Site visit inspection report on compliance with HTA minimum standards

Royal Devon and Exeter Hospital

HTA licensing number 11132

Licensed for the

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

17-18 July 2018

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 Royal Devon and Exeter Hospital (the establishment) had met the majority of the HTA standards, seven shortfalls were found in relation to Consent, Governance and Quality and Premises, Facilities and Equipment.

Particular examples of strengths 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
Progenitor Cell, Haematopoietic, PBSC; PBSC	**E**	**E**	**E**	**E**			

Background to the establishment and description of inspection activities undertaken

The establishment's Haematology Unit provides adult autologous transplant services to patients located mainly in Exeter and Mid and East Devon. Inpatient transplantation takes place on the Yarty Ward, while the pre-transplant assessments take place at the outpatients department of the Haematology Unit.

In the initial medical assessment, either consultants or trained nursing staff will provide information relating to the harvesting of the stem cells. Trained nursing staff seek consent for the procurement of the peripheral blood stem cells (PBSCs), the carrying out of mandatory serology testing, and storage of the cells for a ten year period. Blood samples for the tests are taken no longer than 30 days prior to the stem cell harvest and are sent to the hospital's in-house testing laboratory.

Upon receipt at the testing laboratory, the blood samples are labelled with a unique laboratory ID and are assayed for hepatitis B surface antigen (HBsAg), hepatitis B core antigen (HBc), hepatitis C (HepC), syphilis, human T-lymphotropic virus (HTLV) and HIV antibodies. Confirmatory testing for HepB, HepC and HIV are performed in-house whilst confirmatory testing for syphilis and HTLV are carried out at two separate HTA-licensed establishments. The blood test results are uploaded onto the laboratory's electronic database which is accessible by stem cell transplant staff.

The patient's serology results are reviewed by nursing staff prior to stem cell collection taking place. On the day of harvest, the patient's blood CD34 count is checked pre-apheresis. Staff from the processing laboratory collect the PBSC units in a transport box for overnight storage

at the Blood Transfusion cold room. All units are cryopreserved the day after procurement. If required, the units are diluted with autologous plasma within a closed system prior to overnight storage. If there is insufficient autologous plasma, the units will be sent to another HTA-licensed establishment for dilution with Human Albumin Serum.

Until recently, the establishment had undertaken closed processing for the cryopreservation of stem cells. However, the establishment has temporarily outsourced the cryopreservation of stem cells to the other HTA-licensed establishment, where open processing takes place in a Grade A safety cabinet within a Grade B clean room. These units are also stored at the other HTA-licensed site until required for transplant.

The existing PBSCs stored under the establishment's licence are in two liquid nitrogen tanks set at below -150ºC in a storage room located in a separate building. The controlled-rate freezers for the cryopreservation of PBSCs are also located in this room. There is a quarantine tank available for separate storage of any units with positive serology results. The tanks are linked to a continuous temperature monitoring system which alerts staff remotely if any deviations in temperatures occur. The tanks are also fitted with alarms that sound remotely if the lids are left open for a short period of time. Staff from the processing laboratory are on a rota to manually fill the tanks to ensure the levels of liquid nitrogen are always maintained.

The inspection included a visual inspection of the Yarty ward where the apheresis machine is located and stored, storage areas for reagents and consumables used during apheresis and cell processing, the processing laboratory, the blood transfusion storage cold room, the stem cell storage facility and the testing laboratory. The inspection also included discussions with the DI, who is also the deputy laboratory manager, the CLH contact, who is also a consultant haematologist, the processing lab manager, the quality assurance co-ordinator, the senior ward nurse and key staff at the testing laboratory. Audits included a review of three sets of patient notes and processing records, where evidence of appropriate consent, serology testing, recording of consumables and traceability was checked. Minor discrepancies were found in relation to the consistency of record keeping in the processing records.

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

Consent

Standard	Inspection findings	Level of shortfall
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.		
d) Consent forms comply with the HTA's Codes of Practice.	The establishment does not assess the risk of infectious diseases based on patient's travel history and country of origin. While there is no risk to the patient, there may be implications for shared practices and storage in relation to other patients' units. The consent form does not include the patient consenting to a reduced storage time frame in the event the PBSC collection has a positive serology, in line with the establishment's storage policy.	**Minor**

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.		
b) There are procedures for all licensable activities that ensure integrity of tissue and / or cells and minimise the risk of contamination.	Written procedures are not sufficiently detailed to ensure consistency. Standard operating procedures (SOPs) do not include details of transportation of blood samples to the testing laboratory, receipt of blood samples for HTLV and HBc tests and procedures to ensure blood samples are stored appropriately and assayed within time frames as validated by the test kits. SOPs describing contingency arrangements do not include back-up plans for the failure of the Optia and the blood transfusion cold room.	**Minor**
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.	Although staff are able to describe the procedure for managing quarantine samples, there is no SOP for the handling of positive samples.	**Minor**

GQ2 There is a documented system of quality management and audit.		
d) Processes affecting the quality and safety of tissues and / or cells are validated and undergo regular evaluation to ensure they continue to achieve the intended results.	Although the time from when the cryoprotectant is added to the time when cryopreservation begins is documented, there are no defined maximum time limits that would ensure the integrity of the cells is not compromised.	**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 no procedures at the testing laboratory to report SAEARs within the required timeframe, as set out in Directions 002/2018.	**Minor**

Premises, Facilities and Equipment

Standard	**Inspection findings**	**Level of shortfall**
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.	There are no risk assessments looking at the security of the storage areas for critical consumables and reagents and the storage facility for the PBSC units.	**Minor**
PFE3 There are appropriate facilities for the storage of bodies, body parts, tissues, 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.	The reagents used for PBSC collection are stored in an unlocked cupboard on the ward. There is a high volume of traffic within the ward and no control to prevent unwanted access. Blood culture bottles used for PBSC sterility checks require storage at 2-25ºC but are stored in an unmonitored room in the pathology building.	**Minor**

Advice

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

No.	Standard	Advice
1.	C1d	The DI is advised to refer to guidance available on the European Centre of Disease Prevention and Control (ECDC) and the Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO) website to determine risks of infectious diseases based on travel history and country of origin.
2.	GQ1b	As the controlled-rate freezers are located in a separate building to the processing laboratory, the DI should ensure timers are set to alert staff when cryopreservation is complete to minimise the risk of cells not being transferred to liquid nitrogen storage within the necessary time frame.
3.	GQ1d	The DI is advised to ensure completed actions relating to change control procedures are documented. For example the validation work carried out to confirm potency of PBSCs following a recent change in cryoprotectant.
4.	GQ1r	The establishment has a contingency agreement in place with another HTA-licensed establishment for the procurement of PBSCs in the event of equipment failure. The DI should ensure the agreement sets out the responsibilities of each party for reporting annual activities, application of the Single European Code and serious adverse event and reactions (SAEARs) reporting during transport.
5.	GQ2b	As part of the establishment's ongoing release and disposal procedure, the DI is advised to incorporate a review of sample locations into their internal traceabilty audits.
6.	GQ2b	A small amount of discrepancies in record keeping in processing records were noted during internal audits. The DI is advised to ensure staff are trained to complete all the necessary boxes, and where the information is not as yet available, for example post-apheresis checks on the patient, the reasoning as to why the field is not completed is clearly set out.
7.	GQ8a	The DI is advised to include details of specific SOPs as mitigation actions in the risk assessments.
8.	PFE2b	The establishment is provided with a subset of environmental monitoring data for all open processing carried out by the other HTA-licensed establishment. The DI is advised to review this arrangement to ensure that the full extent of environmental monitoring data of cells processed at the other HTA-licensed establishment is appropriately reviewed.
9.	PFE3c	Processing staff regularly review storage temperature trends for consumables and reagents used during processing. On inspection it was noted that temperatures regularly went below the set 2-8ºC range due to staff manually changing the refrigerator temperature to compensate for the frequent opening of the doors. The DI should ensure staff do not alter the set temperatures and that the reasons behind the deviations in temperatures following the internal investigation are clearly annotated on the monitoring system.

10.	PFE4h	The stem cells are transported in temperature-monitored boxes to other HTA-licensed establishments for processing. The transport boxes are validated annually at ambient temperatures. The DI is advised to compile temperature traces as a validation to demonstrate the boxes can maintain the required 2-6ºC temperature ranges during the hottest and coldest months.
11.	PFE5c	The establishment has plans in place to install an electronic continuous temperature monitoring system in the near future for all storage facilities used for critical reagents and consumables. In the interim period, the DI is advised to test the current alarms devices.
12.	PFE5c	Although the establishment carries out closed processing, settle plates are used to monitor the effectiveness of their decontamination regime. The DI should ensure the incubator used for the settle plates is under a preventative maintenance contract and consider a second incubation at 22-25ºC to detect fungal contamination.
13.	PFE5f	The DI should ensure the cleaning of the apheresis machine carried out between each use is recorded on a log which is easily accessible to all staff as confirmation of decontamination between uses. During the inspection, the green 'I am clean' label used following weekly housekeeping was not on the machine. The DI should ensure all staff carry out procedures as per protocol.
14.	-	The DI should ensure all documents and policies refer to the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended) where appropriate, and not the Human Tissue Act 2004. References to Directions 003/2010 should also be replaced with Directions 002/2018.

Concluding comments

A number of good practices were observed during the inspection. The establishment has a robust procedure to evaluate any delay in engraftment and to take action if necessary. This includes a clearly structured investigational form that details the checks required to determine if the quality and safety of the cells were implicated in the delayed engraftment. The form takes into account checks on staff training and competency, cell count calculations, timings from removal from storage to infusion, expiry dates of consumables and reagents, temperature excursions and presentation of the product. The establishment also has in place a strong training programme for nursing staff responsible for seeking consent. New staff undergo observational training by senior nurses and are then evaluated with a series of test questions which is checked by a consultant haematologist.

There are a number of areas of practice that require improvement, which resulted in seven minor shortfalls. These are related to the absence of sufficient information in the consent form, documented procedures that reflect current practices, procedures for reporting SAEARs, procedures for handling quarantine samples, premise risk assessments, procedures for temperature monitoring and ensuring the security of critical reagents and consumables, and the absence of a defined exposure time of the cryoprotectant before cryopreservation.

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: 13 August 2018

Report returned from DI: 24 August 2018

Final report issued: 24 August 2018

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: 02 November 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
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.
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 002/2018 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.
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.
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 002/2018.
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.