Site visit inspection report on compliance with HTA minimum standards

London Bridge Hospital

HTA licensing number 11069

Licensed for the

- **procurement, testing and storage of human tissues and cells for human application under the Human Tissue (Quality and Safety for Human Application) Regulations 2007**

21-22 March 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 London Bridge Hospital (the establishment) had met some of the HTA standards, one critical, one major and four minor shortfalls were found with regard to the Governance and Quality Systems (GQS) and Premises, Facilities and Equipment (PFE) standards. The critical shortfall relates to the implantation of expired tissue and cells products in three patients and to the need for the establishment to have clearly defined and documented procedures in place to ensure that tissue and cell products are not used beyond their expiry date. The major shortfall relates to the need for the establishment to have robust procedures and records setting out the acceptable storage conditions, including temperature and timeframes required to maintain tissue integrity. The four minor shortfalls were in relation to the traceability of tissue products, risk assessments and incident reporting in third party agreements.

It was identified during the inspection that the establishment has stored new types of tissue and cells products without first notifying the HTA. The HTA considers this a breach of a standard condition of the establishment's licence and will consider the need for regulatory action in relation to this matter separately to the inspection findings reported below.

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

The HTA's regulatory requirements

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

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

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

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

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

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

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

Licensable activities carried out by the establishment

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

'E*' = Establishment is licensed to carry out this activity but is not currently carrying it out.

Tissue category; Tissue type	Procurement	Processing	Testing	Storage	Distribution	Import	Export
Musculoskeletal, Bone; Bone				**E**			
Musculoskeletal, Tendon & Ligament; Tendons				**E**			

Musculoskeletal, Tendon & Ligament; Ligaments				**E**			
Membrane, Fascia Lata; Fascia Lata				**E**			
Progenitor Cell, Hematopoietic, PBSC; PBSC	**E***		**E***				
Skin; Skin				**E***			
Other; Cartilage (ATMP)	**E***		**E***				
Other; Nerve				**E**			

Background to the establishment and description of inspection activities undertaken

London Bridge Hospital (the establishment) is the main hub site and is one of six premises where HTA-licensable activities take place. The establishment has been licensed by the HTA since December 2006. The activities covered under the licence include procurement, donor testing and storage of human tissues and cells under the Human Tissue (Quality and Safety for Human Application) Regulations 2007. The five satellites are:

- Harley Street Clinic, which is licensed for procurement;
- Wellington Hospital, which is licensed for procurement and storage;
- Princess Grace Hospital, which is licensed for procurement and storage; and
- Two Hospital Corporation of America (HCA) laboratories at Shropshire House and Wimpole street, both of which are licensed for donor testing.

Procurement of peripheral blood stem cells (PBSCs) from paediatric patients has not taken place at the Harley Street Clinic since the last routine HTA inspection. This satellite is currently undertaking no licensable activities, but intends to recommence activities once new members of staff are recruited and have completed all required training. Currently, the procurement and serology testing of PBSCs for adult patients takes place at another HTA-licensed establishment under the terms of a service level agreement (SLA).

The hub stores bone, tendon, ligament and meniscus for end use within the establishment. The Princess Grace Hospital stores bone, tendons and ligaments, whilst the Wellington Hospital stores tendons and ligaments, nerves and fascia lata, also for end use within each respective hospital. The London Bridge Hospital has not stored skin since 2015. Amniotic membrane, heart valves and corneas are also used at the establishment, but are not stored for longer than 48hours. Each site maintains a tissue register for every tissue type used in patients where the tissue code, delivery number, patient identity, date received, date charged, theatre team involved in the operation and the expiry date is recorded (*see Advice, item 6*). A human tissue tracker form is used to record tissues removed from storage and used in patients.

The tissue products are purchased from other HTA-licensed tissue suppliers and are stored in dedicated -40°C freezers at the hub and satellite sites. Each -40°C freezer is temperature-monitored and is connected to a wireless callout system that operates around the clock.

Temperature excursions outside the set ranges (above -20°C or below -45°C) trigger the callout system. Power failure also triggers the callout system. In the event of freezer failure, all tissue products will be placed on dry ice and transferred to back-up freezers at one of the other sites.

Chondrocyte procurement for autologous patient treatment takes place infrequently. Since 2015, the establishment has not procured any cartilage for Advanced Therapy Medicinal Product (ATMP) manufacture.

Donor testing is undertaken at the HCA laboratories, which are accredited by the United Kingdom Accreditation Service (UKAS). Blood samples for all the mandatory serology testing, except for HTLV, are sent to the Wimpole Street HCA laboratory. The samples are barcoded, tracked and the test results are recorded on to the laboratory information management system. A separate blood sample for HTLV testing is sent directly to the Shropshire House HCA laboratory and from there to another testing laboratory in France. The French laboratory is accredited and carries out the HTLV testing of all the donors. Any confirmatory serology testing is carried out by the Shropshire House HCA laboratory. Nucleic acid testing (NAT) confirmatory testing is carried out by two other establishments. The London Bridge Hospital has third party agreements (TPAs) with both of the laboratories that perform the NAT confirmatory testing.

This report describes the establishment's sixth routine inspection which took place over two days. Interviews were held with the Designated Individual (DI), Persons Designated at each site and the person responsible for the Quality Systems. A review of documentation relevant to the establishment's licensable activities and a visual inspection of the hub and satellite site where tissue storage and serology testing take place were also included as part of the inspection.

Audits of traceability were carried out on tissue and cell products stored at the Wellington Hospital and the Princess Grace Hospital. The audits included:

- five tissue products tracked back to the tissue register at the Wellington Hospital. Three out of five tissue products were out of date according to the establishment's storage policy and the manufacturer's recommendations (*see shortfall, under GQ4(e), (l)*);
- three tissue products received and used in patients at the Wellington Hospital. Two of the tissue products were traced back to receipt at the Wellington Hospital and the records reviewed were the tissue register, the implantation register and the patient records. No discrepancies were noted.
- two tissue products cross-checked against the tissue register at the Princess Grace Hospital. No discrepancies were noted;
- two tissue products were cross-checked against the implant book. Both tissue products were traced back to receipt at Princess Grace Hospital and the records reviewed were the tissue register, the delivery note, traceability information and the recipient's consent form. No discrepancies were noted.

An audit was also performed on three patient records at the hub. The audit covered the consent for donation and the consent for virology testing. The PBSCs were procured at another HTA-licensed establishment, which is responsible for the mandatory serology testing of the patients. The establishment performs an additional testing of the mandatory serology markers as part of the patient's work-up process. The audit trail was followed to the serology testing labs where date and time of the blood sample being booked-in, processing of the sample and serology results, were confirmed. The serology results, where applicable, were cross-referenced against each of the following identifiers: donor name, date of birth and hospital number. Traceability was maintained throughout. No discrepancies were noted.

Inspection findings

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

However, since the last site visit inspection, the establishment has stored fascia lata and nerve products on a number of occasions. The HTA considers this a breach of the standard condition of the establishment's licence that requires it to seek approval from the HTA prior to it procuring or storing a new type of tissue and/or cells.

The HTA will consider the need for regulatory action in relation to this matter separately to the inspection findings reported below.

Compliance with HTA standards

Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended).

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.		
s) Third party agreements specify that the third party will inform the establishment in the event of a serious adverse reaction or event.	Third party agreements do not include the requirement for third parties to report SAEARs to the establishment within 24 hrs of discovery.	**Minor**
GQ4 There is a systematic and planned approach to the management of 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.	Although staff at the Wellington Hospital keep records of tissue products received by the establishment, information critical to their safe and appropriate storage and use was not consistently documented. For example, during this and the last site visit inspection it was identified that staff do not always amend the expiry date of	**Critical (Cumulative)**

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.	received tissue products to reflect the shorter storage period at -40°C. As a result, the HTA was concerned about the potential storage and use of expired products. A review of the tissue register at Wellington Hospital revealed three samples that were in storage and available for clinical use that were beyond their expiry date.	
GQ7 There are systems to ensure that all adverse events are investigated promptly.	During the site visit inspection the establishment was asked to undertake a review of all the tissue and cell products that were stored to determine if there were any occasions where expired tissue products were used in patients. During this process, staff discovered three expired tissue and cell products that have been implanted into recipients. *(see Advice, item 3)*	
a) There are procedures for the identification, reporting, investigation and recording of adverse events and reactions, including documentation of any corrective or preventative actions.		
PFE3 There are appropriate facilities for the storage of bodies, body parts, tissues, cells, consumables and records.	The establishment has a range of documentation that details the storage requirements of tissue products. However, the requirements set out in these documents are not consistent with each other or with the manufacturer's recommendations. For example, the establishment's policy states that tissue products can only be stored at -40°C for three months. However, a related standard operating procedure (SOP) states that tissue products can be stored at -40°C for up to three years. Furthermore, the tissue register at the London Bridge Hospital states that tissue products can be stored within a temperature range of -10°C to -45°C for six months, and must be disposed of if not used within that period.	
d) There is a documented, specified maximum storage period for tissues and / or cells.		
GQ6 A coding and records system facilitates traceability of bodies, body parts, tissues and cells, ensuring a robust audit trail.		
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.	The audit of the traceability records identified an occasion where traceability was not maintained through to the recipient of the sample *Following the site visit the DI confirmed to the HTA that the recipient of the tissue in question had been identified.*	**Minor**

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.	Although the establishment has documented risk assessments, these do not capture all the risks associated with the activities being carried out under the licence and the full range of control measures in place, which help to mitigate identified risks. (*see Advice, item 4*)	**Minor**

Premises, Facilities and Equipment

Standard	**Inspection findings**	**Level of shortfall**
PFE1 The premises are fit for purpose.		
a) A risk assessment has been carried out of the premises to ensure that they are fit for purpose.	At the time of the site visit the establishment was undertaking building works at the Shropshire House HCA laboratory. A risk assessment has not been carried out of the premises to ensure that they remain fit for use during these works. *(see Advice, item 5)*	**Minor**

PFE3 There are appropriate facilities for the storage of bodies, body parts, tissues, cells, consumables and records.		
c) Tissues and / or cells are stored in controlled, monitored and recorded conditions that maintain tissue and / or cell integrity.	The establishment does not have clearly defined and documented procedures in place setting out the acceptable timeframes and temperatures required to maintain tissue integrity before discard is necessary in the event of temperature deviations or freezer failures. A review of the temperature records for the tissue storage facility at the London Bridge Hospital revealed an occasion in July 2017 where temperatures above -20°C were recorded. Although this deviation from set limits was identified at the time, appropriate action was not taken to establish what impact, if any, this excursion had on the quality and safety of the products in storage at that time.	**Major**

Advice

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

No.	Standard	Advice
1.	GQ3 (e)	The DI is advised to increase awareness of incidents that may need to be escalated to the HTA. Examples of such incidents should be included in staff training programmes. At the hub the theatre assistants have different practices when receiving allografts. As a result, the time of receipt of the tissue products is not always recorded. The DI is advised to provide a refresher training in the receipt protocol.
2.	GQ5 (b)	The establishment intends to add Bone Marrow to the tissue types procured. The DI is advised to ensure the 'virology date' on the transplant plans clearly state when the blood samples were taken, and when the blood samples were actually assayed. The DI is also advised to review the Paediatric Blood and Marrow Transplant Service Guideline and Checklist for Bone Marrow harvest as it does not consider consent taking for the mandatory serology testing, review of the test results and actions in case the test results are positive.
3.	GQ7 (a)	In addressing the shortfall against GQ7 (a,) the DI is advised to formalise an event/incident log to ensure that in the future the following information is included for each event/ incident:

		• the event/ incident; • action taken; • the impact; • the investigation; • when the incident was closed; and • whether or not the incident was reported to the HTA and the rationale for this decision. The DI is also advised to formalise the process for the management of non-reportable incidents in an SOP to ensure that all members of staff understand the process and what it involves. The DI is advised to discuss and record the corrective actions and closure of reportable and non-reportable incidents at governance meetings to raise staff awareness. The DI has appointed Persons Designated (PD) to assist her in the role at the hub and satellites. The DI is advised to consider delegating the responsibility for reporting of SAEARs to PDs to ensure escalation to the HTA within 24 hours in the DI's absence.
4.	GQ8 (a)	With reference to the above shortfall against GQ8(a) the DI is advised to expand the scope of the risk assessments to include: • implantation of expired tissue products; • effect of temperature excursions above -20°C and of the duration of these excursions on the safety and quality of the tissue products; • loss of traceability; • retention/loss of raw data and traceability data; and • timing of donor testing for tissue products procured at the establishment. The DI is also advised to document the full range of control measures in place, which help to mitigate identified risks. In the event of a freezer failure dry ice is supplied from another establishment for the maintenance of the appropriate temperature of the tissue products until they are transferred to a freezer at the satellite or hub. The DI is advised to risk assess the time it takes for the dry ice to arrive from the supplier and the effect it may have on the quality and safety of the tissues.
5.	PFE1(a)	The establishment has plans to expand activities at Shropshire House, which involves a high level of construction work and new staff with access to the facilities. The DI is advised to ensure the security of the premises is risk assessed so access is restricted to authorised staff. As part of the premises risk assessment, the DI should consider the risk of a possible power failure and the control measures in place that ensure continuous power supply.

6.	N/A	The DI is advised to consider introducing an additional column in the Frozen Human Tissue Delivery form to include the size of the tissue product received, which will help staff to locate appropriate tissue products in the freezer.
7.	N/A	The DI is advised to review all documents to ensure reference to the correct legislation - the Human Tissue (Quality and Safety for Human Application) Regulations 2007, not the Human Tissue Act. After 1 April 2018 these references should be to the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended).
8.	N/A	The establishment is advised to record the time the allograft was sent from the other licensed establishment to ensure the allograft was received within the recommended time frame.

Concluding comments

The staff at the Princess Grace Hospital have developed a Human Tissue Tracker form to record details of the movement of tissue products from receipt to end use that contains all the traceability and recipient information. The spreadsheet is a useful tool that links patient consent, traceability information, the delivery note of the tissue product and implantation information; this minimises the risk of traceability being lost.

There are a number of areas of practice that require improvement, including one critical, one major and four minor shortfalls. The HTA has given advice to the Designated Individual with respect to a number of the establishment's forms, training of staff, staff practices, timing of the mandatory serology testing for BM and PBSCs, identification and reporting of SAEARs and expanding the scope of the risk assessments.

The HTA requires that the Designated Individual addresses the major and minor 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 will contact the establishment to confirm any immediate action that is required to address the critical shortfall.

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: 2018-04-23

Report returned from DI: 2018-05-08

Final report issued: 2018-06-01

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: 2018-09-21

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 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.
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.
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.
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 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.