Site visit inspection report on compliance with HTA minimum standards

NHSBT Liverpool

HTA licensing number 11018

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

17 and 18 June 2014

Summary of inspection findings

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

NHSBT Liverpool (the establishment) was found to have met all HTA standards.

NHSBT Liverpool tissue services is the largest tissue bank in the UK. The establishment procures, processes, stores and distributes a wide range of tissues and cells from living and deceased donors. At the time of the inspection, there were no shortfalls on the licence as the establishment had addressed two shortfalls identified during the previous inspection, relating to its oversight of the radiation sterilisation service provided by a third party.

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.

'SLA' = Service Level Agreement; the establishment is licensed for this activity but another establishment (licensed) carries out the activity on their behalf.

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

'N/A' = Not applicable

Tissue type	Procurement	Processing	Testing	Storage	Distribution	Import	Export
Peripheral blood stem cells	**TPA**	**E**	**SLA**	**E**	**E**		
Umbilical cord blood	**TPA**	**E**	**SLA**	**E**	**E**		
Bone Marrow	**TPA**	**E**	**SLA**	**E**	**E**		
Donor lymphocyte infusion	**TPA**	**E**	**SLA**	**E**	**E**		
Bone	**E**	**E**	**SLA**	**E**	**E**		
De-mineralised bone	**N/A**	**E**	**SLA**	**E**	**E**		
Whole skin	**E**	**E**	**SLA**	**E**	**E**		

Heart valves and vessels	**E**	**E**	**SLA**	**E**	**E**		
Pericardium	**E**	**E**	**SLA**	**E**	**E**		
Amniotic membrane	**TPA**	**E**	**SLA**	**E**	**E**		
Cornea and Sclera			**SLA**		**E**		
Tendons / ligaments	**E**	**E**	**SLA**	**E**	**E**		

Background to the establishment and description of inspection activities undertaken

NHSBT Liverpool (the establishment). is licensed for procurement, processing, testing, storage and distribution of human tissue and cells for human application under the Human Tissue (Quality and Safety for Human Application) Regulations 2007. The corporate licence holder NHSBT is a Special Health Authority in England and Wales. The establishment is also licensed under the Human Tissue Act (2004) for the storage of relevant material for the scheduled purpose of research.

The establishment distributes fresh frozen tissue, decontaminated tissue, terminally sterilised tissue, freeze dried tissues and stem cell and immunotherapies to clinical users in the UK. The range of tissues include fresh frozen femoral heads, bone, tendons, heart valves, non-valve conduits, meniscus, skin, amnion, pericardium and demineralised bone (DBM) paste and putty.

The Liverpool Speke site houses the National Referral Centre staffed by nursing staff who take consent for tissue donation, a clean room suite consisting of 14 clean rooms, freezer room, cryopreservation area, and a dedicated retrieval suite where tissues are removed from the deceased. The Stem Cell Immunotherapies (SCI) service processes, stores and distributes haematopoetic stem cells in the form of peripheral blood stem cells, umbilical cord blood, donor lymphocyte infusions and bone marrow. The Quality Assurance team schedules audits, oversees quality control and sign off products for release and distribution. Hospital services package and issue all tissue products to end-users. The customer care team takes orders, collects patient outcome data relating to products supplied by NHSBT, and is the initial point of contact for complaints and any adverse events and reactions relating to those products. The team escalates adverse events and reactions as appropriate, to the lead clinician so that they can be investigated internally and reported to the HTA.

Each week staff review the inventory of products and seek consent from families for donation of specific types of tissues depending on whether or not sufficient tissue is available for distribution. Nurses access the organ donor register and seek consent for tissue donation from relatives of deceased organ and tissue donors. They also seek consent for donation of eyes, athough NHSBT is not currently involved in processing ocular tissue which takes place at Corneal Transplant Service eyebanks. Consent for donation of tissues from living donors is usually sought by the relevant clinician/nursing staff based at the respective hospital.

Tissue Services Donation teams visit hospitals and other sites to procure tissues from the deceased and also manage over 25 satellite sites which procure surplus bone during hip replacement surgery. Tissues from the living such as cord blood and placenta are also collected at hospitals. Theatre staff at the hospitals where procurement takes place receive training from NHSBT Liverpool staff.

All donors are anonymized. Consent documentation, donor assessment and donor test results are filed together in a donor file. Donor testing is undertaken at other HTA licensed sites. Donors are 'approved' by medical staff before tissues donated by them can be cleared for release. Each tissue product type has relevant quality control parameters (including as appropriate, processing records, environmental monitoring records, expiry dates of consummables, pre and post sterility data, sterilisation certificates, *etc*) which which are checked before the tissue product is authorised for release by the Quality Assurance department.

A proprietary pharmaceutical monitoring system continuously monitors the premises including the clean room suite, fridges, freezers and liquid nitrogen storage tanks. Data from this system is stored and backed up. Relevant parameters such as temperature, air pressure and particulates in the clean room during each processing episode are reviewed before the batch records relating to each tissue product is authorised for release. An external maintenance provider validates the clean room suite and the Class II microbiological cabinets. Tissue products are stored as appropriate, in -80^{0}C freezers, ultra low freezers (at -150^{0}C), in the vapour phase of liquid nitrogen or at room temperature, before they are issued.

Tissues are terminally sterilised by another establishment under a third party agreement. Tissues are exposed to an irradiation dose of between 25kGy - 45kGy which meets the recommended dose for bacterial sterilisation (International Atomic Energy Agency international standards 2002). Production staff follow validated protocols. The protocols for packing different types of tissues which are sent away to be terminally sterilised were recently reviewed. Sterilisation indicators are attached to each package containing tissue and a sterilisation certificate is issued for each batch of irradiated tissue products.

The establishment has a policy which covers the testing of tissue for bacteria and fungi and their acceptability for clinical use. The screening strategy for acceptance and rejection of tissues includes bioburden determination and depending on the product type, detection of specific microorganisms and sterility check of the final product. The policy takes into account whether or not tissues are terminally sterilised by irradiation and whether the organisms detected are pathogenic organisms. Representative tissue samples are also taken before and after the tissue is exposed to decontaminating agents in order to evaluate the effectiveness of the decontamination step.

The Research and Development team works closely with the production unit to develop new products and validate new processes. A battery of tests are used to evaluate new products in development including biomechanical properties, sterility, in vitro cytotoxicity, residual water and histology. In the case of DBM products, a sample from each batch is sent to a laboratory for intra muscular implant osteoinduction assay in mice.

A site visit inspection of the Liverpool Speke site of NHSBT, was undertaken on 17 and 18 June 2014. This was the fourth site visit inspection of the establishment. This inspection did not cover satellite sites where procurement of bone from living donors takes place, as the HTA undertakes separate inspections of these satellite sites. The previous inspection of the Liverpool Speke site which took place in June 2012, reviewed processing of cardiovascular tissue, skin and bone. The timetable for this inspection included a visual inspection of the site, observation of bone, and DBM processing in the respective clean rooms and interviews with members of staff. Interviews were held with the Assistant Director,Quality (DI), General Manager, Tissue Services, Lead Consultant, Quality Assurance Manager, Research and Development Manager, Lead Quality Specialist, Tissue Bank Manager, Regional Tissue Donation Manager, staff in Customer Care and Hospital Services and members of staff

undertaking processing and research and development.The inspection team did not interview staff involved in processing stem cell products or heart valves, pericardium or amnion, but focused on the processing of DBM products and dCELL.

A document review was carried out. Documents reviewed included a selection of policies as well as SOPs relating to processing of bone products, operation of an automated bone grinder, processing cortical bone into DBM powder, paste and putty, preparation of dCELL dermis, cleaning of the clean room suite, change control and validation, reporting and managing adverse events, the protocol for handling returned tissues and the packaging details for sending tissues for sterilisation by gamma irradiation. The following third party agreements were reviewed; agreements with sites where procurement of amniotic membrane (placental tissue) takes place, agreement with the transport provider and agreement with the facility where terminal sterilisation takes place. The end user agreements between NHSBT and endusers were also reviewed. Audit trails were undertaken of records relating to freeze dried DBM paste 10cc, frozen irradiated ulna, frozen irradiated whole shapted patella, cryopreserved skin (in quarantine and ready to be issued) frozen amnion, freeze dried cortical strut and processed peripheral blood stem cells. The records reviewed included (as appropriate) storage location, donor files containing medical authorisation, consent form, core donor data form, patient assessment form, site risk assessment, body map, donor test results, GP information and additional tests including testing for Creutzfeldt-Jakob disease (CJD). Processing records which are authorised by staff in the quality assurance team such as records relating to consummables including expiry dates, sterilisation records for re-usable equipment, environmental monitoring data relating to processing episodes, bacteriology test results (pre and post decontamination), controlled rate freezer traces were also reviewed. No discrepancies were noted, apart from a minor oversight where an entry relating to a sterilisation record was duplicated.

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

All applicable HTA standards have been assessed as fully met.

Advice

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

No.	Standard	Advice
1.	GQ1	The establishment has identified the need for closer interaction between the customer care team and teams responsible for reviewing adverse events and reactions and complaints in order to ensure that they are escalated as appropriate. Customer care staff have received training and the DI is advised to ensure that the new procedures are documented as soon as possible.
2.	GQ2	NHSBT provides the HTA with Preparation Process Dossiers (PPD) which cover existing processes as well as new processes. NHSBT inform the HTA when there are any changes to these processes including like for like changes to consumables and equipment. The DI is advised to use the review stage within the two stage change control system in NHSBT when deciding whether or not to inform the HTA of changes to procedures. The criterion for informing the HTA of changes is whether or not the change has the potential to impact on the quality

		and safety of the tissue product. The DI is advised to consider periodic overarching product reviews which capture the wealth of data including patient outcomes, customer feedback, complaints, adverse events and reactions and processing data in order to determine the need for any adjustments to product specifications, processing methods, packaging of tissues for terminal sterilisation and other relevant control parameters. Such reviews will help to prevent any drift to processing methods in relation to primary validation studies and ensure that products continue to achieve the intended results. The reviews will also provide assurance of the quality of tissue products processed and distributed by NHSBT to current and potential customers. The review could also be extended to include the effectiveness of the 'Cambridge cocktail' which is used to decontaminate cardiovascular tissues and tendons.
3.	N/A	The DI is advised to consider providing advice to customers who request tissues and cells from NHSBT on the requirement of an HTA licence if the customer intends to store tissue products containing cells for more than 48 hours.

Concluding comments

All activities undertaken by NHSBT are underpinned by a strong ethical framework and technical expertise. There are effective working relationships between staff in each of the areas. The weekly review of the inventory means that families are not needlessly approached following a bereavement if sufficient amount of tissue is available to be issued. The consent form used by NHSBT is regarded as a model consent form and meets the HTA's standards.

The strong Research and Development team undertakes early stage research and develops new tissue products with input from production staff and external partners. There are effective systems in place to validate products, which is further evidenced by publication of validation studies which cover several NHSBT processes in peer reviewed international journals. This provides assurance that products supplied by NHSBT have been through a robust validation process.

The system of change control ensures that any changes to procedures are reviewed, and if necessary, validated before they are implemented. The continuous monitoring of the facilities including the clean room suite, provides assurance that once tissues enter the NHSBT site at Liverpool, all downstream processing and storage takes place in a monitored environment.

The HTA inspection team was impressed by the professionalism and dedication shown by staff at the establishment, and their commitment to continuous improvement.

The HTA has given advice to the Designated Individual with respect to informing the HTA of any changes to preparation processes and periodic reviews of products in order to ensure that they achieve the intended results.

The HTA has assessed the establishment as suitable to be licensed for the activities specified.

Report sent to DI for factual accuracy: 15 July 2014

Report returned from DI: 18 July 2014

Final report issued: 28 July 2014

Appendix 1: HTA standards

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

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

Consent

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

Governance and Quality

Standard
GQ1 All aspects of the establishment's work are supported by ratified documented policies and procedures as part of the overall governance process.
a) There is an organisational chart clearly defining the lines of accountability and reporting relationships.
b) There are procedures for all licensable activities that ensure integrity of tissue and / or cells and minimise the risk of contamination.
c) There are regular governance meetings, for example health and safety, risk management and clinical governance committees, which are recorded by agendas and minutes.
d) There is a document control system to ensure that changes to documents are reviewed, approved, dated and documented by an authorised person and only current documents are in use.
e) There are procedures for tissue and / or cell procurement, which ensure the safety of living donors.
f) There are procedures for tissue and / or cell procurement, which ensure the dignity of deceased donors.
g) There are procedures to ensure that an authorised person verifies that tissues and / or cells received by the establishment meet required specifications.
h) There are procedures for the management and quarantine of non-conforming consignments or those with incomplete test results, to ensure no risk of cross contamination.
i) There are procedures to ensure tissues and / or cells are not released from quarantine until verification has been completed and recorded.
j) There are procedures detailing the critical materials and reagents used and where applicable, materials and reagents meet the standards laid down by the European directives on medical devices and in vitro diagnostic medical devices.
k) There is a procedure for handling returned products.
l) There are procedures to ensure that in the event of termination of activities for whatever reason, stored tissues and / or cells are transferred to another licensed establishment or establishments.
m) The criteria for allocating tissues and / or cells to patients and health care institutions are documented and made available to these parties on request.
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.