Site visit inspection report on compliance with HTA minimum standards

Addenbrooke's Hospital

HTA licensing number 11072

Licensed for the

- **storage and distribution of human tissues and cells for human application under the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended)**

25-26 April 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 Addenbrooke's Hospital (the establishment) had met the majority of the HTA standards, two major and eight minor shortfalls were found in relation to Governance and Quality Systems and Premises, Facilities and Equipment. The major shortfalls were related to the absence of procedures for the review of serology results and quarantine of vessels prior to their release for use, while the minor shortfalls related to the absence of risk assessments, audits against the full scope of HTA standards, procedures for coding, recording of critical reagents that come in contact with tissues and cells, serious adverse event and reaction (SAEAR) reporting for end users, documented procedures in the event of a termination of activities and storage temperature monitoring.

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

The HTA's regulatory requirements

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

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

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

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

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

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

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

Licensable activities carried out by the establishment

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

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

Tissue Category; Tissue Type	Procurement	Processing	Testing	Storage	Distribution	Import	Export
Cardiovascular, Vessels; Vessels				**E**	**E**		
Musculoskeletal, Bone; Bone				**E**			
Musculoskeletal, Tendon & Ligament; Menisci				**E**			
Musculoskeletal, Tendon & Ligament; Ligaments				**E**			
Musculoskeletal, Tendon & Ligament; Tendons				**E**			
Membrane, Amniotic; Amniotic Membrane				**E**			

Other; Nerve				**E***			
Skin; Skin				**E***			

Background to the establishment and description of inspection activities undertaken

The establishment is part of Cambridge University Hospitals (CUH) NHS Foundation Trust and is one of six HTA-licensed establishments within the Trust. There is a second establishment within CUH that holds a Human Application licence covering licensable activities relating to CUH's stem cell transplant programme. Donor serology testing for the establishment takes place under the governance of this second Human Application licence.

Vessels

The establishment stores liver vessels received with organs to support transplant. Vessels stored for use in a patient other than the primary recipient for over 48 hours are subject to the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (Q&S Regulations). The establishment stores vessels for up to 14 days at 2-6ºC pending use in a different recipient, and, on rare occasions, distributes vessels to other transplant centres.

Serological tests for cadaveric donors of the vessels are uploaded onto a shared electronic offering system (EOS). The serology results are transferred to CUH's electronic patient information system (Epic) where they are made accessible to transplant coordinators and surgeons. The establishment performs a second serology test using blood samples which accompany the livers for confirmatory testing. This ensures donor serology testing for all the mandatory markers is performed in a HTA-licensed laboratory. The second set of results is transferred to Epic from the testing laboratory's electronic management platform and is accessible only to the same subset of authorised staff.

Upon receipt of the organs, theatre nurses record the donor details, the organ details, date and time of retrieval and receipt onto the 'Transplant Organ Tissue and Vessels Register'. Details of vessels sent to other centres are recorded on a vessel log register; also included in the register are details of the recipient, thereby providing records of full traceability from donor to recipient.

The vessels are stored in a locked refrigerator located within theatres. The vessels accompanying the organ are packed individually in sterile pots and, if not required to support the organ transplant, remain unopened and are transferred to storage without re-packaging. If the pot is opened during transplant and subsequently not required, they are re-packaged in a new sterile pot in University of Wisconsin (UW) solution supplemented with antibiotics in theatre. In this situation, the transplant surgeon using the vessels will be informed of the infection status of the previous recipient.

On the day of the inspection, the vessels were being stored in the back-up refrigerator due to breakdown of the main storage refrigerator. Temperatures are recorded continuously on a trace and if the temperature deviates outside the set range, the freezer alarms locally and remotely to staff offices which are manned around the clock. In the event of a breakdown, the establishment had put in place contingency plans to use a drug refrigerator located at a nearby theatre.

Occasionally the establishment receives valved conduit vessels from another HTA-licensed establishment. The vessels are received on dry ice and, if not used within 48 hours, are returned to the other establishment or transferred to freezer storage in the orthopaedic theatres.

Bone, tendons, ligaments, menisci, skin and nerve grafts

The establishment has recently expanded its activities to include the storage of packaged bone, tendons, ligaments, menisci, skin and nerve grafts. During the inspection, the establishment was storing bone, tendon and ligament products purchased from HTA-licensed suppliers. Although licensed for the storage of skin and nerve grafts, the Plastic Surgery Department intends to use these within 48 hours of receipt or to return them to the supplier if the package remains unopened. However, on rare occasions, it may take the decision to stored the tissue for longer periods in the orthopaedic theatre freezer.

All tissue products are stored between -38 and -42ºC in a temperature-monitored freezer located within the theatre department's 'sterile store room'. Storage temperatures are monitored on a continuous basis using chart recorders and a probe system; data from the latter is recorded daily. The freezer alarm is local and there is a new -40ºC freezer installed as a back-up. The establishment has plans to replace the current freezer with a second new -40ºC freezer and put in place an electronic temperature monitoring system which will allow remote call-outs to staff in the event of temperature deviations.

All tissue registers are located within the orthopaedic theatre office where details of the allografts and recipient information are recorded in the 'Bone and Tissue Tracking Register'. Delivery notes, product information sheets and the staff responsible for receipt and removal from storage are recorded in separate registers. Product traceability to the recipients is also recorded on Epic.

Amniotic Membrane

The establishment also stores amniotic membrane for use in ocular procedures at the Cambridge Eye Unit. The amniotic membrane is stored in a locked box in a 2-8ºC refrigerator, within theatres at the clinic. The refrigerator temperature is monitored daily and temperature records are reviewed by the lead nurse. In the event of a fridge malfunction, the establishment has plans to use the anaesthetic refrigerator located adjacent to the main storage fridge.

The eye clinic retains a stock level of around 10-12 amniotic membrane products of various sizes for emergency use. Only trained staff receive the products and complete the 'Tissue Tracking Register' where the product ID, date and time of receipt, expiry date and recipient information are noted down. Product traceability to the patients is also recorded on Epic. The HTA inspection included a visual inspection of the storage facilities for the vessels, bone, tendon and ligament products, and amniotic membranes. The storage facilities for reagents used for vessel re-packaging and the pathology refrigerator used for the storage of donor blood samples prior to being sent to the testing laboratory were also viewed. The inspection included roundtable discussions with the DI, who is also a Consultant Transplant Surgeon, the Compliance Team, Lead Staff Nurses for Orthopaedics, Transplant Theatres and the Eye Clinic and a Transplant Coordinator.

Audits included a review of two bone products received at orthopaedics where the following product information was compared: receipt and implant dates, expiry dates and recipient information available on Epic and the 'Tissue Tracking Register'. A similar audit was performed on an amniotic membrane product in storage against the tissue log register. No discrepancies were found in either of these audits. A further audit was performed on the records associated with two vessels chosen from the 'Transplant Organ Tissue and Vessels Register'. A discrepancy was found against the availability of serology information for one vessel product.

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.		
b) There are procedures for all licensable activities that ensure integrity of tissue and / or cells and minimise the risk of contamination.	The establishment does not have all necessary procedures in place to safeguard the quality and safety of the tissues and cells. For example: • There are no procedures ensuring that donor blood samples are sent to, and received by, the testing laboratory within an agreed and validated timeframe. • There are no documented procedures to ensure that the refrigerator used for the storage of UW solution and antibiotics, and the pathology refrigerator used for the storage of donor blood samples, are appropriately monitored and alarmed. There were no procedures setting out contingency arrangements for these refrigerators. • While standard operating procedures (SOPs) state that purchased tissue products must be used within 10 minutes of removal from the freezer, SOPs do not set out what action is needed in the event this limit is exceeded, nor how the 10 minute limit will be monitored. • There are no SOPs covering how information relating to the receipt, storage and use of tissue products, when purchased from suppliers, should be recorded in tissue registers, log books and Epic at the orthopaedic office.	**Major**

	In addition, procedures described by staff are not accurately reflected in the establishment's documentation. For example: • Staff are able to describe the steps for re-packaging vessels in antibiotic solution in the event the pot is opened in theatre. However, these steps are not detailed within the SOPs. • Although described by staff, the SOP for the receipt of amniotic membrane does not provide details on where products are to be quarantined and steps to take if the product does not meet the required specifications.	
i) There are procedures to ensure tissues and / or cells are not released from quarantine until verification has been completed and recorded.	The establishment has not set out procedures to ensure donor mandatory serology results for liver vessels intended for use under the Q&S Regulations have been received and reviewed by staff prior to vessels being released. There are no quarantine arrangements for vessels prior to review of the results. During the inspection, a vessel available for release did not have the confirmatory serology results for all mandatory infectious markers on Epic. Syphilis results for the vessel from the original donor tests were also not available.	**Major**
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.	While the establishment is able to describe plans in the event of a termination of activities, these procedures are not documented.	**Minor**
GQ2 There is a documented system of quality management and audit.		
b) There is an internal audit system for all licensable activities.	Independent audits are not performed against the full scope of HTA licensable activities.	**Minor**

GQ4 There is a systematic and planned approach to the management of records.		
j) Records are kept of products and material coming into contact with the tissues and / or cells.	While the establishment records the batch numbers of UW solution, batch numbers of sterile pots and antibiotic solutions used in the re-packaging of liver vessels are not documented.	**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 establishment has no procedures in place to apply the Single European Code when distributing tissue products to end users.	**Minor**
GQ7 There are systems to ensure that all adverse events 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.	The information provided to other centres receiving vessels does not include the stipulation to report serious adverse events and adverse reactions (SAEARs) to the DI, to enable escalation onwards to the HTA within 24 hours.	**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.	The establishment has not performed risk assessments identifying all risks associated with licensable activities. For example, principal and contingency storage facilities and release procedures have not been risk assessed.	**Minor**

Premises, Facilities and Equipment

Standard	Inspection findings	Level of shortfall
PFE1 The premises are fit for purpose.		
a) A risk assessment has been carried out of the premises to ensure that they are fit for purpose.	The establishment has not performed risk assessments for the premises encompassing security, suitability of equipment and IT systems.	**Minor**
c) Tissues and / or cells are stored in controlled, monitored and recorded conditions that maintain tissue and / or cell integrity.	The establishment's SOPs detail storage requirements of the tissue products. However, the requirements set out in SOPs are not consistent with actual practices or with the manufacturer's recommendations. For example: • The establishment's temperature records of the orthopaedic freezer indicate that products with a storage requirement of below -40ºC have periods of storage at higher temperatures. • The establishment SOPs for storage of amniotic membrane stipulate storage at between 2-8ºC. This is not in line with the records showing regular temperature deviations above 8ºC.	**Minor**

Advice

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

No.	Standard	Advice
1.	GQ1c	The HTA has recently approved the addition of bone, tendons, ligaments, menisci, neuronal grafts, skin and amniotic membrane onto the establishment's licence. The new tissue types are stored in different departments within CUH under the governance of teams separate from the DI. While the DI has taken steps to ensure appropriate oversight of the licensable activities by appointing Persons Designates (PDs) at each site, the DI should ensure that regular governance meetings are set up between himself and the PDs. The meetings should be minuted and outcomes of discussions and actions should be disseminated to all staff working under the licence.
2.	GQ1p	Under the Trust's agreement with the testing laboratory, it is the responsibility of the establishment to ensure samples are transported to the testing laboratory under defined conditions and using validated methods. The DI is advised to contact the testing laboratory to determine what these

		conditions are to ensure blood samples are tested in line with the validated parameters of the test kits. The conditions for storage and transport should be clearly documented within a SOP and staff should be made aware of the requirements.
3.	GQ2b	The DI should ensure that the number of donor blood samples sent for serology is logged for full traceability. The date and time of testing should also be recorded to ensure samples are assayed within timeframes as specified by the test kits. Currently only the number of blood samples received with the organ are logged within the 'Transplant Organ Tissue and Vessels Register'.
4.	GQ2d	The DI is advised to review the procedures for tissue traceability at orthopaedics to streamline the process, if appropriate. The new procedure should be documented within a SOP.
5.	GQ3g	While all staff have attended a training programme providing information on HTA regulations, a further training programme should be rolled out to new staff to provide knowledge of the HTA standards relevant to the receipt, storage and release of tissue products.
6.	GQ4b	In light of the GQ1i findings, the DI is advised to review the scope of the internal audits to ensure serological status of vessel donors are included in the traceability audits.
7.	GQ4h	While the establishment has set out the required storage periods for the retention of traceability and raw data on a Trust-wide database, this is not translated into practice. On inspection, it came to light that the Eye Clinic was only retaining daily temperature records for six months. As the tissue was only approved on the licence six months previously, there has been no loss of raw data. However, the DI is advised to ensure the raw data retention period is clearly set out in SOPs and that all departments are made aware of the requirements.
8.	GQ4h	Certain data output during processing is recorded on thermal paper which has the potential to fade over time. The DI is advised to ensure all forms of raw data is retained in a suitable format to prevent any loss of information.
9.	GQ4k	When distributing vessels to other centres, the establishment obtains recipient information which is then filed within the release form folders. The DI is advised to ensure this procedure is documented within an SOP to ensure recipient data is always obtained and held for the required 30 year period for full traceability.
10.	GQ7a	While the establishment's SOPs for storage of tissues and cells set out procedures for reporting SAEARs to the HTA within 24 hours, the procedures described may not allow for immediate notification to the DI for escalation within the required timeframe. The inspection team was informed that the SOPs will be amended include the DI's contact number for immediate reporting. The DI should ensure this is implemented and to devise a standalone SOP that clearly sets out the process for reporting SAEARs to the HTA for activities under the Human Application licence. Due to the recent expansion of licensable activities involving separate departments within the hospital, the DI is advised to ensure that the SAEAR reporting responsibilities are also delegated to PDs in other departments in the event the DI is unavailable. The new lines of reporting responsibilities

		should be clearly set out in SOPs and staff should be made aware of the new procedures.
11.	GQ8a/c	The DI should ensure that risk assessments are available to all staff working under the licence once they have been set out and that they are reviewed annually.
12.	PFE4c	Vessels are transported to other centres using couriers which fall under a separate HTA licensing framework. To ensure any incident which may occur during distribution is made known to the DI promptly, the establishment should maintain close communication with the receiving transplant centres to confirm receipt and that conditions during transport were maintained. These procedures should be included in SOPs for tissue distribution.
13.	PFE5c	The freezers used for the storage of vessels and tissue products have temperatures recorded continually using a chart recorder. However, the temperature range shown on the trace is discordant with temperatures recorded on daily log sheets using probe displays. The DI should review the use of both chart recorders and probes, where there may be discrepancies between the two, as the temperature monitoring of the freezers will only rely the calibrated external probe.
14.	-	The DI is advised to review all documents to ensure that they refer to the correct legislation for activities under the Human Application licence. References to the HTA Directions 003/2010 should be replaced with Directions 002/2018 which have superseded them.

Concluding comments

There are a number of strengths observed during the inspection. The Cambridge Transplant Unit has put in place a training presentation that provides staff with a clear visual guide on the procedures involved when receiving, storing and using vessels. This presentation encompasses the regulatory context of the work and provides information on the HTA's remit. In addition, the compliance team performs spot checks on the storage facilities to ensure compliance to the Q&S Regulations and that procedures under the framework of the licence are adhered to. CUH has in place a Human Tissue Meeting Committee which is attended by all the DIs within the Trust to discuss updates in legislative requirements and governance of procedures where there is overlap in activities between licences.

There are areas of practice that require improvement, result in 10 shortfalls. These relate to the absence of documented procedures for licensable activities, procedures to ensure mandatory serological results are available prior to release of tissue, procedures to quarantine of tissue before release, end user reporting of SAEARs, audits against all HTA standards, risk assessments and recording of reagents and consumables. The HTA have given advised to the DI with respect to holding governance meetings, reviewing SOPs, agreements, monitoring of storage facilties, staff training, risk assessments, oversight during distribution, calibration of temperature monitoring systems, retention of raw data and SAEAR reporting.

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: 31 May 2018

Report returned from DI: 19 June 2018

Final report issued: 26 June 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: 18 November 2019

Appendix 1: HTA standards

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

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

Consent

Standard
C1 Consent is obtained in accordance with the requirements of the HT Act 2004, the Human Tissue (Quality and Safety for Human Application) Regulations 2007 and as set out in the HTA's Codes of Practice.
a) If the establishment acts as a procurer of tissues and / or cells, there is an established process for acquiring donor consent which meets the requirements of the HT Act 2004 the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (Q&S Regulations) and the HTA's Codes of Practice
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.
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.
d) Where appropriate, there are procedures to ensure that the premises are of a standard that ensures the dignity of deceased persons.

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.