Site visit inspection report on compliance with HTA minimum standards

Manchester University NHS Foundation Trust - Central Hospitals

HTA licensing number 22596

Licensed for the

- **procurement, processing, testing, storage, distribution and export of human tissues and cells for human application under the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended); and**
- **storage of relevant material which has come from a human body for use for a scheduled purpose**

14 – 15 May 2019

Summary of inspection findings

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

Although the HTA found that Manchester University NHS Foundation Trust - Central Hospitals (the establishment) had met the majority of the HTA standards, two minor shortfalls were found in relation to governance and quality system standards namely, donor selection criteria and documenting the validation of the contingency freezing processes. The HTA has also given advice to the Designated Individual with respect to consent documentation, procedural documentation, agreements with other organisations, risk assessment, processing records and temperature monitoring.

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

The HTA's regulatory requirements

The HTA must assure itself that the Designated Individual, 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 carrying it out.

Tissue Category; Tissue Type	Procurement	Processing	Testing	Storage	Distribution	Import	Export
Progenitor Cell, Hematopoietic, Bone Marrow; Bone Marrow	**E**	**E**	**E**	**E**	**E**		
Progenitor Cell, Hematopoietic, PBSC; PBSC	**E**	**E**	**E**	**E**	**E**		
Progenitor Cell, Hematopoietic, Cord Blood; Cord Blood	**E***	**E**	**E***	**E**	**E**		
Progenitor Cell, Hematopoietic, Unspecified Mature Cell, T Cell; PBMC	**E**	**E**	**E**	**E**	**E**		**E**

Background to the establishment and description of inspection activities undertaken

The establishment is licensed for the procurement, processing, testing, storage, distribution and export of human tissues and cells for human application under the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended) (the Regulations). The establishment is also licensed for the storage of relevant material for use in a scheduled purpose under the Human Tissue Act 2004 (HT Act); however, activity taking place under the HT Act's legislation was not reviewed during this inspection since the establishment informed the inspection team that no activity was taking place under this licence.

The establishment has been licensed by the HTA since October 2009 and this report relates to the fifth routine site visit inspection to assess whether or not the establishment meets the HTA's standards. Annual activity data, pre-inspection discussions with the DI, pre-inspection discussions with the DI's representative and the previous inspection report were used to inform the timetable that was developed for this inspection.

The establishment procures peripheral blood stem cells (PBSCs) and bone marrow for autologous and allogeneic use from adult donors. Paediatric donors can donate bone marrow for autologous and allogeneic use and PBSCs for autologous use. In some cases, for both adult and paediatric donations, donor lymphocyte infusions (DLIs) may also be prepared from procured cells.

Although licensed for the procurement of cord blood, the establishment is not currently undertaking this activity. Cord blood units from HTA-licensed donor registries may be received and processed by the establishment before being issued for end use.

In addition, peripheral blood mononuclear cells (PBMCs) are procured as a starting material for an advanced therapy medicinal product (ATMP). In these cases, donor selection and testing, procurement, and processing take place under the establishment's HTA licence. Procured PBMCs are either sent as fresh cells to a manufacturing site which produces the ATMP or are cryopreserved before being sent to a manufacturing site. In both cases, the ATMP manufacturer is responsible for transport of the procured cells.

The establishment processes cells prior to issuing them as a fresh product and cryopreserves them prior to storage within vapour phase liquid nitrogen. Cells are processed within the establishment's clean room facility. The clean room consists of a grade A air quality cabinet within a room providing a grade B background.

During the inspection, a review of the establishment's governance and quality system was undertaken, looking at audit activity, training records, governance meetings, equipment maintenance and incidents, including reporting procedures. Visits were also undertaken of both adult and paediatric PBSC procurement areas, the establishment's clean room processing facility, storage facility, serological testing laboratory and microbiology laboratory.

During the inspection, four sets of records relating to the processing of cells procured by the establishment were reviewed. In addition, relevant procedural documents relating to the processing were assessed. For each donor, the following documents were reviewed:

Donor 1 Adult, Autologous PBSC

Request to process form, donor consent form, pre-processing planning sheet, records of cell collection bag label creation and sending to the apheresis procurement team, product acceptance checklist (which records the condition of cells on arrival at the processing facility, checks on the donor consent form and signatures at handover of the cells to the laboratory staff), overnight storage sheet (which records whether a dilution is necessary due to high

white blood cell count and the times that the cells are placed into and removed from the fridge), apheresis worksheet (which records consumables used during procurement), the CD34 calculation sheet (which records the two person check of the calculation), plasma depletion worksheet, the cryopreservation worksheet (which records the cryoprotectant calculations), batch sheet (which records consumables and reagents used in processing), the post-processing microbiology results, post-cryopreservation CD34 viability assay results, and donor mandatory serological testing results (including a verification that the testing was performed within 30 days prior to procurement).

Donor 1's cells had also been issued for infusion and the following documents were reviewed:

The medic's transplant protocol detailing the required cell dose for the recipient, the infusion report, the tissue release form (which includes the authorisation for release of the cells, records of checks on donor virology and records of associated raw data such as environmental monitoring during processing), incident report form used to capture any incidents relating to the cells, the temperature records relating to transport of the cells to the ward for end use, the request to issue form (which includes the medic's request for certain bags of cryopreserved cells), the infusion reaction form used to record any infusion-related reactions in the recipient and, finally, all of the environmental monitoring data from the processing of the cells including the non-viable particle counts, settle plate results, finger dab results and the controlled-rate freezer temperature profile.

Donor 2 Paediatric, Autologous PBSC

The same records as Donor 1; however, cells had not been issued at the time of the inspection so no release or infusion related documents were reviewed. During the review of the other documents, it was found that the sample for serological testing had been taken the day prior to the consent for the collection. The establishment clarified that verbal consent for testing would have been sought at the time of the blood draw; however, advice has been given below regarding the recording of consent. In addition, the microbiology sterility results following processing were not filed as expected; however, the results were available electronically and were reviewed.

Donor 3 Paediatric, Allogeneic PBSC

The same records as Donor 1; however, again, cells had not been issued at the time of the inspection so no release or infusion related documents were reviewed. In addition, the independent medical assessment, HTA Accredited Assessment and HTA donor approval documentation were reviewed.

Donor 4 Adult, Allogeneic (related) PBSC

Documentation regarding the donor clearance by the medical team was reviewed along with records of consent and donor testing.

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
GQ2 There is a documented system of quality management and audit.		
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.	Should the establishment's controlled-rate freezer fail, there is a contingency plan through which cells are frozen using a passive freezing process. This process involves cells being frozen in a -80^{o}C freezer before being placed into liquid nitrogen vapour phase storage. The establishment's passive freezing process has not been formally validated.	**Minor**
GQ5 There are documented procedures for donor selection and exclusion, including donor criteria.		
a) Donors are selected either by the establishment or the third party acting on its behalf in accordance with the criteria required by Directions 002/2018.	The establishment's allogeneic donor selection procedures do not reflect all of the donor exclusion criteria as defined in Annex A of Directions 002/2018. The establishment's selection procedure does not include questions regarding Ingestion of, or exposure to, a substance (such as cyanide, lead, mercury, gold) that may be transmitted to recipients in a dose that could endanger their health. or regarding xenotransplantation.	**Minor**

Advice

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

No.	Standard	Advice
1.	C1(d)	The DI is advised to consider including details of the donor serology testing within the consent form for paediatric donors as is the case with the adult consent forms. This may help to provide a record that the donor, or person with parental responsibility if appropriate, has received this information. In addition, the DI is advised to implement a system through which consent for serology testing is documented at the time that it is sought and prior to a testing sample being taken.
2.	C1(d) C2(c)	All donors at the establishment are now tested for Hepatitis E prior to donation. The DI is advised to consider updating the consent forms and donor information to reflect that all donors will be tested for Hepatitis E.
3.	GQ1(b)	Viability assessments may be undertaken on cells that have been in storage for prolonged periods of time when they are requested for infusion. Although taking

		place, this process of viability testing has not been proceduralised within the establishment's suite of standard operating procedures (SOPs). The DI is advised to develop a new SOP or include the viability testing within an existing SOP so that the process is documented.
4.	GQ1(p)	Nurses from another organisation with expertise in paediatric apheresis undertake procurement of paediatric PBSCs. There is a service level agreement in place between the nurses' organisation and the establishment. However, a review of this document found that it had not been updated to include the procurement of PBMCs. The DI is advised to review and update this agreement accordingly. In addition, the document states that it is the nurses' organisation that is responsible for donor testing, processing and storage of donor cells when in fact this is the responsibility of the establishment. The DI is advised to review and update as necessary the matrix of responsibilities within the agreement so that it accurately reflects each party's responsibilities.
5.	PFE1(a)	The establishment has risk assessed the area where adult apheresis procedures are undertaken. Paediatric apheresis procedures are undertaken in clinical areas which are subject to risk assessments. However, the DI is advised to undertake a specific risk assessment relating to the procurement of PBSCs in these areas. In addition, the DI is advised to implement a procedure through which the temperature of the paediatric procurement area is verified prior to procurement commencing. This may help to assure the DI that the temperature of the procurement room is within the range required by the manufacturer of the apheresis equipment.
6.	PFE2(b)	During the review of processing records, examples were found where environmental monitoring settle plate data and post-processing microbiology sterility data had not been filed as expected. These data are currently stored in files separate to the donor files. Although hard copies of these data could not be found, electronic versions were stored on the establishment's electronic system and were available for review. The DI is advised to consider filing all data relating to donors and the processing of their cells in the same file which may help to facilitate review of such data if needed. In addition, when senior staff authorise cells for release, there is only one check box on the authorisation paperwork to record the review of environmental monitoring data and its suitability. The results from non-viable particle counters and microbiological results from settle plates, finger dabs and viable air sampling are received at different times. The DI is advised to consider adding an additional check box to the authorisation for release form so that reviews of non-viable particulate data can be recorded separately to reviews of other environmental monitoring data. This may help in documenting the review of both sets of data and would allow reviews of such data to occur independently from each other while still maintaining a record of each review undertaken.
7.	PFE3(a)	The establishment has recently reviewed and updated the upper and lower temperature alarm limits on its electronic temperature monitoring system. For one of the establishment's probes however, this adjustment did not occur in error meaning that the upper and lower temperature alarm limits for that area do not reflect the upper and lower storage temperature limits of some reagents stored within it. The DI is advised to update the alarm limits of the relevant temperature probe as planned. In addition, the establishment stores a cleaning solution that is used within the processing suite in an unmonitored environment; the solution's manufacturer states that is should not be stored above 25°C. The DI is advised to review

		temperature monitoring arrangements for the cleaning reagent to assure themselves that it is stored in a suitably monitored environment and that establishment staff would be alerted to any deviations in storage temperature that may impact its quality or efficacy.
8.	PFE3(a)	The reagents and consumables used for paediatric apheresis are stored off-site in a temperature-monitored environment. The off-site storage is overseen by the paediatric apheresis nurses however, the DI is advised to implement a procedure through which they can assure themselves, and document, that appropriate storage conditions have been maintained. The DI may wish to consider a system through which storage temperatures are reviewed when reagents and consumables are removed from storage prior to apheresis, this review may then be documented and may help to provide assurance that storage conditions have remained within the required ranges.

Concluding comments

Good practice was also observed during the inspection. The Trust had developed high-level training relating to the HTA and the various legislative requirements. When clinical staff undertake their training, where applicable, this Trust HTA training is included. This helps to assure the DI that staff working under the HTA licence are aware of the regulatory context within which they are working.

There are a number of areas of practice that require improvement, including two minor shortfalls relating to donor selection criteria and documenting the validation of the contingency freezing process. The HTA has given advice to the Designated Individual with respect to consent documentation, procedural documentation, agreements with other organisations, risk assessment, processing records and temperature monitoring.

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: 12 June 2019

Report returned from DI: 18 June 2019

Final report issued: 17 July 2019

Completion of corrective and preventative actions (CAPA) plan

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

Date: 11 November 2019

Appendix 1: HTA standards

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

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

Consent

Standard
C1 Consent is obtained in accordance with the requirements of the HT Act 2004, the Human Tissue (Quality and Safety for Human Application) Regulations 2007 and as set out in the HTA's Codes of Practice.
a) If the establishment acts as a procurer of tissues and / or cells, there is an established process for acquiring donor consent which meets the requirements of the HT Act 2004 the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (Q&S Regulations) and the HTA's Codes of Practice
c) The establishment or the third party's procedure on obtaining donor consent includes how potential donors are identified and who is able to take consent.
d) Consent forms comply with the HTA Codes of Practice.
e) Completed consent forms are included in records and are made accessible to those using or releasing tissue and / or cells for a Scheduled Purpose.
C2 Information about the consent process is provided and in a variety of formats.
a) The procedure on obtaining consent details what information will be provided to donors. As a minimum, the information specified by Directions 002/2018 is included.
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.
n) The establishment ensures imports from non EEA states meet the standards of quality and safety set out in Directions 002/2018.
o) There is a complaints system in place.

p) There are written agreements with third parties whenever an activity takes place that has the potential to influence the quality and safety of human tissues and / or cells.
q) There is a record of agreements established with third parties.
r) Third party agreements specify the responsibilities of the third party and meet the requirements set out in Directions 002/2018.
s) Third party agreements specify that the third party will inform the establishment in the event of a serious adverse reaction or event.
t) There are procedures for the re-provision of service in an emergency.
GQ2 There is a documented system of quality management and audit.
a) There is a quality management system which ensures continuous and systematic improvement.
b) There is an internal audit system for all licensable activities.
c) An audit is conducted in an independent manner at least every two years to verify compliance with protocols and HTA standards, and any findings and corrective actions are documented.
d) Processes affecting the quality and safety of tissues and / or cells are validated and undergo regular evaluation to ensure they continue to achieve the intended results.
GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills.
a) There are clearly documented job descriptions for all staff.
b) There are orientation and induction programmes for new staff.
c) There are continuous professional development (CPD) plans for staff and attendance at training is recorded.
d) There is annual documented mandatory training (e.g. health and safety and fire).
e) Personnel are trained in all tasks relevant to their work and their competence is recorded.
f) There is a documented training programme that ensures that staff have adequate knowledge of the scientific and ethical principles relevant to their work, and the regulatory context.
g) There is a documented training programme that ensures that staff understand the organisational structure and the quality systems used within the establishment.
h) There is a system of staff appraisal.
i) Where appropriate, staff are registered with a professional or statutory body.
j) There are training and reference manuals available.
k) The establishment is sufficiently staffed to carry out its activities.
GQ4 There is a systematic and planned approach to the management of records.
a) There are procedures for the creation, identification, maintenance, access, amendment, retention and destruction of records.

b) There is a system for the regular audit of records and their content to check for completeness, legibility and accuracy and to resolve any discrepancies found.
c) Written records are legible and indelible. Records kept in other formats such as computerised records are stored on a validated system.
d) There is a system for back-up / recovery in the event of loss of computerised records.
e) The establishment keeps a register of the types and quantities of tissues and / or cells that are procured, tested, preserved, processed, stored and distributed or otherwise disposed of, and on the origin and destination of tissues and cells intended for human application.
f) There are procedures to ensure that donor documentation, as specified by Directions 002/2018, is collected and maintained.
g) There is a system to ensure records are secure and that donor confidentiality is maintained in accordance with Directions 002/2018.
h) Raw data which are critical to the safety and quality of tissues and cells are kept for 10 years after the use, expiry date or disposal of tissues and / or cells.
i) The minimum data to ensure traceability from donor to recipient as required by Directions 002/2018 are kept for 30 years after the use, expiry or disposal of tissues and / or cells.
j) Records are kept of products and material coming into contact with the tissues and / or cells.
k) There are documented agreements with end users to ensure they record and store the data required by Directions 002/2018.
l) The establishment records the acceptance or rejection of tissue and / or cells that it receives and in the case of rejection why this rejection occurred.
m) In the event of termination of activities of the establishment a contingency plan to ensure records of traceability are maintained for 10 or 30 years as required.
GQ5 There are documented procedures for donor selection and exclusion, including donor criteria.
a) Donors are selected either by the establishment or the third party acting on its behalf in accordance with the criteria required by Directions 002/2018.
b) The testing of donors by the establishment or a third party on behalf of the establishment is carried out in accordance with the requirements of Directions 002/2018.
c) In cases other than autologous donors, donor selection is carried out by authorised personnel and signed and reviewed by a qualified health professional.
d) There is a system in place either at the establishment or at a third party acting on its behalf to record results of donor selection and associated tests.
e) Testing of donor samples is carried out using CE marked diagnostic tests.
f) Samples taken for donor testing are clearly labelled with the time and place the sample was taken and a unique donor identification code.

GQ6 A coding and records system facilitates traceability of tissues and / or cells, ensuring a robust audit trail.
a) There is a donor identification system which assigns a unique code to each donation and to each of the products associated with it.
b) An audit trail is maintained, which includes details of when the tissues and / or cells were acquired and from where, the uses to which the tissues and / or cells were put, when the tissues and / or cells were transferred elsewhere and to whom.
c) The establishment has procedures to ensure that tissues and / or cells imported, procured, processed, stored, distributed and exported are traceable from donor to recipient and vice versa.
d) The requirements of the Single European Code are adhered to as set out in Directions 002/2018.
GQ7 There are systems to ensure that all adverse events, reactions and/or incidents are investigated promptly.
a) There are procedures for the identification, reporting, investigation and recording of adverse events and reactions, including documentation of any corrective or preventative actions.
b) There is a system to receive and distribute national and local information (e.g. HTA regulatory alerts) and notify the HTA and other establishments as necessary of serious adverse events or reactions.
c) The responsibilities of personnel investigating adverse events and reactions are clearly defined.
d) There are procedures to identify and decide the fate of tissues and / or cells affected by an adverse event, reaction or deviation from the required quality and safety standards.
e) In the event of a recall, there are personnel authorised within the establishment to assess the need for a recall and if appropriate initiate and coordinate a recall.
f) There is an effective, documented recall procedure which includes a description of responsibilities and actions to be taken in the event of a recall including notification of the HTA and pre-defined times in which actions must be taken.
g) Establishments distributing tissue and / or cells provide information to end users on how to report a serious adverse event or reaction and have agreements with them specifying that they will report these events or reactions.
h) Establishments distributing tissues and / or cells have systems to receive notifications of serious adverse events and reactions from end users and notify the HTA.
GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately.
a) There are documented risk assessments for all practices and processes.
b) Risk assessments are reviewed regularly, as a minimum annually or when any changes are made that may affect the quality and safety of tissues and cells.
c) Staff can access risk assessments and are made aware of local hazards at training.
d) A documented risk assessment is carried out to decide the fate of any tissue and / or cells stored prior to the introduction of a new donor selection criteria or a new processing step, which enhances the quality and safety of tissue and / or cells.

Premises, Facilities and Equipment

Standard
PFE1 The premises are fit for purpose.
a) A risk assessment has been carried out of the premises to ensure that they are fit for purpose.
b) There are procedures to review and maintain the safety of staff, visitors and patients.
c) The premises have sufficient space for procedures to be carried out safely and efficiently.
e) There are procedures to ensure that the premises are secure and confidentiality is maintained.
f) There is access to a nominated, registered medical practitioner and / or a scientific advisor to provide advice and oversee the establishment's medical and scientific activities.
PFE2 Environmental controls are in place to avoid potential contamination.
a) Tissues and / or cells stored in quarantine are stored separately from tissue and / or cells that have been released from quarantine.
b) Where processing of tissues and / or cells involves exposure to the environment, it occurs in an appropriate, monitored environment as required by Directions 002/2018.
c) There are procedures for cleaning and decontamination.
d) Staff are provided with appropriate protective clothing and equipment that minimise the risk of contamination of tissue and / or cells and the risk of infection to themselves.
PFE3 There are appropriate facilities for the storage of tissues and / or cells, consumables and records.
a) Tissues, cells, consumables and records are stored in secure environments and precautions are taken to minimise risk of damage, theft or contamination.
b) There are systems to deal with emergencies on a 24 hour basis.
c) Tissues and / or cells are stored in controlled, monitored and recorded conditions that maintain tissue and / or cell integrity.
d) There is a documented, specified maximum storage period for tissues and / or cells.
PFE4 Systems are in place to protect the quality and integrity of tissues and / or cells during transport and delivery to its destination.
a) There is a system to ensure tissue and / or cells are not distributed until they meet the standards laid down by Directions 002/2018.
b) There are procedures for the transport of tissues and / or cells which reflect identified risks associated with transport.
c) There is a system to ensure that traceability of tissues and / or cells is maintained during transport.
d) Records are kept of transportation and delivery.
e) Tissues and / or cells are packaged and transported in a manner and under conditions that

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

Disposal

Standard
D1 There is a clear and sensitive policy for disposing of tissues and / or cells.
a) The disposal policy complies with HTA's Codes of Practice.
b) The disposal procedure complies with Health and Safety recommendations.
c) There is a documented procedure on disposal which ensures that there is no cross contamination.

D2 The reasons for disposal and the methods used are carefully documented.
a) There is a procedure for tracking the disposal of tissue and / or cells that details the method and reason for disposal.
b) Disposal arrangements reflect (where applicable) the consent given for disposal.

Human Tissue Act 2004 Standards

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

Governance and quality system standards
GQ1 All aspects of the establishments work are governed by documented policies and procedures as part of the overall governance process
a) Ratified, documented and up-to-date policies and procedures are in place, covering all licensable activities.
b) There is a document control system.
c) There are change control mechanisms for the implementation of new operational procedures.
d) Matters relating to HTA-licensed activities are discussed at regular governance meetings, involving establishment staff.

e) There is a system for managing complaints.
GQ2 There is a documented system of audit
a) There is a documented schedule of audits covering licensable activities. b) Audit findings include who is responsible for follow-up actions and the timeframes for completing these.
GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills
a) Qualifications of staff and all training are recorded, records showing attendance at training. b) There are documented induction training programmes for new staff. c) Training provisions include those for visiting staff. d) Staff have appraisals and personal development plans.
GQ4 There is a systematic and planned approach to the management of records
a) There are suitable systems for the creation, review, amendment, retention and destruction of records. b) There are provisions for back-up / recovery in the event of loss of records. c) Systems ensure data protection, confidentiality and public disclosure (whistleblowing).
GQ5 There are systems to ensure that all adverse events are investigated promptly
a) Staff are instructed in how to use incident reporting systems. b) Effective corrective and preventive actions are taken where necessary and improvements in practice are made.
GQ6 Risk assessments of the establishment's practices and processes are completed regularly, recorded and monitored
a) There are documented risk assessments for all practices and processes requiring compliance with the HT Act and the HTA's Codes of Practice. b) Risk assessments are reviewed regularly. c) Staff can access risk assessments and are made aware of risks during training.

Traceability standards
T1 A coding and records system facilitates the traceability of bodies and human tissue, ensuring a robust audit trail
a) There is an identification system which assigns a unique code to each donation and to each of the products associated with it.

b) A register of donated material, and the associated products where relevant, is maintained.
c) An audit trail is maintained, which includes details of: when and where the bodies or tissue were acquired and received; the consent obtained; all sample storage locations; the uses to which any material was put; when and where the material was transferred, and to whom.
d) A system is in place to ensure that traceability of relevant material is maintained during transport.
e) Records of transportation and delivery are kept.
f) Records of any agreements with courier or transport companies are kept.
g) Records of any agreements with recipients of relevant material are kept.
T2 Bodies and human tissue are disposed of in an appropriate manner
a) Disposal is carried out in accordance with the HTA's Codes of Practice.
b) The date, reason for disposal and the method used are documented.

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

Appendix 2: Classification of the level of shortfall (HA)

Where the HTA determines that a licensing standard is not met, the improvements required will be stated and the level of the shortfall will be classified as 'Critical', 'Major' or 'Minor'. Where the HTA is

not presented with evidence that an establishment meets the requirements of an expected standard, it works on the premise that a lack of evidence indicates a shortfall.

The action an establishment will be required to make following the identification of a shortfall is based on the HTA's assessment of risk of harm and/or a breach of the HT Act or associated Directions.

1. **Critical shortfall:**

   A shortfall which poses a significant direct risk of causing harm to a recipient patient or to a living donor,

   Or

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

   Or

   A number of 'major' shortfalls, none of which is critical on its own, but viewed cumulatively represent a systemic failure and therefore are considered 'critical'.

   A critical shortfall may result in one or more of the following:

   (1) A notice of proposal being issued to revoke the licence

   (2) Some or all of the licensable activity at the establishment ceasing with immediate effect until a corrective action plan is developed, agreed by the HTA and implemented.

   (3) A notice of suspension of licensable activities

   (4) Additional conditions being proposed

   (5) Directions being issued requiring specific action to be taken straightaway

2. **Major shortfall:**

   A non-critical shortfall.

   A shortfall in the carrying out of licensable activities which poses an indirect risk to the safety of a donor or a recipient

   or

   A shortfall in the establishment's quality and safety procedures which poses an indirect risk to the safety of a donor or a recipient;

   or

   A shortfall which indicates a major deviation from the Human Tissue (Quality and Safety for Human Application) Regulations 2007 or the HTA Directions;

   or

   A shortfall which indicates a breach in the relevant Codes of Practices, the HT Act and other relevant professional and statutory guidelines;

   or

   A shortfall which indicates a failure to carry out satisfactory procedures or a failure on the part of the designated individual to fulfil his or her legal duties;

   or

A combination of several ‘minor’ shortfalls, none of which is major on its own, but which, viewed cumulatively, could constitute a major shortfall.

In response to a major shortfall, an establishment is expected to implement corrective and preventative actions within 1-2 months of the issue of the final inspection report. Major shortfalls pose a higher level of risk and therefore a shorter deadline is given, compared to minor shortfalls, to ensure the level of risk is reduced in an appropriate timeframe.

3. **Minor shortfall:**

   A shortfall which cannot be classified as either critical or major and, which can be addressed by further development by the establishment.

   This category of shortfall requires the development of a corrective action plan, the results of which will usually be assessed by the HTA either by desk based review or at the time of the next inspection.

   In response to a minor shortfall, an establishment is expected to implement corrective and preventative actions within 3-4 months of the issue of the final inspection report.

Follow up actions

A template corrective and preventative action plan will be sent as a separate Word document with both the draft and final inspection report. You must complete this template and return it to the HTA within 14 days of the issue of the final report.

Based on the level of the shortfall, the HTA will consider the most suitable type of follow-up of the completion of the corrective and preventative action plan. This may include a combination of

- a follow-up site-visit inspection
- a request for information that shows completion of actions
- monitoring of the action plan completion
- follow up at next desk-based or site-visit inspection.

After an assessment of your proposed action plan you will be notified of the follow-up approach the HTA will take.