Site visit inspection report on compliance with HTA minimum standards

Birmingham Children's Hospital

HTA licensing number 11005

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**

7-8 November 2017

Summary of inspection findings

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

Although the HTA found that Birmingham Children's Hospital (the establishment) had met the majority of the HTA standards, 14 minor shortfalls were found in relation to accurate documentation of practices, terms of end user agreements, internal and independent audits, recording of raw data during processing, validation for microbial testing, risk assessments relating to premises and practices, equipment maintenance contracts, cleaning logs and storage of reagents.

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

The HTA's regulatory requirements

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

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

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

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

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

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

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

Licensable activities carried out by the establishment

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

'E*' = Establishment is licensed to carry out this activity, but is not currently doing so.

'SLA' = Service level agreement; the establishment is licensed for this activity but another establishment carries out the activity on their behalf.

Tissue Category; Tissue Type	Procurement	Processing	Testing	Storage	Distribution	Import	Export
Cardiovascular, Valves; Heart Valves	**E***	**E**	**SLA**	**E**	**E**		
Progenitor Cell, Haematopoietic, Bone Marrow; Bone Marrow	**E**		**E/SLA**		**E**		
Progenitor Cell, Haematopoietic, PBSC; PBSC	**E**		**E/SLA**		**E**		
Mature Cell, T Cell (DLI); DLI	**E**		**E/SLA**		**E**		
Membrane, Amniotic; Amniotic Membrane				**E**			

Musculoskeletal Bone; Cranial Flap	**E**		**E/SLA**	**E**			
Ocular; Cornea				**E**			
Ocular; Sclera				**E**			
Skin; Skin	**E***		**E***	**E**			

Background to the establishment and description of inspection activities undertaken

The establishment is part of the Birmingham Women's and Children's NHS Foundation Trust. The establishment operates a heart valve bank (HVB), the core activity of which is the processing of heart valves from donor hearts, and a stem cell transplant programme for autologous and allogeneic treatment of paediatric patients.

Heart Valve Bank (HVB)

Hearts are distributed to the establishment as part of the National Fulfilment Scheme (NFS), which allocates donated cardiovascular tissue to patients listed nationally. Under the NFS, hearts from deceased donors are received at the HVB from centres around the UK, under the appropriate agreements. The establishment is one of four independent heart valve processing centres and receives hearts from donors located mainly in the West Midlands. Once processed by the establishment, the valves are cryopreserved and stored at the HVB for use locally or for distribution. Where valves are deemed unsuitable for transplantation, they may be stored for research if appropriate consent is in place.

In all cases, consent for the donation and serological testing for mandatory markers is performed by another HTA-licensed establishment. Test results are uploaded onto a shared electronic offering system by the other HTA-licensed establishment where they can be reviewed by the establishment prior to processing. Upon receipt, HVB staff carry out further assessments on donor travel and medical history to ensure suitability of the donor prior to processing of the heart.

The hearts are processed in a dedicated clean room. The microbiological safety cabinets (MSC) in the clean room maintain a Grade A environment within a Grade B background. Following dissection, valves are incubated in an antibiotic solution overnight at room temperature. The following day, the valves are packaged and cryopreserved for storage at -190ºC. Dissection and packaging of the valves is performed in separate MSCs. Environmental monitoring is conducted in accordance with the requirements of HTA Directions 003/2010. During the initial dissection process, settle plates are used. For the final packaging stage, non-viable automated particle counting, settle plates and finger dabs are performed. Any remaining heart tissue may be stored at -20ºC in a dedicated freezer at the HVB or sent immediately to another tissue bank for research use, if suitable consent is in place.

On rare occasions, the HVB stores cranial bone flaps for autologous use in the hospital. The bone flaps are autoclaved, labelled with the patient ID and stored in a dedicated area within the storage facility. The establishment also purchases and stores additional heart valves, ocular tissue, amniotic membranes and skin from other HTA-licensed establishments for use locally at the hospital. All storage equipment is linked to a continuous temperature monitoring system that alerts staff on a 24-hour basis should any deviations in temperature occur.

The inspection included a visual inspection of the HVB, where the clean room for processing heart valves and storage facilities for the tissues and cells and processing records were viewed. The inspection also included discussions with the DI, who is also a Consultant

Anaesthetist, and Tissue Processing Specialist Staff. Six processing records for heart valves were reviewed for evidence of appropriate consent, serology, recording of consumables and reagents, environmental monitoring and traceability. No discrepancies were found.

Stem Cell Transplant (SCT) programme

The SCT programme in the Paediatric Stem Cell Unit is part of the Blood, Stem Cell Transplant and Cancer Group at the establishment. Peripheral blood stem cells (PBSCs) and bone marrow (BM) are procured for autologous and allogeneic transplant. Consent for the treatment is taken by trained consultants. Blood samples for serology testing of mandatory markers is taken within 30 days of the harvest. All mandatory testing, processing, storage and distribution of the cells are carried out at another HTA-licensed establishment under terms of an appropriate agreement. Specialist nurses take responsibility for coordinating transport of the cells to the other establishment. Additional testing for mandatory serology is performed at the establishment's own testing laboratory. The cells are returned to the establishment for subsequent transplantation.

The inspection included a visual inspection of the facilities where the procurement kits and reagents for PBSCs and BM are stored and round table discussions with key members of staff including the Clinical Programme Director who is also the Lead Haematology Consultant, the Quality Manager and members of the Specialist Nursing Team. Six sets of patient records for sibling and autologous donors were audited for evidence of appropriate consent, traceability and processing records. Discrepancies were found relating to the consistency of record keeping for traceability and processing records.

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

Governance and Quality

Standard	Inspection findings	Level of shortfall
GQ1 All aspects of the establishment's work are supported by ratified documented policies and procedures as part of the overall governance process.		
b) There are procedures for all licensable activities that ensure integrity of tissue and / or cells and minimise the risk of contamination.	The establishment's practices are not accurately reflected in the documentation. For example, • The standard operation procedure (SOP) for microbial contamination checks do not include the checks performed on transport fluid and washing medium used during processing; • The SOP for contingency arrangements does not include the back-up controlled rate freezer or -150ºC electric freezer. The SOP also does not include the contingency arrangement in the event of a breakdown of the refrigerator used for vessel storage; and • The HVB also has SOPs in circulation that are not applicable to the establishment's current practices, for example SOPs for storage of kidneys and for snap-freezing of cranial flaps.	**Minor**
g) There are procedures to ensure that an authorised person verifies that tissues and / or cells received by the establishment meet required specifications	Although the HVB staff are able to describe the correct procedure for tissue receipt, there is no documented SOP and steps to take when the received tissue does not conform to required standards.	**Minor**
r) Third party agreements specify the responsibilities of the third party and meet the requirements set out in Directions 003/2010.	The establishment's end user agreements do not stipulate the requirement to report Serious Adverse Events and Reactions (SAEARs) to the DI within 24 hours of discovery of the event, that tissue is not stored over 48 hours except on HTA-licensed premises and for traceability data to be retained for 30 years.	**Minor**
s) Third party agreements specify that the third party will inform the establishment in the event of a serious adverse reaction or event.		

GQ2 There is a documented system of quality management and audit.		
b) There is an internal audit system for all licensable activities.	The HVB internal audits do not assess compliance against the full scope of licensable activities. Completed audits do not include corrective actions to ensure the discrepancies found are not repeated.	**Minor**
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.	While the HVB and SCT programme are audited annually by an external company, the audit does not assess the establishment's compliance against all HTA standards.	**Minor**
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.	The establishment performs an antibiotic incubation step that is used to reduce the microbial burden during processing of heart valves. The extent of microbiological contamination of the tissue is currently assessed using a sample following incubation in antibiotics. During the inspection, the establishment was unable to provide assurance that the antibiotics do not interfere with the microbial growth tests. No documented validation for the acceptability of this process was made available given the presence of the antibiotic.	**Minor**
GQ4 There is a systematic and planned approach to the management 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.	During a review of the SCT patient records, it was noted that the majority of the forms were inconsistently completed. Missing information included the absence of the second sign-off in the apheresis care pathway, confirmation of absence of incidents during infusion, anticoagulant batch details and the name of staff responsible for the stem cell collection in the final 'collection checklist'. The discrepancies have a potential to affect traceability during incident investigations.	**Minor**
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.	Pressure recordings of the clean room are not recorded on all days processing takes place. While pressure differentials are recorded Monday to Friday irrespective of any processing taking place, pressure readings during weekends are not logged even though processing may occur.	**Minor**

GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately.		
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.	While the HVB has risk assessments for processing and storage of tissue, the assessments are not reviewed annually. Recent changes associated with the implementation of new equipment and the employment of new processing staff have not been considered.	**Minor**

Premises, Facilities and Equipment

Standard	**Inspection findings**	**Level of shortfall**
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.	The HVB has no formal documentation to capture all risks associated with premises and facilities.	**Minor**
PFE2 Environmental controls are in place to avoid potential contamination.		
c) There are procedures for cleaning and decontamination.	While the SCT programme staff are able to describe the daily and weekly procedures for cleaning of the apheresis machine, there is no record showing weekly decontamination of the machine.	**Minor**
PFE3 There are appropriate facilities for the storage of bodies, body parts, tissues, 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.	Reagents used for apheresis are stored in a temperature-monitored room. However, records indicate that the temperature of the room frequently deviates from the limits set by the reagent manufacturer. The establishment had not identified these excursions nor taken appropriate corrective action. *Note: Following identification of this shortfall during the inspection, the establishment has addressed this by moving the reagent to a temperature-controlled area. The HTA has assessed the information provided as satisfactory and considers this standard to be met.*	**Minor**

PFE4 Systems are in place to protect the quality and integrity of bodies, body parts, tissues and cells during transport and delivery to a destination.		
h) Packaging and containers used for transportation are validated to ensure they are fit for purpose.	The HVB very occasionally uses transport boxes for storage of frozen tissue in theatre. While staff are able to describe the validation performed to ensure maintenance of temperatures for up to five days, this validation is not documented.	**Minor**
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. e) There are documented agreements with maintenance companies.	There are no maintenance contracts in place for the particle counter used for environmental monitoring during processing or for the cryostore tanks used for storage of tissue. Both pieces of equipment have not been inspected in accordance with the manufacturer's instructions. The establishment has an agreement in place for maintenance of the clean room. The agreement does not cover testing of the HEPA filters which are under the responsibility of the hospital's estates department. The establishment was unable to provide evidence that the filters have been routinely checked and re-qualified to ensure that it is functioning as required.	**Minor**

Advice

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

No.	Standard	Advice
1.	GQ1b	The DI should to implement an alarm system to ensure staff are alerted when the control rate freezing programme is complete to enable prompt transfer to liquid nitrogen storage.
2.	GQ1j	The DI is advised to record the batch number of EDTA tubes used for serology testing.
3.	GQ2d	The DI should explore ways to strengthen ties with the microbiology laboratory to ensure there is adequate oversight over the activities carried out at the laboratory under authority of the HTA licence.
4.	GQ2d	The DI is advised to review the protocol for the microbial analysis of environmental monitoring plates to ensure the procedure employed is appropriate for the HVB's requirements and in line with guidance from the

		European Pharmacopeia and European Directorate for the Quality of Medicines. The basis for any differences in procedures should be documented.
5.	GQ3d	Although the gowning procedure for entering the clean room is assessed during staff induction, there is no refresher training or revalidation of gowning procedures following this induction. The DI is advised to implement gowning revalidation checks to ensure that staff continue to follow the correct gowning procedure.
6.	GQ4h	The HVB uses a tissue log book for recording the time of tissue receipt and the staff responsible for delivering or receiving the tissue. The DI is advised to amend the form to also record the reference number and type of tissue that is received to ensure full traceability when multiple shipments arrive on the same day.
7.	GQ5b	The DI is advised to clearly document in the relevant SOP the required temperature range and timeframes for storage of blood samples for NAT testing, as set out in the agreement between the external testing laboratory and the establishment. Staff should be trained to ensure they are aware of the requirements.
8.	GQ7a	The DI is advised to appoint further staff at the HVB and SCT unit as Persons Designated to ensure all SAEARs are reported to the HTA within 24 hours of discovery of the event.
9.	GQ7a	The SCT unit has in place a good system to ensure any incidents that occur are investigated and steps are taken to ensure they are not repeated. For example following contamination of a harvest, a review of the SOP with procurement personnel was performed. However, this action was not documented. The DI should to ensure these preventative actions are formally recorded for closure.
10.	GQ7a	The DI should ensure the SCT programme's SOP for reporting incidents includes the description of events that need to be escalated to the HTA during procurement and testing, in addition to end use, in accordance to the "Guide to Quality and Safety Assurance for Human Tissues and Cells for Patient Treatment".
11.	PFE1a	The establishment has plans to move the SCT unit to a new premise shortly. The DI is advised to notify the HTA prior to the move to ensure the premise is assessed for suitability.
12.	PFE2b	The DI is advised to ensure the monitoring of the grade B areas using settle plates takes place during operational procedures. Additional monthly monitoring checks of clean rooms should be performed during operation or during simulation exercises.
13.	PFE3a	The DI is advised to update the SOP relating to storage of reagents and consumables used for apheresis in line with the recent change in storage rooms.
14.	PFE3a	The DI is advised to contact the manufacturer of the cryopreservation media used during processing to confirm the appropriate temperature range for its storage. The manufacturer currently only specifies storage at room temperature.

15.	-	The DI is advised to review the Quality Manual to ensure that it refers to the Human Tissue (Quality and Safety for Human Application) Regulations 2007.

Concluding comments

There were a number of strengths and areas of good practice observed during the inspection. Upon receipt of a donor heart, the HVB staff perform a comprehensive review of the donors' medical and travel history in line with the most recent Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee (JPAC) donor selection guidelines. This is clearly documented within the tissue processing records. Being a paediatric unit, the SCT staff also take great care to ensure that donors and recipients are supplied with information in a manner and format appropriate for their age and level of understanding, which include stories and videos.

There are a number of areas of practice that require improvement, which resulted in 14 minor shortfalls. The HTA has given advice to the Designated Individual with respect to setting alarm alerts during control rate freezing procedures, recording of consumables, environmental monitoring of clean rooms, changes to new premises, appointing new PDs, incident reporting actions and closure, updating SOPs in relation to new storage facilities and storage of blood samples prior to NAT assays.

The HTA requires that the Designated Individual addresses the shortfalls by submitting a completed corrective and preventative action (CAPA) plan within 14 days of receipt of the final report (refer to Appendix 2 for recommended timeframes within which to complete actions). The HTA will then inform the establishment of the evidence required to demonstrate that the actions agreed in the plan have been completed.

The HTA has assessed the establishment as suitable to be licensed for the activities specified subject to corrective and preventative actions being implemented to meet the shortfalls identified during the inspection.

Report sent to DI for factual accuracy: 6 December 2017

Report returned from DI: 14 December 2017

Final report issued: 22 December 2017

Completion of corrective and preventative actions (CAPA) plan

Based on information provided, the HTA is satisfied that the establishment has completed the agreed actions in the CAPA plan and in doing so has taken sufficient action to correct all shortfalls addressed in the Inspection Report.

Date: 27 September 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.
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

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 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.