Site visit inspection report on compliance with HTA minimum standards

Derriford Hospital

HTA licensing number 11093

Licensed for the

- **procurement, 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)**

13-14 November 2018

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 Derriford Hospital (the establishment) had met the majority of the HTA standards, one major and seven minor shortfalls were found in relation to the Governance and Quality Systems (GQS) and the Premises, Facilities and Equipment (PFE) standards. The major shortfall was in relation to temperature monitoring. The seven minor shortfalls relate to the establishment's agreements, independent audit, donor selection criteria, training of staff, environmental monitoring during processing, the format and recording of the Single European Code (SEC) and raw data retention.

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.

'SLA' = Service level agreement; another licensed establishment carries out the activity on behalf of the establishment.

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

'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, PBSC; PBSC	**E/TPA**	**SLA**	**E/TPA**	**SLA**	**E**		
Mature Cell, T cell (DLI); T cell (DLI)	**E/TPA**	**SLA**	**E/TPA**	**SLA**	**E**		
Musculoskeletal, Bone; Bone	**E**		**E**	**E**			
Musculoskeletal, Tendon & Ligament; Tendon				**E**			
Musculoskeletal, Bone; Bone Strut				**E**			
Other; Skeletal Muscle (ATMP)	**E***		**E***				**E***

Background to the establishment and description of inspection activities undertaken

Derriford Hospital is part of the Plymouth Hospitals NHS Trust and is licensed for the procurement, testing, storage, distribution and export of human tissues and cells under the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended).

The Haematology unit serves those who are living in Plymouth, East Cornwall and South Devon. The clinical programme operates as part of the South West Peninsula Transplant Service (SWPTS) along with Royal Cornwall Hospital and Torbay Hospital. The establishment procures autologous and allogeneic peripheral blood stem cell (PBSC) collections and donor lymphocytes for patient treatment and holds JACIE accreditation.

The procurement and testing of PBSCs takes place at Derriford Hospital, and also at Royal Cornwall Hospital under the terms of a third party agreement (TPA). Donor / patient selection, pre-assessment and consent to the harvest is a consultant-led process.

Bloods for the mandatory serology tests are taken within thirty days prior to, or on the day of, procurement. For patients at Royal Cornwall and Torbay Hospital most of the samples for mandatory serology testing, apart from those taken for HTLV-1 testing, are sent for analysis at the testing laboratories within the hospitals, which operate under TPAs with Derriford Hospital. Harvested cells are transported from Royal Cornwall Hospital to the establishment

along with a blood sample for HTLV-1 testing. Patients are referred to Derriford Hospital by Torbay Hospital for PBSCs harvest.

For patients at Derriford Hospital the samples for mandatory serology testing are sent to the diagnostic immunology laboratory within the hospital, which has Clinical Pathology Accreditation (CPA). The diagnostic immunology laboratory also performs NAT testing for HIV, HBV and HCV markers.

The licensable activities of processing and storage are undertaken by another HTA-licensed establishment under the terms of a service level agreement (SLA). Derriford staff that hold honorary contracts with the other licensed establishment transfer, process and cryopreserve the PBSCs and cells for donor lymphocyte infusions (DLIs) within the clean room facilities of the other licensed establishment *(see shortfall under PFE2(b)).* Cryopreserved cells for transplantation are returned to the establishment upon request.

There are regular planning and governance meetings across the SWPTS sites and between the licensed establishments involved in the delivery of this transplant programme.

The establishment also procures femoral heads from patients undergoing primary elective total hip replacement surgery and stores tendons and struts sourced from another licensed establishment. Donor selection and consent take place at the orthopaedic outpatient department. Potential donors are identified by the trained pre-assessment nurses who also provide the patients with an information booklet, take the donor's medical history and assess their overall fitness for the surgery.

Blood samples for the mandatory serological testing are taken from the donor on the day of donation along with a swab and bone chips from the cut end of the femoral head. The femoral head is placed in a sterile tamper-evident screw-capped pot which is, in turn, placed in a second sterile tamper-evident screw-capped pot followed by a non-sterile plastic bag. The outer collection pot is labelled with a unique donation number, the date of harvest and weight of the femoral head. The blood sample is sent to the diagnostic immunology laboratory, within the hospital, where serological testing is performed for all the mandatory markers.

The femoral heads are then placed in the quarantine -80°C freezer and details of each procurement are entered into the bone donation register and "log of bone" spreadsheet. The Quality Manager monitors when 180 days post-harvest is coming up and notifies the orthopaedic pre-assessment nurses, who contact the patients to come in for repeat serology tests. The orthopaedic unit is currently considering moving to NAT testing for HIV, HBV and HCV.

Once the serology and microbiology test results are reviewed, and if all results are negative, the Quality Manager transfers the femoral head to the approved use -80°C freezer. The bone donation register and "log of bone" spreadsheet are updated. Any samples with a positive result are disposed of according to the Trust's disposal policy.

Both freezers are temperature-monitored and linked to a wireless call-out system. Temperature excursions outside the set ranges alert the Trust's switchboard, and, in turn, the Quality Manager is notified, in and out of standard working hours *(see advice item, 6).*

The establishment also occasionally receives and stores tendons and struts from another HTA-licensed establishment, under the terms of a SLA. The tendons are ordered on demand on a named-patient basis and stored in the -80°C approved use freezer. Also, a small stock of struts are kept at all times and stored at ambient room temperature. Records of the tendons and struts are maintained in the bone donation register and electronic database.

More recently, the establishment started taking part in the Cook Myosite clinical trial involving an Advanced Therapy Medicinal Product (ATMP), where autologous muscle cells are harvested and expanded to form the final ATMP product for female patients with stress

urinary incontinence (SUI). Donor selection, consent and testing for the mandatory serology markers will be carried out under this licence *(see advice item, 1).*

This report describes the establishment's fifth routine inspection, which took place on 13-14 November 2018. The establishment has been licensed by the HTA since 2007. Discussions were held with the Designated Individual (DI), the Haematology and Orthopaedic Quality Managers, apheresis staff from the apheresis units at Derriford Hospital and Royal Cornwall Hospital, the Quality Lead and staff from the testing laboratory at Royal Cornwall Hospital.

The inspection included a visual inspection of the premises at Derriford Hospital and Royal Cornwall Hospital where tissue storage and serology testing takes place, as well as the apheresis rooms and storage areas containing the ACD-A.

Audits of traceability were carried out and included the storage location of one strut and four femoral heads; locations in the quarantine and release freezers and ambient temperature storage area were cross-checked against the bone donation register and "log of bone" spreadsheet. One discrepancy was identified *(see advice item, 4).* A total of three donor and four recipient files were reviewed to ensure that they contained all relevant documentation, including consent forms, serology results and microbiology results, and included information such as the Single European Code (SEC). A number of discrepancies were identified *(see shortfall under GQ6 (d)).*

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
GQ1 All aspects of the establishment's work are supported by ratified documented policies and procedures as part of the overall governance process.		
r) Third party agreements specify the responsibilities of the third party and meet the requirements set out in Directions 002/2018.	Although the establishment has third party agreements in place, these need to be amended to include all the responsibilities of each party including: • serious adverse events and reactions (SAEARs) reporting; and • retention of critical traceability records (30 years) and raw data (10 years). *Prior to the final report being issued the DI submitted evidence of the actions taken in relation to the above shortfall. The HTA has assessed this evidence as satisfactory and considers this standard to be met.*	**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.		
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.	Although the establishment conducted an independent audit, the scope of the audit did not include all applicable HTA standards.	**Minor**
GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills.		
c) There are continuous professional development (CPD) plans for staff and attendance at training is recorded.	Refresher training and ongoing competency assessment for apheresis staff at Royal Cornwall Hospital was not documented in staff training records.	**Minor**

GQ4 There is a systematic and planned approach to the management of records.		
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.	Royal Cornwall Hospital has a procedure for raw data retention for the requisite ten years. However, it was noted during the inspection that the temperature records for the ACD-A storage area have not been retained for March 2017 and August 2018. *Prior to the final report being issued the DI submitted evidence of the actions taken in relation to the above shortfall. The HTA has assessed this evidence as satisfactory and considers this standard to be met.*	**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 and Royal Cornwall Hospital have documented procedures for donor selection and exclusion. These do not include all of the donor exclusion criteria as set out in Annex A of the Guide to Quality and Safety Assurance for Human Tissues and Cells for Patient Treatment. For example, the medical history of allogeneic PBSC's and bone graft donors 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". *Prior to the final report being issued the DI submitted evidence of the actions taken in relation to the above shortfall. The HTA has assessed this evidence as satisfactory and considers this standard to be met.*	**Minor**

GQ6 A coding and records system facilitates traceability of bodies, body parts, tissues and cells, ensuring a robust audit trail.		
d) The requirements of the Single European Code are adhered to as set out in Directions 002/2018.	The other licensed establishment provides the SEC code to Derriford Hospital. Derriford Hospital applies the SEC to autologous and allogeneic PBSC units in the accompanying documentation following harvest. However, on one occasion the SEC was not recorded in the donor's medical records and was not included in the corresponding recipient's clinical records. Also, the format of the SEC is not in line with requirements. For example, the establishment's unique donation number is composed of fourteen alpha-numeric characters, instead of thirteen. *Prior to the final report being issued the DI submitted evidence of the actions taken in relation to the above shortfall. The HTA has assessed this evidence as satisfactory and considers this standard to be met.*	**Minor**

Premises, Facilities and Equipment

Standard	**Inspection findings**	**Level of shortfall**
PFE2 Environmental controls are in place to avoid potential contamination.		
b) Where processing of tissues and / or cells involves exposure to the environment, it occurs in an appropriate, monitored environment as required by Directions 002/2018.	Establishment staff aseptically process PBSCs in the clean room facility of another HTA-licensed establishment. During the review of processing records it was noted that the time periods for processing and monitoring were not documented, and therefore confirmation that monitoring took place concurrent with the processing event could not be obtained. Furthermore, it was noted that during a longer processing procedure continuous air particle monitoring was not maintained for the entire processing event, since the particle monitor sampling time was limited to 20 minutes.	**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.	At Derriford Hospital the anticoagulant ACD-A is stored in a cabinet with no minimum and maximum temperature monitoring. The thermometer used to monitor the cabinet stores temperature data for a period of 24 hours only. Establishment staff monitor and document the temperature during working hours on Monday to Friday only, and there is no provision for reviewing and recording temperatures over the weekend and bank holidays. As a result, there is a risk that any deviations that take place over the weekend may go unnoticed. At Royal Cornwall Hospital the ACD-A is stored in a temperature-monitored cabinet with a defined temperature range. However, the minimum – maximum function on the temperature loggers used to monitor the cabinet temperature is not always programmed. Furthermore, the temperature loggers change frequently and the establishment does not keep a record of the in-use temperature logger. As a result there is a risk that the temperature of the ACD-A will not be continuously monitored and data related to licensable activities lost. The manufacturer of ACD-A recommends a storage temperature of 15-25˚C. A review of the temperature records at both sites indicated a number of occasions, where temperatures over 25˚C were recorded. Although the deviations were identified, appropriate action was not taken to establish what impact, if any, these excursions had on the quality and safety of the product.	**Major (cumulative)**

c) Tissues and / or cells are stored in controlled, monitored and recorded conditions that maintain tissue and / or cell integrity.	The testing laboratory's procedure at Royal Cornwall Hospital is for samples for mandatory serology testing to be stored in the reception fridge. Samples that are received later in the day are centrifuged the following day and the serum is also stored in the reception fridge until tests are complete. Any serum remaining following testing is frozen at -20˚C. Establishment staff perform daily spot-checks of the fridge and freezer temperatures, but do not record the minimum – maximum temperature range. The required range for the reception fridge is 2-8˚C. A review of the temperature records indicated that temperatures for this fridge routinely went over 8˚C. These deviations were not identified and appropriate action was not taken to establish what impact, if any, these excursions had on the quality and safety of the samples for the mandatory serology testing. Furthermore, the inspection team identified an incident where a serum sample for syphilis testing was stored in the reception fridge for a period of nine days before it was tested. The establishment was not able to provide assurance that the quality of the sample was maintained for the duration of storage.	

Advice

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

No.	Standard	Advice
1.	GQ1 (b)	The SOP on serology testing for PBSC harvests states that the virology sample must be taken 30 days before or 7 days after collection. The DI is advised to update the wording on the SOP to the effect of: blood samples must be taken for testing within 30 days prior to donation. The clinical plan for the harvest of autologous muscle-derived cells states that the mandatory serology tests must be completed within 30 days prior to the biopsy procedure. The DI is advised to update the wording on the establishment's procedure to the effect of: blood samples for the testing of the mandatory serological markers must be taken at the time of donation or, if not possible, within seven days post-donation. The DI is further advised to ensure this is in place before commencing the work on this clinical study.
2.	GQ1 (r), (s)	In addressing the shortfall above against GQ1 (r), (s) the DI is advised to review local procedures for the identification of adverse events and reactions,

		such as the one at Royal Cornwall Hospital testing laboratory, to ensure that they are consistent with the requirements, as set out in the revised TPA.
3.	GQ2 (c)	The DI is advised to schedule the independent audit to occur in the intervening year between HTA inspections.
4.	GQ6 (d)	Following the transposition of the import and coding directives to UK law, struts have been purchased from another licensed establishment and are currently placed into storage. The DI is advised to update the Bone Donation Register and spreadsheet to capture the SEC for these and any future products purchased. Going forward the establishment intends to input the SEC manually into the Bone Donation Register, spreadsheet and recipient's clinical records. The DI is advised to consider a second person verification to minimise the risk of transcription errors that may result in loss of traceability. The DI is also advised to update the establishment's procedures for the clinical study with autologous muscle-derived cells to include the allocation and application of the SEC-DI, as a minimum on the accompanying documentation of the starting material prior to distribution to the ATMP manufacturer.
5.	PFE2 (b)	In addressing the shortfall above against PFE2b, the DI is advised to remind staff to record in the "Donor Lymphocyte Processing" form the start and stop time of processing and air sampling of PBSCs. This will enable the DI, during audits, to ascertain whether monitoring is being conducted for the full duration of critical processing.
6.	PFE3 (b)	Current practice is for the bone bank Quality Manager to be notified by email and telephone, in and out of hours, if the temperature of the freezers deviates from the required set range. The DI is advised to identify at least one other member of staff in the orthopaedic department who could respond to freezer alarm notifications to ensure staff are available at all times to respond to temperature excursions.
7.	PFE4 (h)	The establishment last validated the insulated boxes used to transport PBSC units from Royal Cornwall Hospital to Derriford Hospital in 2010. The DI is advised to revalidate the transportation boxes and consider worst-case temperature and transit times to ensure they continue to achieve the intended results.

Concluding comments

There are a number of areas of practice that require improvement, including one major and seven minor shortfalls.

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: 2018/12/08

Report returned from DI: 2018/12/18

Final report issued: 2018/12/27

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: 2019/07/22

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 002/2018 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 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.
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.
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.
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.
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.