Site visit inspection report on compliance with HTA minimum standards

Queen's Medical Centre

HTA licensing number 11035

Licensed for the

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

15-16 February 2017

Summary of inspection findings

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

Although the HTA found that Queen's Medical Centre, (the establishment) had met the majority of the HTA standards, shortfalls were found, particularly in relation to governance and quality systems. The shortfalls relate to the establishment's independent audit and donor selection criteria.

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	Testing	Storage	Distribution
Femoral Head	**E**	**TPA**	**E**	**E**
Rib	**E**	**TPA**	**E**	**E**
Tendons and Ligaments			**E**	
Struts			**E**	
Amniotic Membrane			**E**	
Limbal Stem Cells	**E***			

Background to the establishment and description of inspection activities undertaken

Queen's Medical Centre Hospital (the hub) is one of three hospitals where licensable activities take place. The activities covered under the licence are procurement, donor testing, storage and distribution of human tissues and cells under the Human Tissue (Quality and Safety for Human Application) Regulations 2007. There are two further hospital sites, which are satellite sites to the hub. The satellites are City Hospital, Nottingham and Nottingham Woodthorpe Hospital. The majority of licensable activities under this license relate to femoral heads procured from patients undergoing elective hip replacement surgery. More recently, the range of activities under this licence has expanded to include other tissue types and the bone bank has become a tissue bank.

Donor selection, consenting and procurement of femoral heads takes place at the satellites (the hub does not procure femoral heads). At the satellites, all patients scheduled for a hip replacement operation are given an information sheet concerning bone donation during the pre-operative assessment visit. The pre-assessment nurses identify potential donors and the implications of bone donation are explained. If the patient agrees to donate their femoral head, the pre- assessment nurses seek consent, take past medical history including travel history and assess overall fitness for the surgery.

At Nottingham Woodthorpe hospital, blood samples for the mandatory serological testing are taken from the donor on the day of the pre-assessment visit. At City Hospital, blood samples for the mandatory serological testing are taken, by the anaesthetist, on the day of the surgery. In addition to the serological testing, theatre staff take a swab and a small bone sample for sterility testing. Donor testing for all mandatory serology markers and microbiological testing of tissues is carried out by the East Midlands Pathology Services laboratory at Queen's Medical Centre. The establishment has a third party agreement (TPA) with this laboratory.

On the day of the procurement, the femoral head is placed in an inner sterile bag, which is, in turn, placed in a sterile tamper evident screw capped pot. The patient identity sticker with a unique identification number is affixed to the outside of the pot, which is then placed in an outer, non-sterile plastic bag. The collection pots along with the sterile inner bags, unique bone bank number and related labels are provided by the designated individual (DI) at the hub.

Following procurement, femoral heads may be stored in a −80 ^{o}C freezer at the satellites, prior to transfer to the hub by either Trust transport or a courier. Validated transport boxes ensure the femoral heads remain frozen for up to a period of four hours.

All femoral heads, awaiting initial serology tests, prior to being placed in the −80 ^{o}C quarantine freezer of the bone bank, are weighed and details of each procurement are entered into the bone bank register and an electronic database. The establishment also determines the Rhesus status of all donors, in the event a femoral head is used in recipients of childbearing age.

Once the initial serology and microbiology tests are confirmed to be negative, femoral heads are moved from the quarantine freezer to the bottom half of a second −80 ^{o}C freezer and the bone bank register and electronic database are updated. Any samples with a positive result are disposed of according to the Trust's disposal policy.

The DI or the research technician, who deputises for the tissue bank at the hub, contact all donors after 180 days to arrange for the repeat mandatory serological testing and arrange either to collect a blood sample at the hub or the satellites during their 6 month post-surgery review. On occasion, a home visit or collection of bloods from the GP is arranged. Once all the test results are reviewed, and if all results are negative, the femoral heads are moved to the top half, the “ready for release” section of the second freezer and the “ready for use” sticker is affixed to the pot. The bone bank register and electronic spreadsheet are also updated accordingly. More recently, the additional use of a smaller −80 ^{o}C freezer, within theatres at the hub, allows clinical staff to access ready for release femoral heads for trauma surgery.

Occasionally the establishment procures ribs for autologous use. These are stored on a separate shelf in the -80°C quarantine freezer and records are maintained in a separate register. The same set of serology testing is performed, as for allogeneic bone. If the tissue is required for end use before 180 days, then the consultant surgeon will be asked to sign a disclaimer to indicate that nucleic acid amplification technique (NAT) testing has not been performed, as the laboratory does not undertake NAT testing. The surgeon will take full responsibility for the use of the tissue.

The hub also stores tendons and ligaments stored in a separate section of the second freezer. Amniotic membrane is stored at the establishment for ocular surgery and it is purchased from another licenced tissue supplier. The establishment maintains traceability records for every tissue used in patients by recording: the size and tissue code, patient identity, date of order, fate of tissue, surgeon involved in operation and the product label is affixed against this information.

In preparation to participate in a multi-centre clinical trial to assess the efficacy of autologous cultivated limbal stem cell transplantation in patients with ocular burns, the establishment has recently added limbal stem cells to its licence. Donor selection, consent and procurement will be undertaken by the establishment. The procured tissue sample will be distributed to another site for processing into an Advanced Therapy Medicinal Product (ATMP). Distribution to the other site and serology testing is not taking place under the establishment’s licence and will be the responsibility of the manufacturer. Once processed into an ATMP, which will occur under the authority of a Medicines and Healthcare products Regulatory Agency (MHRA) licence, the ATMP will be returned for autologous administration into the trial participant.

The establishment has been licensed by the HTA since January 2007. This report describes the establishment’s fifth routine inspection, which took place over two days on the 15-16 February 2017. Discussions were held with the Designated Individual (DI), the research technician at the hub, the pre-assessment nurse at Nottingham City Hospital and the team leader for ophthalmology theatres during the visual inspection. A review of documentation relevant to the establishment’s licensable activities and a visual inspection of the areas of the establishment where tissue storage and serology testing take place were also undertaken as part of the inspection.

Audits of traceability were carried out and included storage locations of one strut and of three femoral heads, at both the quarantine and the “ready for release” freezers, cross-checked

against the bone bank register. As part of the traceability audit the patient files of the three femoral heads were reviewed along with another four donor and recipient files, to ensure that they contained all the relevant documentation, including serology and microbiology test results. There were a few inconsistencies in the completion of the consent forms (see advice below).

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
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.	Although internal audits are conducted that cover the range of activities carried out under the licence, there is currently no independent audit against HTA standards. (See Advice item 5 below)	**Minor**
GQ5 There are documented procedures for donor selection and exclusion, including donor criteria.		
a) Donors are selected either by the establishment or the third party acting on its behalf in accordance with the criteria required by Directions 003/2010.	The establishment has documented procedures for donor selection and exclusion. These do not include all of the donor exclusion criteria as set out in Annex A of the Guide to Quality and Safety Assurance for Human Tissues and Cells for Patient Treatment. For example, the medical history and donor information leaflet form 1.0 do not include questions regarding “Ingestion of, or exposure to, a substance (such as cyanide, lead, mercury, gold) that may be transmitted to recipients in a dose that could endanger their health” or give consideration to the possibility the donor may have undergone “transplantation with xenografts”	**Minor**

Advice

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

No.	Standard	Advice
1.	C1a	The DI is advised to reference all the mandatory serology tests to be performed on the donors on the patient information sheet and the consent form for the limbal stem cell clinical trial. The DI should consider including provisions on the patient information sheet and consent form on how the participants will be informed and advised on future implications of positive test results and whether this may result in their exclusion from the clinical trial.
2.	C1d	A number of discrepancies were noted during the audit of the establishment's donor details forms. Examples include: • the white and blue copy of the consent form was not always dated • the date the first mandatory serology bloods were obtained and the test results returned, were not always completed. The DI is advised to review the records as part of the release procedure of femoral heads to ensure everything is corrected and all the information is available. The DI is also advised to review the content of the forms to ensure there is no duplication of information.
3.	GQ1d	The DI is advised to review the standard operating procedures (SOPs) to reflect current practices and references. Examples of these include, but are not limited to: • The SOP for retrieval of autologous rib states that if the tissue is required for use before 180 days then NAT testing is performed. Current practice is for the consultant surgeon to sign a disclaimer taking full responsibility for use of the tissue, as NAT testing is not performed by the laboratory. • The SOP detailing the storage of autologous graft cites compartment 5D of the quarantine freezer. The DI is advised to update the SOP with the current compartment of the quarantine freezer where autologous graft are stored, as detailed in the freezer plan. The DI is also advised to review the wording of the SOP detailing the procedure for carrying out internal audits. This SOP makes reference to the HTA carrying out an external audit of the establishment. The HTA inspection does not fulfil the requirement for an independent audit every two years.
4.	GQ1r	The DI is advised to review the wording on Serious Adverse Events or Serious Reactions (SAEARS) contained within agreements, to be reported to the establishment within 24hrs of discovery instead of as soon as observed, as this may be subject to different interpretations.
5.	GQ2c	The DI is advised to schedule the independent audit to occur in the intervening year between HTA inspections.
6.	GQ4k	The Nottingham bone bank collects any documentation related to the tissue from procurement to end use and keeps it for the required 30 years. The DI is advised to review the wording of sections of the End User agreements to ensure the information needed to fulfil this requirement is included within the agreements.

7.	GQ8	The DI is advised to review the risk assessment on the release of bone for therapeutic use, as it does not consider the release of Rhesus negative femoral heads.

Concluding comments

The HTA observed a number of good practices during the course of the inspection. Overall, the hub and satellites have effective systems of communication with frequent meetings across the establishment. Oversight and access to the quarantine and release freezers at the establishment is limited to the DI and the research technician. In circumstances of medical emergency, where a Rhesus negative bone may be urgently required, clinical staff have access to the small freezer within theatres. The establishment undertakes annual validation of the temperature of the transportation boxes and calibration of the temperature loggers and compares the data acquired to the data first obtained in 2010. This ensures that there are no temperature excursions over the years that may negatively affect the femoral heads during transport.

Two areas of practice were identified during the inspection that require improvement, each resulting in minor shortfalls. The establishment is committed to continuous service improvement and prior to the end of the inspection, the DI amended the donor information leaflets to include all the donor exclusion criteria as required in Annex A of the Guide to Quality and Safety Assurance for Human Tissues and Cells for Patient Treatment. The HTA has also given advice to the DI with respect to updating the SOPs and a risk assessment, reviewing the wording of sections of agreements and amending the patient information sheet and consent form for the limbal stem cell clinical trial.

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 / subject to compliance with the additional conditions applied to the licence.

Report sent to DI for factual accuracy: 14/03/ 2017

Report returned from DI: 16/03/ 2017

Final report issued: 24/03/ 2017

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: 18 July 2017

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.
n) The establishment ensures imports from non EEA states meet the standards of quality and safety set out in Directions 003/2010.
o) There is a complaints system in place.
p) There are written agreements with third parties whenever an activity takes place that has the potential to influence the quality and safety of human tissues and / or cells.
q) There is a record of agreements established with third parties.
r) Third party agreements specify the responsibilities of the third party and meet the requirements set out in Directions 003/2010.

s) Third party agreements specify that the third party will inform the establishment in the event of a serious adverse reaction or event.
t) There are procedures for the re-provision of service in an emergency.
GQ2 There is a documented system of quality management and audit.
a) There is a quality management system which ensures continuous and systematic improvement.
b) There is an internal audit system for all licensable activities.
c) An audit is conducted in an independent manner at least every two years to verify compliance with protocols and HTA standards, and any findings and corrective actions are documented.
d) Processes affecting the quality and safety of tissues and / or cells are validated and undergo regular evaluation to ensure they continue to achieve the intended results.
GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills.
a) There are clearly documented job descriptions for all staff.
b) There are orientation and induction programmes for new staff.
c) There are continuous professional development (CPD) plans for staff and attendance at training is recorded.
d) There is annual documented mandatory training (e.g. health and safety and fire).
e) Personnel are trained in all tasks relevant to their work and their competence is recorded.
f) There is a documented training programme that ensures that staff have adequate knowledge of the scientific and ethical principles relevant to their work, and the regulatory context.
g) There is a documented training programme that ensures that staff understand the organisational structure and the quality systems used within the establishment.
h) There is a system of staff appraisal.
i) Where appropriate, staff are registered with a professional or statutory body.
j) There are training and reference manuals available.
k) The establishment is sufficiently staffed to carry out its activities.
GQ4 There is a systematic and planned approach to the management of records.
a) There are procedures for the creation, identification, maintenance, access, amendment, retention and destruction of records.
b) There is a system for the regular audit of records and their content to check for completeness, legibility and accuracy and to resolve any discrepancies found.
c) Written records are legible and indelible. Records kept in other formats such as computerised records are stored on a validated system.
d) There is a system for back-up / recovery in the event of loss of computerised records.

e) The establishment keeps a register of the types and quantities of tissues and / or cells that are procured, tested, preserved, processed, stored and distributed or otherwise disposed of, and on the origin and destination of tissues and cells intended for human application.
f) There are procedures to ensure that donor documentation, as specified by Directions 003/2010, is collected and maintained.
g) There is a system to ensure records are secure and that donor confidentiality is maintained in accordance with Directions 003/2010.
h) Raw data which are critical to the safety and quality of tissues and cells are kept for 10 years after the use, expiry date or disposal of tissues and / or cells.
i) The minimum data to ensure traceability from donor to recipient as required by Directions 003/2010 are kept for 30 years after the use, expiry or disposal of tissues and / or cells.
j) Records are kept of products and material coming into contact with the tissues and / or cells.
k) There are documented agreements with end users to ensure they record and store the data required by Directions 003/2010.
l) The establishment records the acceptance or rejection of tissue and / or cells that it receives and in the case of rejection why this rejection occurred.
m) In the event of termination of activities of the establishment a contingency plan to ensure records of traceability are maintained for 10 or 30 years as required.
GQ5 There are documented procedures for donor selection and exclusion, including donor criteria.
a) Donors are selected either by the establishment or the third party acting on its behalf in accordance with the criteria required by Directions 003/2010.
b) The testing of donors by the establishment or a third party on behalf of the establishment is carried out in accordance with the requirements of Directions 003/2010.
c) In cases other than autologous donors, donor selection is carried out by authorised personnel and signed and reviewed by a qualified health professional.
d) There is a system in place either at the establishment or at a third party acting on its behalf to record results of donor selection and associated tests.
e) Testing of donor samples is carried out using CE marked diagnostic tests.
f) Samples taken for donor testing are clearly labelled with the time and place the sample was taken and a unique donor identification code.
GQ6 A coding and records system facilitates traceability of tissues and / or cells, ensuring a robust audit trail.
a) There is a donor identification system which assigns a unique code to each donation and to each of the products associated with it.
b) An audit trail is maintained, which includes details of when the tissues and / or cells were acquired and from where, the uses to which the tissues and / or cells were put, when the tissues and / or cells were transferred elsewhere and to whom.

c) The establishment has procedures to ensure that tissues and / or cells imported, procured, processed, stored, distributed and exported are traceable from donor to recipient and vice versa.
GQ7 There are systems to ensure that all adverse events, reactions and/or incidents are investigated promptly.
a) There are procedures for the identification, reporting, investigation and recording of adverse events and reactions, including documentation of any corrective or preventative actions.
b) There is a system to receive and distribute national and local information (e.g. HTA regulatory alerts) and notify the HTA and other establishments as necessary of serious adverse events or reactions.
c) The responsibilities of personnel investigating adverse events and reactions are clearly defined.
d) There are procedures to identify and decide the fate of tissues and / or cells affected by an adverse event, reaction or deviation from the required quality and safety standards.
e) In the event of a recall, there are personnel authorised within the establishment to assess the need for a recall and if appropriate initiate and coordinate a recall.
f) There is an effective, documented recall procedure which includes a description of responsibilities and actions to be taken in the event of a recall including notification of the HTA and pre-defined times in which actions must be taken.
g) Establishments distributing tissue and / or cells provide information to end users on how to report a serious adverse event or reaction and have agreements with them specifying that they will report these events or reactions.
h) Establishments distributing tissues and / or cells have systems to receive notifications of serious adverse events and reactions from end users and notify the HTA.
GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately.
a) There are documented risk assessments for all practices and processes.
b) Risk assessments are reviewed regularly, as a minimum annually or when any changes are made that may affect the quality and safety of tissues and cells.
c) Staff can access risk assessments and are made aware of local hazards at training.
d) A documented risk assessment is carried out to decide the fate of any tissue and / or cells stored prior to the introduction of a new donor selection criteria or a new processing step, which enhances the quality and safety of tissue and / or cells.

Premises, Facilities and Equipment

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

d) Where appropriate, there are procedures to ensure that the premises are of a standard that ensures the dignity of deceased persons.
e) There are procedures to ensure that the premises are secure and confidentiality is maintained.
f) There is access to a nominated, registered medical practitioner and / or a scientific advisor to provide advice and oversee the establishment's medical and scientific activities.
PFE2 Environmental controls are in place to avoid potential contamination.
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 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.