distribution, receipt, processing, and storage of human tissue. However, the DI is advised to expand the scope of these documents to include the taking of consent and the import of relevant material to ensure that all licensable activities have been appropriately risk assessed.
8.	PFE5a	The DI is advised to update the establishment's cleanroom pressure differential log sheets to include relevant action limits for the various areas within the facility.
9.	PFE5c	The DI is advised to adjust the lower limit for the temperature monitoring alarm in the room used to store demineralised bone products so that it is consistent with the storage parameters for such products. Signage in this room should be adjusted accordingly.

Concluding comments

The HTA saw numerous examples of good practice during the course of the inspection.

Although Biovault Scientific Ltd should update its contingency plans to ensure that records are transferred to another HTA-licensed premises in the event of closure, the plans on the whole are well-thought out and include financial provision for the movement and continued storage of samples should the need arise. The establishment's approach to risk assessment is similarly robust, and typifies a commitment on the part of the establishment to the

development and implementation of robust governance and quality systems to support the work taking place under the authority of their licence. The establishment has also sought and received accreditation from a number of external bodies, such as Joint Accreditation Committee-ISCT (Europe) & EBMT (JACIE), and also holds ISO 9001 and ISO 13485 accreditation for its quality management systems. The establishment also participates in the UK National External Quality Assessment Service (NEQAS) scheme to help ensure that the results of laboratory tests carried out in-house continue to be reliable.

The processing and storage facilities themselves are well maintained and are continually being developed to support working practices. Several changes were noted since the last inspection, including modifications to the monitoring and alarm system that's linked to the storage equipment which should help further safeguard the establishment's samples.

Four areas of practice were identified during the inspection that require improvement, resulting in one major and three minor shortfalls. These relate to the validation work completed by the establishment in relation to the processing of umbilical cord tissue, the establishment's current approach to non-viable particulate monitoring, and to the need for independent audits to be completed every two years aimed at assessing compliance against HTA standards. The latter was addressed during the course of the inspection. Robust systems should also be in place to ensure that imported tissues meet equivalent standards of quality and safety to those set out in Directions.

The HTA has given advice to the Designated Individual with respect to a number of the establishment's procedures, documents and working practices with a view to helping the organisation further develop its working practices. Prior to finalisation of the inspection report, the DI provided a range of evidence to demonstrate that action had been taken in response to the majority of advice items noted above.

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.

The HTA has assessed the establishment as suitable to be licensed for the activities specified subject to corrective and preventative actions being implemented to meet the shortfalls identified during the inspection.

Report sent to DI for factual accuracy: 23 May 2014

Report returned from DI: 30 May 2014

Final report issued: 16 June 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) If the establishment acts as a procurer of tissues and / or cells, there is an established process for acquiring donor consent which meets the requirements of the HT Act 2004 the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (Q&S Regulations) and the HTA's Codes of Practice
b) If there is a third party procuring tissues and / or cells on behalf of the establishment the third party agreement ensures that consent is obtained in accordance with the requirements of the HT Act 2004, the Q&S Regulations and the HTA's Codes of Practice.
c) The establishment or the third party's procedure on obtaining donor consent includes how potential donors are identified and who is able to take consent.
d) Consent forms comply with the HTA Codes of Practice.
e) Completed consent forms are included in records and are made accessible to those using or releasing tissue and / or cells for a Scheduled Purpose.
C2 Information about the consent process is provided and in a variety of formats.
a) The procedure on obtaining consent details what information will be provided to donors. As a minimum, the information specified by Directions 003/2010 is included.
b) If third parties act as procurers of tissues and / or cells, the third party agreement details what information will be provided to donors. As a minimum, the information specified by Directions 003/2010 is included.
c) Information is available in suitable formats and there is access to independent interpreters when required.
d) There are procedures to ensure that information is provided to the donor or donor's family by trained personnel.
C3 Staff involved in seeking consent receive training and support in the implications and essential requirements of taking consent.
a) Staff involved in obtaining consent are provided with training on how to take informed consent in accordance with the requirements of the HT Act 2004 and Code of Practice on Consent.
b) Training records are kept demonstrating attendance at training on consent.

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) There are procedures for tissue and / or cell procurement, which ensure the safety of living donors.
f) There are procedures for tissue and / or cell procurement, which ensure the dignity of deceased donors.
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) The criteria for allocating tissues and / or cells to patients and health care institutions are documented and made available to these parties on request.
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.
GQ2 There is a documented system of quality management and audit.
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.
GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills.
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.
GQ4 There is a systematic and planned approach to the management of records.
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.
d) There is a system for back-up / recovery in the event of loss of computerised records.

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) There are procedures to ensure that donor documentation, as specified by Directions 003/2010, is collected and maintained.
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) Records are kept of products and material coming into contact with the tissues and / or cells.
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.
GQ5 There are documented procedures for donor selection and exclusion, including donor criteria.
a) Donors are selected either by the establishment or the third party acting on its behalf in accordance with the criteria required by Directions 003/2010.
b) The testing of donors by the establishment or a third party on behalf of the establishment is carried out in accordance with the requirements of Directions 003/2010.
c) In cases other than autologous donors, donor selection is carried out by authorised personnel and signed and reviewed by a qualified health professional.
d) There is a system in place either at the establishment or at a third party acting on its behalf to record results of donor selection and associated tests.
e) Testing of donor samples is carried out using CE marked diagnostic tests.
f) Samples taken for donor testing are clearly labelled with the time and place the sample was taken and a unique donor identification code.
GQ6 A coding and records system facilitates traceability of tissues and / or cells, ensuring a robust audit trail.
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.
GQ7 There are systems to ensure that all adverse events, reactions and/or incidents are investigated promptly.
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) A documented risk assessment is carried out to decide the fate of any tissue and / or cells stored prior to the introduction of a new donor selection criteria or a new processing step, which enhances the quality and safety of tissue and / or cells.

Premises, Facilities and Equipment

Standard
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) Where appropriate, there are procedures to ensure that the premises are of a standard that ensures the dignity of deceased persons.
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) Where processing of tissues and / or cells involves exposure to the environment, it occurs in an appropriate, monitored environment as required by Directions 003/2010.
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.
PFE3 There are appropriate facilities for the storage of tissues and / or cells, consumables and records.
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.
PFE4 Systems are in place to protect the quality and integrity of tissues and / or cells during transport and delivery to its destination.
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.
PFE5 Equipment is appropriate for use, maintained, quality assured, validated and where appropriate monitored.
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) Instruments and devices used for procurement are sterile, validated and regularly maintained.
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

Standard
D1 There is a clear and sensitive policy for disposing of tissues and / or cells.
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.
D2 The reasons for disposal and the methods used are carefully documented.
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.

Human Tissue Act 2004 Standards

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 (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 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 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 breach in the relevant Codes of Practices, the HT Act and other relevant professional and statutory guidelines;

or

A shortfall which indicates a failure to carry out satisfactory procedures 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.

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.