Site visit inspection report on compliance with HTA minimum standards

Queen Elizabeth Hospital Birmingham

HTA licensing number 11100

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 (as amended); and**

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

5 – 7 February 2019

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 Queen Elizabeth Hospital Birmingham (the establishment) had met the majority of the HTA standards, six minor shortfalls were found in relation to the Consent (C) standards, Governance and Quality Systems (GQS) standards and the Premises, Facilities and Equipment (PFE) standards. The shortfalls related to the donor selection criteria, third party agreements, retention of raw data for ten years, the Single European Code (SEC), risk assessments and the monitoring of critical equipment.

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
Cardiovascular, Vessels; Vessels (Including Illiac)			**E**	**E**	**E**		
Mature Cell, T Cell (DLI); DLI	**E**		**E**				
Musculoskeletal, Bone; Bone				**E**			
Musculoskeletal, Tendon & Ligament				**E**			
Other; Nerve				**E**			
Progenitor Cell, Haematopoietic, PBSC; PBSC	**E**		**E**				
Progenitor Cell, Hematopoietic, Unspecified; Peripheral Blood Mononuclear Cells (PBMC)	**E**		**E**				
Skin; skin	**E**		**E**	**E**			

Background to the establishment and description of inspection activities undertaken

This report refers to the activities carried out by Queen Elizabeth Hospital Birmingham (the establishment). The establishment was issued a HTA licence in July 2006. Queen Elizabeth

Hospital Birmingham is part of University Hospitals Birmingham NHS Foundation Trust (FT). Since the last inspection, a new Designated Individual (DI) has been appointed.

The establishment is licensed under the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended; the Q&S Regulations) for the procurement, testing, storage and distribution of tissues and cells for human application. The establishment is also licensed for the storage of relevant material for use for a scheduled purpose under the Human Tissue Act 2004 (HT Act). Although licensed for this activity, the establishment does not currently store relevant material for use for a scheduled purpose. The organisation is also accredited by the Joint Accreditation Committee - European Society for Blood and Marrow Transplantation (EBMT) and the International Society for Cellular Therapy (ISCT) (JACIE) and was last inspected as part of its ongoing accreditation in April 2017.

The DI is a Consultant Pathologist; the Corporate LH (CLH) is University Hospitals Birmingham NHS FT, and the CLH Contact (CLHC) is the Director of Operations in the Division containing Clinical Laboratory Services (CLS). There are ten Persons Designated (PDs) on the licence: a Consultant Burns and Plastics Surgeon, three members of the Liver Unit Theatre Team, two members of the Trauma Theatre Team, two members of the Bone Marrow Transplant/Apheresis Team, a Biomedical Scientist (BMS) within the testing laboratory, and the Tissue Services Operations Manager.

Licensed activities at the establishment relate to a wide range of tissue and cell types, as shown in the table above.

Cryopreserved skin, bone, ligaments and nerve allografts

The establishment stores cryopreserved bone, tendons, peripheral nerves and split skin from cadaveric donors. The tissue is purchased from three HTA-licensed suppliers under the terms of written agreements. The suppliers are responsible for donor selection, consent, procurement, serological testing and transportation.

The allografts are received into the Tissue Services Department by authorised personnel. All allograft details are entered onto a requisitions and deliveries file, and paper copies of dispatch sheets are kept separately. The details from the requisitions and deliveries file, including the unique graft number and SEC, are transferred onto a Tissue Services database and a spreadsheet, which are backed-up as part of the Trust Information Technology (IT) system.

All allograft products are stored securely at -80°C in labelled, lockable ‘tissue bank’ freezers (bone and tendon allografts within the Clinical Room, Burns Centre and cryopreserved skin and nerve grafts within the Medication 2 room). The freezer plugs are labelled with a sign stating ‘Do not unplug’. Non-conforming units are stored on separate freezer shelves. The freezers are linked to the continuous temperature-monitoring unit. Arrangements are in place for service, calibration and contingency. Printed ‘Tissue Record Forms’ listing the inventory contained within the freezers are attached to the freezer doors. The inventory is checked every morning (Monday – Friday) by Tissue Services.

When required for engraftment, allograft products are removed by two trained and competent staff and taken to the operating theatres for thawing before use. The date/time of removal, recipient patient number, theatre number and the names of the staff removing the products are documented on the printed ‘Tissue Record Form’. This information is transferred to the Tissue Services database spreadsheet, when there is usage.

Details of tissue disposed, including when, where and the reason for disposal, is entered into the spreadsheet. Tissue disposal is by incineration as per the Trust anatomical waste procedure.

Whole skin patches for autologous treatment

The establishment procures and stores skin tissue from burns patients as an autologous treatment to assist the natural healing and repair process. The skin is stored, for a maximum period of 5 days, in a temperature-monitored refrigerator (within the Medication 2 room) before use. A sticker is attached to the container in which the skin is stored, stating the expiry date. Units pending mandatory serology test results are stored on a separate shelf in the refrigerator. At the time of the inspection, there was no autologous skin stored in the refrigerator.

Demineralised Bone Matrix

The establishment purchases demineralised bone matrix (DBM) from two HTA-licensed suppliers. A comprehensive log is maintained of the quantities, batch numbers and expiry dates of the packs received and used. The material is stored at room temperature in a locked and temperature-monitored cupboard.

Liver Vessels

The establishment receives and stores liver vessels retrieved during the organ retrieval process. The organ and associated vessels (mainly iliac arteries and veins) are retrieved within the Trust, or at other hospitals as part of the National Organ Retrieval Service (NORS). The Trust holds an organ donation and transplant (ODT) licence (HTA licensing number 40042) for organ retrieval and transplant.

The liver vessels may be used at the time of organ transplant or during an additional revision procedure following transplant. Liver vessels stored for more than 48 hours for use in a patient other than the primary organ transplant recipient are subject to the Q&S Regulations and fall under the current licence. The establishment stores liver vessels for up to 14 days pending use in a different recipient. Occasionally the establishment distributes vessels to another HTA-licensed organisation for transplant, for which there is a documented Memorandum of Understanding (MoU) agreement in place. The agreement documents the requirements for serious adverse events and reactions (SAEARs) reporting and the maintenance of traceability records from transportation to the outcome for the vessel (e.g. transplantation or disposal) for 30 years.

Peripheral Blood Stem Cells (PBSCs) and Donor Lymphocyte Infusion (DLI)

The establishment provides an adult stem cell collection and allogeneic and autologous stem cell transplantation service for patients.

Since the last inspection, the apheresis unit, and the location at which procurement is undertaken, has moved to a separate building from the main hospital and is now located within the Centre for Clinical Haematology. Processing, cryopreservation and storage are carried out at a separate HTA-licensed establishment (‘processing centre’) under the terms of an SLA.

Donor selection (medical assessment including social history) and consent for PBSC and DLI collections, as well as for mandatory serology tests, take place within the department. Patients are consented by consultants or apheresis nursing staff. In the case of directed, related donations, medical assessments are conducted by an independent qualified medical practitioner. A single consent form is used, which records consent for cell mobilisation, collection, processing, testing and storage.

Duplicate samples for mandatory serology testing are taken up to 30 days prior to cell collection and on the day of collection. Samples are tested separately by the Department of Clinical Microbiology (considered as the primary result), and the processing centre.

The apheresis unit contains four apheresis machines. Following collection, cells are

packaged (the SEC-Donor Identification (DI), is applied) and transported to the processing centre using validated procedures. Transplant products are returned by processing centre staff using similar validated procedures. Reagents and consumables for apheresis are stored in a secure, temperature-monitored storage area.

The processing centre performs total nucleated cell count, immunophenotype, cell viability and biological function assays for all collections, as well as human leukocyte antigen tissue typing and sterility analysis. Haematocrit levels, blood group and chimerism analysis are performed in the Department of Laboratory Haematology within CLS.

Tests on pre-apheresis, pre-processed and pre-cryopreserved product are performed, as appropriate, as well as tests on the product prior to transplant. The establishment has acceptance and release criteria for cell transplant based on the above set of markers. Products with minimal cell counts are disposed of by the processing centre.

Peripheral Blood Mononuclear Cells (PBMCs) as a starting material for an Advanced Therapy Investigational Medicinal Product (ATIMP)

The Research department, located within the Centre for Clinical Haematology, is participating in a clinical trial in which PBMCs are procured as a starting material for an ATIMP (a Chimeric Antigen Receptor, CAR-T cell therapy). The cells are transported to a facility within the EU, where the ATIMP is manufactured.

Donor selection and the seeking of consent for cell procurement, as well as for mandatory serology tests, takes place in the Centre for Clinical Haematology. Patients are provided with a patient information sheet at a pre-meeting at which general eligibility is assessed. Consent is taken in accordance with specific procedures using both Trust and separate ethically-approved consent forms. Blood samples for mandatory serology testing are taken 30 days prior to and on the day of procurement. The standard 'Autologous Transplant Pathway' is followed for the procurement of PBMCs.

The trial organiser provides kits for transportation and accompanying labels; these are stored in a secure room within the Centre for Clinical Haematology. The SEC-DI is applied at the time of packaging of the unit for transportation; the SEC-DI is recorded in the Research trial log spreadsheet. Cells are transported on the same day as procurement by courier; there is an agreement in place between the trial organisation and the courier.

Testing

The Department of Clinical Microbiology within the establishment is accredited by the United Kingdom Accreditation Service (UKAS) to International Organization for Standardization (ISO) standard 15189:2012. Samples are tested using CE-marked diagnostic kits on automated testing equipment according to manufacturer's instructions. Tests for HTLV-1, HIV-1 and 2, HBsAg, HBc, HCV and Treponema pallidum are carried out. Confirmatory serology and Nucleic Acid Amplification Technique (NAT) testing is also carried out in this department. In addition the testing lab also routinely tests for Toxoplasma gondii and Cytomegalovirus (CMV). The department routinely takes part in external quality assessment schemes for the above tests.

Samples intended for certain serological tests (e.g. HTLV-1) are tested in batches and hence kept in a refrigerator for up to five days prior to analysis, in cases where this storage time is exceeded, the serum is stored frozen. The temperature of the refrigerator and freezer is monitored manually but this record is not always completed.

The Department performs liver vessel donor testing for vessels stored under the Q&S Regulations. A proportion of donor samples are supplied to the department in tubes that are not validated for use with the laboratory equipment. These blood samples are not tested; this is recorded within the laboratory report. In this situation, the test results on the Electronic

Offering System (EOS) are used. When a liver vessel is used, a sample of the vessel storage solution is tested within the department for sterility; any positive results are reported to the appropriate Consultant. Unused vessel disposal is by incineration as per the Trust anatomical waste procedure.

The Inspection Process

Six allograft units (two nerve grafts, one tendon, one tri-cortical ileum wedge, one femoral strut and one cryopreserved skin) were selected at random from the freezer and labelling details were compared to the Tissue Record Forms. There was one discrepancy noted on the Tissue Record Form for the tendon, between the expiry date within the SEC and the separately recorded expiry date. Upon investigation by the establishment, it was confirmed that an incorrect label had been provided to them by the supplier. A correct label was issued by the supplier and the product and records were updated. There were no other discrepancies noted.

Two sets of patient records were reviewed for patients who had received allograft products (one nerve graft and one femoral strut). The date/time of use and the SEC were recorded in the records and there were no discrepancies noted.

Two sets of patient records (consent documentation and results of serological tests) were reviewed for patients who had autologous skin procured. The date of procurement and for one patient, the date of use, was recorded. For the second patient, the tissue was not used and the date of disposal was recorded. The results of the serological tests were cross-referenced to the testing laboratory results system; no discrepancies were noted.

Two liver vessels recorded as currently stored in the refrigerator, were selected at random from the ‘Stored Vessel Record’ form. The labelling details of the stored liver vessels were compared to the Stored Vessel Record; there were no discrepancies noted.

Five sets of patient records were reviewed for patients from which liver vessels were retrieved during the organ retrieval process and stored under the Q&S Regulations. The records included consent documentation and results of serological and microbiological analysis. For one patient record, the results of the serological tests were cross-referenced to the testing laboratory results system; there were no discrepancies noted for all the records reviewed.

The ‘Release Form’ for a vessel distributed to another HTA-licensed establishment was reviewed and it was noted that although the SEC had been applied, the format was not correct.

Four sets of patient records were reviewed for PBSC donations (two autologous and two allogeneic). The review included medical assessment, donor/recipient consent forms, processing worksheets and results of serological and microbiological analysis. There were no discrepancies noted.

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

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

Consent

Standard	Inspection findings	Level of shortfall
C1 Consent is obtained in accordance with the requirements of the Human Tissue Act 2004 (HT Act) and as set out in the Code of Practice.		
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, the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (Q&S Regulations) and the HTA's Codes of Practice.	The sibling donor screening questionnaire does not include questions regarding "Ingestion of, or exposure to, a substance (such as cyanide, lead, mercury) that may be transmitted to recipients in a dose that could endanger their health" or "Transplantation with xenografts" as set out in Annex A of the Guide to Quality and Safety Assurance for Human Tissues and Cells for Patient Treatment.	**Minor**

Governance and Quality

Standard	Inspection findings	Level of shortfall
GQ1 All aspects of the establishment's work are supported by ratified documented policies and procedures as part of the overall governance process.		
r) Third party agreements specify the responsibilities of the third party and meet the requirements set out in Directions 002/2018.	There is an agreement with the courier undertaking the transportation of liver vessels to the end user. The agreement refers to the requirements of The Quality & Safety of Organs Intended for Transplantation and not the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended).	**Minor**
GQ4 There is a systematic and planned approach to the management of records.		
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.	Failure of the system used to monitor and record the temperature of equipment (e.g. refrigerators and freezers for allograft storage) has resulted in the loss of data for up to 24 hours on more than one occasion (e.g. July 2018, November 2018). Although daily visual checks of temperature are undertaken, these are not recorded.	**Minor**

GQ6 A coding and records system facilitates traceability of bodies, body parts, tissues and cells, ensuring a robust audit trail.		
d) The requirements of the Single European Code are adhered to as set out in Directions 002/2018.	Although a SEC label is applied prior to the distribution of liver vessels for end use, the structure of the SEC does not meet the requirements as set out in Directions 002/2018.	**Minor**
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.	Although the establishment has documented risk assessments, these do not capture all the risks associated with the activities being carried out under the licence and the control measures in place, which help to mitigate identified risks. For example, the risks associated with the procurement of PBSCs from more than one patient at the same time, the transfer of blood samples from the Clinical Haematology Department to the processing laboratory, the receipt of incorrect documentation, and the availability of staff to undertake HTA activities, have not been formally assessed.	**Minor**

Premises, Facilities and Equipment

Standard	**Inspection findings**	**Level of shortfall**
PFE5 Equipment is appropriate for use, maintained, quality assured, validated and where appropriate monitored.		
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.	Samples pending mandatory serology testing may be stored in the refrigerator/freezer in the testing laboratory. A review of the temperature monitoring records for this equipment indicated temperatures outside of the defined acceptable ranges on multiple occasions. Information was not consistently recorded in the 'Details of out of range events' column and there was no evidence to demonstrate investigation of the temperature excursions. Samples may be stored in a refrigerator within the Haematology department, prior to transportation to the processing laboratory. Temperature monitoring was in place for this equipment, but did not include monitoring at the weekends.	**Minor**

Advice

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

No.	Standard	Advice
1.	GQ1i	The DI is advised to consider adding further detail to the procedure PTS_S4 (Storage of Liver Vessels) in relation to the 'Release of Vessels' and the recording of the assessment of suitability of the vessel by the Consultant when the release is concessionary (e.g. if a vessel is used beyond the expiry date).
2.	GQ1s	The DI is advised to consider including a reference to SAEARs reporting requirements in the agreement between the testing and the external testing laboratories.
3.	GQ3a	The responsibilities of the PD in the testing laboratory are clearly defined and included within the job description for that staff member's role. The DI is advised to consider this approach for all PD roles.
4.	GQ4b	During a review of internal audits, it was noted that the SEC was recorded in the medical notes but that this was not documented in the audit. The DI is advised to consider including the presence/absence of the SEC within internal audit reports.
5.	GQ4h GQ4i	The DI is advised to consider including the specific requirements for the retention of traceability (donor to recipient) records for 30 years and raw data for 10 years, in the agreement between Tissue Services and the testing laboratory.
6.	GQ7a	The DI is advised to consider further development of SAEARs training, awareness of their investigation, dissemination of information and implementation of follow-up.
7.	GQ7c	The DI is advised to consider identifying personnel within the transfusion department to be responsible for reporting/managing SAEARs.
8.	PFE5f	The apheresis equipment is cleaned daily and this is indicated by attaching a green 'Clean' label' to the machine. The equipment is also cleaned after use and this is recorded on the 'Stem Cell Collection Run Sheet'. The DI is advised to consider a separate cleaning log that can be retrieved for audit purposes.

Concluding comments

There are a number of areas of practice that require improvement, including six minor shortfalls. The HTA has given advice to the Designated Individual with respect to Governance and Quality Systems and Premises, Facilities and Equipment.

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: 07 March 2019

Report returned from DI: 18 March 2019

Final report issued: 02 April 2019

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: 25 June 2019

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 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.
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 002/2018.
o) There is a complaints system in place.
p) There are written agreements with third parties whenever an activity takes place that has the potential to influence the quality and safety of human tissues and / or cells.
q) There is a record of agreements established with third parties.
r) Third party agreements specify the responsibilities of the third party and meet the requirements set out in Directions 002/2018.

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

e) The establishment keeps a register of the types and quantities of tissues and / or cells that are procured, tested, preserved, processed, stored and distributed or otherwise disposed of, and on the origin and destination of tissues and cells intended for human application.
f) There are procedures to ensure that donor documentation, as specified by Directions 002/2018, is collected and maintained.
g) There is a system to ensure records are secure and that donor confidentiality is maintained in accordance with Directions 002/2018.
h) Raw data which are critical to the safety and quality of tissues and cells are kept for 10 years after the use, expiry date or disposal of tissues and / or cells.
i) The minimum data to ensure traceability from donor to recipient as required by Directions 002/2018 are kept for 30 years after the use, expiry or disposal of tissues and / or cells.
j) Records are kept of products and material coming into contact with the tissues and / or cells.
k) There are documented agreements with end users to ensure they record and store the data required by Directions 002/2018.
l) The establishment records the acceptance or rejection of tissue and / or cells that it receives and in the case of rejection why this rejection occurred.
m) In the event of termination of activities of the establishment a contingency plan to ensure records of traceability are maintained for 10 or 30 years as required.
GQ5 There are documented procedures for donor selection and exclusion, including donor criteria.
a) Donors are selected either by the establishment or the third party acting on its behalf in accordance with the criteria required by Directions 002/2018.
b) The testing of donors by the establishment or a third party on behalf of the establishment is carried out in accordance with the requirements of Directions 002/2018.
c) In cases other than autologous donors, donor selection is carried out by authorised personnel and signed and reviewed by a qualified health professional.
d) There is a system in place either at the establishment or at a third party acting on its behalf to record results of donor selection and associated tests.
e) Testing of donor samples is carried out using CE marked diagnostic tests.
f) Samples taken for donor testing are clearly labelled with the time and place the sample was taken and a unique donor identification code.
GQ6 A coding and records system facilitates traceability of tissues and / or cells, ensuring a robust audit trail.
a) There is a donor identification system which assigns a unique code to each donation and to each of the products associated with it.
b) An audit trail is maintained, which includes details of when the tissues and / or cells were acquired and from where, the uses to which the tissues and / or cells were put, when the tissues and / or cells were transferred elsewhere and to whom.

c) The establishment has procedures to ensure that tissues and / or cells imported, procured, processed, stored, distributed and exported are traceable from donor to recipient and vice versa.
d) The requirements of the Single European Code are adhered to as set out in Directions 002/2018.
GQ7 There are systems to ensure that all adverse events, reactions and/or incidents are investigated promptly.
a) There are procedures for the identification, reporting, investigation and recording of adverse events and reactions, including documentation of any corrective or preventative actions.
b) There is a system to receive and distribute national and local information (e.g. HTA regulatory alerts) and notify the HTA and other establishments as necessary of serious adverse events or reactions.
c) The responsibilities of personnel investigating adverse events and reactions are clearly defined.
d) There are procedures to identify and decide the fate of tissues and / or cells affected by an adverse event, reaction or deviation from the required quality and safety standards.
e) In the event of a recall, there are personnel authorised within the establishment to assess the need for a recall and if appropriate initiate and coordinate a recall.
f) There is an effective, documented recall procedure which includes a description of responsibilities and actions to be taken in the event of a recall including notification of the HTA and pre-defined times in which actions must be taken.
g) Establishments distributing tissue and / or cells provide information to end users on how to report a serious adverse event or reaction and have agreements with them specifying that they will report these events or reactions.
h) Establishments distributing tissues and / or cells have systems to receive notifications of serious adverse events and reactions from end users and notify the HTA.
GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately.
a) There are documented risk assessments for all practices and processes.
b) Risk assessments are reviewed regularly, as a minimum annually or when any changes are made that may affect the quality and safety of tissues and cells.
c) Staff can access risk assessments and are made aware of local hazards at training.
d) A documented risk assessment is carried out to decide the fate of any tissue and / or cells stored prior to the introduction of a new donor selection criteria or a new processing step, which enhances the quality and safety of tissue and / or cells.

Premises, Facilities and Equipment

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

c) The premises have sufficient space for procedures to be carried out safely and efficiently.
d) Where appropriate, there are procedures to ensure that the premises are of a standard that ensures the dignity of deceased persons.
e) There are procedures to ensure that the premises are secure and confidentiality is maintained.
f) There is access to a nominated, registered medical practitioner and / or a scientific advisor to provide advice and oversee the establishment's medical and scientific activities.
PFE2 Environmental controls are in place to avoid potential contamination.
a) Tissues and / or cells stored in quarantine are stored separately from tissue and / or cells that have been released from quarantine.
b) Where processing of tissues and / or cells involves exposure to the environment, it occurs in an appropriate, monitored environment as required by Directions 002/2018.
c) There are procedures for cleaning and decontamination.
d) Staff are provided with appropriate protective clothing and equipment that minimise the risk of contamination of tissue and / or cells and the risk of infection to themselves.
PFE3 There are appropriate facilities for the storage of tissues and / or cells, consumables and records.
a) Tissues, cells, consumables and records are stored in secure environments and precautions are taken to minimise risk of damage, theft or contamination.
b) There are systems to deal with emergencies on a 24 hour basis.
c) Tissues and / or cells are stored in controlled, monitored and recorded conditions that maintain tissue and / or cell integrity.
d) There is a documented, specified maximum storage period for tissues and / or cells.
PFE4 Systems are in place to protect the quality and integrity of tissues and / or cells during transport and delivery to its destination.
a) There is a system to ensure tissue and / or cells are not distributed until they meet the standards laid down by Directions 002/2018.
b) There are procedures for the transport of tissues and / or cells which reflect identified risks associated with transport.
c) There is a system to ensure that traceability of tissues and / or cells is maintained during transport.
d) Records are kept of transportation and delivery.
e) Tissues and / or cells are packaged and transported in a manner and under conditions that minimise the risk of contamination and ensure their safety and quality.
f) There are third party agreements with courier or transport companies to ensure that any specific transport conditions required are maintained.
g) Critical transport conditions required to maintain the properties of tissue and / or cells are defined and documented.

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

Disposal

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

Human Tissue Act 2004 Standards

Consent standards
C1 Consent is obtained in accordance with the requirements of the Human Tissue Act 2004 (HT Act) and as set out in the code of practice
a) Consent procedures are documented and these, along with any associated documents, comply with the HT Act and the HTA's Codes of Practice.
b) Consent forms are available to those using or releasing relevant material for a scheduled purpose.
c) Where applicable, there are agreements with other parties to ensure that consent is obtained in accordance with the requirements of the HT Act and the HTA's Codes of Practice.
d) Written information is provided to those from whom consent is sought, which reflects the requirements of the HT Act and the HTA's Codes of Practice.
e) Language translations are available when appropriate.
f) Information is available in formats appropriate to the situation.
C2 Staff involved in seeking consent receive training and support in the essential requirements of taking consent
a) There is suitable training and support of staff involved in seeking consent, which addresses the requirements of the HT Act and the HTA's Codes of Practice.
b) Records demonstrate up-to-date staff training.
c) Competency is assessed and maintained.

Governance and quality system standards
GQ1 All aspects of the establishments work are governed by documented policies and procedures as part of the overall governance process
a) Ratified, documented and up-to-date policies and procedures are in place, covering all licensable activities.
b) There is a document control system.
c) There are change control mechanisms for the implementation of new operational procedures.
d) Matters relating to HTA-licensed activities are discussed at regular governance meetings, involving establishment staff.
e) There is a system for managing complaints.
GQ2 There is a documented system of audit
a) There is a documented schedule of audits covering licensable activities.
b) Audit findings include who is responsible for follow-up actions and the timeframes for completing these.

GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills
a) Qualifications of staff and all training are recorded, records showing attendance at training.
b) There are documented induction training programmes for new staff.
c) Training provisions include those for visiting staff.
d) Staff have appraisals and personal development plans.
GQ4 There is a systematic and planned approach to the management of records
a) There are suitable systems for the creation, review, amendment, retention and destruction of records.
b) There are provisions for back-up / recovery in the event of loss of records.
c) Systems ensure data protection, confidentiality and public disclosure (whistleblowing).
GQ5 There are systems to ensure that all adverse events are investigated promptly
a) Staff are instructed in how to use incident reporting systems.
b) Effective corrective and preventive actions are taken where necessary and improvements in practice are made.
GQ6 Risk assessments of the establishment's practices and processes are completed regularly, recorded and monitored
a) There are documented risk assessments for all practices and processes requiring compliance with the HT Act and the HTA's Codes of Practice.
b) Risk assessments are reviewed regularly.
c) Staff can access risk assessments and are made aware of risks during training.

Traceability standards
T1 A coding and records system facilitates the traceability of bodies and human tissue, ensuring a robust audit trail
a) There is an identification system which assigns a unique code to each donation and to each of the products associated with it.
b) A register of donated material, and the associated products where relevant, is maintained.
c) An audit trail is maintained, which includes details of: when and where the bodies or tissue were acquired and received; the consent obtained; all sample storage locations; the uses to which any material was put; when and where the material was transferred, and to whom.
d) A system is in place to ensure that traceability of relevant material is maintained during transport.
e) Records of transportation and delivery are kept.
f) Records of any agreements with courier or transport companies are kept.
g) Records of any agreements with recipients of relevant material are kept.

T2 Bodies and human tissue are disposed of in an appropriate manner
a) Disposal is carried out in accordance with the HTA's Codes of Practice.
b) The date, reason for disposal and the method used are documented.

Premises, facilities and equipment standards
PFE1 The premises are secure and fit for purpose
a) An assessment of the premises has been carried out to ensure that they are appropriate for the purpose.
b) Arrangements are in place to ensure that the premises are secure and confidentiality is maintained.
c) There are documented cleaning and decontamination procedures.
PFE2 There are appropriate facilities for the storage of bodies and human tissue
a) There is sufficient storage capacity.
b) Where relevant, storage arrangements ensure the dignity of the deceased.
c) Storage conditions are monitored, recorded and acted on when required.
d) There are documented contingency plans in place in case of failure in storage area.
PFE3 Equipment is appropriate for use, maintained, validated and where appropriate monitored
a) Equipment is subject to recommended calibration, validation, maintenance, monitoring, and records are kept.
b) Users have access to instructions for equipment and are aware of how to report an equipment problem.
c) Staff are provided with suitable personal protective equipment.

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 shortfall which poses a significant risk to human safety and/or dignity or is a breach of the Human Tissue Act 2004 (HT Act) or associated Directions,

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 breach in the relevant Codes of Practices, the HT Act and other relevant professional and statutory guidelines;

or

A shortfall which indicates a failure to carry out satisfactory procedures 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.

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.