Site visit inspection report on compliance with HTA minimum standards

Royal Victoria Infirmary

HTA licensing number 11122

Licensed for the

- **procurement, processing, testing, 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 under the Human Tissue Act 2004.**

19 – 21 November 2013

Summary of inspection findings

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

Although the HTA found that Royal Victoria Infirmary (the establishment) had met the majority of the HTA standards, one minor shortfall was found, in relation to control over transport conditions for distribution of femoral heads.

Since previous inspections, the establishment continues to improve its systems, including acting on advice given in the last inspection report.

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

The HTA's regulatory requirements

The HTA must assure itself that the Designated Individual, Licence Holder, premises and practices are suitable.

The statutory duties of the Designated Individual are set down in Section 18 of the Human Tissue Act 2004. They are to secure that:

- the other persons to whom the licence applies are suitable persons to participate in the carrying-on of the licensed activity;
- suitable practices are used in the course of carrying on that activity; and
- the conditions of the licence are complied with.

The HTA developed its licensing standards with input from its stakeholders. They are designed to ensure the safe and ethical use of human tissue and the dignified and respectful treatment of the deceased. The HTA inspects the establishments it licences against four groups of standards:

- consent
- governance and quality systems
- premises facilities and equipment
- disposal.

This is an exception-based report: only those standards that have been assessed as not met are included. Where the HTA determines that a standard is not met, the level of the shortfall is classified as 'Critical', 'Major' or 'Minor' (see Appendix 2: Classification of the level of shortfall). Where HTA standards are fully met, but the HTA has identified an area of practice that could be further improved, advice is given to the DI.

Reports of HTA inspections carried out from 1 November 2010 are published on the HTA's website.

Licensable activities carried out by the establishment

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

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

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

Tissue type	Procurement	Processing	Testing	Storage	Distribution
HSC	**E**	**E**	**E**	**E**	**E**
Bone	**E**	**E***	**E***	**E**	**TPA**
Heart valves	**E**	**E***	**E***	**E**	**E**
Iliac vessels	**E**	**N/A**	**E**	**E**	**E**
Pancreatic islets	**E**	**E**	**E**	**E**	**E**
hESC	**E***	**E***	**E***	**E**	**E***
Cord blood	**E**	**E**	**E**	**E**	**E**

Background to the establishment and description of inspection activities undertaken

The establishment's licence covers a range of activities at the hub (Royal Victoria Infirmary, (RVI)) and two satellite sites: Newcastle Bio-Manufacturing Facility (NBF), at the Centre for Life; and the Freeman Hospital. At the RVI, the establishment procures, processes and stores haematopoietic stem cells (HSCs) for cellular therapies and conducts mandatory testing of donors. The RVI also stores cord blood which is either obtained through cord blood registries, or procured for directed donations. Some of the HSCs are used in two clinical trials. One for the transplantation of autologous limbal stem cells and another to use tolerogenic dendritic cells to treat autoimmune conditions, such as rheumatoid arthritis. Procurement of these cells, and testing of the donors, takes place under the HTA licence. Processing takes place under an MHRA licence.

NBF recently processed its first batch of pancreatic islet cells for autologous use, procured and implanted at the Freeman Hospital. The NBF also stores human embryonic stem cells (hESCs) in ultra cool, liquid nitrogen vapour phase. More processing activity is planned in the future with other cell types.

The Freeman Hospital stores bone, heart valves and iliac vessels. Femoral heads are stored in a -34°C freezer. One shelf is used for storage of bone distributed for use at the RVI and a separate shelf is used for bone used at the Freeman Hospital. There is also a -180°C freezer used for storage of heart valves and a 4°C fridge for storage of iliac vessels. All storage units are within theatres.

Other distribution activity at the establishment includes distribution of pancreatic islet cells for autologous use. The first batch of cells processed at the NBF were packaged and sent back to the Freeman Hospital for reimplantation into the patient, accompanied by the transplant surgeon. There is also regular distribution of HSCs procured at the adult apheresis unit at the Freeman Hospital, to the processing laboratory at the RVI and back to the Freeman Hospital for reinfusion.

Serology testing takes place at the Freeman Hospital for the three sites. Sterility testing and environmental qualification of the cleanroom suites used for processing by the RVI and the NBF is completed under an agreement with a third party.

This was the establishment's fourth routine inspection and was conducted over three days. The previous inspection, in 2011, found one major shortfall in relation to the use of personal protective equipment and several minor shortfalls against training, record keeping and temperature monitoring. These were addressed by the establishment through completion of a corrective and preventive action plan. The establishment has demonstrated a commitment to compliance with HTA standards. Since the last inspection it has acted on pieces of advice from the HTA, such as implementing regular alarm testing of its fridges and freezers used to store iliac vessels, bone and heart valves and monitoring the temperature where apheresis kits and anticoagulants are stored at the Freeman Hospital.

This inspection encompassed a document review, interviews with staff and traceability audits. The visual inspection included an observation of an HSC cryopreservation process at the RVI, an inspection of the processing facilities at the NBF and review of storage areas at the RVI, NBF and Freeman Hospital. This was the first inspection conducted since processing activity commenced at the NBF. The visual inspection specifically excluded the processing laboratories at RVI used for the expansion of limbal stem cells and dendritic cells to create advanced therapy medicinal products (ATMPs). Processing of these cells is governed under an MHRA licence. The procurement, consent and mandatory donor testing is governed under the HTA licence. These elements were discussed with staff and procurement areas were seen during the visual inspection of the apheresis unit at the Freeman Hospital, where the HSCs are procured.

The establishment also stores purchased amniotic membrane which is used as a dressing in opthalmology, but due to time constraints, this was not specifically reviewed during the inspection.

The traceability audits included a review of sets of patient notes from:

- the limbal stem cell trial;
- the tolerogenic dendtiric cell trial;
- haematology;
- orthopaedics; and
- the autologous islet cell transplantation programme.

Patient notes were reviewed to trace material from the storage area to the patient notes, or to trace material from the donor to the recipient. Records were also reviewed to confirm completion of mandatory tests and for cell and tissue identifiers. There were anomalies found for one orthopaedic patient record and for the autologous islet cell recipient record. These are discussed in more detail in the advice section below.

During the visual inspection, the inspection team also completed a traceability audit of:

- two femoral heads from the shelves in the freezer to the bone register kept at the Freeman Hospital;
- one EU homograft heart valve from the order form, to the register, to the storage freezer and to the current holdings log;
- an iliac vessel awaiting disposal was checked against the form and the physical location in the fridge; and
- an HSC donation number and donor details at the Freeman Hospital apheresis unit were traced from the bag on the machine, to the barcodes and donor details on the traceability forms used the following day at the RVI during the processing.

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

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.		
f) There are third party agreements with courier or transport companies to ensure that any specific transport conditions required are maintained.	Femoral heads are stored at the Freeman Hospital. Some are designated for use at the RVI. These are sent unaccompanied to the RVI by taxi. Establishment staff explained that this was because bone may be needed at short notice. This practice is not consistent with current processes across the establishment. For example, HSCs are distributed between the apheresis unit at the Freeman Hospital and the processing laboratory at the RVI by a courier company engaged under the terms of a third party agreement. The DI should ensure processes are in place to maintain critical transport conditions and that necessary TPAs are in place. Refer to advice against GQ8(a).	**Minor**
g) Critical transport conditions required to maintain the properties of tissue and / or cells are defined and documented.		

Advice

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

No.	Standard	Advice
1.	GQ2(c)	The establishment had an independent audit around the time of the last inspection at the end of 2011. Establishment staff advised that they will organise another independent inspection shortly. The HTA advises this should be completed as soon as possible to ensure this standard continues to be fully met.
2.	GQ4(b)	The establishment has an audit schedule in place and completed audits of records to address HTA standards such as traceability. Steps are underway to improve recording of actions needed following an audit and monitoring the follow-up steps taken. The DI is advised to continue with work to improve processes around documentation of audits.
3.	GQ4(h) and (m)	NBF has a Site Master File in place which specifies arrangements for transfer of cells in the event of suspension or termination of activities at NBF. When the document is next reviewed, the DI is advised to update this document to specify retention periods for transferred tissues and records.
4.	GQ5(b) and GQ6(c)	The establishment recently transplanted its first batch of autologous islet cells procured at the Freeman Hospital and processed at the NBF, before immediate reimplantation at the Freeman Hospital. The records and patient notes for the islet cell processing and transplant were reviewed. There were some anomalies found, specifically: • mandatory test results were not available at the time of the transplantation. This was recorded as a deviation by the establishment and addressed, including test results being recorded in the notes following the transplant; and • the code for the first batch of islets was not recorded in the recipient notes. The DI is advised to raise awareness with transplant staff about recording this for future islet transplantation operations, to ensure full traceability is maintained and manage any anomalies through the existing audit schedule.
5.	GQ6(c)	A femoral head record was traced from the register at the Freeman Hospital to patient notes at the RVI, where the bone was used. The paperwork allowed traceability of two femoral heads to the recipient, however the notes did not record the femoral head identifying code in the patient notes. The DI is advised to continue with the existing audit schedule to identify and address such anomalies.
6.	GQ8(a)	The establishment distributes femoral heads between sites, by taxi. The DI may wish to ensure a risk assessment is completed to evaluate the potential safety of this practice and / or any changes implemented to this process. Refer to the minor shortfall against PFE4(f) and (g).

7.	PFE2(b)	The establishment processes material in cleanroom suites at the RVI and the NBF. To further reduce the risk of contamination of viable and non-viable particles, the DI is advised to consider the following. For the RVI: • reposition the settle plates used during processing, from the back of the cabinet, closer to the areas of activity; • maintain an appropriate amount of residual timing after alcohol spray, when using the transfer hatches between controlled environments to the storage area; • reintroduce the recently discontinued additional environmental monitoring step between processing and before cleaning by contractors; • ensure disposal, on receipt, of any outer wrapping or packaging used to protect tissues and cells during transport,in order to safeguard the cleanroom suite against extraneous contamination; and • risk assess the decision not to conduct in-process monitoring for closed systems. For the NBF: • review the current method of in-particle monitoring, to ensure best practice; • place signage in the processing suite, to identify the flow of the controlled environments; and • secure the Grade D egress into the fire escape / maintenance area.
8.	PFE2(b)	The bone freezer at the Freeman Hospital has a protocol on the front of the freezer which instructs staff on how to handle bone products. This includes a step to check that the temperature is within the appropriate limits. The DI is advised to include the freezer limits on the protocol, for ease of reference.
9.	PFE3(a)	As part of the cryopreservation process, HSCs processed at the RVI are stored overnight in a freezer with blood products. The DI is advised to consider other storage options to reduce the risk of mix-up or cross-contamination.

Assessment of preparation process dossier

Prior to the inspection the HTA assessed a preparation process dossier (PPD) for autologous transplantation of pancreatic islets. This is a process offered at other sites in the UK and other centres around the world, but was a new process to be offered at the establishment. The process was authorised. NBF anticipates increasing its processing activities in the near future, which will most likely include different cell types and novel processes. The establishment staff confirmed they would submit further PPDs as required, in line with advice from the inspection team.

Concluding comments

There were a number of strengths and areas of good practice observed during this inspection. Staff demonstrated an underlying culture of commitment to quality and safety of tissues and cells used for patient treatment, across the establishment. There is good communication in place and dedicated staff are continuously improving systems, including harmonising governance systems across the licence to ensure staff remain supported in their clinical duties. Staff demonstrated pride in what they do and showed initiative by contributing to system improvements. For example, the team working with iliac vessels uses transplant packs to consistently document all traceability data for the vessels. The person designate in this area extended this existing system to ensure appropriate paperwork was developed for the recent, single islet procedure. Other work units also have strong documentation in place to record traceability, such as the use of a transport form by staff in the apheresis unit at the Freeman Hospital and processing staff in the processing laboratory at the RVI, to record the chain of custody of HSCs between sites. Staff at the NBF have ensured that any new processes undertaken for third parties will be preceded by full test runs, as further evidence of the establishment's commitment to quality. Staff at the establishment are further supported by robust training and induction procedures, including use of competency assessments and procedural questionnaires to evidence awareness and understanding of standard operating procedures.

There were areas of practice identified that require improvement, including one minor shortfall. The HTA has given advice to the Designated Individual with respect to audits, references to retention periods in the event of transfer of cells, tissue or records, risk assessment of processes and changes to processes, environmental monitoring, clarifying use of premises, such as controlled access to areas, including freezer limits for easier reference and reducing the risk of mix-up or cross-contamination during all processing and transport steps.

The HTA requires that the Designated Individual addresses the minor shortfall by submitting a completed corrective and preventive 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 preventive actions being implemented to meet the shortfall identified during the inspection.

Report sent to DI for factual accuracy: 19 December 2013

Report returned from DI: 24 December 2013

Final report issued: 2 January 2014

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: 10 July 2014

Appendix 1: HTA standards

The HTA standards applicable to this establishment are shown below; those not assessed during the inspection are shown in grey text. Individual standards which are not applicable to this establishment have been excluded.

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

Consent

Standard
C1 Consent is obtained in accordance with the requirements of the HT Act 2004, the Human Tissue (Quality and Safety for Human Application) Regulations 2007 and as set out in the HTA's Codes of Practice.
a) If the establishment acts as a procurer of tissues and / or cells, there is an established process for acquiring donor consent which meets the requirements of the HT Act 2004 the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (Q&S Regulations) and the HTA's Codes of Practice
b) If there is a third party procuring tissues and / or cells on behalf of the establishment the third party agreement ensures that consent is obtained in accordance with the requirements of the HT Act 2004, the Q&S Regulations and the HTA's Codes of Practice.
c) The establishment or the third party's procedure on obtaining donor consent includes how potential donors are identified and who is able to take consent.
d) Consent forms comply with the HTA Codes of Practice.
e) Completed consent forms are included in records and are made accessible to those using or releasing tissue and / or cells for a Scheduled Purpose.
C2 Information about the consent process is provided and in a variety of formats.
a) The procedure on obtaining consent details what information will be provided to donors. As a minimum, the information specified by Directions 003/2010 is included.
b) If third parties act as procurers of tissues and / or cells, the third party agreement details what information will be provided to donors. As a minimum, the information specified by Directions 003/2010 is included.
c) Information is available in suitable formats and there is access to independent interpreters when required.
d) There are procedures to ensure that information is provided to the donor or donor's family by trained personnel.
C3 Staff involved in seeking consent receive training and support in the implications and essential requirements of taking consent.
a) Staff involved in obtaining consent are provided with training on how to take informed consent in accordance with the requirements of the HT Act 2004 and Code of Practice on Consent.
b) Training records are kept demonstrating attendance at training on consent.

Governance and Quality

Standard
GQ1 All aspects of the establishment's work are supported by ratified documented policies and procedures as part of the overall governance process.
a) There is an organisational chart clearly defining the lines of accountability and reporting relationships.
b) There are procedures for all licensable activities that ensure integrity of tissue and / or cells and minimise the risk of contamination.
c) There are regular governance meetings, for example health and safety, risk management and clinical governance committees, which are recorded by agendas and minutes.
d) There is a document control system to ensure that changes to documents are reviewed, approved, dated and documented by an authorised person and only current documents are in use.
e) There are procedures for tissue and / or cell procurement, which ensure the safety of living donors.
f) There are procedures for tissue and / or cell procurement, which ensure the dignity of deceased donors.
g) There are procedures to ensure that an authorised person verifies that tissues and / or cells received by the establishment meet required specifications.
h) There are procedures for the management and quarantine of non-conforming consignments or those with incomplete test results, to ensure no risk of cross contamination.
i) There are procedures to ensure tissues and / or cells are not released from quarantine until verification has been completed and recorded.
j) There are procedures detailing the critical materials and reagents used and where applicable, materials and reagents meet the standards laid down by the European directives on medical devices and in vitro diagnostic medical devices.
k) There is a procedure for handling returned products.
l) There are procedures to ensure that in the event of termination of activities for whatever reason, stored tissues and / or cells are transferred to another licensed establishment or establishments.
m) The criteria for allocating tissues and / or cells to patients and health care institutions are documented and made available to these parties on request.
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 preventive actions.
b) There is a system to receive and distribute national and local information (e.g. HTA regulatory alerts) and notify the HTA and other establishments as necessary of serious adverse events or reactions.
c) The responsibilities of personnel investigating adverse events and reactions are clearly defined.
d) There are procedures to identify and decide the fate of tissues and / or cells affected by an adverse event, reaction or deviation from the required quality and safety standards.
e) In the event of a recall, there are personnel authorised within the establishment to assess the need for a recall and if appropriate initiate and coordinate a recall.
f) There is an effective, documented recall procedure which includes a description of responsibilities and actions to be taken in the event of a recall including notification of the HTA and pre-defined times in which actions must be taken.
g) Establishments distributing tissue and / or cells provide information to end users on how to report a serious adverse event or reaction and have agreements with them specifying that they will report these events or reactions.
h) Establishments distributing tissues and / or cells have systems to receive notifications of serious adverse events and reactions from end users and notify the HTA.
GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately.
a) There are documented risk assessments for all practices and processes.
b) Risk assessments are reviewed regularly, as a minimum annually or when any changes are made that may affect the quality and safety of tissues and cells.
c) Staff can access risk assessments and are made aware of local hazards at training.
d) A documented risk assessment is carried out to decide the fate of any tissue and / or cells stored prior to the introduction of a new donor selection criteria or a new processing step, which enhances the quality and safety of tissue and / or cells.

Premises, Facilities and Equipment

Standard
PFE1 The premises are fit for purpose.
a) A risk assessment has been carried out of the premises to ensure that they are fit for purpose.
b) There are procedures to review and maintain the safety of staff, visitors and patients.
c) The premises have sufficient space for procedures to be carried out safely and efficiently.
d) Where appropriate, there are procedures to ensure that the premises are of a standard that ensures the dignity of deceased persons.

e) There are procedures to ensure that the premises are secure and confidentiality is maintained.
f) There is access to a nominated, registered medical practitioner and / or a scientific advisor to provide advice and oversee the establishment's medical and scientific activities.
PFE2 Environmental controls are in place to avoid potential contamination.
a) Tissues and / or cells stored in quarantine are stored separately from tissue and / or cells that have been released from quarantine.
b) Where processing of tissues and / or cells involves exposure to the environment, it occurs in an appropriate, monitored environment as required by Directions 003/2010.
c) There are procedures for cleaning and decontamination.
d) Staff are provided with appropriate protective clothing and equipment that minimise the risk of contamination of tissue and / or cells and the risk of infection to themselves.
PFE3 There are appropriate facilities for the storage of tissues and / or cells, consumables and records.
a) Tissues, cells, consumables and records are stored in secure environments and precautions are taken to minimise risk of damage, theft or contamination.
b) There are systems to deal with emergencies on a 24 hour basis.
c) Tissues and / or cells are stored in controlled, monitored and recorded conditions that maintain tissue and / or cell integrity.
d) There is a documented, specified maximum storage period for tissues and / or cells.
PFE4 Systems are in place to protect the quality and integrity of tissues and / or cells during transport and delivery to its destination.
a) There is a system to ensure tissue and / or cells are not distributed until they meet the standards laid down by Directions 003/2010.
b) There are procedures for the transport of tissues and / or cells which reflect identified risks associated with transport.
c) There is a system to ensure that traceability of tissues and / or cells is maintained during transport.
d) Records are kept of transportation and delivery.
e) Tissues and / or cells are packaged and transported in a manner and under conditions that minimise the risk of contamination and ensure their safety and quality.
f) There are third party agreements with courier or transport companies to ensure that any specific transport conditions required are maintained.
g) Critical transport conditions required to maintain the properties of tissue and / or cells are defined and documented.
h) Packaging and containers used for transportation are validated to ensure they are fit for purpose.
i) Primary packaging containing tissues and / or cells is labelled with the information required by Directions.

j) Shipping packaging containing tissues and / or cells is labelled with the information required by Directions.
PFE5 Equipment is appropriate for use, maintained, quality assured, validated and where appropriate monitored.
a) Critical equipment and technical devices are identified, validated, regularly inspected and records are maintained.
b) Critical equipment is maintained and serviced in accordance with the manufacturer's instructions.
c) Equipment affecting critical processes and storage parameters is identified and monitored to detect malfunctions and defects and procedures are in place to take any corrective actions.
d) New and repaired equipment is validated before use and this is documented.
e) There are documented agreements with maintenance companies.
f) Cleaning, disinfection and sanitation of critical equipment is performed regularly and this is recorded.
g) Instruments and devices used for procurement are sterile, validated and regularly maintained.
h) Users have access to instructions for equipment and receive training in the use of equipment and maintenance where appropriate.
i) Staff are aware of how to report an equipment problem.
j) For each critical process, the materials, equipment and personnel are identified and documented.
k) There are contingency plans for equipment failure.

Disposal

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

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 preventive 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 preventive actions within 3-4 months of the issue of the final inspection report.

Follow up actions

A template corrective and preventive 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 preventive 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.