Site visit inspection report on compliance with HTA minimum standards

NHSBT Bristol

HTA licensing number 22518

Licensed for the

- **procurement, processing, storage, distribution, import and export 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**

14, 15 and 16 March 2017

Summary of inspection findings

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

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

Particular examples of strengths and good practice are included in the concluding comments section of the report.

The HTA's regulatory requirements

The HTA must assure itself that the Designated Individual, Licence Holder, premises and practices are suitable.

The statutory duties of the Designated Individual are set down in Section 18 of the Human Tissue Act 2004. They are to secure that:

- the other persons to whom the licence applies are suitable persons to participate in the carrying-on of the licensed activity;
- suitable practices are used in the course of carrying on that activity; and
- the conditions of the licence are complied with.

The HTA developed its licensing standards with input from its stakeholders. They are designed to ensure the safe and ethical use of human tissue and the dignified and respectful treatment of the deceased. The HTA inspects the establishments it licences against four groups of standards:

- consent
- governance and quality systems
- premises facilities and equipment
- disposal.

This is an exception-based report: only those standards that have been assessed as not met are included. Where the HTA determines that a standard is not met, the level of the shortfall is classified as 'Critical', 'Major' or 'Minor' (see Appendix 2: Classification of the level of shortfall). Where HTA standards are fully met, but the HTA has identified an area of practice that could be further improved, advice is given to the DI.

Reports of HTA inspections carried out from 1 November 2010 are published on the HTA's website.

Licensable activities carried out by the establishment

'E' = Establishment is licensed to carry out this activity.

Tissue type	Procurement	Processing	Testing	Storage	Distribution	Import	Export
PBSC*	**E**	**E**		**E**	**E**		**E**
Bone marrow		**E**		**E**	**E**		
Donor lymphocyte infusions	**E**	**E**		**E**	**E**		
Umbilical cord blood		**E**		**E**	**E**		**E**
Ocular tissue – cornea and sclera		**E**		**E**	**E**		

* Peripheral blood stem cells

Background to the establishment and description of inspection activities undertaken

The HTA licence held by NHSBT Bristol covers activities undertaken in Bristol, by the Therapeutic Apheresis Services (TAS), the Stem Cell and Immunotherapies (SCI) Laboratory, the Bristol Eye Bank, the NHS Cord Blood Bank and the British Bone Marrow Registry. These services are part of several national services managed by NHSBT, a Strategic Health Authority under the Department of Health. The HTA Designated Individual (DI) is the Associate Director of Quality and the corporate licence holder contact is the Chief Executive Officer of NHSBT.

This was the fourth inspection of NHSBT Bristol and included a visual inspection of the TAS and the hub site. Discussions were held with the DI, Head of Laboratory of the Stem Cell and Immunotherapies Laboratory, Clinical Director Apheresis Services, Nursing Lead Apheresis Services, Head of Laboratory of the Cord Blood Bank, the BBMR Manager, Tissue and Eye Services Manager, Therapeutic Apheresis Nurses Regional Quality Manager, Quality Assurance Managers, Tissue Practitioners at the Eye Bank and the Facilities Manager at the hub site at Filton.

This inspection did not cover the storage of relevant material for use for scheduled purposes.

Therapeutic Apheresis Services (TAS) Bristol

The TAS is a satellite site located at level 7 Haematology and Oncology Centre within the grounds of the University Hospital Bristol Foundation Trust. The TAS undertakes around 300 apheresis collections each year; around 20 collections are sent to other countries in accordance with arrangements made by the BBMR.

The TAS has five beds; four apheresis machines are used to collect stem cells for patient treatment. Patients are referred from Bristol and regional hospitals at Weston-super-Mare, Cheltenham and Bath. The apheresis machines are taken to the wards at the Bristol Children's Hospital if paediatric patients have to be apheresed. Clinical care is provided under the supervision of the Clinical Director at TAS who is also the DI under HTA licence 22538, held by University Hospitals Bristol Foundation Trust. Staff employed by the Trust undertake donor work up, donor assessment and seek consent for procurement of PBSC from autologous or allogeneic donors. They also seek consent from donors listed on a registry when stem cells are sent to recipients outside the UK. The Antony Nolan registry is responsible for seeking consent from donors listed on the registry, if the donation is for patients within the UK.

Apheresis nurses seek consent for the apheresis procedure before donors are connected to the machines. The machines are maintained under a service contract and staff clean them before and after each apheresis session. Staff training is recorded, and all incidents are logged and investigated. Consumables such as the anticoagulant Acid-Citrate-Dextrose Formula A (ACD-A) are stored in an adjoining room which is temperature monitored. Stem cells and around 150-200ml of plasma are collected during each apheresis session.

Each collection is labelled with a unique code (International Society for Blood Transfusion - ISBT code). The labels are printed from the NHSBT IT system and attached to each collection, and each donor blood sample sent away for infectious disease testing. The unique code ensures traceability from procurement through to processing, storage, distribution and end-use.

Stem cell collections, plasma from the donor and the blood samples are packed in insulated transport boxes along with pre-chilled ice packs. NHSBT transport pick up the boxes from the TAS, sign a handover form and transport the collection to the hub site at Filton. The journey can take around 30-40 minutes.

Stem cell processing and storage

The SCI laboratories at the hub site at Filton receive and process around 300 apheresis collections, 60 bone marrow collections, 50 donor lymphocyte collections and over 2000 units of cord blood each year. The laboratory aims to process and cryopreserve all collections within 24 hours of collection.

Samples for donor testing are transported to NHSBT Manchester where mandatory donor testing takes place. NHSBT Manchester is licensed for testing as a satellite site of HTA licence 11018.

The stem cell transplant programme is accredited by JACIE (Joint Accreditation Committee ISCT; International Society for Cellular Therapy and EMBT; European Society for Blood and Marrow Transplantation) for collection and processing of PBSC from adult and paediatric donors for autologous and allogeneic use.

Stem cells are processed in a dedicated clean room, which was not inspected. On the day of the inspection, this clean room was not operational as repairs were being undertaken on the air circuit breaker, which controls the automatic switch over to a generator in the event of a power failure. The establishment intends to use two adjacent clean rooms to manufacture investigational medicinal products under a licence from the Medicines and Healthcare products Regulatory Agency (MHRA).

Open processing of stem cell collections and donor lymphocyte infusions take place in Class II safety cabinets in the clean room (Grade A/B environment). Dimethyl sulphoxide is added to the collection which is placed in the controlled rate freezer within 30 minutes after addition of the cryopreservative. The controlled rate freezer is located in the cryostore and frozen collections are stored in the vapour phase of liquid nitrogen storage tanks. The tanks are temperature-monitored and filled automatically; the level of liquid nitrogen is checked manually on Mondays, Wednesdays and Fridays. All stem cell collections are tested for viability, CD34+ dose and CD3+ content. Bacteriology testing of stem cell products is undertaken at NHSBT Colindale (HTA licence 22600).

Cord Blood processing and storage

Cord blood is collected at hospitals around London and sent to NHSBT Colindale (HTA licence 22600) before it arrives at the Stem Cell Laboratory in Filton, where processing takes place. The establishment is accredited by the Foundation for the Accreditation of Cellular Therapy (NetCord FACT). Cord blood is processed within 24 hours of collection using a proprietary closed processing system. Hydroxyethyl starch (HES) is added to sediment red blood cells. The collection is transferred into a closed processing set and centrifuged to reduce the volume of stem cells to around 20ml. Dimethy sulphoxide is added to the processed cord blood contained in a cryopreservation bag, which is wrapped within an overwrap bag. The collection is then placed in a magnetic steel canister in preparation for controlled rate freezing and storage. A closed robotic sample handling system automatically loads the collection into the integrated controlled rate freezer where it is cooled to -50^0C before it is automatically transferred into liquid nitrogen for storage in liquid nitrogen at -196^0C. This closed system enables individual handling of each unit and prevents other units

from being exposed to transient warming events. The establishment currently stores over 20,000 units of cord blood.

All stem cell collections from cord blood are registered on the British Bone Marrow Registry, Bone Marrow Donors Worldwide and NETCORD. Healthcare professionals from the UK and around the world search these registries for patients who need stem cell transplants from matching donors.

British Bone Marrow Registry (BBMR) activities

BBMR staff are responsible for administrative support and arrange for over 20 donations from volunteer donors each month. The Registry is accredited by the World Marrow Donor Association. Fresh bone marrow is procured at several sites and distributed to the hub site at Filton. Recipient centres outside the UK make transport arrangements with couriers in accordance with agreements with international stem cell registries. Couriers arrive at Filton with a transport container, which is used to transport donations to end users. BBMR staff provide information on the donation and documentation, which enables the courier to pass through customs.

Bristol Eye Bank

NHSBT Bristol started processing and storing corneas and sclera from deceased donors in 2017. This followed the transfer of activities, from the Corneal Transplant Service (CTS) Eye Bank located at Bristol Eye Hospital (HTA Licence 11045) to NHSBT. The procedures followed by the Eye Bank at NHSBT Bristol are based on documented procedures used at the CTS Eye Bank, which was established in 1986, and released over 20,000 corneas for patient treatment.

The Eye Bank has a clean room suite, several incubators, office space and an area where ocular tissues are received. The clean room suite was installed and validated in 2016 and consists of changing rooms, a tissue processing room and a tissue assessment room. In January 2017, the HTA authorised a Preparation Process Dossier for processing and storing ocular tissue at NHSBT Bristol. A local eye procurement team working under the HTA licence 11018 held by NHSBT Liverpool undertakes local eye retrievals. Eyes are given a unique ISBT code and an Eye Bank number - the right and left eye from each donor is additionally labelled A or B respectively. Donor blood samples are sent to NHSBT Colindale where donor testing of blood from deceased donors takes place.

Eyes are transferred into a Class II safety cabinets (Grade A environment) in the tissue processing room, washed with iodine followed by sodium thiosulphate, before they are dissected to remove the corneoscleral disc. The cornea is suspended in organ culture medium containing antibiotics and fetal calf serum for up to four weeks at 34^0C. The corneas are kept in quarantine and microbiology testing of the culture medium is undertaken after seven days of storage, before the tissue is cleared for further evaluation. Regular checks take place to monitor any visible growth or change in colour of the medium containing the corneoscleral discs.

Corneas are assessed in the Class II safety cabinets flow cabinet in the tissue assessment clean room. Corneas are stained with trypan blue, followed by treatment with hypotonic sucrose solution to visualise the cell membranes. Light microscopy is used to assess the shape and size of cells, extent of Descemet membrane folding and endothelial cell density. Cell density of the corneal discs must exceed 2,200 cells/mm^2 in order for corneas to be released for transplantation. A photograph is taken and sent along with the cornea to the end

user. Before release, the discs are transferred to organ culture medium containing dextran for 24 hours in order to reverse the stromal oedema, which occurs during storage. A sample of this final storage solution is sampled and tested for microbial contamination. The establishment ensures that around five units of sclera are dissected in the processing clean room and stored in 70% ethanol in a flame-proof cabinet ready for issue, if requested by ophthalmic surgeons.

Environmental monitoring and temperature monitoring

Viable and non-viable particle monitoring takes place during open processing. Sessional settle plates (typticase soy agar and sabourand agar plates) are placed in the Class II safety cabinets (Grade A environment) and operators perform finger dabs at the end of each session. There is a set programme of environmental monitoring using contact plates, settle plates, swabs and active air sampling at rest. Incubation of plates exposed during processing takes place within the stem cell laboratory; the results are reviewed weekly and compared with the alert levels and action levels. Plates for six monthly monitoring are incubated in the Quality Assurance Laboratory.

The Eye Bank uses a proprietary continuous particle monitoring system to monitor non-viable particles in the Class II safety cabinets and in the background areas.

A proprietary temperature monitoring system monitors the temperature of the liquid nitrogen storage tanks, fridges, freezers and room temperature. This proprietary system triggers a series of alarms in the event of a temperature deviation.

An external contractor is responsible for undertaking annual dispersed oil particulate (DOP) filter testing to check the integrity of the filter, ducts and filter housing in the clean rooms. The service includes monitoring of the clean room and checks on particle counts, air speed and room air changes.

Document review and audits

Documents reviewed included standard operating procedures (SOPs), policies, minutes of meetings, risk assessments, internal audits, training records, environmental monitoring data and temperature monitoring records. Discussions were also held on training plans, task-based training and tools used to identify training needs.

During the inspection, the HTA team was provided with the Eye Bank training matrix which listed the key SOPs which individual staff at the Eye Bank had read and understood. Following the inspection, the Eye Bank provided additional documents including training plans and ‘Task Based Training Records’ relating to two critical processes, namely Corneal Excision (SOP5085/1) and Endothelial Assessment (SOP4988). The HTA notes that observational assessment records mentioned in the training plans were not provided. However, NHSBT provided two batch processing records which documented the name of the trainee and the trainer to evidence the supervision of trainees (see Advice item 2).

Audit trails were undertaken of two ocular tissue donations. The records reviewed included consent forms, procurement site risk assessments, collection forms, donor assessment form, donor test results, consumables used during procurement and processing, endothelial assessment, microbiology quality checks and environmental monitoring. There were no discrepancies.

Several audits were undertaken. Records of four apheresis donations at the TAS – one autologous donation, one related allogeneic donation and two allogeneic donations were

traced. Patient identifiers and serology test results were reviewed; they included donor testing within 30 days of donation and on the day of donation. No discrepancies were noted.

Audit trails of processing records relating to one autologous donation and one cord blood unit which was processed, stored and distributed to France (including temperature monitoring of the dry shipper used during transport), one apheresis collection sent to the United States were also reviewed. Records of clean room gowning validation, sterile fill monitoring, hatch pass through monitoring and exit suit monitoring undertaken by staff in the SCI laboratory were reviewed. Records reviewed included, as appropriate, consent, donor testing, collection reports, processing records, records of consumables and reagents used, environmental monitoring and freezing profiles. There were no discrepancies.

BBMR activities relating to one bone marrow donation procured at another licensed establishment and exported to Germany were reviewed. Records reviewed included forms and letters relating to collection of bone marrow, donor testing and documents provided to the courier who transported the collection to Germany.

Incident reporting and management procedures relating to several incidents were reviewed. Staff report all occurrences – unexpected events and deviations using an electronic or paper based system. All reports are reviewed by Quality Assurance staff, who undertake a risk assessment which covers the likelihood of recurrence and impact in order to assign it as an incident (a corrective and preventative action (CAPA) plan has to be put in place) or an occurrence (where no CAPA is required). Each report is assigned to an owner who is responsible for implementing any required actions. Incidents are closed once quality management staff have reviewed and are satisfied with the actions taken.

The HTA inspection team discussed change control procedures relating to repairs being undertaken in the cleanroom where stem cell processing takes place. Quality Assurance staff outlined their procedures including communication, risk assessments and the procedure for bringing the cleanroom back into operation after these repairs were completed. The risk and impact assessment, took into account, people, processes, plant (and equipment) products and regulatory requirements. Quality Assurance staff sought input from stakeholders who would be affected if the clean room was closed and made arrangements to redirect stem cell processing to another NHSBT site whilst the repairs were taking place.

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

All applicable HTA standards have been assessed as fully met.

Advice

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

No.	Standard	Advice
1.	GQ1b	The DI is advised to review and update worksheets and other documentation in use at the Eye Bank to ensure that they reference the NHSBT Eye Bank at the hub site at Filton.
2.	GQ3e	The Eye Bank currently has three members of staff. Three new members of staff are expected to join the Eye Bank over the next two months. Only one member of staff, the Deputy Eye Bank Manager is trained and experienced in all activities undertaken under the licence. The DI is advised to: • review the Training Plan documents and implementation of the training plans for Corneal Excision (SOP5085/1) and Endothelial Assessment (SOP4988) for accuracy and use of language; • monitor the implementation and use of FRM5076 to record training and competency assessments when a procedure has a criticality score of greater than 15. Whilst FRM5076 is mentioned in the current Eye Bank training plan documents, this form is not being used in the Eye Bank. However, the HTA was informed that actions have been taken to implement the use of this form when Eye Bank staff receive training in critical processes; and • consider reviewing the training materials listed on page two of the training plan documents with a view to streamlining the procedure and reducing the number of forms which have to be completed by operational staff (trainers and trainees) to evidence competencies and sign-off. These steps will help the DI to assure himself that training is recorded in accordance with documented procedures and that all staff, including new members of staff, are competent in licensable activities undertaken at the Eye Bank.
3.	PFE 5	The DI is advised to consider swabbing the microscope used to assess the quality of corneas in the Tissue Assessment Room in order to monitor the effectiveness of cleaning before and after the microscope has been used.

Concluding comments

Staff at the Stem Cell Laboratory, BBMR and the Cord Blood Bank have good systems of communication. There are regular meetings with staff at other NHSBT SCI laboratories to review engraftment data for cell therapy products and improve practices. Cell potency assays (colony forming units) are performed when a unit which has been stored for more than 10 years is released. SCI laboratory staff have regular appraisals and are provided with learning and development opportunities.

Staff employed by NHSBT and Bristol NHS Foundation Trust attend joint quality management group meetings each quarter, which cover stem cell collections, adult and paediatric

transplants and incidents. Staff monitor neutrophil and platelet engraftment. There is an effective system of training, observational audits and snapshot audits at the TAS site. The snapshot audit tool for auditing consent covers the consent discussion, description of the procedure, right to withdraw consent and risk/benefit discussions. The consent form used by the TAS staff 'Patient agreement to Investigation or Treatment – (Consent Form 1 FRM403/5)' provides prompts and names of information leaflets for the health professional, which helps to ensure that all key points are mentioned when providing information to donors. There is also a section prompting the consent seeker to document any particular concerns raised by the patient and record religious, spiritual or cultural beliefs.

The HTA has given advice to the Designated Individual with respect to reviewing training plans and their implementation in the Eye Bank, reviewing worksheets and monitoring cleaning of the microscope used in the Eye Bank.

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

Report sent to DI for factual accuracy: 12 April 2017

Report returned from DI: 8 May 2017

Final report issued: 26 May 2017

Appendix 1: HTA standards

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

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

Consent

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

C3 Staff involved in seeking consent receive training and support in the implications and essential requirements of taking consent.
a) Staff involved in obtaining consent are provided with training on how to take informed consent in accordance with the requirements of the HT Act 2004 and Code of Practice on Consent.
b) Training records are kept demonstrating attendance at training on consent.

Governance and Quality

Standard
GQ1 All aspects of the establishment's work are supported by ratified documented policies and procedures as part of the overall governance process.
a) There is an organisational chart clearly defining the lines of accountability and reporting relationships.
b) There are procedures for all licensable activities that ensure integrity of tissue and / or cells and minimise the risk of contamination.
c) There are regular governance meetings, for example health and safety, risk management and clinical governance committees, which are recorded by agendas and minutes.
d) There is a document control system to ensure that changes to documents are reviewed, approved, dated and documented by an authorised person and only current documents are in use.
e) There are procedures for tissue and / or cell procurement, which ensure the safety of living donors.
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.
e) Testing of donor samples is carried out using CE marked diagnostic tests.
f) Samples taken for donor testing are clearly labelled with the time and place the sample was taken and a unique donor identification code.
GQ6 A coding and records system facilitates traceability of tissues and / or cells, ensuring a robust audit trail.
a) There is a donor identification system which assigns a unique code to each donation and to each of the products associated with it.
b) An audit trail is maintained, which includes details of when the tissues and / or cells were acquired and from where, the uses to which the tissues and / or cells were put, when the tissues and / or cells were transferred elsewhere and to whom.
c) The establishment has procedures to ensure that tissues and / or cells imported, procured, processed, stored, distributed and exported are traceable from donor to recipient and vice versa.
GQ7 There are systems to ensure that all adverse events, reactions and/or incidents are investigated promptly.
a) There are procedures for the identification, reporting, investigation and recording of adverse events and reactions, including documentation of any corrective or preventative actions.
b) There is a system to receive and distribute national and local information (e.g. HTA regulatory alerts) and notify the HTA and other establishments as necessary of serious adverse events or reactions.

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

Premises, Facilities and Equipment

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

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

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

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

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 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.