Site visit inspection report on compliance with HTA minimum standards

Moorfields Eye Hospital

HTA licensing number 11040

Licensed for the

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

- **storage of relevant material which has come from a human body for use for a scheduled purpose**

11 & 12 July 2017

Summary of inspection findings

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

Although the HTA found that Moorfields Eye Bank (the establishment) had met many of the HTA standards, seven major shortfalls and four minor shortfalls were found in relation to 'Governance and Quality Systems' and 'Premises, Facilities and Equipment'.

Key personnel issues, including poor handover from the outgoing to incoming DI and loss of a member of the technical team to long term leave, have contributed to several systematic problems; these include SAEARs management, key aspects of governance, processing and critical equipment maintenance.

Examples of good practice were observed during the inspection and these 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 Paragraph 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.

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

Tissue category	Tissue type	Procurement	Processing	Testing	Storage	Distribution	Import	Export
Ocular	Cornea	**E / TPA**	**E**	**TPA**	**E**	**E**	**E**	**E***
Ocular	Sclera	**E / TPA**	**E**	**TPA**	**E**	**E**	**E**	**E***
Membrane, Amniotic	Amniotic Membrane				**E**			

Background to the establishment and description of inspection activities undertaken

Consent and procurement

Ocular Tissue Donor Coordinators liaise with hospitals in London to identify potential donors by working closely with their bereavement teams. The establishment is also alerted to potential donors by staff at hospitals and hospices in London and South East England, as well as by donor families who call the establishment directly. The coordinators check the national organ donor register and contact relatives to discuss eye donation and/or donation of tissue for research. The coordinators seek consent and undertake patient assessments based on the medical and behavioural history of the potential donor provided by the donor's family and GP. Donor acceptance criteria is based on current JPAC guidance.

Cadaveric donor ocular tissue is procured by trained members of staff from the establishment and transported to the establishment on ice in standard consumer cool bags. This is in line with the establishment's procurement standard operating procedure (SOP).

Tissue may also be procured by teams acting under the authority of a Third Party Agreement with the establishment. The establishment has also received donated tissue from a Danish eye bank. In all cases, donor blood samples are also obtained for mandatory serology tests, and testing is undertaken under a service level agreement with another HTA-licensed establishment.

Processing and storage

Processing is carried out by three members of staff, two with many years' experience and one new to the role (less than one year of technical experience). The establishment has a clean room suite for the processing of eye tissue. The processing room comprises Grade A cabinets within a Grade B background air quality environment. The eyes undergo a surface decontamination step before the corneas and sclera are dissected. Sclera are split into four pieces per eye, and each piece is stored separately in alcohol for up to 12 months. Corneas are incubated in organ culture medium at 31ºC for up to 28 days before transfer to de-swelling media for up to 4 days. The establishment's processing activities also include cutting corneas for Descemet's Stripping Automated Endothelial Keratoplasty (DSAEK) cases. DSAEK cuts are carried out using a microkeratome.

Import, Export and Distribution outside the UK

Corneal tissue is imported on a routine basis from a single supplier in the US. There is a formal agreement in place with the supplier. The imported tissue is supplied ready for transplant, and no processing of this material takes place at the establishment. No tissue is exported or distributed outside the UK.

Donor suitability and issue for end use

Tissue requests from Moorfields' consultants are matched with tissues suitable for transplant, and from this information a daily issue list is produced by the establishment. Tissues are used by Moorfields' consultants within Moorfields Eye Hospital's main City Road site or at other Moorfields Eye Hospital locations based around London and the South East.

Storage for research

The establishment currently stores a small amount of material for research under this licence. Material for research is also sometimes transferred to the UCL Institute of Ophthalmology, research licence 12177.

Audits

1. *Tissue in storage on the premises*

   Two donor identification numbers were chosen at random by the inspectors from the establishment's electronic database. Donor files were examined for signed consent documents, microbiology testing results, serology testing results, processing records and procurement site risk assessments.

2. *Tissue released for end use*

   The same procedure was followed as for Audit 1 above, and in addition two records associated with release for end use were examined. Some anomalies were found relating to recording of lab results for donated material and donor serology testing. See advice against GQ1j and GQ5.

3. *Tissue imported from the US*

Four donor identification numbers were chosen at random by the inspectors from the establishment's electronic database. Accompanying paperwork was examined.

4. Critical materials batch / lot numbers

The establishment records batch/lot numbers of critical materials in three ways: (1) paper processing records (also scanned), (2) paper records are transposed by the technical team onto the electronic processing records and (3) batch/lot numbers of in-use critical materials are also recorded on a white board located in the office and viewable from the tissue receipt/initial prep lab (used mainly for ordering purposes). Consumables kept in the lab were audited to ensure that batch/lot numbers were consistent with the white board, and anomalies were noted (see advice against GQ1j). Upon discussing the anomalies, the establishment confirmed during the inspection that the white board would henceforth be used only for ordering purposes, and that batch/lot numbers for critical materials used during processing would continue to be recorded onto paper processing records, transposed into electronic records and paper records would be scanned and stored with donor files.

Inspection findings

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

Compliance with HTA standards

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

Governance and Quality

Standard	Inspection findings	Level of shortfall
GQ1 All aspects of the establishment's work are supported by ratified documented policies and procedures as part of the overall governance process.		
c) There are regular governance meetings, for example health and safety, risk management and clinical governance committees, which are recorded by agendas and minutes.	Eye bank level meetings are not currently minuted. Under the current DI, there has been one formal minuted eye bank level meeting; eye bank level matters tend to be discussed informally by the small team.	**Major (cumulative)**
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.	There was a file of hard copy SOPs in the establishment office; some of these had been superseded by updated SOPs that were only available in electronic form. Critical SOPs were not sufficiently controlled; for example, the SOP that described the current antibiotic wash step used during the organ culture storage of corneas was only available as an uncontrolled electronic SOP.	

g) There are procedures to ensure that an authorised person verifies that tissues and / or cells received by the establishment meet required specifications.	The SOP for tissue receipt (MLEB-DOC-SOP-E1.02) does not mention any quality checks of the tissue itself.	
r) Third party agreements specify the responsibilities of the third party and meet the requirements set out in Directions 003/2010.	The agreement with the US supplier of ocular tissue does not state the requirement for HTLV1 testing, a key issue for US imports because HTLV1 testing is required by the US FDA for ocular tissue. As a general point with regard to TPAs, language such as 'without delay' is used to describe the timeframe in which the third party must notify the DI of suspected serious adverse events and reaction (SAEARs) this is too vague. The third party should notify the DI immediately. The choice of language is of particular importance for the ocular tissue imported from the US, where reporting to the US FDA is allowed to take up to 15 days (as opposed to the UK's 24 hour reporting requirement).	

GQ2 There is a documented system of quality management and audit.		
a) There is a quality management system which ensures continuous and systematic improvement.	Establishment staff demonstrate a strong concern for quality; however, the quality management system requires significant development in order to ensure continuous and systematic improvement. Specifically, the systems for managing incidents, critical equipment maintenance and tissue non-conformances have failed to produce continuous improvement despite significant time and effort spent by staff dealing with the individual matters. Quality governance must be improved such that when issues affecting quality and safety arise, there are appropriate channels for their efficient and effective management. The establishment also has inadequate systems in place to manage organisational change; for example, the handover from the outgoing DI to the interim DI and then on to the newly appointed DI did not ensure appropriate quality governance.	**Major (cumulative)**
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.	When new critical equipment was obtained for performing DSAEK cuts using a different method, there was no formal training for technical staff, the method was not validated and a PPD was not submitted for HTA approval as required. Conversations with staff and evaluation of processing records for DSAEK cuts on inspection revealed that although the majority of DSAEK cuts were within set parameters for release, there are systematic problems with thickness and ability to measure the cuts. There is no system in place for regular ongoing evaluation of the DSAEK cuts.	

GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills.		
e) Personnel are trained in all tasks relevant to their work and their competence is recorded.	Training records were not up-to-date for multiple members of staff. The processing records suggest that staff had achieved competence in a number of areas (and this was confirmed by staff during the inspection); however, there was no formal record of the training given or the competence achieved.	**Major (cumulative)**
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.	There is consent training in place for coordinators; however, there is not a formal training programme in place for other staff.	
g) There is a documented training programme that ensures that staff understand the organisational structure and the quality systems used within the establishment.	It was clear that staff understand the organisational structure; however, knowledge of the quality systems used within the establishment, in particular the Trust-level incident reporting system, was not adequate.	
k) The establishment is sufficiently staffed to carry out its activities.	The establishment is not sufficiently staffed. The administrator has recently changed roles to become a technical member of staff to fill in for another member of the technical team who is on long term sick leave. This has left two experienced technical team members, one new member and the DI to handle all processing, lab management and quality management. It was clear that during busy times, periods of intense tissue processing or when a staff member is ill or on leave that quality could be detrimentally affected.	
GQ4 There is a systematic and planned approach to the management 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.	There is a record of planned audits, but audits are not taking place on a regular basis. During the inspection, several instances of fields left blank and areas with missing information were noted in 2/2 processing records audited.	**Minor**

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.	Policies do not provide for the retention of raw data for the required 10 year period.	**Minor**
GQ5 There are documented procedures for donor selection and exclusion, including donor criteria.		
c) In cases other than autologous donors, donor selection is carried out by authorised personnel and signed and reviewed by a qualified health professional.	Currently, the establishment's tissue coordinators perform the evaluation of allogenic donors, including donor serology testing results and medical history. One of the two coordinators is a qualified nurse; however, although very experienced, the other coordinator is not a qualified healthcare professional.	**Minor**
GQ7 There are systems to ensure that all adverse events 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.	The team noted several incidents that have occurred since the last inspection which should have been reported to the HTA as SAEARs.	**Major (cumulative)**
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.	The incident reporting SOP clearly states that the DI should report SAEARs to the HTA, but not the manner in which incident should be investigated to determine whether or not an incident is reportable as a SAEAR.	
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.	The procedures in place currently do not adequately define the decision making process.	

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.	End user agreements do not appropriately describe how and when suspected SAEARs should be reported back to the establishment.	
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 a number of risk assessments in place relating to licensable activities, these have not been reviewed regularly and do not adequately encompass the full range of activities taking place under their licence. For example, there was no evidence of any actions taken with regard to assessing risk of major changes to practice, for example the implementation of the new method and equipment for performing DSAEK cuts.	**Major (cumulative)**
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.		

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 003/2010.	No finger dabs or settle plates are used when performing DSAEK cuts. In-process particle monitoring is carried out but not documented. Action is only taken if a particle counter alarms. A monthly at-rest test is performed. Room pressure monitoring is captured in a room pressure log. Adjacent rooms of different grades should have a pressure differential of 10-15 Pascals. The room pressure log showed numerous incidences of pressure cascade failure between rooms without any assessment of the impact of this. Although it was confirmed on the day of the inspection that a service visit to remedy the issue was booked for early September, there was no documented assessment of pressure issue's potential impact on quality and safety of tissue.	**Major**
PFE4 Systems are in place to protect the quality and integrity of bodies, body parts, tissues and cells during transport and delivery to a destination.		
h) Packaging and containers used for transportation are validated to ensure they are fit for purpose.	Standard consumer cool bags used by the technical team to transport tissue from procurement sites back to the establishment have not been validated.	**Minor**
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.	The new microkeratome used for performing DSAEK cuts was not validated and is not present on the critical equipment list.	**Major (cumulative)**
b) Critical equipment is maintained and serviced in accordance with the manufacturer's instructions.	Several items have not been serviced regularly, including -80 freezer, new microkeratome for DSAEK cuts, pachymeter and particle monitors.	

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.	There have been ongoing problems with DSAEK cuts resulting in the release of tissue that was unfit for purpose and numerous occasions where tissue was released for human application despite falling outside the establishment's release criteria. The issues with out-of-spec DSAEK cuts stem in part from problems with the new microkeratome itself as well as problems with the pachymeter. The establishment does not have formal procedures for maintenance or maintenance contracts for either of these pieces of critical equipment. The magnehelic gauges on the air handling system have been reading out-of-specification for several months The clean room was attended by a maintenance company on 29 June 2017 which recommended a whole suite rebalance citing that pressure cascades were commonly below targets set (with the exception of grade B areas). The reason for the ongoing delay prior to corrective action taking place was unclear.	
d) New and repaired equipment is validated before use and this is documented.	The new microkeratome used for performing DSAEK cuts was not validated.	
e) There are documented agreements with maintenance companies.	The establishment was not able to produce documented agreements with maintenance companies. A number of items of critical equipment lacked service contracts: -80 freezer, new microkeratome for DSAEK cuts, pachymeter, particle monitors and air handling system.	
k) There are contingency plans for equipment failure.	Formal contingency plans are not in place for the malfunctioning of the pachymeter, even though this is a regular occurrence that has contributed to SAEs (unreported).	

Advice

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

No.	Standard	Advice
1.	GQ1b, j	During the audit of tissue that had been released for transplantation, it was noted that the number of colonies recorded on TSA plates was not present on a direct printout from the donor records database. It was discussed during the inspection that when microbiology results are negative (i.e. no growth), the electronic system does not allow for entry of '0' or text, so the field must be routinely left blank. As a result, the establishment's records are often incomplete and do not provide evidence that this monitoring took place. The establishment is working on a systems solution to this data entry issue. In addition, some details for critical materials coming into contact with the tissue was missing from the direct printout of database records. The DI is advised to continue scanning and saving paper lab records relating to microbiology and critical materials coming into contact with donor material to ensure that these details are present in donor records.
2.	GQ1j	The DI is advised to ensure that the batch numbers are recorded appropriately for tissue pots, as the pots themselves are not printed with a batch number and are stored loose in the receipt lab.
3.	GQ3f	Microbiology training should be provided for staff who do not have a formal health professional or life sciences qualification.
4.	GQ4b, c	The DI is advised to ensure staff are aware of how to use the new records database and its limitations. The DI should continue with plans to further develop the system and interface, including planned audits, to better suit the needs of the eye bank.
5.	GQ4j	The DI is advised to ensure that lab paper records of batch / lot numbers are routinely scanned and traceable to donor and recipient.
6.	GQ4k	The DI is advised to add a section to the donor tissue information sheet for surgeons to detail any incidents or issues with the tissue. Currently, the some surgeons note issues on a large blank area of the form. A prompt may increase feedback and highlight any quality trends.
7.	GQ5	Upon auditing records for a sample of donor tissue that had been released for transplant, it was noted that a West Nile Virus test was ordered due to the donor's travel history (the donor had travelled to Italy within the last 12 months). The establishment's exclusion criteria state that if a potential donor has travelled to an area affected by West Nile Virus within four weeks of the potential donation, then the donor should be excluded. Dates of travel were not present within the donor records, so the HTA was unable to determine whether or not the donor should have been excluded. The DI is advised to ensure that such details are recorded and made readily accessible within donor records.

Assessment of existing conditions/shortfalls against standards

There were four open CAPAs from the previous inspection that were open at the time of this inspection; these are summarised in the table below.

Standard	Short description of finding	CAPA progress	Further action required
GQ1b	Lack of procedures to describe some aspects of the quality system and import	Documentary evidence covering the procedures has been received and reviewed by the HTA.	Some amendments required. This CAPA is now closed. Outstanding issues relating to updating policies and procedures will roll over into the CAPA plan relating to this inspection. See shortfall against GQ1.
GQ2a	Incident follow -up and independent audit	Documentary evidence covering independent audits and their scheduling was reviewed on inspection and deemed to be satisfactory. A major shortfall was identified relating to incident follow-up.	None; this CAPA is now closed. Outstanding issues relating to incident follow-up will roll over into the CAPA plan relating to this inspection. See shortfall against GQ7.
GQ4b	Audit of records for completeness	Donor records and database audited on inspection. A new database has been implemented which deals with the previous issues of missing information and records are complete.	None; this CAPA is now closed. See advice against GQ4b, c.
GQ8a	Risk assessments for transport and import.	A list of risk assessments was reviewed on inspection, but these had not been carried out.	Risk assessments should be carried out according to a schedule. This CAPA is now closed and the outstanding actions relating to risk assessments will roll over in to the CAPA plan relating to this inspection. See shortfall against GQ8 in this report).

Concluding comments

There are a number of areas of practice that require improvement, including seven major shortfalls and four minor shortfalls. The HTA has given advice to the Designated Individual with respect to research tissue storage, record keeping, microbiology training and communication.

Despite the significant number of shortfalls against standards, staff demonstrated a genuine concern for quality and commitment to their work. It is evident upon review of clinical outcomes that in the vast majority of cases the preparation of ocular tissue by the establishment is suitable and the tissue is safe for transplantation.

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: 6 September 2017

Report returned from DI: 15 September 2017

Final report issued: 4 October 2017

Completion of corrective and preventative actions (CAPA) plan

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

Date: 1 June 2020

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 003/2010 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 003/2010 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.
f) There are procedures for tissue and / or cell procurement, which ensure the dignity of deceased donors.
g) There are procedures to ensure that an authorised person verifies that tissues and / or cells received by the establishment meet required specifications.
h) There are procedures for the management and quarantine of non-conforming consignments or those with incomplete test results, to ensure no risk of cross contamination.
i) There are procedures to ensure tissues and / or cells are not released from quarantine until verification has been completed and recorded.
j) There are procedures detailing the critical materials and reagents used and where applicable, materials and reagents meet the standards laid down by the European directives on medical devices and in vitro diagnostic medical devices.
k) There is a procedure for handling returned products.
l) There are procedures to ensure that in the event of termination of activities for whatever reason, stored tissues and / or cells are transferred to another licensed establishment or establishments.
m) The criteria for allocating tissues and / or cells to patients and health care institutions are documented and made available to these parties on request.
n) The establishment ensures imports from non EEA states meet the standards of quality and safety set out in Directions 003/2010.
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 003/2010.

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 003/2010, is collected and maintained.
g) There is a system to ensure records are secure and that donor confidentiality is maintained in accordance with Directions 003/2010.
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 003/2010 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 003/2010.
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 003/2010.
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 003/2010.
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.
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 003/2010.
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 003/2010.
b) There are procedures for the transport of tissues and / or cells which reflect identified risks associated with transport.
c) There is a system to ensure that traceability of tissues and / or cells is maintained during transport.
d) Records are kept of transportation and delivery.
e) Tissues and / or cells are packaged and transported in a manner and under conditions that minimise the risk of contamination and ensure their safety and quality.
f) There are third party agreements with courier or transport companies to ensure that any specific transport conditions required are maintained.
g) Critical transport conditions required to maintain the properties of tissue and / or cells are defined and documented.
h) Packaging and containers used for transportation are validated to ensure they are fit for purpose.

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

Disposal

Standard
D1 There is a clear and sensitive policy for disposing of tissues and / or cells.
a) The disposal policy complies with HTA's Codes of Practice.
b) The disposal procedure complies with Health and Safety recommendations.
c) There is a documented procedure on disposal which ensures that there is no cross contamination.
D2 The reasons for disposal and the methods used are carefully documented.
a) There is a procedure for tracking the disposal of tissue and / or cells that details the method and reason for disposal.
b) Disposal arrangements reflect (where applicable) the consent given for disposal.

Human Tissue Act 2004 Standards

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

Governance and quality system standards
GQ1 All aspects of the establishments work are governed by documented policies and procedures as part of the overall governance process
a) Ratified, documented and up-to-date policies and procedures are in place, covering all licensable activities. b) There is a document control system. c) There are change control mechanisms for the implementation of new operational procedures. d) Matters relating to HTA-licensed activities are discussed at regular governance meetings, involving establishment staff. e) There is a system for managing complaints.
GQ2 There is a documented system of audit
a) There is a documented schedule of audits covering licensable activities. b) Audit findings include who is responsible for follow-up actions and the timeframes for completing these.

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

Traceability standards
T1 A coding and records system facilitates the traceability of bodies and human tissue, ensuring a robust audit trail
a) There is an identification system which assigns a unique code to each donation and to each of the products associated with it.
b) A register of donated material, and the associated products where relevant, is maintained.
c) An audit trail is maintained, which includes details of: when and where the bodies or tissue were acquired and received; the consent obtained; all sample storage locations; the uses to which any material was put; when and where the material was transferred, and to whom.
d) A system is in place to ensure that traceability of relevant material is maintained during transport.
e) Records of transportation and delivery are kept.
f) Records of any agreements with courier or transport companies are kept.
g) Records of any agreements with recipients of relevant material are kept.

T2 Bodies and human tissue are disposed of in an appropriate manner
a) Disposal is carried out in accordance with the HTA's Codes of Practice. b) The date, reason for disposal and the method used are documented.

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

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

Where the HTA determines that a licensing standard is not met, the improvements required will be stated and the level of the shortfall will be classified as 'Critical', 'Major' or 'Minor'. Where the HTA is not presented with evidence that an establishment meets the requirements of an expected standard, it works on the premise that a lack of evidence indicates a shortfall.

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

1. **Critical shortfall:**

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

   Or

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

   Or

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

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

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

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

   (3) A notice of suspension of licensable activities

   (4) Additional conditions being proposed

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

2. **Major shortfall:**

   A non-critical shortfall.

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

   or

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

   or

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

   or

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

or

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

or

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

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

3. **Minor shortfall:**

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

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

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

Follow up actions

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

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

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

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