Site visit inspection report on compliance with HTA minimum standards

Nottingham University Hospitals City Campus

HTA licensing number 11073

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

04 October 2016

Summary of inspection findings

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

Although the HTA found that Nottingham University Hospitals City Campus (the establishment) had met the majority of the HTA standards, one minor shortfall was found with regard to the Premises, Facilities and Equipment (PFE) standards. The minor shortfall was in relation to weaknesses in cleanroom procedures and cleanroom gowning. Advice has been given relating to the Consent, Governance and Quality Systems, PFE and Disposal standards, as well as to licence management.

Particular examples of 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 (DI), Licence Holder (LH), premises and practices are suitable.

The statutory duties of the DI 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 licenses 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.

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

Tissue type	Procurement	Processing	Testing	Storage	Distribution	Import	Export
DLI	**E**	**E**		**E**	**TPA**		
PBSC	**E**	**E**		**E**	**TPA**		
UCB				**E**			

DLI = cells for donor lymphocyte infusion.

PBSC = peripheral blood stem cells.

UCB = umbilical cord blood.

Background to the establishment and description of inspection activities undertaken

This report refers to the activities carried out by Nottingham University Hospitals City Campus (the establishment). The establishment was issued an HTA licence in June 2007. This was the fifth HTA site visit inspection of the establishment, the last was in September 2014. The current inspection was a routine one to assess whether the establishment is continuing to meet the HTA's standards.

Nottingham University Hospitals NHS Trust consists of the City Hospital, the Nottingham Children's Hospital and the Queen's Medical Centre. The establishment serves a haematology patient population of approximately two million across the East Midlands Region.

The establishment is licensed under the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (Q&S Regulations) for the procurement, processing, 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 these activities, the establishment does not currently carry out serological testing for human application or store relevant material for use for a scheduled purpose (*see Advice item 1*). 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 by this organisation in March 2013.

The DI is a Professor of Haematology and is the Bone Marrow Transplant (BMT) Programme Director. The Corporate LH (CLH) is Nottingham University Hospitals NHS Trust and the CLH Contact (CLHC) is the Trust Chief Executive Officer. There are three Persons Designated (PDs) on the licence: the BMT Programme Quality Manager, the Stem Cell Laboratory Manager and the Quality Assurance Officer.

The establishment provides an adult stem cell collection and allogeneic and autologous stem cell transplantation service for patients within the Haematology and Oncology Departments of the Trust. Approximately 195 autologous peripheral blood stem cell (PBSC) collections are carried out annually, along with 30 allogeneic (related directed) PBSC collections and five allogeneic collections of cells for donor lymphocyte infusion (DLI).

Transplanted cells include those from directed related and autologous donations within the hospital, as well as from tissue-typed ('matched') unrelated donations. Matched unrelated PBSC and umbilical cord blood (UCB) donations are managed by the Anthony Nolan and NHS Stem Cell Registry under service level agreement (SLA). In total, approximately 70 allogeneic and 100 autologous PBSC transplants are undertaken annually along with five UCB allogeneic transplants.

Donor selection (medical assessment) and consent for PBSC and DLI collections, as well as for mandatory serology tests, take place within the purpose built Centre for Clinical Haematology. Consent for collection also occasionally takes place at one other local hospital. Patients are consented by trained consultants working to well-defined procedures. 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.

Samples for mandatory serology testing are taken up to 30 days prior to cell collection and are transported by Trust porters to the Department of Clinical Microbiology, Queen's Medical Centre campus. This laboratory is licensed by the HTA for serological testing and is accredited the United Kingdom Accreditation Service (UKAS) to International Organization for Standardization (ISO) standard 15189 (2012).

The Centre for Clinical Haematology contains three apheresis machines. Following collection, cells are packaged and transported by establishment staff to the processing facility using validated procedures. Transplant products are returned to the Centre by the same staff using similar validated procedures. Reagents and consumables for apheresis are stored in a secure temperature-monitored storage area. A separate alarmed and monitored refrigerator is available within the Centre for short-term storage of both fresh collections and products pending transplant.

The processing facility is located within the Clinical Sciences Building and consists of a cleanroom containing two laminar air flow cabinets which maintain a grade A tissue processing environment in a background of grade C.

The processing steps create both cryobags and ampoules ('pilot samples') for each collected unit. Pilot samples allow for post storage and pre-transplant quality control analysis. Temperature-sensitive reagents and consumables are stored in an alarmed and monitored refrigerator.

Cryobags and pilot samples are cryopreserved using controlled-rate freezers. Following cryopreservation, samples with known clear serology results are stored in the liquid nitrogen storage area in liquid nitrogen storage vessels (cryovessels) and the corresponding pilot samples are stored in separate cryovessels for further analysis. Once serology and environmental monitoring data have been reviewed, along with processing records, by the Stem Cell Laboratory Manager, samples are designated and approved for release. Separate cryovessels are used to store serologically positive samples and those with results still pending (*see Advice item 7*).

All cryovessels are linked to a continuous temperature monitoring unit which feeds into a wireless callout system. Temperature excursions outside the set ranges trigger both audible alarms and the callout system and the system is tested regularly. There are oxygen depletion monitors linked to an alarm system. The main storage cryovessels are linked to an automated filling system and the cryovessels used for quarantined samples are filled manually twice a week. Contracts are in place for contingencies, including emergency off-site storage.

A variety of tests to ensure cellular quality and safety are carried out. Total nucleated cell count (TNCC), haematocrit levels and blood group analysis are performed in the Department of Clinical Pathology at the City Hospital campus. Human leukocyte antigen (HLA) tissue typing is carried out at NHSBT laboratories, Sheffield. CD34/CD45 immunophenotype, cell viability and colony-forming unit biological function assays are performed within the Clinical Sciences Building. Sterility analysis (for both bacteria and fungi) is carried out in the Department of Clinical Microbiology, Queen's Medical Centre campus.

The establishment performs pre-apheresis tests for TNCC, pre-processing TNCC and pre-cryopreservation analysis for CD34/CD45 immunophenotype and cell viability. Colony-forming unit biological function is performed post-processing. Further tests for TNCC, CD34/CD45 immunophenotype, cell viability and colony-forming unit biological function are conducted on the product or pilot samples prior to transplant, along with chimerism, blood group and further microbiology testing as required. There are release criteria based on this set of tests.

The establishment occasionally distributes cells to end users on request. These are cases where there are cells already in storage and patient care has transferred to another transplant centre. Transport arrangements are arranged by the recipient centre.

The timetable for the current site visit inspection was developed after consideration of the establishment's previous inspection reports, communications with the HTA since the last inspection and annual activity data. The inspection included a visual inspection of the site (Centre for Clinical Haematology and Clinical Sciences Building). Discussions and interviews were held with key staff and documentation was reviewed. Interviews were held with the DI, two PDs (BMT Programme Quality Manager, Stem Cell Laboratory Manager), the PBSC and BM Collection Facility Director and a Nurse Specialist - PBSC Quality Management Supervisor. Audits of traceability were also carried out:

Four PBSC products were selected at random from the cryovessels and labelling details were compared to the electronic database and paper records. The following information was cross

referenced: donor name, hospital identification number, date of procurement, bag number and cryovessel storage location. There were no discrepancies noted.

The electronic and paper records of six PBSC donations were reviewed (four autologous, two paired directed donations and corresponding transplants). They included: medical collection and donor/recipient consent forms; apheresis care plans; and processing worksheets. The worksheets included operators involved, sample volumes, cellular yields, reagent/consumable batch numbers, approval for 'cleared' storage, cryopreservation records, number of vials frozen, results of serological and microbiological analysis; environmental monitoring data and sample labels. There were no discrepancies noted.

Inspection findings

The HTA found the DI and the CLH 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

Premises, Facilities and Equipment

Standard	Inspection findings	Level of shortfall
PFE2 Environmental controls are in place to avoid potential contamination.		
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.	The practices described in standard operating procedures (SOPs) and observed by the inspection team in the grade A laminar air flow cabinets and in the grade C laboratory were not consistent with the formal designation of these areas and introduced the risk of contamination.	**Minor**
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.	<u>Protective clothing:</u> Gowning procedures were not always consistent with the requirements of a grade C background as additional gowning was only put into practice during cell manipulation. Staff wore lab coats which had been stored in an ungraded corridor in the grade C area. Lint-free non-shedding lab coats, overshoes and elasticated hats were only worn during cell manipulation in the cabinets. Other manipulations in the cabinets did not require this level of gowning even in the presence of sterile consumables planned for use with cells. It is not clear from procedures that staff should use a clean non-shedding lab coat for each batch of cells to minimise the risk of contamination. <u>Processing:</u> Staff did not spray gloved hands with ethanol before introducing them into the cabinet to carry out operations that did not involve cells even in the presence of sterile consumables. The sharps bin inside the cabinet, which contained sharps that had been in contact with processed cells, was being re-used for the next processing procedure. This creates a potential source of contamination for subsequent samples that are processed. The instructions in the appropriate document (SOP D101) to spray all equipment with ethanol before placing it in the cabinets were unclear. It was unclear clear whether items such as racks that were in the cabinets were sterilised before use. <u>Environmental monitoring:</u> Although there was microbiological monitoring of the grade C area using settle plates, such monitoring did not take place during any of the operational procedures or during simulation exercises.	

Advice

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

No.	Standard	Advice
1.	N/A	The DI is advised to consider removing the activity of 'Testing' on the licence held under the Q&S Regulations and to consider revoking the licence held under the HT Act from their portfolio of HTA licences as neither of these licences is being used.

2.	C1a, D1a	The establishment is reaching capacity for the storage of cells for human application. 'Cleared' cells are occasionally being stored in empty quarantine cryovessels. The DI is advised to ensure that this procedure is risk assessed. The DI is also advised to consider including a set storage period on the consent form and to consider modifying procedures to indicate steps to be taken when that set period has expired.
3.	GQ3e	The DI is advised to consider updating the SOP on staff training to ensure that the training form has been countersigned once competency is achieved.
4.	GQ5a	The DI is advised to consider adding more detail to the SOP on donor selection (medical assessment) under the section which covers recent travel abroad. The SOP has not been updated to include Zika virus. The DI is advised to consider including a link to the Joint United Kingdom Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee (JPAC) Donor Selection Guidelines and to the Geographical Disease Risk Index rather than including a list of individual infections.
5.	GQ7c	The DI is advised to ensure that the SOP for the identification and reporting of serious adverse events and adverse reactions (SAEARs) is updated to include all personnel who should report SAEARs in the DI's absence.
6.	PFE2d	The DI is advised to ensure that suitable signage is in place so that staff are aware that they are entering a grade C area and should be gowned appropriately.
7.	PFE3a	The DI is advised to consider labelling and locking all cryovessels which contain human tissue to prevent sample mix-ups and to ensure that staff are aware of the need to manage these samples in line with the regulatory requirements.
8.	PFE5a	Apheresis machines are maintained by the manufacturer. The DI is advised to set up a notice so that all staff are aware when the next maintenance visit is due.

Concluding comments

During the inspection areas of good practice were noted:

- There are good lines of communication between staff, including the use of a shared diary system to ensure that all clinical and laboratory staff are aware of upcoming apheresis, processing and transplant activities.
- The consent procedure is consultant led and the consent training programme is comprehensive.
- There is a HTA Tissue Management Group, consisting of the Trust's DIs, PDs and other senior staff which meets every six months.
- The establishment makes good use of two-person checks covering its activities. These include staff-staff checks (e.g. placement of products in storage and retrieval from storage, confirmation of identity prior to thawing) and staff-patient checks (e.g. confirmation of patient details after labelling apheresis product and upon receipt of cells prior to transplant.

There are a number of areas of practice that require improvement, including one minor shortfall. The HTA has given advice to the DI with respect to the Consent, Governance and Quality Systems, Premises, Facilities and Equipment and Disposal standards, as well as to licence management.

The HTA requires that the DI 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: 01 November 2016

Report returned from DI: 10 November 2016

Final report issued: 06 December 2016

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: 15 May 2018

Appendix 1: HTA standards

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

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

Consent

Standard
C1 Consent is obtained in accordance with the requirements of the HT Act 2004, the Human Tissue (Quality and Safety for Human Application) Regulations 2007 and as set out in the HTA's Codes of Practice.
a) If the establishment acts as a procurer of tissues and / or cells, there is an established process for acquiring donor consent which meets the requirements of the HT Act 2004 the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (Q&S Regulations) and the HTA's Codes of Practice
b) If there is a third party procuring tissues and / or cells on behalf of the establishment the third party agreement ensures that consent is obtained in accordance with the requirements of the HT Act 2004, the Q&S Regulations and the HTA's Codes of Practice.
c) The establishment or the third party's procedure on obtaining donor consent includes how potential donors are identified and who is able to take consent.
d) Consent forms comply with the HTA Codes of Practice.
e) Completed consent forms are included in records and are made accessible to those using or releasing tissue and / or cells for a Scheduled Purpose.
C2 Information about the consent process is provided and in a variety of formats.
a) The procedure on obtaining consent details what information will be provided to donors. As a minimum, the information specified by Directions 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.
g) There are procedures to ensure that an authorised person verifies that tissues and / or cells received by the establishment meet required specifications.
h) There are procedures for the management and quarantine of non-conforming consignments or those with incomplete test results, to ensure no risk of cross contamination.
i) There are procedures to ensure tissues and / or cells are not released from quarantine until verification has been completed and recorded.
j) There are procedures detailing the critical materials and reagents used and where applicable, materials and reagents meet the standards laid down by the European directives on medical devices and in vitro diagnostic medical devices.
k) There is a procedure for handling returned products.
l) There are procedures to ensure that in the event of termination of activities for whatever reason, stored tissues and / or cells are transferred to another licensed establishment or establishments.
m) The criteria for allocating tissues and / or cells to patients and health care institutions are documented and made available to these parties on request.
o) There is a complaints system in place.
p) There are written agreements with third parties whenever an activity takes place that has the potential to influence the quality and safety of human tissues and / or cells.
q) There is a record of agreements established with third parties.
r) Third party agreements specify the responsibilities of the third party and meet the requirements set out in Directions 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.
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.
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.

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
• Consent forms comply with the HTA's Code of Practice • Consent forms are in records and are made accessible to those using or releasing relevant material for a scheduled purpose • If the establishment obtains consent, a process is in place for acquiring consent in accordance with the requirements of the HT Act 2004 and the HTA's Codes of Practice • Where applicable, there are agreements with third parties to ensure that consent is obtained in accordance with the requirements of the HT Act 2004 and the HTA's Codes of Practice • Consent procedures have been ethically approved
C2 Information about the consent process is provided and in a variety of formats
• Standard operating procedures (SOPs) detail the procedure for providing information on consent • Agreements with third parties contain appropriate information • Independent interpreters are available when appropriate • Information is available in suitable formats, appropriate to the situation • Consent procedures have been ethically approved
C3 Staff involved in seeking consent receive training and support in the implications and essential requirements of taking consent
• Standard operating procedures (SOPs) detail the consent process • Evidence of suitable training of staff involved in seeking consent • Records demonstrate up-to-date staff training • Competency is assessed and maintained

Governance and quality system standards
GQ1 All aspects of the establishments work are supported by ratified documented policies and procedures as part of the overall governance process
• Policies and procedures are in place, covering all activities related to the storage of relevant material for research in connection with disorders, or the functioning, of the human body • Appropriate risk management systems are in place • Regular governance meetings are held; for example, health and safety and risk management committees, agendas and minutes

- Complaints system

GQ2 There is a documented system of quality management and audit

- A document control system, covering all documented policies and standard operating procedures (SOPs).
- Schedule of audits
- Change control mechanisms for the implementation of new operational procedures

GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills

- **Qualifications of staff and training are recorded, records showing attendance at training**
- **Orientation and induction programmes**
- **Documented training programme, (e.g. health and safety, fire, risk management, infection control), including developmental training**
- **Training and reference manuals**
- **Staff appraisal / review records and personal development plans are in place**

GQ4 There is a systematic and planned approach to the management of records

- Documented procedures for the creation, amendment, retention and destruction of records
- Regular audit of record content to check for completeness, legibility and accuracy
- Back-up / recovery facility in the event of loss of records
- Systems ensure data protection, confidentiality and public disclosure (whistle-blowing)

GQ5 There are documented procedures for distribution of body parts, tissues or cells

- A process is in place to review the release of relevant material to other organisations
- An agreement is in place between the establishment and the organisation to whom relevant material is supplied regarding the tracking and use of material and eventual disposal or return

GQ6 A coding and records system facilitates traceability of bodies, body parts, tissues and cells, ensuring a robust audit trail

- There is an identification system which assigns a unique code to each donation and to each of the products associated with it
- An audit trail is maintained, which includes details of when and where the relevant material was acquired, the consent obtained, the uses to which the material was put, when the material was transferred and to whom

GQ7 There are systems to ensure that all adverse events are investigated promptly
• Corrective and preventive actions are taken where necessary and improvements in practice are made • System to receive and distribute national and local information (e.g. HTA communications)
GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately
• Documented risk assessments for all practices and processes • Risk assessments are reviewed when appropriate • Staff can access risk assessments and are made aware of local hazards at training

Premises, facilities and equipment standards
PFE1 The premises are fit for purpose
• A risk assessment has been carried out of the premises to ensure that they are appropriate for the purpose • Policies in place to review and maintain the safety of staff, authorised visitors and students • The premises have sufficient space for procedures to be carried out safely and efficiently • Policies are in place to ensure that the premises are secure and confidentiality is maintained
PFE 2 Environmental controls are in place to avoid potential contamination
• Documented cleaning and decontamination procedures • Staff are provided with appropriate protective equipment and facilities that minimise risks from contamination • Appropriate health and safety controls are in place
PFE3 There are appropriate facilities for the storage of bodies, body parts, tissues and cells, consumables and records.
• Relevant material, consumables and records are stored in suitable secure environments and precautions are taken to minimise risk of damage, theft or contamination • Contingency plans are in place in case of failure in storage area • Critical storage conditions are monitored and recorded • System to deal with emergencies on 24-hour basis • Records indicating where the material is stored in the premises

PFE 4 Systems are in place to protect the quality and integrity of bodies, body parts, tissues and cells during transport and delivery to a destination

- Documented policies and procedures for the appropriate transport of relevant material, including a risk assessment of transportation
- A system is in place to ensure that traceability of relevant material is maintained during transport
- Records of transportation and delivery
- Records are kept of any agreements with recipients of relevant material
- Records are kept of any agreements with courier or transport companies

PFE5 Equipment is appropriate for use, maintained, quality assured, validated and where appropriate monitored

- Records of calibration, validation and maintenance, including any agreements with maintenance companies
- Users have access to instructions for equipment and receive training in use and maintenance where appropriate
- Staff aware of how to report an equipment problem
- Contingency plan for equipment failure

Disposal Standards

D1 There is a clear and sensitive policy for disposing of human organs and tissue

- Documented disposal policy
- Policy is made available to the public
- Compliance with health and safety recommendations

D2 The reason for disposal and the methods used are carefully documented

- Standard operating procedures (SOPs) for tracking the disposal of relevant material detail the method and reason for disposal
- Where applicable, disposal arrangements reflect specified wishes

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 Human Tissue Act 2004, Human Tissue (Quality and Safety for Human Application) Regulations 2007 or the HTA Directions.

1. **Critical shortfall:**

   A shortfall which poses a significant risk to 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 represents a systemic failure and therefore is 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 straight away.

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 the proposed action plan the establishment will be notified of the follow-up approach the HTA will take.