Site visit inspection report on compliance with HTA minimum standards

King's College Hospital

HTA licensing number 11062

Licensed for the

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

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

04-06 June 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 King's College Hospital (the establishment) had met the majority of the HTA standards, five minor shortfalls were identified. These related to the scope and content of establishment procedures, the completeness of processing records and alignment with documented procedures, the content of agreements, validation of microbial testing and environmental monitoring procedures, systems for the back-up of computerised records, and the impact assessment undertaken as part of the investigation into a temperature excursion that occurred in a reagent and consumables storage area.

In addition to this, since the last inspection, the establishment has undertaken the procurement and processing of autologous islets prior to the licence being updated to reflect the procurement activity, or authorisation of the relevant updated preparation process dossier (PPD). The HTA considers this a breach of the standard condition of the establishment's licence, which requires it to seek approval from the HTA prior to it procuring a new type of tissue and/or cells, or making changes to authorised processing procedures. The HTA will consider the need for regulatory action in relation to this matter separately to the inspection findings reported below.

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.

'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
Mature Cell, Pancreatic Islet Cells; Pancreatic islets		**E**			**E**		
Mature Cell, Hepatocyte; Hepatocytes		**E**		**E**			
Cardiovascular, Vessels; Vessels				**E**	**E**		
Other; Fascia lata	**E**		**TPA**				

Background to the establishment and description of inspection activities undertaken

This report refers to the activities carried out by the King's College Cell Isolation section within the Cellular Therapy Unit (CTU). Activities undertaken under the authority of the establishment's Human Tissue (Quality and Safety for Human Application) Regulations 2007 (Q&S Regulations) licence include the processing and storage of hepatocytes from allogeneic liver donors, processing and distribution of islets from allogeneic and autologous pancreas donors, the storage, testing and distribution of vessels from liver donors, and the procurement and testing of fascia tissue from organ donors.

The establishment is also licensed for the storage of relevant material for use for a scheduled purpose under the Human Tissue Act 2004 (HT Act), and release stored vessels and hepatocytes for research purposes if they are not suitable for clinical use. This inspection focused on activities falling under the Q&S Regulations.

The CTU consists of a shared clean room suite with associated storage and office areas, based at King's College Hospital (KCH). Areas within the suite are dedicated to specific activities, with separate areas for islet and hepatocyte processing activities undertaken by the Cell Isolation Section. Vessel and fascia activities taking place under this licence are also managed by a separate team, with vessels being stored in a fridge in theatre so that they are readily available if needed in organ transplant surgery.

Donor selection, consent and serological testing for donations from cadaveric donors of all three tissue types is undertaken by another establishment licensed under the Quality and Safety of Organs Intended or Transplantation Regulations (2012). Test results are uploaded onto NHS Blood and Transplant's Electronic Offering System (EOS), which establishment staff review prior to accepting organs for processing. Where vessels procured during liver retrievals are stored for future use in a recipient other than the recipient of the associated liver, the establishment undertakes additional serology testing in accordance with the Q&S Regulations, under the authority of its own licence.

Pancreatic Islets

Pancreata from deceased donors are distributed to the establishment as part of the National Pancreas Allocation Scheme, when the pancreas itself is not suitable for use in solid organ transplantation. The establishment is one of three HTA-licensed islet isolation centres in the UK, and shares an on-call rota arrangement for the processing of allogenic islets with one of these. Upon a pancreas becoming available and receipt of a corresponding request from a clinician to undertake islet purification, establishment staff review the EOS record to initially determine if the pancreas can be accepted for processing. Upon receipt of the organ into the establishment, it undergoes an examination by a senior operator to ensure it meets the establishment's criteria before processing activities begin.

The processing pathway involves sequential dissection, digestion and cell purification steps to isolate islet cells from the surrounding tissues and cells. Each step is undertaken in a separate, dedicated microbiological safety cabinet, which is maintained and monitored to ensure the required grade A environment is achieved within the surrounding grade B clean room. Processing is undertaken by a senior operator with support from other operators. Operators complete finger dabs and then change gloves when moving between cabinets, and samples are taken throughout the process for microbiological testing. The purified islets are maintained in media for between 24 and 48 hours before being released to the clinician who requested the islet isolation. Only processed cells that have met the required viable islet numbers, and where the pre-release Gram stain is negative, are released for end use. Final

packaging of the cells takes place in an isolator within the clean room suite. Results from microbiology testing are reviewed and reported retrospectively, as they become available.

The establishment has been selected to participate in a funded autologous islet transplantation programme, which is intended to support eligible patients in retaining some insulin-production function after undergoing a complete pancreatectomy procedure. Potential patients suitable for this procedure are identified by clinicians. Should the patient be selected and undergo the procedure, the explanted pancreas is examined by establishment staff. This examination is to determine whether the size and condition of the organ is likely to support successful islet recovery. Depending on the volume of cell digest recovered in early processing stages, the final purification step may be eliminated in order to maximise the numbers of viable islet cells recovered. Cells are returned to the patient during the same surgical procedure as the pancreatectomy or shortly afterwards through means of a catheter. Records from three procedures undertaken for KCH patients and one undertaken for a patient located at a different hospital were examined during the inspection, in addition to a detailed examination of two processing records for allogeneic islet purification.

Hepatocytes

The establishment operates the only clinical hepatocyte isolation programme in the UK. Livers that are unsuitable for whole or split organ transplantation are received from centres around the UK under an agreement with the Liver Transplant Unit based at KCH. Livers received directly from the KCH Liver Transplant Unit are also allocated by the National Liver Allocation Scheme.

Establishment staff are on-call 24-hours a day to receive livers for processing. When notified of a suitable donor liver, staff first review the EOS record before accepting the organ. Upon receipt, the organ is examined by a senior operator against a set of acceptance criteria before processing begins. Perfusion, digestion and purification are undertaken in separate, dedicated microbiological safety cabinets, which are monitored to ensure a grade A processing environment is achieved within the surrounding dedicated grade B clean room. Processing activities are undertaken by a senior operator with support from other operators. Operators complete finger dabs and then change gloves when moving between cabinets, and samples are taken throughout the process for microbiological testing. Final product acceptance is based upon Gram stain results (supported by microbiological test results which are available later), and the presence and percentage of viable hepatocytes in the purified suspension. Cells not required for immediate transplantation are preserved in cryoprotectant and frozen using a controlled-rate freezing process before being transferred to liquid nitrogen storage tanks. Storage tanks are located in a secure room and the establishment transfers cells to and from the room using a dry shipper. There is a quarantine tank for the storage of cells with pending serological infectious disease marker results. Stored cells are returned to an isolator in the clean room suite for final processing prior to release, and may also be used as a starting material for a Medicines and Healthcare products Regulatory Agency (MHRA) licensed “specials” product.

The Islet and Hepatocyte processing teams operate closely but independently of one another within the shared CTU facility. Each team undertakes audits and meetings related to their activities, and these sit within an overarching CTU quality management system encompassing control of shared areas, routine environmental monitoring, equipment maintenance and monitoring, and higher level governance meetings.

Critical facility systems, including room pressures, storage temperatures, particle monitoring readings and CO_2 concentrations, are monitored continuously using a centralised system. The system is pre-set with alert and action limits, and a system is in place to ensure staff are alerted to excursions as soon as they occur, including those that may occur outside of

standard working hours. Staff are also able to review room status using information panels within the processing rooms before starting processing activities.

Liver Vessels and Fascia

Liver vessels (and occasionally rectus muscle fascia) are procured from deceased solid organ donors. The vessels are received into the theatres packaged with the donor liver in a validated transport container. Each vessel is individually packaged in a suitably labelled sterile pot. If vessels are not used in the transplant operation for which the liver was received, they are booked in to storage by authorised staff and may be stored for up to five days in a centrally-monitored and alarmed fridge in the KCH theatres. Temperature measurements are taken daily by theatre staff. When vessels are stored for future use, a serology sample that is received with the vessels is sent for testing in accordance with the Q&S Regulations. If the vessel is not used within five days it is destroyed by incineration or, if suitable consent is in place, sent to another establishment for use in research. Occasionally the establishment may distribute vessels to other establishments. Procedures are in place to undertake and document this activity, and assign a unique Single European Code (SEC) to the vessels in accordance with regulatory requirements.

Since the last inspection, the establishment has procured rectus muscle fascia on a named-patient basis in order to support post-operative wound closure. The fascia is obtained from deceased solid organ donors by the KCH retrieval team, following the consent and donor selection systems used for solid organ donation. Additional consent is specifically sought for the procurement of the fascia tissue. Donor serological testing is undertaken by the establishment in accordance with the requirements of the Q&S Regulations, and the procured tissue is not stored.

Inspection activities

This was the establishment's fifth routine site inspection. The inspection team undertook a visual inspection of the clean room processing facility and associated reagent, consumables and hepatocyte cell storage areas. An in-depth review of islet and hepatocyte batch manufacturing records (BMRs) was conducted, and records relating to the storage, testing and distribution of vessels were examined. Round table discussions with key members of staff from the various teams involved in establishment activities were held, as well as round table discussions examining the wider governance and quality systems, which included a review of training files, agreements, risk assessments, meeting minutes, and deviation and non-conformance records.

Inspection findings

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

However, since the last inspection the establishment has undertaken the procurement and processing of autologous islets, prior to the licence being updated to reflect the procurement activity, or authorisation of the relevant updated preparation process dossier (PPD). The HTA considers this a breach of the standard condition of the establishment's licence, which requires it to seek approval from the HTA prior to it procuring a new type of tissue and/or cells, or making changes to authorised processing procedures. The HTA will consider the need for regulatory action in relation to this matter separately to the inspection findings reported below.

Compliance with HTA standards

Human Tissue (Quality and Safety for Human Application) Regulations 2007 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.	During the inspection several examples were identified where documented procedures did not reflect the establishment's practices. These included, but were not limited to: • the standard operating procedure (SOP) for vessel storage states that vessels are stored at 2-6°C. The actual storage temperature range is 4-8°C; • the SOP describing the release of hepatocytes for human application describes an eight hour expiry period, when the actual expiry period is 24 hours; and • step 7.9 of the BMR for islet processing captures the undertaking of steps in the processing pathway which are not described in the corresponding SOP. Examples were also identified where SOPs and BMRs did not contain sufficient detail to ensure required processes were consistently followed. These included, but were not limited to: • the SOP for microbiological sampling in islet processing does not provide guidance to staff on the procedures to be followed in the event of a positive result; • the SOP describing the sign-off of islet processing records by the main operator and quality manager does not include instructions on what should be checked in the batch manufacturing record and associated paperwork; • the BMR for islet processing does not capture all the final preparation steps undertaken prior to the release of cells for distribution, and therefore confirmation that the steps have been performed in accordance with the SOP	**Minor**

	is not recorded; • the combined procedure/BMR for hepatocyte processing does not describe or capture the steps taken when transferring purified cells from the controlled-rate freezer into storage in liquid nitrogen; and • the SOP describing the packaging of islets for distribution requires staff to include one to four cool packs, but does not provide any guidance on how to decide the correct number to use during any given distribution event.	
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. r) Third party agreements specify the responsibilities of the third party and meet the requirements set out in Directions 002/2018.	The agreement between KCH and the establishment which supplies organs and vessels, undertakes some courier activities and will provide a contingency for the storage of records in the event of the termination of activities at the establishment, remains in draft. Since the last inspection, KCH has processed autologous islets on behalf of another establishment. An appropriate agreement, setting out the roles and responsibilities of each party, was not in place for this work. The agreement with the third party testing laboratory does not cover the serological testing undertaken by the laboratory, nor does it contain sufficient information to meet the requirements for third party agreements as set out in Directions 002/2018.	**Minor**
GQ2 There is a documented system of quality management and audit.		
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.	The establishment undertakes microbial testing of samples taken at several points in the islet and hepatocyte processing pathways. Where samples are taken immediately after antibiotic treatment steps, the establishment has not undertaken validation studies to determine whether any residual antibiotics that might be present in the sample have been removed or neutralised, and therefore do not affect the reliability of the test results. Establishment procedures allow for environmental monitoring agar plates to be incubated for various lengths of time to enable them to be analysed on normal working days. The establishment identified the need to validate this activity in 2016, but	**Minor**

	this has not yet been undertaken.	
GQ4 There is a systematic and planned approach to the management of records.		
d) There is a system for back-up / recovery in the event of loss of computerised records.	The establishment has a central computerised system for monitoring and storing critical data such as room and equipment temperatures, particle monitoring data, room pressures, and carbon dioxide (CO_2) levels in incubators. Records captured since the system was installed are stored on a stand-alone personal computer (PC). The PC is supported by an uninterrupted power supply, however there are no systems or procedures in place to safeguard the stored data through regular back-up to a separate storage location.	**Minor**

Premises, Facilities and Equipment

Standard	Inspection findings	Level of shortfall
PFE3 There are appropriate facilities for the storage of bodies, body parts, tissues, 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.	In 2018, an area used to store reagents and consumables experienced a temperature excursion above the defined upper limit for the room. Although this deviation was documented, the investigation did not consider the potential impact on the stored consumables and reagents. In addition, the defined upper and lower temperature limits for the room are not aligned with the manufacturer's recommended storage temperatures for all the reagents stored in the room.	**Minor**

Advice

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

No.	Standard	Advice
1.	GQ1b	The DI is advised to document the maximum number of people permitted in the various clean room areas at any one time, to help ensure that limits identified during the qualification of the facility are adhered to.

2.	GQ4a	To reduce the risk of introducing contaminants into the grade A environment, completion of the BMR during islet processing is undertaken by supporting technicians working with the senior member of staff. The DI is advised to introduce a sign-off point at the end of each processing stage in the BMR capturing the name of the person who undertook the processing activity and their signed confirmation that they carried out the preceding steps in accordance with the BMR and SOP. The DI is further advised to review the islet and hepatocyte BMRs to ensure all required information is being captured. For example, provide separate lines for recording aerobic and anaerobic sampling bottle lot information in the islet BMR, a line to prompt operators to record the end of the first part of the processing pathway in the hepatocyte BMR, acceptable centrifuge operating ranges and the start time for controlled-rate freezing in the hepatocyte BMR. Although the establishment routinely audits records, the inspection identified a number of instances where forms had not been completed as required. These included records of cleaning undertaken at the end of processing, and return to use forms following repair or routine maintenance of establishment equipment. The DI is advised to review procedures for the auditing of records, including those related to vessel activities, to ensure that they are sufficiently robust to identify such instances in a timely manner, and take appropriate actions to assess and manage the impact of any errors that may be detected.
3.	GQ7a	The DI is advised to ensure that there are robust systems in place so that all staff involved in vessel activities are aware of how to escalate potential SAEARs events. This will help to ensure that potential SAEARs are reported to the HTA within 24 hours, in line with the regulatory requirement.
4.	PFE5a	The DI is advised to consider implementing a system for updating the time settings of stand-alone equipment in line with Greenwich Mean Time (GMT) and British Summer Time (BST), to ensure that times recorded on equipment print-outs align with times recorded within the accompanying BMR.
5.	PFE5c	During the inspection it was noted that a freezer that had been identified as being faulty had been taken out of use in the quality management system but had not been suitably labelled and removed from use in the laboratory. The freezer did not contain any critical reagents or samples. The DI is advised to update procedures to ensure that when faulty equipment is identified it is clearly marked, removed from use, and that staff are made aware.

Assessment of existing conditions/shortfalls against standards

At the time of the inspection two shortfalls from the previous inspection remained open. These related to contingency arrangements for the storage of hepatocytes, and the serology testing of stored vessels in accordance with the Q&S Regulations. During the inspection the HTA reviewed the steps taken by the establishment, and considers that both shortfalls have now been addressed.

Concluding comments

The HTA found the Designated Individual and the Licence Holder to be suitable in accordance with the requirements of the legislation. There are a number of areas of practice that require improvement, including five minor shortfalls. These related to the scope and content of establishment procedures, the completeness of processing records and alignment

with documented procedures, the content of agreements, validation of microbial testing and environmental monitoring procedures, systems for the back-up of computerised records, and the impact assessment undertaken as part of the investigation into a temperature excursion that occurred in a reagent and consumables storage area.

The HTA has given advice to the Designated Individual with respect to documenting the number of operators permitted to work in a clean room area at any one time, updating records to improve clarity, expanding the content of risk assessments, undertaking a review of reagent and consumables storage requirements against the action and alert temperature limits assigned to those areas, ensuring the clocks for stand-alone equipment are updated to reflect GMT and BST, and ensuring systems are in place to clearly identify faulty equipment and remove it from use.

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: 04 July 2019

Report returned from DI: 11 July 2019

Final report issued: 05 August 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: 23 December 2021

Appendix 1: HTA standards

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

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

Consent

Standard
C1 Consent is obtained in accordance with the requirements of the HT Act 2004, the Human Tissue (Quality and Safety for Human Application) Regulations 2007 and as set out in the HTA's Codes of Practice.
a) If the establishment acts as a procurer of tissues and / or cells, there is an established process for acquiring donor consent which meets the requirements of the HT Act 2004 the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (Q&S Regulations) and the HTA's Codes of Practice
b) If there is a third party procuring tissues and / or cells on behalf of the establishment the third party agreement ensures that consent is obtained in accordance with the requirements of the HT Act 2004, the Q&S Regulations and the HTA's Codes of Practice.
c) The establishment or the third party's procedure on obtaining donor consent includes how potential donors are identified and who is able to take consent.
d) Consent forms comply with the HTA Codes of Practice.
e) Completed consent forms are included in records and are made accessible to those using or releasing tissue and / or cells for a Scheduled Purpose.
C2 Information about the consent process is provided and in a variety of formats.
a) The procedure on obtaining consent details what information will be provided to donors. As a minimum, the information specified by Directions 002/2018 is included.
b) If third parties act as procurers of tissues and / or cells, the third party agreement details what information will be provided to donors. As a minimum, the information specified by Directions Directions 002/2018 is included.
c) Information is available in suitable formats and there is access to independent interpreters when required.
d) There are procedures to ensure that information is provided to the donor or donor's family by trained personnel.
C3 Staff involved in seeking consent receive training and support in the implications and essential requirements of taking consent.
a) Staff involved in obtaining consent are provided with training on how to take informed consent in accordance with the requirements of the HT Act 2004 and Code of Practice on Consent.
b) Training records are kept demonstrating attendance at training on consent.

Governance and Quality

Standard
GQ1 All aspects of the establishment's work are supported by ratified documented policies and procedures as part of the overall governance process.
a) There is an organisational chart clearly defining the lines of accountability and reporting relationships.
b) There are procedures for all licensable activities that ensure integrity of tissue and / or cells and minimise the risk of contamination.
c) There are regular governance meetings, for example health and safety, risk management and clinical governance committees, which are recorded by agendas and minutes.
d) There is a document control system to ensure that changes to documents are reviewed, approved, dated and documented by an authorised person and only current documents are in use.
e) There are procedures for tissue and / or cell procurement, which ensure the safety of living donors.
g) There are procedures to ensure that an authorised person verifies that tissues and / or cells received by the establishment meet required specifications.
h) There are procedures for the management and quarantine of non-conforming consignments or those with incomplete test results, to ensure no risk of cross contamination.
i) There are procedures to ensure tissues and / or cells are not released from quarantine until verification has been completed and recorded.
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.