Site visit inspection report on compliance with HTA minimum standards

The Jack Copland Centre

HTA licensing number 11010

Licensed for the

- **procurement, processing, testing, storage, distribution and import/export of human tissues and cells for human application under the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended)**

20 - 23 August 2018

Summary of inspection findings

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

Although the HTA found that the Jack Copland Centre (the establishment) had met the majority of the HTA standards, ten minor shortfalls were found in relation to Governance and Quality and Premises, Facilities and Equipment. The shortfalls relate to the absence of recent risk assessments relating to licensable activities; the temperature monitoring of the store room where ACD-A is stored; not replacing the temperature monitoring device according to the SOP; timings for obtaining blood samples for donor serology testing of donors of PBMCs; the requirement for internal and independent audits; terms of end user agreements; defining the exposure time of tissues and cells to cryoprotectant before cryopreservation; absence of contingency arrangements for the failure of the controlled-rate freezer and the application of the SEC.

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.

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

Tissue type	Procurement	Processing	Testing	Storage	Distribution	Import / export
Progenitor Cell, Haematopoietic, Peripheral Blood Stem Cells (PBSC); PBSC	E/TPA	E	E	E	E	
Progenitor Cell, Hematopoietic, Bone Marrow; Bone Marrow	E*/TPA	N/A	N/A	N/A	N/A	
Mature Cell, T Cell Donor Lymphocytes for Adoptive Lymphocyte	E*/TPA	E*	E*	E	E	

Immunotherapy (DLI); DLI						
Musculoskeletal; Bone, Bone	E/TPA	N/A	E	E	E	
Musculoskeletal; Tendon & Ligament;	E*	E*	E*	E	E*	
Mature cells; Pancreatic Islet cells	TPA	E	E/TPA	E	E	
Membrane, Amniotic; Amniotic Membrane	N/A	N/A	N/A	E	E	
Cardiovascular, Valves; Heart Valves	E	E*	E/TPA	E	E	
Skin; Skin	E	E/SLA	E/TPA	E	E	
Reproductive; Ovarian Tissue	E/TPA	E	E/TPA	E	E	
Reproductive; Testicular Tissue	E/TPA	E	E/TPA	E	E	
Progenitor Cell, Haematopoietic, Unspecified; Peripheral Blood Mononuclear Cells (PBMC)	E/TPA	E	E/TPA		E	

Background to the establishment and description of inspection activities undertaken

The Scottish National Blood Transfusion Service (SNBTS) manages all of the public tissue banking activity in Scotland. SNBTS consists of a hub based in Edinburgh. The hub has recently relocated to a new purpose built site known as the Jack Copland Centre (JCC) and now includes a testing laboratory and the National Microbiology Reference Unit (NMRU) on site. In addition to the hub, there are five satellite establishments:

- Dundee - East of Scotland Tissue and Cell Bank (ESTCB)
- Aberdeen – North East of Scotland Tissue and Cell Bank (NESTCB)
- Inverness – North of Scotland Tissue and Cell Bank (NSTCB)
- Glasgow – West of Scotland Tissue and Cell Bank (WSTCB)
- Edinburgh – Scottish Centre for Regenerative Medicine (SCRM)

Tissues are obtained from both living and cadaveric donors; cadaveric tissue is obtained from multi organ donors and / or tissue only donors depending on the type of tissue.

Consent is taken by trained staff and donor selection is based on agreed donor selection guidelines which are published on the Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee (JPAC) website and as set out in the Quality and Safety for Human Application Regulations 2007.

Microbiological and mandatory virology testing is carried out at the laboratories based at the JCC. Mandatory testing consists of serology tests. The NMRU undertakes HTLV-1 testing as well as nucleic acid tests for HIV, HCV and HBV, HEV and where indicated, West Nile Virus.

Processing of most tissues and cells is undertaken at the hub and the satellite site NESTCB, which also processes haematopoietic stem cells. Processing is carried out within cleanrooms. All open processing is carried out within a Grade A safety cabinet in a Grade B background. This currently includes processing of haematopoietic stem cells and ovarian tissue. Islet processing is carried out within a Grade A safety cabinet in a Grade C background. Environmental monitoring is carried out in accordance with Annex I of the EU Guidelines to Good Manufacturing Practice and the requirements of Directions 002/2018, and examination of contact and settle plates is carried out by the quality team at the establishment or by agreement with local specialist laboratories.

The JCC is in the process of reviewing all activities undertaken at the satellite sites and NESTCB will cease processing in due course. Prior to the move to the JCC, the establishment decided to temporarily cease the processing of tendons and heart valves. Following the move to the JCC, a review of the management of the heart valve and tendon activities was undertaken and a decision was taken to stop procurement and processing activities associated with tendons. Heart valves are also currently not being processed at the JCC but any heart valves in storage continue to be issued, under a concessional release process.

Depending on tissue type, storage is at the hub, or at one of the satellite tissue banks. PBSCs are stored at the NESTCB, ESTCB, and WSTCB and at the hub. Bone products for end use are stored at all locations.

This inspection was conducted in two phases. The first phase from 25-28 June 2018, consisted of visits to each of the satellite sites with the exception of the Edinburgh satellite SCRM. Detailed reports for each of the satellite sites inspected in June are available on the HTA's website. The second site visit was undertaken from 20 -23 August 2018 and consisted of site visits to the Royal Infirmary Edinburgh where PBSCs, PBMCs as starting material and femoral heads are procured; SCRM where PBMCs are processed for Advanced Therapeutic Medicinal Products (ATMPs) manufacture and finally the JCC. SCRM is the designated contingency site for processing of tissue and cells when processing facilities at the JCC are being serviced or not operational.

At each site, the inspection team carried out a visual inspection of the premises, audit of traceability, document review and held roundtable discussions with key staff.

The audits undertaken at each site were as follows:

- Edinburgh - Scottish Centre for Regenerative Medicine (SCRM)

Three sets of records for the procurement of PBMC were reviewed. It was noted that the mandatory serology tests were not undertaken on the day of procurement, or within seven days after procurement. In addition, one of the samples had been procured after the amended Quality and Safety Regulations came into force on 1 April 2018. The Single

European Code Donation Identification Sequence (SEC-DI) had not been applied to this tissue.

- Edinburgh - Jack Copland Centre (JCC)

Processing records relating to one PBSC collection and three pancreatic islets were reviewed for presence of testing results, processing details, environmental monitoring, transport records and disposal records. The quality team undertake a retrospective audit of each the pancreatic islet file however, it was noted that one set of records had not been audited.

The documentation for the concessionary release of three heart valves and one ovarian cryopreservation processing record were reviewed.

The quarantine location records for one femoral head and one tendon procured before the establishment stopped processing were confirmed against the electronic records. The location, mandatory serology and microbiology results of a femoral head and a patella tendon held in separate issue freezers were also checked. The audit trail of one femoral head that was initially issued to Glasgow subsequently returned and then issued to Inverness was reviewed to ascertain times in transit and tissue return procedures.

Finally, the receipt and storage records of three amniotic membranes purchased from another HTA-licensed establishment were also reviewed.

No discrepancies were found apart from the absence of the retrospective audit of one of the pancreatic islet 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

Governance and Quality

Standard	Inspection findings	Level of shortfall
GQ2 There is a documented system of quality management and audit.		
b) There is an internal audit system for all licensable activities.	Edinburgh hub: No internal audits have been conducted for any of the licensable activities undertaken at the previous or current hub site.	**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.	Edinburgh hub: Due to the ongoing move to the JCC, an independent audit of the hub's activities to assess compliance against relevant HTA standards has not been carried out	**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.	Edinburgh hub The time limit from the addition of cryoprotectant to the PBSC units to the commencement of cryopreservation has not been defined and documented.	**Minor**
GQ5 There are documented procedures for donor selection and exclusion, including donor criteria		
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.	Edinburgh SCRM: Mandatory serology testing of patients for the MATCH trial was not undertaken, as required, on the day of procurement.	**Minor**
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.	Edinburgh JCC and SCRM: There are no contingency procedures in the event of a controlled-rate freezer (CRF) failing to reach the required temperature.	**Minor**
GQ6 A coding and records system facilitates traceability of tissues and / or cells, ensuring a robust audit trail.		
d) The requirements of the Single European Code are adhered to as set out in Directions 002/2018.	Edinburgh SCRM: The application of the Single European Code (SEC-DI) to the procured PBMC is not in accordance to Directions 002/2018.	**Minor**
GQ7 There are systems to ensure that all adverse events, reactions and/or incidents are investigated promptly.		

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.	Edinburgh hub Third party agreements do not stipulate the requirement to report SAEARs to the HTA, within 24 hours discovery of the event.	**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.	Edinburgh hub: The risk assessments have not been updated to reflect recent changes in activities.	**Minor**

Premises, Facilities and Equipment

Standard	Inspection findings	Level of shortfall
PFE3 There are appropriate facilities for the storage of tissues and / or cells, consumables and records.		
c) Tissues and / or cells are stored in controlled, monitored and recorded conditions that maintain tissue and / or cell integrity.	Edinburgh Hub: The anticoagulant ACD-A is stored in a temperature-monitored room with a minimum/maximum temperature range of 6-25˚C. The manufacturer recommends a storage temperature of 15-25˚C. A review of the previous month's temperature records indicate temperatures over 25˚C were recorded for three consecutive days. There was no evidence that any action had been taken to ensure that the existing stock of ACD-A could still be used.	**Minor**
PFE5 Equipment is appropriate for use, maintained, quality assured, validated and where appropriate monitored.		
b) Critical equipment is maintained and serviced in accordance with the manufacturer's instructions.	The temperature-monitoring device is used to monitor the temperature of the room where the ACD-A is stored, is calibrated every two years. However, the SOP states that the temperature-monitoring device should be replaced every two years.	**Minor**

Advice

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

No.	Standard	Advice
1	C1a	National: The DI is advised to include reference to the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended) within the donor selection criteria of the "Competency Framework for Tissue and Bone

		Nursing-Deceased and Live Donor Femoral Head Procurement".
2	GQ1b	Edinburgh - JCC: The DI is advised to review the establishment's standard operating procedures (SOPs) and policies following the move to the JCC and the rationalization of activities at the satellite sites so that . For example, - the SOP on testing of serology samples does not include a centrifugation step and does not reflect the maximum sample storage timeframes if the samples are not tested immediately e.g. 72h at ambient temperature then a maximum 7 days at 2-8 °C; - the records retention policy is not in keeping with requirements; for example, the equipment logbook is kept for the lifetime of the equipment plus four years and internal Quality Check records for eight years; and - during processing of pancreatic islets, two members of staff decide when the enzymatic digestion step should cease. However, only one member of staff signs the processing records.
3	GQ1b	Edinburgh – SCRM: The Edinburgh satellite site is shared with another establishment. The DI is advised to monitor what is moved through communal areas to minimize the risk of potential contamination to tissues and cells
6	GQ1t	National: If there is a failure of the clean room plant during processing staff will continue to process the tissue or cells to completion. The DI is advised to ensure that these units are marked as tissue for concessionary release.
7	GQ2d	Edinburgh – JCC: During the processing of tendons and heart valves, the tissue is first soaked in antibiotics, which are subsequently washed off. The DI is advised, before re-commencing processing of tendons and heart valves to undertake validation studies to demonstrate that the no residual antibiotic remains after the washing steps thereby masking the presence of bacterial contamination.
8	GQ3e	Edinburgh – JCC: As part of the move from the old hub site to the JCC, staff underwent an evaluation of the ovarian processing protocol. The DI is advised to record this in relevant training records.
11	GQ7b	Edinburgh – JCC: The DI is advised to share any learnings from the root cause analysis and the corrective and preventative actions resulting from any SAEARS with staff at all sites.
12	PFE2b	Edinburgh – JCC and SCRM The DI is advised to review the position of non-viable particulate detectors to ensure the accurate readouts during processing are obtained.
13	PFE2c	Edinburgh – JCC:

		The DI is advised that the boxes used to transport PBSC units to and from the RIE should be appropriately decontaminated between use.
15	PFE3a	Edinburgh – JCC: Antibiotics used during the processing of pancreatic islets are stored in a -20°C freezer. If there is an upper temperature deviation, there is a time lag of 30 minutes before the alarm is triggered. The DI is advised to review the alarm settings so that the alarm is triggered immediately a temperature deviation occurs.
21	PFE5a	Edinburgh – JCC: The procured femoral heads are weighed prior to storage in the -80°C quarantine freezer. The balance is checked against a 300 gram, calibrated weight but this process is not documented. The DI is advised to implement a procedure for documenting the check of the balance prior to use, obtain calibrated weights that reflect the lower weight ranges of the procured bones and to ensure that the weights are calibrated at appropriate intervals.
23	PFE5c	Edinburgh – JCC: The DI is advised to document the contingency arrangements for flow cytometry analysis of PBSC CD34 counts pre-and post-apheresis and how results will be communicated. The DI is also advised that an assessment of the transport times between the contingency site and the hospital undertaken to ensure samples are processed in a timely manner.

Concluding comments

Although the HTA found that the JCC had met the majority of the HTA standards, ten minor shortfalls were found in relation to Governance and Quality and Premises, Facilities and Equipment. The shortfalls relate to the absence of recent risk assessments relating to licensable activities; the temperature monitoring of the store room where ACD-A is stored; not replacing the temperature monitoring device according to the SOP; timings for obtaining blood samples for donor serology testing of donors of PBMCs; the requirement for internal and independent audits; terms of end user agreements; defining the exposure time of tissues and cells to cryoprotectant before cryopreservation; absence of contingency arrangements for the failure of the controlled-rate freezer and the application of the SEC. In addition, the HTA has given advice to the Designated Individual with a view to helping the establishment further develop its working practices.

The HTA requires that the Designated Individual addresses the shortfall 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 shortfall identified during the inspection.

Report sent to DI for factual accuracy: 21 September 2018

Report returned from DI: 3 October 2018

Final report issued: 22 October 2018

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: 1 October 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

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.
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 002/2018.
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.

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 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 failure to carry out satisfactory procedures for the release of tissues and cells or a failure on the part of the designated individual to fulfil his or her legal duties;

   or

   A combination of several 'minor' shortfalls, none of which is major on its own, but which, viewed cumulatively, could constitute a major shortfall by adversely affecting the quality and safety of the tissues and cells.

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

3. **Minor shortfall:**

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

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

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

Follow up actions

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

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

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

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