



Site visit inspection report on compliance with HTA minimum standards

Leicester Royal Infirmary

HTA licensing number 11031

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

20-21 September 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 Leicester Royal Infirmary (the establishment) had met the majority of the HTA standards, eight minor shortfalls were found in relation to Governance and Quality Systems and Premises, Facilities and Equipment. The shortfalls were related to agreements, risk assessments, independent audits, temperature monitoring systems, donor exclusion criteria, Serious Adverse Event And Reaction (SAEAR) reporting procedures and documented procedures for ensuring blood samples are obtained in line with Directions 002/2018.

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	E		
Progenitor Cell, Haematopoietic, Bone Marrow; Bone Marrow	E	E	E	E	E		
Mature Cell, T Cell (DLI); DLI	E	E	E	E	E		

Background to the establishment and description of inspection activities undertaken

The establishment's Haematopoietic Progenitor Cell Transplant Programme offers adult autologous and allogeneic matched related transplant services. Unrelated donor stem cells received for transplant at the establishment are managed under an agreement with another HTA-licensed establishment.

All apheresis collections and stem cell transplantation takes place at the Clinical Haematology unit at the establishment. However, pre-transplant medical assessments can take place both at the establishment and at the haematology unit at Northampton General Hospital; patients are then referred on to the establishment for subsequent apheresis collection. During the initial medical assessment, consultants will provide information relating

to the harvesting of the stem cells and obtain consent for the procedure, mandatory serology testing and storage of the cells for a five-year period. This is followed up with a second appointment with nursing staff to ensure the patients or donors clearly understand the procedure and have an opportunity to ask any further questions.

Blood samples obtained from patients and donors are sent to an in-house testing laboratory at the establishment. The samples are assayed for hepatitis B, hepatitis C, syphilis and HIV by both automated immunoassay and nucleic acid amplification tests. Samples are subjected to plate-based assays for Human T-Lymphotropic Virus (HTLV) and hepatitis E. All confirmatory tests are performed in-house except for HTLV, which is sent to another HTA-licensed establishment for confirmation.

On the day of harvest, the patient's blood CD34 count is checked pre-apheresis at the immunology laboratory. Following the collection, stem cell laboratory staff collect the PBSC units for cryopreservation. All harvests are tested pre-cryopreservation for CD34 counts. The processing facility consists of two clean rooms – one with a Grade B background and another with a Grade C. The microbiological safety cabinets in the clean rooms maintain a Grade A environment within the respective backgrounds. Processing of high risk samples will take place within the cabinet in the Grade B clean room. All environmental monitoring is conducted in accordance with the requirements of Directions 002/2018 and Annex I of the EU Guidelines to Good Manufacturing Practice.

Any units requiring overnight storage prior to cryopreservation will be stored in a dedicated box in a temperature monitored cold room at the laboratory. If required, the units are diluted with Human Albumin Serum prior to overnight storage. If red blood cell depletion or CD34 selection is requested, the units are sent to another HTA-licensed establishment for processing.

The PBSC units are stored under the establishment's licence in ten ultra-low temperature freezers set at below -150°C in a storage room located in a separate building. The two -80°C freezers for passive freezing of the PBSCs are also located in this room. There are two empty freezers available for contingencies. Units with positive serology results are stored in separate stacks and labelled as 'high risk'. The freezers are linked to a continuous temperature monitoring system which alerts staff remotely if any deviations in temperatures occur.

The establishment also procures DLIs as starting material for Advanced Therapy (Investigational) Medical Products in a clinical trial. The clinical trial is carried out under agreements with other establishments which are regulated by the Medicines and Healthcare products Regulatory Agency (MHRA) within the UK. Staff responsible for the collection of the tissues and cells follow existing procedures at the establishment for consent, medical history assessment and timings for obtaining blood samples for mandatory serology tests.

The establishment is also HTA-licensed for storage of relevant material for use for a scheduled purpose under the Human Tissue Act 2004. Although licensed for this activity, the establishment does not currently store any relevant material.

The inspection included a visual inspection of the Clinical Haematology unit where the apheresis machine is located and stored, storage areas for reagents and consumables used during apheresis and cell processing, the stem cell storage facility, the immunology laboratory and the virology testing laboratory. The inspection also included discussions with the DI, who is also a Consultant Haematologist and Medical Programme Director, the Transplant Director, who is also the prospective DI, the Cell Processing Lead Biomedical Scientist and the Transplant Programme Quality Manager. 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. A record for a patient recruited onto the clinical trial was also reviewed. No discrepancies were found.

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

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.		
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.	Confirmatory HTLV tests is performed by a third party. Staff were unaware of this procedure and were unable to produce an agreement for this activity.	Minor
GQ2 There is a documented system of quality management and audit.		
c) An audit is conducted in an independent manner at least every two years to verify compliance with protocols and HTA standards, and any findings and corrective actions are documented.	Audits of the procedures at the Stem Cell Laboratory are performed by staff responsible for second sign-off of processing records. As such, the audits of records are not conducted in a sufficiently independent manner.	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 establishment's medical assessment does not include questions to exclude possible donors who have ingested, or had an exposure to, a substance (such as cyanide, lead, mercury, gold) that may be transmitted to recipients in a dose that could endanger their health.	Minor

<p>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.</p>	<p>Written procedures for donor serology testing are not sufficiently clear to ensure alignment with the Directions. The establishment's standard operating procedure (SOP) for obtaining blood samples state "all tests will be carried out within 30 days of collection for all HPC donors". This is not in line with Annex B of the Guide to Quality and Safety Assurance for Human Tissues and Cells for Patient Treatment which sets out that "blood samples must be taken for testing within 30 days prior to donation".</p>	<p>Minor</p>
<p>GQ6 A coding and records system facilitates traceability of bodies, body parts, tissues and cells, ensuring a robust audit trail.</p>		
<p>d) The requirements of the Single European Code are adhered to as set out in Directions 002/2018.</p>	<p>The establishment does not have documented procedures for the application of the Single European Code (SEC) Donation Identification Sequence (DIS) to starting material sent to the manufacturing facility.</p>	<p>Minor</p>
<p>GQ7 There are systems to ensure that all adverse events are investigated promptly.</p>		
<p>a) There are procedures for the identification, reporting, investigation and recording of adverse events and reactions, including documentation of any corrective or preventative actions.</p>	<p>The establishment has not outlined the procedures for SAEARs reporting for the testing and immunology laboratory to ensure reporting to the HTA takes place as set out in the "Guide to Quality and Safety Assurance for Human Tissues and Cells for Patient Treatment" which forms the Annex to Directions 002/2018.</p>	<p>Minor</p>
<p>GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately.</p>		
<p>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.</p>	<p>The establishment's risk assessments are not all reviewed annually to identify new risks or to consider operational changes that may affect licensable activities.</p>	<p>Minor</p>

Premises, Facilities and Equipment

Standard	Inspection findings	Level of shortfall
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.	<p>The establishment does not have systems in place to ensure temperature sensitive consumables and reagents are stored within appropriate temperature ranges. For example:</p> <ul style="list-style-type: none"> the cryoprotectant used in processing is not stored within the 20-30°C temperature range as recommended by the manufacturer. apheresis kits are not stored in a temperature monitored room. 	Minor

Advice

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

No.	Standard	Advice
1.	GQ1d	The establishment is currently migrating to an electronic document management system. The DI should ensure any hard copies of documents in circulation are appropriately controlled.
2.	GQ1d	The DI should include in SOPs for stem cell processing the list of consumables and reagents required for preparation and transfer into the clean room. The list is currently printed out on a separate laminated card which is not controlled.
3.	GQ2b	The DI is advised to review all SOPs to remove references to control rate freezing procedure previously carried out in the laboratory, following a move to a passive freezing protocol.
4.	GQ2b	The DI should ensure the Quality Manual is updated to remove references to previously licensed import and export activities.
5.	GQ2b	The establishment's findings following internal audits are discussed at the establishment's Quarterly Standards meetings and any actions are taken forward by consultants. The DI should ensure staff responsible for the follow-up actions and the steps taken to address the findings are clearly documented to show completion of actions.
6.	GQ2d	The establishment currently carries out manual trypan blue assays to assess the viability of every unit one week post-cryopreservation. The DI is advised to consider a review of this arrangement to ensure that the ongoing quality

		programme also evaluates other criteria quality criteria such as CD34 counts and potency, and consideration given to units that have been stored for longer periods time
7.	GQ7a	The DI should ensure all adverse incidents that occur at the immunology and testing laboratory that may impact HTA-licensed activities are escalated to appropriate staff members at the Stem Cell Laboratory. Incidents could include, for example, assay kits stored temporarily above the recommended temperature range or a recall of kits by the manufacturer. This will help the DI ensure that the appropriate corrective and preventative actions have been taken in response to any given incident.
8.	GQ8a	The DI is advised to review the format of risk assessments to ensure that there are control measures in place for each discrete activity. The current approach of embedded mitigating steps into SOPs and not reproducing those in separate risk assessments does not facilitate the review the process.
9.	PFE2b	The DI is advised to incorporate into their ongoing environmental monitoring programme swabbing of hatches and heat sealers to check that the cleaning is effective.
10.	-	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.

Concluding comments

There are a number of areas of practice that require improvement resulting in eight minor shortfalls. These relate to the procedures to ensure all agreements are available and recorded, exclusion of donors in line with the criteria set out in Directions 002/2018, donor testing timings, SAEAR reporting, reviewing of risk assessments, application of the SEC, independent audits and temperature monitoring systems. The HTA has given advice to the Designated Individual with respect to updating documents, document control, SAEAR reporting procedures and ongoing procedures to evaluate the quality of cryopreserved stem cells.

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 October 2018

Report returned from DI: 23 October 2018

Final report issued: 1 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
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 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.
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.
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.