Site visit inspection report on compliance with HTA minimum standards

Royal Brompton Hospital

HTA licensing number 11048

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**

17-18 January 2019

Summary of inspection findings

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

Although the HTA found that Royal Brompton Hospital (the establishment) had met the majority of the HTA standards, one major and six minor shortfalls were found in relation to Governance and Quality and Premises, Facilities and Equipment standards. The major shortfall was in relation to the establishment's procedures. The six minor shortfalls relate to the establishment's third party agreements, internal and independent audits, serious adverse event and reaction (SAEARs) reporting by third parties, and risk assessments.

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.

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

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

Tissue Category; Tissue Type	Procurement	Processing	Testing	Storage	Distribution	Import	Export
Cardiovascular, Valves; Heart Valves	**SLA/TPA**	**E**	**E/SLA/TPA**	**E**	**E**		**E**
Cardiovascular, Vessels; Conduits	**SLA/TPA**	**E**	**E/SLA/TPA**	**E**	**E**		**E**

Background to the establishment and description of inspection activities undertaken

Royal Brompton Hospital (RBH) (the establishment) has been licensed by the HTA since July 2006. The HTA licence covers the procurement, testing, processing, storage, distribution and export of human tissues and cells under the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended), and the storage of relevant material under the

Human Tissue Act 2004. The Heart Valve Bank (HVB) within the establishment dissects, processes and stores human heart valves (homografts) in the form of aortic and pulmonary valves and conduits. The HVB also stores hearts and valves for use in research.

The majority of donor hearts referred to Royal Brompton HVB are from deceased multi-organ donors. The allocation of homografts is facilitated by NHS Blood and Transplant (NHSBT) National Referral System (NRC), which holds the database for all cardiac homografts and ensures equitable distribution across England. Specialist Nurses for Organ Donation (SNODs) employed by NHSBT, refer potential donors to the NRC once consent and assessment have been completed. The establishment has a Service Level Agreement (SLA) with NHSBT, which sets out the relationship between the two establishments and the referral zone for homografts to be sent to the HVB, which includes: London, South East and Eastern regions. The SNODs also collect blood samples for the mandatory serology testing just prior to death.

In the past the HVB also received homografts from tissue only donors under the terms of third party agreements (TPAs) with other hospitals. The establishment is looking to re-commence this activity in the coming year (*see Advice item, 1*). Under these arrangements donor assessment, consent, retrieval of the homografts and blood samples will be performed by qualified members of the pathology department at the third party hospital premises.

Occasionally, homograft referrals are made from living donors, who undergo a heart transplant and donate their own explanted hearts for valves. Adult and paediatric donors are referred by Recipient Transplant Co-ordinators (RTCs) based at Harefield Hospital and another establishment, respectively. The blood samples for the mandatory serological testing are taken from the donor on the day of the surgery, prior to the commencement of immuno-suppression therapy.

Upon arrival the containers with the homografts and a blood sample are placed into a temperature-monitored fridge or onto a trolley, if the fridge is full, either by HVB staff during working hours, or trained porters out of hours. Prior to entering the dissection laboratory, staff at the HVB check the transport box is intact, packaging is compliant with the specifications given by the HVB and all the required documents for donation of the heart, are available. A “Tissue Receipt Check List” at the front of the Donor File is completed, to reflect how the homograft was received.

Following these checks the homografts are taken in a microbiological laminar flow safety cabinet within the dissection laboratory (background grade D). Once dissected, the heart valves and/or conduits are placed into a nutrient antibiotic solution and incubated for a minimum of 24 hours at 37°C. If the tissue is deemed unsuitable for clinical use, it will not be processed any further. For donor hearts with research consent the cardiac tissue and any dissected valves will be stored for research.

Staff from the Virology and Microbiology department at the Royal Brompton Hospital come to the dissection laboratory, at the HVB, to prepare the samples for microbiological testing. This takes place within a second laminar flow safety cabinet, where antibiotic solutions are prepared (*see Advice item, 5*). Following dissection of the homografts the blood samples for the mandatory serological testing are centrifuged. The serum and tissue samples from each processed donor heart are sent to the RBH Virology and Microbiology department within the hospital.

Donor testing for multi-organ deceased donors is carried out by NHSBT. Donor testing for paediatric living donors is carried out by the other establishment (*see Shortfall under, GQ1p*). On occasion, hearts received from multi-organ and paediatric living donors have not been screened for all the mandatory tests. Staff at the HVB complete a virology test request form, and serum is sent by the RBH Virology and Microbiology department to another HTA-licensed establishment for serology and nucleic acid testing (NAT), under an SLA. For adult living

donors the mandatory serological tests and NAT testing are mostly performed by the other HTA-licensed establishment, but on occasion serological tests are performed at the in-house testing lab (*see Shortfall under, GQ1b*).

Following incubation, the dissected heart valves and conduits are moved via a transfer hatch to the clean room (background grade C) and prepared for cryopreservation within a laminar flow positive pressure isolator. The establishment performs environmental monitoring throughout processing of the homografts in the form of contact plates, settle plates, finger dabs and non-viable particle counts.

Cryopreserved cardiac tissue is stored within three dedicated-use -140°C ultra-low temperature (ULT) freezers for quarantine, research and released cardiac tissue. The establishment also has a -80°C freezer to store returned cardiac tissue and antibiotics. The ULT and -80°C freezers are installed with a wireless temperature-monitoring system. Temperature excursions outside the set ranges trigger the wireless temperature monitoring system. The freezers are connected to an auto-dialer which is activated to the switchboard. If the operator does not acknowledge the alarm, the auto-dialer will proceed to dial up to three other numbers until an acknowledgement is received.

Freshly frozen valves and conduits are placed in the quarantine ULT freezer. Once the serology and microbiology tests are confirmed to be negative, the documentation is completed and environmental monitoring data is checked, the Donor File is countersigned by the Designated Individual (DI) and the HVB Manager. All grafts deemed suitable for clinical use are transferred to the release ULT freezer. Grafts deemed unsuitable for clinical use or research are disposed of according to the Trust's disposal policy.

Cryopreserved heart valves and conduits are distributed to the end user within an insulated "Human Tissue" box that contains dry ice. Unused cardiac tissue can be returned to the HVB within 48 hours, provided the transport container has not been tampered with (*see Advice item, 8*).

This report describes the establishment's sixth routine inspection, which took place on 17-18 January 2019. Discussions were held with the DI who is also Head of Surgical Research and Education and a former Cardiothoracic Surgeon, the HVB Manager and HTA Person Designate (PD), the HVB Quality Lead, the Tissue Governance Manager and key members of the RBH Virology and Microbiology department. A review of documentation relevant to the establishment's licensable activities and a visual inspection of the premises, where tissue processing and storage takes place, were also included as part of the inspection.

Audits of traceability were carried out and included the storage locations of five heart valves and one conduit in the quarantine, release, research ULT freezers and -80°C freezer, which were cross-checked against the current stock sheet. No discrepancies were identified. A total of five sets of donor records were reviewed to ensure they contained all relevant documentation. Records of consent forms, serology and microbiology results, processing, sterility testing (transport medium and cryomedium), consumables used during processing, cryopreservation, environmental monitoring and sign-off by the DI and HVB manager, were reviewed where relevant. A number of discrepancies were identified (*see Advice item, 4*).

Inspection findings

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

It was identified during this inspection that although Royal Brompton HVB receives cardiac tissue from living adult donors from Harefield Hospital, there are currently no appropriate licensing arrangements in place covering this activity. This issue will be addressed as part of

the follow-up to this inspection to ensure that activities are appropriately licensed under the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended).

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.		
b) There are procedures for all licensable activities that ensure integrity of tissue and / or cells and minimise the risk of contamination.	Although Royal Brompton Hospital has a number of standard operating procedures (SOPs) detailing the mandatory serology testing of heart valve donors, these do not always reflect the current working practices and are not sufficiently clear. For example: • The SOP for processing of donor samples states that all samples for serology and NAT testing are sent by the in-house testing lab to the other HTA-licensed establishment for testing. The establishment's practice for adult living donors is for the serology tests to be carried out at Royal Brompton virology testing laboratory and/or the other HTA-licensed establishment; for paediatric donors the serology samples may be tested at the establishment undertaking the procurement of the cardiac tissue and/or be sent to the other HTA-licensed establishment. • The SOP detailing the procedure for the receipt and processing of microbiology test results states that for living donor explanted hearts the transplant centres should carry out some or all serology tests. The SOP makes no reference to some or all the serology tests being carried out by the other HTA-licensed establishment. • Although the SOP detailing the management of donated hearts makes reference to blood samples from living donors being sent for serology testing to Royal Brompton virology testing laboratory, it makes no reference to the fact that some or all serology tests and all the NAT tests can be carried out at the other HTA-licensed establishment. *(see Advice item, 1)*	**Major**

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.	Royal Brompton Hospital has a third party agreement with another establishment for the procurement of cardiac tissue from living paediatric donors. This does not include donor testing for the mandatory serological markers carried out by the other establishment.	**Minor**
s) Third party agreements specify that the third party will inform the establishment in the event of a serious adverse reaction or event.	The establishment's agreement with the courier needs to be amended to include the requirement for third parties to report SAEARs to the establishment within 24 hours of discovery.	**Minor**
GQ2 There is a documented system of quality management and audit.		
b) There is an internal audit system for all licensable activities.	The internal audits do not cover the full range of activities carried out by the establishment. *(see Advice item, 4)*	**Minor**
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.	The establishment has not conducted an independent audit to verify compliance with all applicable HTA standards since the last site visit. *(see Advice item, 4)*	**Minor**
GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately.		
a) There are documented risk assessments for all practices and processes.	Although the establishment has documented risk assessments, these do not capture all the risks associated with the activities being carried out under the licence. *(see Advice item, 6)*	**Minor**

Premises, Facilities and Equipment

Standard	Inspection findings	Level of shortfall
PFE1 The premises are fit for purpose.		
a) A risk assessment has been carried out of the premises to ensure that they are fit for purpose.	The establishment has not carried out a risk assessment to ensure the premises are fit for purpose. *Prior to the final report being issued the DI provided the HTA with a premises risk assessment.*	**Minor** *The HTA has assessed this information as satisfactory and considers this standard to be met.*

Advice

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

No.	Standard	Advice
1.	GQ1 (b),	In addressing the shortfall above against GQ1 (b), the DI is advised to review the establishment's procedures on testing to provide clarity when donor testing is carried out at the other licensed establishment, and/ or at RBH Virology and Microbiology laboratory. The DI is also advised to update the procedures on donor testing to include the testing arrangements of homografts received from tissue only donors, before this activity resumes. The DI is advised to review the standard operating procedures (SOPs) on the transport of cardiac tissue to ensure they reflect current practices and references. For example, SOP004 states that there is a courier company used as well as the Royal Brompton and Harefield NHS Trust shuttle bus. Also, SOP0048 on tissue return states that during working hours every effort should be made to use the Trust shuttle bus. Currently, the shuttle bus is not operating and the establishment uses the courier for the transport of homografts to and from RBH.
2.	GQ1 (c)	The DI is advised to expand the list of participants at existing HTA–related governance meetings to include representatives from the RBH Virology and Microbiology department.

		The DI is also advised to cascade the meeting minutes to all staff working under the licence, to ensure continuing improvement of processes and practices.
3.	GQ1 (d)	During the review of the establishment's risk assessments it was noted that several of these were neither dated nor signed. The DI is advised to review and update all documents to ensure they are dated and signed.
4.	GQ2 (b), (c), GQ5 (b)	The DI is advised to expand the scope of the internal audits to include mandatory serology testing performed under the licence to ensure it is carried out in accordance with the requirements of Directions 002/2018. The DI is also advised to schedule the independent audit to occur in the intervening year between HTA inspections.
5.	GQ3 (c)	The DI is advised to document any refresher training and ongoing competency assessment for all members of staff from RBH Virology and Microbiology department that come into the dissection laboratory to prepare the samples for the microbiological testing.
6.	GQ8 (a)	The DI is advised to expand the scope of the risk assessments to include testing of mandatory serology markers performed under the licence. Once transport with the shuttle bus commences again, the DI is advised to risk assess the transport of cardiac tissue from Harefield Hospital to better reflect that the shuttle bus driver brings in the container with the homograft and blood samples to the reception at the RBH. The DI is also advised to consider the time needed to validate critical reagents, such as the in-house antibiotic solution and the impact this may have on release of homografts and delivery of services.
7.	PFE4 (h)	The establishment recently updated the inside material of the insulated boxes used to transport cardiac tissues. Prior to this the establishment last validated the transport boxes in 2014. The DI is advised to revalidate the transport boxes and consider worst case temperature and transit times to ensure they continue to achieve the intended results.

Concluding comments

The HTA observed a number of good practices during the course of the inspection.

The establishment uses a red and green "traffic light" colour system to label the Donor Files, where red stickers are used for cardiac tissues in quarantine and green stickers for all the cardiac tissues suitable for release. For living donors the establishment uses amber-coloured stickers. The establishment also uses a label for cardiac tissues that have been implanted and has a sticker affixed on cardiac tissues returned from an end user. The latter alerts staff when the tissue was removed from the ULT freezer, when it was placed in the -80°C freezer and the new reduced expiry date. The labeling system used by the establishment minimises the risk of cardiac tissue being issued incorrectly or being used past its expiry date.

The team constantly strives to improve their practices as exemplified by the prompt action to address advice given during the inspection related to scanning of the paper copies of the environmental monitoring data from the particle monitor to ensure appropriate archiving of these records.

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

The HTA requires that the Designated Individual addresses the shortfalls by submitting a completed corrective and preventative action (CAPA) plan within 14 days of receipt of the final report (refer to Appendix 2 for recommended timeframes within which to complete actions). The HTA will then inform the establishment of the evidence required to demonstrate that the actions agreed in the plan have been completed.

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

Report sent to DI for factual accuracy: 2019/02/13

Report returned from DI: 2019/03/21

Final report issued: 2019/04/17

Completion of corrective and preventative actions (CAPA) plan

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

Date: 2019/06/03

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.
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.
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.
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 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.