Site visit inspection report on compliance with HTA minimum standards

John Radcliffe Hospital

HTA licensing number 11106

Licensed for the

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

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

13-14 February 2019

Summary of inspection findings

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

Although the HTA found that John Radcliffe Hospital (the establishment) had met the majority of the HTA standards, one minor shortfall was identified. This related to particle monitoring of aseptic processes. In addition, the HTA has provided advice in relation to standards under the governance and quality and premises, facilities and equipment standards.

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

The HTA's regulatory requirements

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

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

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

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

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

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

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

Licensable activities carried out by the establishment

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

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

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

'SLA' = Service level agreement; the establishment is licensed for this activity but another establishment (licensed) carries out the activity on their behalf.

'SLA*' = Service level agreement; the establishment is licensed for this activity, which another licensed establishment carries out on their behalf. However, the establishment is not currently carrying out this activity.

Tissue Category; Tissue Type	Procurement	Processing	Testing	Storage	Distribution	Import	Export
Reproductive, Ovarian; Ovarian Tissue	**E/TPA**	**E**	**SLA**	**E**	**E**		**E**
Reproductive, Testicular; Testicular Tissue	**E/TPA**	**E**	**SLA**	**E**	**E**		**E**
Cardiovascular, Valves; Heart Valves and Conduits	**E/TPA**	**E**	**SLA**	**E**	**E**		**E**
Ocular; Cornea	**E***		**SLA***		**E***		

Background to the establishment and description of inspection activities undertaken

The Oxford Cell and Tissue Bank (OCTB, the establishment), is based at John Radcliffe Hospital and falls within the Oxford University Hospitals NHS Foundation Trust (OUHFT). The establishment has been licensed under the Human Tissue (Quality and Safety for Human Application) Regulations since 2007, and also holds a licence for storage of relevant material for a scheduled purpose under the Human Tissue Act 2004. This inspection focused on activities under the Human Tissue (Quality and Safety for Human Application) Regulations (2007).

OCTB was formally known as the Oxford Heart Valve Bank (OHVB), but in recent years has increasingly focused on the procurement, processing and storage of reproductive tissue. To support this the establishment's structure has been realigned to fall under the OUHFT Children's Services Directorate. The OCTB Manager is the HTA Designated Individual (DI), and the Lead Consultant for the service is the HTA Corporate Licence Holder Contact (CLHc).

The establishment contracts another licensed establishment to undertake mandatory serological and additional nucleic acid tests (NAT) under the terms of a service level agreement (SLA). Blood samples are centrifuged and stored at -80°C awaiting transport by dedicated courier to the testing establishment.

The establishment is also licensed to procure ocular tissue which is then sent to another HTA licensed establishment for processing. However, at the time of the inspection, this activity was not taking place as it was on hold. Records relating to the last ocular tissue procurement, which took place in 2017, were reviewed during the inspection. Under the agreement between the two licensed establishments, staff sought consent, undertook donor assessment and retrieved donor eyes along with a blood sample for serological testing. The eyes and serology sample were then sent to the other licensed establishment for donor testing, processing, storage and distribution.

<u>Reproductive Tissue</u>

Autologous ovarian and testicular tissue from eligible donors is removed and preserved with the aim of restoring reproductive function in the future to young patients undergoing gonadotoxic chemo- or radio-therapy.

Patients are referred to the service by clinicians at various treatment centres around the UK. Tissue is procured in theatres either at John Radcliffe Hospital, or at the treatment centres

themselves under the terms of third party agreements (TPAs). Information about the process is provided in advance and consent is sought by the OCTB Lead Consultant. As part of the service, patients are asked to consent to the use of up to ten percent of donated tissue for research purposes, provided a minimum quantity is available for future autologous use. Young donors are re-consented for the on-going storage of tissue when they reach 18 years of age.

Surgical staff are trained in procurement procedures by establishment staff. In most cases, establishment staff attend each procurement, taking with them pre-prepared sterile equipment packs and controlled forms upon which to document patient details and procurement activities. They are present during the World Health Organisation (WHO) surgical safety checklist sign-in and sign-out procedures. A blood sample for serological testing is collected during the procedure. Establishment staff pack and transport the tissue and blood sample to the OCTB in accordance with documented procedures for processing.

The establishment has recently trained a member of staff at a distant treatment centre to carry out procurement activities without establishment staff being present. Procured tissue is transported to the OCTB by courier. The training and reference materials used to train this member of staff were viewed during the inspection.

Reproductive tissue is processed in microbiological safety cabinets, which provide a grade A environment in a surrounding suite maintained to grade B specifications. The tissue is weighed and dissected. Tissue slices are immersed in cryoprotectant medium and undergo controlled-rate freezing, before being transferred to long term storage in the vapour phase of liquid nitrogen tanks. Samples are retained for histological analysis. The transport and final suspension media are tested for microbiological contamination, and a sample of previously-sterile absorbent material is also snipped during processing and sent for microbiological analysis, as a proxy for the tissue itself.

Heart Valves and Conduits

Heart valves and conduits are procured from donated heart tissue. This may be obtained within the Trust or from the national organ transplant network, in cases where the heart itself could not be used for transplant.

For tissue supplied by the organ transplant pathway, initial consent, donor selection and serology information is assessed by establishment staff via the national electronic offering system (EOS). Within the Trust, tissue coordinators liaise with bereavement services and mortuary staff, review patient files and the organ donor registry to identify potential suitable donors. The nearest relations of the patient are contacted to discuss the possibility of donation. Time is given for the family to consider the request and if agreement is given, formal consent for both the donation and serological testing is sought. Establishment staff attend the mortuary with a pre-prepared sterile procurement kit and transport the tissue and serology sample back to the OCTB for processing.

The initial dissection takes place in a microbiological safety cabinet within a grade C clean room. Following antibiotic treatment, the tissue is transferred to the grade B cleanroom. Final processing of the valves and conduits takes place in a grade A cabinet within the grade B suite. The tissue is immersed in cryopreservation medium before being transported to a controlled-rate freezer and subsequent long term storage in the vapour phase of a quarantine liquid nitrogen storage tank. If release checks are completed satisfactorily the tissue is transferred to a post-release storage tank. Tissue is issued to clinicians within the Trust or in the case of heart valves, via a national database.

Premises and Equipment

Since the last inspection the establishment has relocated the controlled-rate freezers and the quarantine and long-term storage liquid nitrogen vessels from a portacabin to a permanent building within the hospital. Access to the room is restricted with a keypad lock and the room is included in routine checks by hospital Security. The room is equipped with oxygen monitors and alarms. Vessels are automatically refilled and monitored to alert staff of events such as overfilling.

Temperature-controlled storage equipment, including the liquid nitrogen vessels, fridges and freezers, are maintained under a service agreement and independently monitored by a contracted company. In the event of an out-of-hours temperature excursion, establishment staff respond to alerts from the monitoring company on a rota basis.

The clean room suite and grade A cabinets are subject to sessional, daily and monthly monitoring by the establishment, as well as biannual maintenance and testing by a contracted maintenance company. Pressure gradients in the clean room suite are checked daily prior to processing. Sessional monitoring includes the use of tryptone soya and Sabouraud dextrose agar (TSA and SDA respectively) settle plates in the grade A and B areas, particle monitoring in grade A and operator finger dabs. Monthly monitoring includes active air sampling and surface monitoring via contact plates and swabs. Environmental monitoring data is monitored for trends and reported at establishment governance meetings. The suite undergoes daily surface cleaning and wider room cleaning against a schedule. Disinfectants used to clean the equipment, consumables and suite are specified and rotated to help maintain efficacy.

The former vessel storage area has been re-purposed as a laboratory for the incubation and initial analysis of environmental monitoring agar plates, finger dab plates and process simulation broths. Two new incubators in this laboratory, one operating at 20-25°C and the other at 30-35°C, are monitored using calibrated data loggers pending installation of monitoring points for the independent monitoring system used for other equipment on site.

This was the establishment's sixth routine inspection. The visit included a visual inspection of tissue and reagent storage areas, observation of gowning, spraying-in, media preparation and tissue processing in the clean room suite, a visit to the microbiology lab performing sterility testing of samples taken during and at the end of processing, and a visit to the portacabin area used to incubate environmental monitoring plates. Document review and round table discussions were performed for each licensed tissue type. Wider governance procedures to assess records relating to consent, donor selection, serological and NAT tests, processing, sterility testing, cryopreservation, review and release procedures, release for research, maintenance and calibration records, staff training and ongoing assessment, document control procedures, governance meetings, routine and independent audits, incident handling and risk assessments were also reviewed.

Inspection findings

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

Compliance with HTA standards

Premises, Facilities and Equipment

PFE2 Environmental controls are in place to avoid potential contamination.		
b) Where processing of tissues and / or cells involves exposure to the environment, it occurs in an appropriate, monitored environment as required by Directions 002/2018.	The establishment has one particle monitor serving two grade A processing environments (microbiological safety cabinets). This means that on occasions when both cabinets are used concurrently, the activity deemed to be the most critical is monitored, and activities such as the preparation of medium coming into contact with the stored tissue are not. This practice is not compliant with the requirements of Directions 002/2018. During observation of tissue being processed at the establishment, and a review of patient records, it was noted that the particle monitor is not consistently started prior to tissue first being exposed to the Grade A environment, and may stop measuring after collecting a one cubic metre sample. As a result, monitoring is not in place for the full duration of tissue processing. In addition, the particle monitor settings are not routinely updated in line with clock changes to British Summer Time and Greenwich Mean Time, resulting in occasions when the monitoring times cannot be easily aligned to the recorded processing timings. The establishment's procedures specify the requirements for microbial monitoring of the clean room suite. In January 2019, swab plates were not performed as required by the establishment's procedures. In December 2018, TSA plates were not sequentially incubated at 20-25°C and then 30-35°C in accordance with the establishment's procedures. These deviations and the rationale supporting them were not formally documented in the establishment's internal reporting systems.	**Minor**

Advice

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

No.	Standard	Advice
1.	General	The DI is advised to update the form which documents the release of tissue for use in research under the Human Tissue Act 2004 to ensure it references the current code of practice for research (Code E).
2.	General	The establishment is licensed for the procurement of corneas but is not currently performing this activity. The DI is advised to notify the HTA prior to this activity recommencing to ensure records of establishment activities reflect planned work.
3.	GQ1b	The DI is advised to consider updating the SOP that describes environmental monitoring procedures within the clean room facility (OCTB/QS/SOP/G21), to remove the greater than (>) symbol on limits assigned to the grade B and C areas. This would avoid ambiguity and directly reflect the guidance on the grading of such areas.
4.	GQ2b	A comprehensive schedule for audits is in place. However, a number of audits planned in 2018 and early 2019 have not yet been completed. The DI is advised to ensure that audits are performed in accordance with the schedule. Where necessary information is not available due to, for example, a reliance on external parties, this should be captured as an audit finding and associated actions documented within the CAPA plan.
5.	GQ3k	At present one member of staff performs environmental monitoring activities for the establishment, with a second member of staff in training. Given the increasing activity levels at the establishment the DI is advised to consider expanding this training to further staff members to ensure sufficient cover at busy times and in the event of staff sickness or annual leave.
6.	GQ4b	Environmental monitoring results are captured as handwritten entries on pre-prepared forms by the operator. These are then transferred to patient records through an intermediate spreadsheet. The DI is advised to include a second check of the transfer of such data, or include this process in routine audits, to help ensure that transcription errors do not occur during the process.
7.	GQ4h	Stored reproductive tissue is not assigned an expiry date due to the relative youth of the donors and developing knowledge in this treatment area. The DI is advised to ensure procedures are in place to ensure that all raw data critical to the quality and safety of stored tissue is identified and kept for 10 years after the use, expiry date or disposal of the tissue, in line with the regulatory requirement. For example, controlled temperature storage equipment is monitored by an external contract company. The terms of the agreement with this company stipulate that records will be retained for 30 years, which, due to the indefinite storage period, may result in the loss of raw data prior to the 10 year retention period being achieved.
8.	GQ5b	The DI is advised to inform the HTA of any occasion in which it is known or suspected that there will be insufficient sample available to conduct testing of donors (for example infant heart valve donors where the volume of blood for testing received is insufficient for the analysis) in accordance with the requirements of Directions 002/2018.

9.	PFE2b	The DI is advised to consider revising the SOP describing gowning procedures (OCTB/QS/SOP/G01) to include a requirement to remove make-up before entering the clean room suite, to support clean room microbial compliance and consistency with relevant guidance (EU GMP Annex I of Directive 2003/94/EC).
10.	PFE3a	The DI is advised to ensure that where disinfectant reagents have been assigned a temperature range by the manufacturer, they are stored in a suitably monitored environment. The DI is further advised to ensure that all disinfectant bottles are labelled with the required 'in-use' expiry date immediately after opening.
11.	PFE4f	The establishment contracts a courier to transport serology samples directly to the testing establishment. In the forthcoming renewal of the agreement with the courier company, the DI is advised to update it so that the establishment's requirement for direct transportation without deviation or avoidable delay is included.
12.	PFE4h	During revalidation of the transportation boxes the DI is advised to consider testing the boxes under extremes of hot and cold external temperatures in order to determine performance under 'worst-case' seasonal conditions in vehicles that are not temperature-controlled.
13.	PFE5c	The DI is advised to consider updating procedures to put in place controls to minimise the risk of pressure gauge readings being missed on days when aseptic processes are being undertaken. The DI is further advised to consider creating a template for the documentation of pressure gauge readings, to support timely and accurate completion of records.
14.	PFE5g	The establishment pre-prepares bags of disinfected consumables for use in specific aseptic processes. At the time of the inspection these bags were located on the floor in the corner of the preparation room. The DI is advised to consider the use of an alternative storage area or a robust outer container. This would support the integrity and cleanliness of the pre-prepared bag and simplify movement of packs for activities such as room cleaning.

Concluding comments

The OCTB has an effective system of governance. The establishment structure and management Board has been realigned as the focus of activities has shifted from heart to reproductive tissue, providing input from key medical, surgical, fertility and microbiology partners. There is a comprehensive programme of clean room monitoring and ongoing staff competency assessment. The establishment has taken steps to minimise the risk of error and contamination through, for example, the use of pre-prepared consumables packs specific to each processing activity. Training materials are detailed and available in a variety of formats to support staff training, particularly staff involved in procurement working at other establishments under the terms of a TPA. Tissue release procedures require review and approval of records from both the DI and Lead Consultant, or nominated deputies.

Although the HTA found that the establishment had met the majority of the HTA standards, one minor shortfall was identified. This related to particle monitoring of aseptic processes. In addition, the HTA has provided advice in relation to standards under the governance and quality and premises, facilities and equipment standards.

The HTA requires that the Designated Individual addresses the shortfall by submitting a completed corrective and preventative action (CAPA) plan within 14 days of receipt of the

final report (refer to Appendix 2 for recommended timeframes within which to complete actions). The HTA will then inform the establishment of the evidence required to demonstrate that the actions agreed in the plan have been completed.

The HTA has assessed the establishment as suitable to be licensed for the activities specified subject to corrective and preventative actions being implemented to meet the shortfall identified during the inspection.

Report sent to DI for factual accuracy: 14 March 2019

Report returned from DI: 28 March and 15 April 2019

Final report issued: 17 April 2019

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: 26 June 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 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.
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 002/2018.
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.

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 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.