Site visit inspection report on compliance with HTA minimum standards

Royal Hallamshire Hospital

HTA licensing number 11030

Licensed for the

- **procurement, testing, storage and distribution of human tissues and cells for human application under the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended)**

12-13 June 2019

Summary of inspection findings

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

Although the HTA found that the Royal Hallamshire Hospital (the establishment) had met the majority of the HTA standards, one major shortfall was found relating to document control, which was also identified at the last inspection. 12 minor shortfalls were found in relation to Governance and Quality Systems (GQS) and Premises, Facilities and Equipment (PFE) standards. The shortfalls were related to internal and independent audits, staff appraisal, audit of records, donor confidentiality, donor selection and testing, the Single European Code (SEC), incident reporting, risk assessments, temperature monitoring and equipment maintenance.

It was identified during the inspection that the establishment has undertaken the storage of tendons without first notifying the HTA. The HTA is carrying out an investigation into this activity and will consider the need for regulatory action in relation to this matter separately to the inspection findings reported below.

Particular examples of good practice are included in the concluding comments section of the report.

The HTA's regulatory requirements

The HTA must assure itself that the Designated Individual, 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 Category; Tissue Type	Procurement	Processing	Testing	Storage	Distribution	Import	Export
Musculoskeletal, Bone; Bone	**E**		**E**	**E**	**E**		
Other, Cartilage (ATMP)	**E**		**E**		**E**		

Background to the establishment and description of inspection activities undertaken

The bone bank at the Royal Hallamshire Hospital is licensed under the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended) for procurement, donor testing, storage and distribution of human tissues and cells for human application. The establishment's HTA licence also covers the satellite site at Northern General Hospital. Sheffield Teaching Hospitals NHS Foundation Trust is the Corporate Licence Holder (CLH) and the CLH contact is the Medical Director of the Trust.

The establishment has recently varied the licence to undertake procurement of cartilage tissue at both the satellite and hub, which is sent for Advanced Therapy Medicinal Product (ATMP) manufacturing in Germany. This will be sent back to the establishment for Autologous Chondrocyte Implantation (ACI). The shipping box is provided by the manufacturer and it contains the consumables used for procurement and sample collection. The documentation related to the licensable activities for the cartilage tissue were reviewed.

The establishment is in the initial stages of seeking patients for this treatment and has not yet started procurement.

The bone bank is jointly managed by the Department of Laboratory Medicine and the Department of Orthopaedics. Procurement of bone takes place in theatres at the hub and satellite. Both of these theatres have quarantine freezers for the short-term storage of freshly procured bone, and 'ready to use' freezers for the storage of released bone ready for implantation. The main storage area is located in a secure room near the mortuary at Royal Hallamshire Hospital, where the bone is stored in four dedicated freezers. The satellite also receives and stores bone strut grafts and tendons from HTA-licensed suppliers within the UK for use in orthopaedic surgical procedures; these products are also stored within the -80ºC freezers in the theatres. Since the last inspection the theatres at the hub have relocated to a newly refurbished theatre area in the main hospital.

Femoral heads are procured at both the hub and satellite from patients undergoing hip replacement surgery. Pre-assessment nurses who have been trained to seek consent, identify potential donors and provide information on bone donation. They interview potential donors and assess their medical and travel history. The initial blood sample is taken for mandatory donor testing, seven days after the surgery. Potential donors are given the opportunity to withdraw consent, and a second confirmatory consent for bone donation is sought if the surgical procedure takes place 30 days or more after the date of initial consent.

Donor testing for the mandatory serology markers and microbiology testing of tissues is carried out at the microbiology and virology laboratories at the Northern General Hospital, which is accredited by United Kingdom Accreditation Service (UKAS). Repeat serology testing is undertaken after 180 days.

The majority of femoral heads procured at the establishment are for allogeneic use. Femoral heads are procured and washed using sterile Hartmann's solution. Theatre staff swab the femoral head and remove a bone chip from the cut end of the bone in order to test for microbial contamination. The femoral head is packaged in the theatres in two sterile pots and tamper-evident tape is secured to the seal of the lid and the pot, under the supervision of orthopaedic surgeons. The pots are labelled with a unique bone bank number and donor addressograph, and placed into a tamper-evident bag. The name of the person who handled the femoral head is recorded on the procurement form along with the size, weight and the batch number of the consumables and reagents used. Once procured, the bone is not removed from the pots until it is opened in theatres, just before implantation into a recipient.

Following procurement, femoral heads are placed in the -80°C quarantine freezer. The establishment has two quarantine freezers. However, at the time of inspection, one of the quarantine freezers was broken and out of action. The first and second (180-day repeat) serology test results, as well as the microbiology test results, are recorded on the bone bank register and electronic spreadsheet. The Designated Individual (DI) and Medical Director of the bone bank review the donor file, which contains the procurement report, mandatory donor test results (including repeat 180-day results) and results following microbial analysis of bone chips and swabs, before they authorise the release of bone for surgical use. Femoral heads are disposed of if the mandatory test results are positive or if microbial contamination is detected on the swabs and/or bone chips.

Once the serology and microbiology test results are reviewed and signed-off, the bone bank coordinator transfers the femoral head to one of the two 'release' -80°C freezers in the bone bank. The bone bank register, location in the freezer, the electronic spreadsheet and the 'freezer contents log' secured onto the front of the freezers are updated every time a femoral head is moved.

The bone bank supply femoral heads to the theatres upon request from the theatre nurses. A small number of released femoral heads (approximately six at any one time) are stored in the

‘ready for use’ freezers at both hub and satellite to be readily available for patient use. Theatre nurses remove bone for implantation from ‘ready to use’ freezers and transfer it to the theatres where it is thawed ready for implantation. Femoral heads are swabbed once again in theatres before implantation, and the swabs are tested for the presence of any microbial contamination. Orthopaedic surgeons record the use of bone and relevant recipient data in the theatre implant sheet, which is returned to the bone bank; the relevant records are filed in the recipient’s clinical notes.

Freezers at the bone bank and theatres at the hub are monitored using a wireless temperature system, which is linked to alarms connected to the hospital switchboard. In the event of a temperature deviation from the required storage temperature, the hospital switchboard would subsequently notify the bone bank staff. The freezer temperatures at the bone bank are additionally recorded by staff using the freezer display on weekdays. The freezers at the satellite are not linked to the wireless temperature system; temperatures are manually recorded on weekdays using the freezer display. The temperatures of the freezers at the satellite are not recorded on the weekends or bank holidays. The -80°C freezers at both the hub and satellite are plugged into a power sockets but are not hard-wired to the mains electricity supply. The freezer alarms and the response from switchboard staff are tested each month.

This was the sixth routine inspection of the establishment to assess whether the establishment is continuing to meet the required HTA standards. The visual inspection included a visit to the bone bank freezer storage area at the hub, the freezer storage areas at the theatres at both the hub and satellite, and the microbiology and serology testing laboratories at the satellite.

Discussions relating to the licensable activities were held with the DI, who is also the laboratory manager at the Department of Laboratory Medicine, the bone bank manager, who is also the mortuary supervisor at the hub, pre-assessment and orthopaedic theatre nurses, mortuary staff, biomedical scientists responsible for testing activities, and the quality manager at the Department of Laboratory Medicine at the Northern General Hospital.

Documentation relevant to the establishment’s licensable activities at both the hub and satellite were reviewed, including standard operating procedures (SOPs) covering donor selection, document control and storage and authorisation of bone for implantation. Staff training records, competency assessments, temperature monitoring records, including manual paper and electronic records, risk assessments, audit reports, maintenance records and disposal records were also reviewed.

A traceability audit was carried out which included six femoral heads chosen from the freezer contents logs at the bone bank. Four femoral heads were chosen from the freezer contents log from the ‘ready to use’ freezers in the orthopaedic theatres at both sites. The femoral heads were cross-checked with the electronic database and the paper records stored at the bone bank. The corresponding donor files of the femoral heads were reviewed to ensure that they contained all the relevant documentation, including donor medical history forms, consent forms, and the serology and microbiology test results. For two of the donors, the microbiology results for the swabs and bone chips, and the serology test results were traced back to the electronic database at the testing laboratory where the details were confirmed. One of the femoral heads that was temporarily stored in the theatres at the hub, had been discarded due to the femoral head reaching the expiry date and the documentation for disposal was reviewed. At the time of inspection an achilles tendon was found to be stored in the ‘ready to use’ freezer at the satellite. The delivery note, Single European Code (SEC) and paper records were also checked for this product.

There were inconsistencies with the filling-in and completion of the temperature monitoring forms and a minor discrepancy with the expiry date of one of the femoral heads that was

stored in the theatres 'ready to use' freezer at the satellite. Although the correct expiry date was seen on the femoral head pot and the paperwork, this was incorrectly logged as one day later than the expiry date on the electronic database.

Inspection findings

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

It was identified during the inspection that the establishment has undertaken the storage of tendons without first notifying the HTA. The HTA is carrying out an investigation into this activity and will consider the need for regulatory action in relation to this matter separately to the inspection findings reported below.

Compliance with HTA 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.	The establishment has not put adequate systems in place for document control and for archiving older versions of documents. For example, older versions of SOPs and forms were seen in circulation at the satellite. For one set of forms, two different versions were seen in the same document wallet. This issue was also identified at the last inspection. However, the establishment has not implemented the corrective and preventative actions that were agreed following that visit, which included creating a list of documents to be stored as hard copies and carrying out an annual audit of the documents at both sites.	**Major**
GQ2 There is a documented system of quality management and audit.		
b) There is an internal audit system for all licensable activities.	The establishment's audit reports lack essential information to fully understand the scope of the audit conducted, what exactly was audited and what the findings were. Due to the lack of findings, there were no corrective actions documented.	**Minor**
c) An audit is conducted in an independent manner at least every two years to verify compliance with	An independent audit was conducted in February 2019; the audit was a review of the bone bank processes, and whilst it	**Minor**

protocols and HTA standards, and any findings and corrective actions are documented.	covered some of the HTA standards, there was insufficient evidence to demonstrate that this was carried out against all of the applicable HTA standards.	
GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills.		
h) There is a system of staff appraisal.	Although the Trust has systems in place for appraisals, it was noted that several bone bank staff have not had regular appraisals for a number of years.	**Minor**
GQ4 There is a systematic and planned approach to the management 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.	At the satellite, there are two freezers located in the orthopaedic theatres. During a review of the temperature records, it was noted that there were several months of temperature records missing. In addition to this, there were consistently several days per month during which the temperatures had not been recorded and there was no documented explanation. See *Advice*, item 5, below	**Minor**
g) There is a system to ensure records are secure and that donor confidentiality is maintained in accordance with Directions 002/2018.	Femoral heads sent from the satellite site to the hub are accompanied by a 'chain of custody form. This form, which contains donor identifiable information, must be signed by the driver responsible for transporting the femoral head. The current system in place does not ensure that donor confidentiality is maintained in accordance with Directions 002/2018.	**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 002/2018.	The procedures for donor selection do not include whether the donor has had a xenograft transplant in the past. Although, there is reference to toxic chemical exposure, the 'consent/self-deferment form for femoral head donation' does not specify whether the donor has ever ingested, or been exposed, to a substance (such as cyanide, lead, mercury, gold) that may be transmitted to recipients in a dose that could endanger their health.	**Minor**

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 002/2018.	During the audit of serology testing records, it was noted that the blood samples from one donor were not received into the testing laboratory until two days after collection. The establishment was unable to account for the storage of the blood samples during this period. The test kits used for the majority of the serology testing allow for the blood samples to be stored at ambient temperature following collection. However, the blood samples for the HTLV I/II testing should be kept at 2-8ºC, as specified by the manufacturer of the kits. The establishment could not demonstrate that samples collected for HTLV I/II testing were stored at the manufacturer's required storage temperature following collection.	**Minor**
GQ6 A coding and records system facilitates traceability of bodies, body parts, tissues and cells, ensuring a robust audit trail.		
d) The requirements of the Single European Code are adhered to as set out in Directions 002/2018.	The establishment has chosen to apply the SEC to femoral heads released for end use both internally and externally as required. It was noted that the SEC-DI part of the sequence was incorrect as the unique donation number contained an additional alpha-numeric character. In addition to this, the SEC-PI part of the sequence was not being applied. The current format of the SEC does not comply with the requirements as set out in Directions 002/2018.	**Minor**
GQ7 There are systems to ensure that all adverse events 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.	There are two freezers located in the theatres at the satellite; one is used to store released, 'ready for use' bone, and the second is used to temporarily store procured bone. During a review of the temperature records, it was noted that there was a temperature excursion above the establishment's set action limit for the freezer used to stored procured bone; action was not taken until one day later. During this time, the freezer had been used to store a procured femoral head. The local incident procedures were not implemented in relation to this excursion, and theatre staff and the bone bank	**Minor**

	manager were not informed. There was no record of this incident and the establishment could not demonstrate what action had been taken to assess the impact of the excursion on the quality and safety of the femoral head in storage at that time.	
GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately.		
c) Staff can access risk assessments and are made aware of local hazards at training.	During inspection, it was apparent that there was a lack of awareness of how to access risk assessments for the staff in the theatres and what risk assessments were available to staff working under the licence.	**Minor**

Premises, Facilities and Equipment

Standard	**Inspection findings**	**Level of shortfall**
PFE3 There are appropriate facilities for the storage of tissues and / or cells, consumables and records.		
c) Tissues and / or cells are stored in controlled, monitored and recorded conditions that maintain tissue and / or cell integrity.	The temperatures of the two freezers in the theatres at the satellite are recorded manually on weekdays using the freezer display; temperatures are not recorded on weekends or bank holidays. Currently, the maximum and minimum temperatures of the freezers are not recorded at any time. The current system of temperature monitoring of the freezers at the satellite does not provide adequate assurance that bone is stored within the required temperature range at all times.	**Minor**
PFE5 Equipment is appropriate for use, maintained, quality assured, validated and where appropriate monitored.		
b) Critical equipment is maintained and serviced in accordance with the manufacturer's instructions.	The -80ºC bone bank freezers at both the hub and satellite were last serviced in June 2017. The annual servicing of the freezers has not been maintained in accordance with the manufacturer's instructions.	**Minor**

Advice

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

No.	Standard	Advice
1.	GQ1c	The DI is advised to ensure regular governance meetings are held and that representatives attend from the different multi-disciplinary areas related to the licensable activities.
2.	GQ1k	The DI is advised to update SOP 7.6/02 “Return of tissue to the bone bank after issue for implant” to ensure that it is clearer when grafts can be returned once despatched to the end users.
3.	GQ2b PFE3c	The bone bank freezer temperature graphs are printed off monthly and filed in the respective folders. During a review of the paper and electronic temperature records, it was not clear what had caused a peak in temperature in May 2019. The DI is advised to put systems in place to clearly capture the reasons for any temperature deviations. This would enable the establishment to have a clearer record of what happened at the time and identify trends to facilitate internal audit activities and help improve storage practices.
4.	GQ3e	The DI is advised to arrange documented refresher training for the staff carrying out the internal audits to ensure that staff are more familiar with the audit process.
5.	GQ4b	The DI is advised to implement a regular documented review of the temperature monitoring records to check for completeness, legibility and accuracy and to resolve any discrepancies before filing records for storage.
6.	GQ4f	The DI is advised to put a system in place for the ward nurses to capture the volumes of liquid or blood infused into donor’s before, during and after surgery, and to communicate this information to the testing laboratory staff as the haemodilution may affect the testing results. This may help the testing laboratory to ensure that adjustments can be made to the algorithm, as required.
7.	GQ8a	Prior to commencement of cartilage tissue ATMP work, the DI is advised to expand the current risk assessments to include consent, procurement, donor selection and donor testing activities.
8.	GQ8a, PFE5k	During the inspection, it was observed that one of the quarantine freezers was out of action. Whilst the establishment has a contingency arrangement with the theatres, there may not be sufficient capacity to store and segregate the different types of bones. The DI is advised to risk assess and formalise an agreement with other departments to provide assurance that in the event of freezer breakdown, there is an adequate contingency storage provision.
9.	PFE3d	It was noted that the establishment had disposed of a large number of femoral heads in 2018, due to the products reaching their expiry date. During inspection, it was seen that a femoral head with a longer expiry date had been selected for use in the theatres, when there was a femoral head with a shorter expiry date available. In order to minimise disposal of bone, the DI is advised to put systems in place to ensure that staff are aware of the need to select bones with shorter expiry dates first, unless a bone of a specific weight and/or Rhesus status is required for transplantation.
10.	PFE5c	The back-up freezer probes are calibrated annually, and these are used to check that the freezer probes are recording the correct temperatures. The DI is advised to formally capture this process in an SOP, which should also include

		the frequency of documented checks and the acceptance limits to ensure that the freezer probes are working to specification. The SOP should also include what actions should be taken if the probes are not recording temperatures within an acceptable tolerance of the reference probe. The DI is also advised to record the outcome of the freezer alarm testing on the relevant documentation and ensure that this is carried out in accordance with the SOP.
11.	PFE5f	The DI is advised to clearly document the cleaning of the freezers on the appropriate form and ensure this is performed at the correct frequency.

Concluding comments

The HTA observed several examples of good practice during the course of the inspection.

The establishment display colour-coded signs on the freezers located in the theatres at both sites, so that the staff can clearly differentiate the freezer used to store freshly procured bone and the freezer used to store released bones. The 'ready to use' freezers are secured by padlock, and the keys must be signed out by authorised staff to gain access.

The freezer contents log has a map of where individual femoral heads are located, which is updated every time a femoral head is moved, and this is affixed to the front of each freezer door, which minimises the risk of mixing up products.

There are a number of areas of practice that require improvement, including one major shortfall relating to document control, which was also identified at the last inspection. The 12 minor shortfalls were related to internal and independent audits, staff appraisal, audit of records, donor confidentiality, donor selection and testing, the Single European Code (SEC), incident reporting, risk assessments, temperature monitoring and equipment maintenance.

The HTA has given advice to the Designated Individual with respect to governance meetings, updating documents, facilitating internal audits, refresher training, review of records, haemodilution factors, risk assessments, and contingency storage provisions, stock control, formally capturing the temperature probe calibration process, recording the outcome of the freezer alarm testing and recording cleaning of the freezers

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: 11 July 2019

Report returned from DI: 15 July 2019

Final report issued: 05 August 2019

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: 01 July 2020

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
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 002/2018 is included.
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.
n) The establishment ensures imports from non EEA states meet the standards of quality and safety set out in Directions 002/2018.
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 002/2018.
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 002/2018, is collected and maintained.
g) There is a system to ensure records are secure and that donor confidentiality is maintained in accordance with Directions 002/2018.
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 002/2018 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 002/2018.
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 002/2018.
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 002/2018.
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.
d) The requirements of the Single European Code are adhered to as set out in Directions 002/2018.
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.

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.
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.
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 002/2018.
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.

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

Where the HTA determines that a licensing standard is not met, the improvements required will be stated and the level of the shortfall will be classified as 'Critical', 'Major' or 'Minor'. Where the HTA is not presented with evidence that an establishment meets the requirements of an expected standard, it works on the premise that a lack of evidence indicates a shortfall.

The action an establishment will be required to make following the identification of a shortfall is based on the HTA's assessment of risk of harm and/or a breach of the HT Act or associated Directions.

1. **Critical shortfall:**

   A shortfall which poses a significant direct risk of causing harm to a recipient patient or to a living donor,

   Or

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

   A critical shortfall may result in one or more of the following:

   (1) A notice of proposal being issued to revoke the licence

   (2) Some or all of the licensable activity at the establishment ceasing with immediate effect until a corrective action plan is developed, agreed by the HTA and implemented.

   (3) A notice of suspension of licensable activities

   (4) Additional conditions being proposed

   (5) Directions being issued requiring specific action to be taken straightaway

2. **Major shortfall:**

   A non-critical shortfall.

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

   or

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

   or

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

   or

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

   or

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

   In response to a major shortfall, an establishment is expected to implement corrective and preventative actions within 1-2 months of the issue of the final inspection report. Major shortfalls pose a higher level of risk and therefore a shorter deadline is given, compared to minor shortfalls, to ensure the level of risk is reduced in an appropriate timeframe.

3. **Minor shortfall:**

   A shortfall which cannot be classified as either critical or major and, which can be addressed by further development by the establishment.

   This category of shortfall requires the development of a corrective action plan, the results of which will usually be assessed by the HTA either by desk based review or at the time of the next inspection.

   In response to a minor shortfall, an establishment is expected to implement corrective and preventative actions within 3-4 months of the issue of the final inspection report.

Follow up actions

A template corrective and preventative action plan will be sent as a separate Word document with both the draft and final inspection report. You must complete this template and return it to the HTA within 14 days of the issue of the final report.

Based on the level of the shortfall, the HTA will consider the most suitable type of follow-up of the completion of the corrective and preventative action plan. This may include a combination of

- a follow-up site-visit inspection
- a request for information that shows completion of actions
- monitoring of the action plan completion
- follow up at next desk-based or site-visit inspection.

After an assessment of your proposed action plan you will be notified of the follow-up approach the HTA will take.