Site visit inspection report on compliance with HTA minimum standards

Royal Orthopaedic Hospital

HTA licensing number 12379

Licensed for the

- **procurement, storage and distribution 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**

13-14 July 2016

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 The Royal Orthopaedic Hospital (the establishment) had met the majority of the HTA standards, seven shortfalls under the Human Tissue (Quality and Safety for Human Application) Regulations 2007 were found. These were in relation to the absence of HTLV-1 testing as well as the limited scope of risk assessments and internal and independent audits, the lack of documented procedures for the transportation of tissue to other premises and a formal procedure which covers the establishment's response to reports of serious adverse events and reactions (SAEARs) by end users. A further three shortfalls were found in relation to compliance under the Human Tissue (HT) Act, 2004. These relate to absent or out-of-date standard operating procedures (SOPs), the limited scope of the risk assessments and the lack of freezer maintenance.

Particular examples of 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.

Tissue type	Procurement	Processing	Testing	Storage	Distribution	Import	Export
Bone			**E**	**E**	**E**		
Tendons and cartilage				**E**			
Cartilage/ chondral tissue	**E**						

Background to the establishment and description of inspection activities undertaken

The Royal Orthopaedic Hospital, based in Birmingham has been providing orthopaedic services since the late 1880s. The establishment is licensed under the Human Tissue (Quality and Safety for Human Application) Regulations 2007 for the storage and distribution of femoral heads, cartilage and tendons and for the procurement of cartilage tissue for patient treatment. The establishment has been licensed since 2008. The establishment has a satellite licence at the Department of Musculoskeletal Pathology based at the University of Birmingham. This satellite site is licensed by the HTA under the Human Tissue Act 2004 (HT Act) for the storage of relevant material which has come from a human body for use for a scheduled purpose. There was a recent change in DI. The current DI is the Divisional General Manager of services including Theatres and Pathology.

The establishment purchases femoral heads from another HTA-licensed establishment. On receipt of the tissue at the hub site, checks are made on the integrity of the outer and inner packaging and to ensure that the product is received in a frozen state. For each femoral head, the unique International Standard for Blood and Transplant 128 “G number” applied to the product by the supplier, date and time of receipt and details of first and second checker are entered into the bone register against a unique in-house number created by the establishment. The tissue is stored in a -80°C freezer. The temperature of the freezer is displayed digitally and is recorded manually by establishment staff from Monday to Saturday. In the event of a temperature deviation both in or out of hours, an alarm is received by the porters who will then notify the DI. There is a power back-up for the freezer and the digital display has a battery back-up. In addition, a -40°C freezer located next to the -80°C serves as a back-up freezer. Advice will be sought from the allograft supplier regarding the shelf-life of any tissue which has been transferred to the back-up freezer. The establishment aims to maintain a stock level of five femoral heads.

The establishment also purchases other allografts such as tendons and menisci from two other licensed establishments. The procedure for receipt and registering these products is the same as that described for femoral heads. All entries for these tissues are highlighted in yellow to distinguish them from entries for the femoral heads. The tissues are stored on a separate shelf in the -80°C freezer.

Allografts are only requested when the patient is on the operating table and the surgeon is certain that tissue is required. In such cases the date and time of removal of the allograft from the freezer, details of the recipient, the name of the surgeon, the theatre and the signature of the person issuing the allograft are entered into the bone register.

The establishment also stores demineralised bone products purchased from another HTA-licensed establishment. As storage of acellular products for end use is not currently licensed, the systems used for the storage of the demineralised bone products were not assessed as part of this inspection.

The establishment occasionally distributes bone products to a private hospital and to other nearby hospitals. The day before an elective procedure, staff at these other hospitals contact the bone bank staff to request an allograft. The recipient’s name, date of birth and the name of the surgeon requiring the allograft is entered into the bone register. The next day the tissue is placed along with cool packs in an insulated container and transported by the courier. The allograft will be disposed of if it is not used by the receiving hospital.

In 2016, the establishment procured cartilage from two patients; the cartilage biopsy was used as a starting material for an advanced therapy medicinal product (ATMP). The expanded chondrocytes were returned to the establishment and implanted into the donor to treat damaged knee cartilage, a procedure known as autologous chondrocyte implantation (ACI). The establishment has a service level agreement with an ATMP manufacturer licensed by the Belgian Federal Agency for Medicines and Health Products.

The donor is initially consented during the pre-operation assessment and re-consented on the day of the procedure. Two consent forms are used; one supplied by the Trust and the second by the ATMP manufacturer. On the day of procurement, the ATMP manufacturer’s representative arrives from Belgium and delivers a procurement kit; named individuals within the establishment are allowed to take receipt of the kit. Each kit is marked with a unique number which is also used to label the material and relevant records from procurement to end use. The cartilage biopsy is placed in transport medium and packaged with a blood sample and handed back to the representative who is responsible for transporting it back to Belgium for donor testing for HIV 1 and 2, Hepatitis B and C and syphilis and manufacturing of the ATMP.

The establishment has on occasion procured bone from patients suffering from cancer. The bone is packaged in a Perspex container, sealed and sent to another hospital for immediate irradiation before re-implantation. The last procurement of a humerus occurred in 2014. The establishment has indicated that they wish to continue this activity even though it occurs on an infrequent basis.

The satellite site at the Department of Musculoskeletal Pathology stores relevant material within a Research Tissue Bank which has received approval by a recognised National Research Ethics Service (NRES) committee. The establishment distributes samples to other research institutions under material transfer agreements. The release of tissue for research purposes is dependent on approval by the Tissue Bank's Research Governance Committee. All tissue sent to the department for diagnostic purposes is allocated a unique number within an electronic database. Consent forms are checked to determine whether the patient has consented for their sample to be used in research. The samples are processed appropriately; are placed in colour-coded cassettes and aliquots of frozen tissue, blood, urine and other relevant material are stored at -80°C in colour-coded vials. Cassettes and vials are colour-coded to distinguish between samples from oncology or orthopaedic patients and to provide a visual prompt for staff to identify samples which have consent for research and samples which are being stored in a diagnostic archive. If more than one portion is stored at -80°C, then the number of sub-samples created is also recorded on the database.
The samples are stored in two freezers one of which is full. There is one additional freezer, containing extracted nucleic acid samples, which has been designated as a back-up freezer. The temperature of the freezer is monitored and recorded during the working week. The freezers are alarmed to a mobile phone to notify the DI both in and out of hours in the event of a deviation from the required storage temperature. The DI will in turn contact the staff.

This was the fifth inspection of the site. The visual inspection covered areas where the licensable activity of storage takes place. Reviews of documentation were undertaken and interviews were held with key members of staff.

As part of the inspection process, a traceability audit was carried out. For the hub, the details of a femoral head and tendon entered into the bone register were verified against the tissue stored in the freezer, two patient notes were reviewed and cross-checked against the bone register, notes relating to the irradiation of a humerus contained within the patient's notes were also reviewed. Details of two cartilage procurements were reviewed. There were a few minor discrepancies in the bone register These mainly related to the absence of a record of the time the allograft was removed from the freezer; however, full traceability was maintained.

At the satellite, three specimens were selected from the electronic database and cross-checked against their locations in the freezer. Two further samples were selected from the freezer and their details verified against the database records. Signed consent forms from all of the patients who had donated these tissue samples were also reviewed. No discrepancies were identified but advice and guidance is given with respect to sample location records and ensuring consistency in completing consent forms.

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.		
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.	A number of the SOPs were out-of-date or required updating in order to reflect the recent change in DI and changes to practices.	**Minor**
s) Third party agreements specify that the third party will inform the establishment in the event of a serious adverse reaction or event.	The third party agreement with the private hospital does not specify that any SAEARs should be reported to the establishment within 24 hours of discovery.	**Minor**
GQ2 There is a documented system of quality management and audit.		
b) There is an internal audit system for all licensable activities.	The establishment carries out two internal audits annually. The audit records reviewed referred to samples outside the audit timeframe. For example, the audit conducted for the period July to December 2014 audited femoral heads that were used in 2015. The follow up actions to address non-conformances identified during the audits were not documented. In addition, the name of the person who conducted the audit was not documented. The ACI activity is not included within the system of internal audits.	**Minor**
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 an independent audit was carried out this did not extend to the ACI activities.	**Minor**

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.	Under Annex II of Directive 2006/17/EC, HTLV-1 antibody testing must be performed for donors living in, or originating from, high prevalence areas, or with sexual partners originating from those areas, or where the donor's parents originate from those areas. HTLV-1 antibody testing for cartilage procurement is not performed nor are there any assessments in place to ascertain whether such additional testing is required.	**Minor**
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.	Risk assessments are not reviewed on a regular basis. The scope of risk assessments is limited and does not extend to ACI or irradiation of bone tissue activities.	**Minor**
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.		

Premises, Facilities and Equipment

Standard	**Inspection findings**	**Level of shortfall**
PFE4 Systems are in place to protect the quality and integrity of bodies, body parts, tissues and cells during transport and delivery to a destination.		
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.	The establishment distributes femoral heads mainly to a local hospital. Staff were able to describe the process they follow, but the procedure has not been formally documented. The procedure for packaging and transporting the tissue has not been validated to demonstrate that the quality and safety of the allograft is maintained.	**Minor**
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.		

Human Tissue Act 2004 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.	A number of the SOPs were out-of-date or required updating in order to reflect the recent change in DI and changes to practices These include the SOP for assigning the colours of cassettes and vials and the contingency arrangements in case of freezer failure.	**Minor**
GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately.	The risk assessments only relate to use of tissue in the absence of an HTA licence but do not extend to risks relating to tissues such as storage conditions, transport conditions and loss of traceability.	**Minor**

Premises, Facilities and Equipment

Standard	Inspection findings	Level of shortfall
PFE5 Equipment is appropriate for use, maintained, quality assured, validated and where appropriate monitored.	During the audit trail the freezer alarm sounded but the DI was not alerted. Furthermore, the temperature on the digital display did not alter. There was no evidence that the freezers have been serviced.	**Minor**

Advice

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

No.	Standard	Advice
1.	PFE3c	The DI informed the HTA inspection team that provision has been made to relocate the freezer used to store allografts to a larger room. The DI is advised to carry out a risk assessment ahead of the move to the new facility as part of the change control procedure.
2.	N/A	The establishment undertakes the surgical resection and irradiation of cancerous bone. The bone is removed in surgery, cleaned, packed and transferred to another hospital to be irradiated. The irradiated bone is then promptly returned to the establishment, where it is surgically implanted in its original anatomical location. Although this activity has not taken place for over 18 months the DI has indicated that there is still a possibility that this activity might take place in the future. The DI is advised that, should the establishment wish to restart this procedure, an application must be made to the HTA to have the licensable activity of 'processing' added to the establishment's licence before the activity can take place. In addition, the DI would need to submit a preparation process dossier (PPD) to the HTA, describing the procedure and providing evidence that the

		irradiation procedure achieves the desired result and does not render the tissue clinically ineffective. The preparation process must be authorised by the HTA before the establishment can undertake this activity.
3.	C1 (HT Act, 2004)	All consent forms reviewed were signed at the bottom by the donor and person seeking consent. Each form has information and lists options for consent and there is a check box besides each item and these are either initialled, ticked or left blank by the donor. The DI is advised to consider re-designing the form so that staff and the donors are aware of how they should be completed or carry out training to ensure that the consent seeker can give guidance to donors in order to ensure that there is consistency in the way these forms are completed.
4.	GQ1 (HT Act, 2004)	The DI hold weekly meeting with staff at the satellite. The DI is advised to continue to raise staff awareness of the legal requirements under the HT Act.
5.	GQ4 (HT Act, 2004)	The DI is advised to ensure that the sample location is not erased from the system even after all of the sample has been removed and used for research. This is to an ensure that an audit trail relating to the previous location of the sample continues to be maintained.
6.	GQ4 (HT Act, 2004)	The DI is advised to number all of the sub-samples stored in the freezer so that they can be identified and their traceability maintained. Samples should be stored according to the storage SOP i.e. diagnostic samples first and research samples next.
7.	GQ6 (HT Act, 2004)	The DI is advised to amend the MTA to ensure that organisations receiving relevant material for research dispose of the tissue on completion of their research work.
8.	General	The DI is advised that once the SOPs have been reviewed and issued that there is a system in place to document that staff have read them.

Concluding comments

During the inspection a number of good practices were noted. The satellite site had a comprehensive document which details on-going training and competency of staff for day-to-day activities. The colour-coding system greatly facilitated differentiating samples consented for research from other samples. At the hub site, femoral heads are not issued until the surgeon is certain that an allograft is required.

There are a number of areas of practice that require improvement, including seven minor shortfalls under the Q&S Regulations and three minor shortfalls under the HT Act, 2004. The HTA has also given advice to the Designated Individual with respect to a number of the establishment's procedures and documents with a view to helping the organisation further develop its working practices.

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: 05 August 2016

Report returned from DI: 07 September 2016

Final report issued: 07 September 2016

Completion of corrective and preventative actions (CAPA) plan

Based on information provided, the HTA is satisfied that the establishment has completed the agreed actions in the CAPA plan and in doing so has taken sufficient action to correct all shortfalls addressed in the Inspection Report.

Date: 05 February 2018

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.
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.
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.
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.