Site visit inspection report on compliance with HTA minimum standards

King's Cell Isolation Unit

HTA licensing number 11062

Licensed for the

- **processing, storage and distribution of human tissues and cells for human application under the Human Tissue (Quality and Safety for Human Application) Regulations 2007; and**
- **storage of relevant material which has come from a human body for use for a scheduled purpose**

23 March 2017

Summary of inspection findings

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

Although the HTA found that King's Cell Isolation Unit (the establishment) had met the majority of the HTA standards, four shortfalls were found in relation to Governance and Quality. These were related to the absence of procedures in the event of termination of activities, internal audits of records and forms, testing requirements for liver vessels and procedures for documenting mandatory tests results.

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

The HTA's regulatory requirements

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

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

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

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

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

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

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

Licensable activities carried out by the establishment

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

Tissue type	Procurement	Processing	Testing	Storage	Distribution	Import	Export
Pancreatic islets		**E**			**E**		
Hepatocytes		**E**		**E**	**E**		
Other vessels				**E**	**E**		

Background to the establishment and description of inspection activities undertaken

This report refers to the activities carried out by King's Cell Isolation Unit (the establishment) based at King's College Hospital. The establishment is licensed for processing, storage and distribution under the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (Q&S Regulations). The establishment is also licensed for storage of relevant material for use for a scheduled purpose under the Human Tissue (HT) Act 2004. Although licensed for this activity, the establishment does not currently store relevant material for a scheduled purpose under the HT Act.

The establishment is part of the Cell Therapy Unit (CTU) which is a dedicated cell therapy production facility that includes the Cell and Gene Therapy and the Mesenchymal Stromal Cell groups at the hospital. The establishment's core activity is the isolation of hepatocytes from donor livers and islet cells from donor pancreata for transplants. The establishment also

stores vessels for transplantation should they be needed for surgery where the the recipient's own vessels are inadequate.

Serological testing for cadaveric donors for all three tissue types are carried out by another HTA-licensed establishment and test results are uploaded onto the NHS Blood and Transplant Electronic Offering System (EOS) so they can be reviewed by the establishment prior to processing or transplantation.

Pancreatic Islets

Pancreata are distributed to the establishment as part of the National Pancreas Allocation Scheme, which allocates donated pancreata to patients listed nationally. Pancreata from deceased donors are received from centres around the UK, under the terms of an appropriate agreement. The establishment is one of three isolation centres in the UK and shares an on-call rota with another HTA-licensed establishment for the processing of pancreatic islets. The establishment may accept pancreata which are declined for whole organ transplant should they meet the criteria for processing, which include the extent of damage and cold ischaemic time. Once processed by the establishment, the isolated islet cells are distributed, within 48 hours, to islet transplantation centres around the UK for clinical use. Where islets are deemed unsuitable for transplantation or islet isolation they may be used for research if appropriate consent is in place. This may take place outside the common allocation scheme.

The establishment processes roughly 50 pancreata per year. The pancreata are received into the establishment by trained staff from the pancreas processing team. Donor details and serology test results of the pancreas are accessed by staff ousing the EOS system. The islet isolation procedures are performed in a dedicated Grade A/B clean room with separate flow cabinets for dissection, digestion and purification respectively. Samples are taken for assessment of microbiological contamination throughout the procedure. The final product is released by the pancreas processing team based on numbers of viable islet cells and negative Gram staining, which is backed up by microbiology cultures retrospectively post-infusion.

Hepatocytes

The establishment operates the only clinical hepatocyte isolation programme in the UK. The establishment receives whole livers from centres around the UK, under an agreement with the Liver Transplant Unit based at King's College Hospital. The establishment may receive whole livers from the Liver Transplant Unit directly, but the allocation is undertaken by National Liver Allocation Scheme. The establishment's liver processing team reviews donor details and serology results on EOS prior to processing.

The establishment processes approximately 20 livers per year. Only donor livers that are deemed unsuitable for whole, or split organ transplant are processed by the establishment to obtain hepatocytes. Staff are on-call 24 hours a day in case a suitable liver becomes available for processing. The livers are collected from theatres by trained staff. Hepatocytes are isolated in dedicated Grade A/B clean rooms with separate flow cabinets for perfusion, digestion and purification respectively. The final product is assessed by numbers of viable cells, negative Gram staining and is backed up with microbiology cultures. The final hepatocyte products are not distributed to other organisations. If not required for immediate transfusion, the hepatocytes are cryopreserved using control rate freezers and stored at -190°C.

All hepatocytes are stored in a locked liquid nitrogen tank on a separate floor within the CTU. Only staff from the liver processing team have access to the storage tank, which is located within a secured room. The tank is monitored by an electronic monitoring system that alerts staff on-call 24 hours a day by mobile if the temperature deviates outside the set range. The liver processing team has its own dedicated dry shipper for transport between the processing

rooms and the storage room. There is a quarantine stack within the liquid nitrogen tank for processed hepatocytes with pending serology results. Stock audits of hepatocyte batches are performed annually.

Liver Vessels

The establishment stores liver vessels procured during the organ retrieval process. The organ and the associated vessels are procured within the hospital by the Liver Transplant Team, or may be distributed to the establishment from other retrieval centres.

Vessels stored for more than 48 hours for use in a patient other than the primary recipient are subject to the Q&S Regulations. The establishment stores vessels for up to 5 days at 2-8°C pending use in a different recipient and occasionally distributes vessels to other organisations for transplant. Serology test results are transcribed from EOS data by theatre staff onto the Transplant Vessels and Tissue form, which is stored with the vessels. For vessels intended for distribution, the staff complete a Blood Vessel Transfer form using results from the Transplant Vessels and Tissue form. The Blood Vessel Transfer form accompanies the vessel to receiving transplant centres.

The vessels are received into the operating theatre packaged with donor livers in validated, sterile containers by authorised staff. The vessels are packed individually in sterile pots in preservation fluid and arrive labelled with a unique ID number, date of birth, blood group, date of retrieval and specimen name. Vessels remain unopened at all times during storage. Vessels stored for longer than 5 days are disposed of by theatre staff by incineration and are bagged separately from clinical waste. Distribution of liver vessels is arranged by the Transplant Coordinators employed by another HTA-licensed establishment, who will liase with the consultant surgeon on call to assess supply of vessels before distribution.

The vessels are stored in a locked refridgerator in the operating theatre, which is only accessible by authorised staff. There is daily temperature recording of the refrigerator temperature and temperature mapping is performed annually. Stock is reviewed daily.

Inspection Process

This was the fourth routine inspection of the establishment. The inspection included a visual inspection of the processing rooms for islets and hepatocytes, and the storage facility for hepatocytes; discussions with key members of staff including the Designated Invidual (DI) who is also the Director of the CTU, the Head of Production of Liver Processing, the Head of Production for Pancreas Processing, the Quality Manager for Liver Processing, the Quality Manager for Pancreas Processing and the Senior Sister for Liver Transplant; a review of three processing records for islets and three processing records for hepatocytes; and an audit trail looking at traceability of donor and recipient details for two batches of hepatocytes on the establishment's electronic database. Two sets of clinical notes for patients receiving islet infusions were also checked for consent and processing records. Discrepancies were found relating to the consistency of record keeping for processing records.

Inspection findings

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

Compliance with HTA standards

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

Governance and Quality

Standard	Inspection findings	Level of shortfall
GQ1 All aspects of the establishment's work are supported by ratified documented policies and procedures as part of the overall governance process.		
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.	There is no procedure or written agreement with another HTA-licensed establishment for transfer of stored hepatocytes in the event of termination of activities.	**Minor**
GQ4 There is a systematic and planned approach to the management of records.		
b) There is a system for the regular audit of records and their content to check for completeness, legibility and accuracy and to resolve any discrepancies found.	The establishment has a team of 30 theatre staff who are responsible for completing the forms used for the storage of vessels and for vessel distribution. During the inspection it was noted that the majority of the forms were filled in inconsistently. It was also noted that several islet processing records were incomplete. Out of the three records reviewed, a release form was not included in one processing record and the EOS form was not included in two.	**Minor**
GQ5 There are documented procedures for donor selection and exclusion, including donor criteria.		
b) The testing of donors by the establishment or a third party on behalf of the establishment is carried out in accordance with the requirements of Directions 003/2010.	Where vessels are being stored under the Q&S Regulations, blood samples for mandatory testing must have been obtained just prior to death or, if possible as soon as possible after death, and in any case within 24 hours of death. Such blood samples must be tested in a HTA-licensed testing laboratory. The establishment does not have procedures in place to ensure that donor mandatory serology testing for liver vessels intended for use under the Q&S Regulations meet these requirements.	**Minor**

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.	The donor exclusion criteria, as set out in the "Guide to Quality and Safety Assurance fror Human Tissue and Cells for Patient Treatment" which forms the Annex to Directions 003/2010, includes history, clinical evidence, or laboratory evidence of HTLV-1. The establishment does not transcribe results of HTLV-1 tests onto the Transplant and Vessel Form used with storage of vessels, or onto the Blood Vessel Transfer Form used for vessel distribution. As such, there is no documentation of the HTLV-1 status of the vessels stored and distributed for transplantation. This practice is also reflected in the establishment's policy for vessel storage and transplant (HTX-P-PR-031), which states the donor exclusion criteria encompassing HIV, HBV and HCV, but not HTLV-1.	**Minor**

Advice

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

No.	Standard	Advice
1.	C1b/2a	The DI is advised to review information provided to paediatric and adult donor families to ensure that the information provided for consent is sufficiently clear. In particular it should be clear as to the possibility of cells being isolated, from donated organs, to be used for treatment in the event that the organ cannot be used for a whole organ transplant.
2.	GQ1b	The establishment's practice for retaining vessels for a maximum of 5 days at 2-8°C is not reflected in the quality manual and policy for storage and transplant of vessels, which state storage of vessels for up to 14 days. The DI is advised to update these documents accordingly to ensure they are in line with current practices.
3.	GQ1r	The DI is advised to review the wording of agreements with third parties to ensure that they include reference to the correct legislation (e.g. the Human Tissue (Quality and Safety for Human Application) Regulations 2007). References to HTA Directions 001/2006 should also be replaced with HTA Directions 003/2010 which have superceded them.
4.	GQ3f	As part of the training programme, the DI is advised to ensure all staff working under the licence have good knowledge of the ethical value and regulatory context of working with human tissues and cells and have records of staff who have attending this training.
5.	GQ4b	When completing the Blood Vessel Transfer Forms the DI is advised to ensure staff refer to the original copy of EOS data when transcribing results onto the form.

6.	GQ4m	The DI is advised to ensure there are procedures in place to transfer tissue traceability records and raw data to the Trust archives, in the event of termination of activities.
7.	GQ7c	The DI is advised to appoint Persons Designated who are able to report serious adverse events and reactions (SAEARs) in the DI's absence and to notify the HTA of the appointments. The amended chain of personnel responsible for reporting SAEARs should be included in the staff training programme.
8.	GQ7g	The DI is advised to ensure the Blood Vessel Transfer form used for distribution of vessels to other transplantation centres includes the responsibility of the receiving centre to report serious adverse events or adverse reactions (SAEARs) to the DI.
9.	PFE4e	The DI should put in place procedures to periodically review the dry shipper's data logger information to ensure it continues to perform as expected.

Concluding comments

There were a number of good practices observed during the inspection. The establishment has in place robust procedures for the processing of islets and hepatocytes to safeguard the quality of the final product. This includes two-person checks when performing calculations, steps to test the reliability of air particle monitoring during processing and implementation of visible instructions for staff carrying out controlled rate freezing to ensure adherence to new protocols.

Four areas of practice were identified during the inspection that require improvement, each resulting in minor shortfalls. These relate to the absence of procedures in an event of a termination of activities, audits of forms and records, procedures to assure testing requirements under the Q&S Regulations are in place and are appropriately recorded on relevant documents. The HTA has given advice to the Designated Individual with respect to reviewing policies, protocols and agreements to ensure they are in line with practices, appointing PDs and ensuring end user forms include SAEARs reporting to the HTA.

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: 10 April 2017

Report returned from DI: 20 April 2017

Final report issued: 21 April 2017

Completion of corrective and preventative actions (CAPA) plan

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

Date: 14 February 2020

Appendix 1: HTA standards

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

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

Consent

Standard
C1 Consent is obtained in accordance with the requirements of the HT Act 2004, the Human Tissue (Quality and Safety for Human Application) Regulations 2007 and as set out in the HTA's Codes of Practice.
b) If there is a third party procuring tissues and / or cells on behalf of the establishment the third party agreement ensures that consent is obtained in accordance with the requirements of the HT Act 2004, the Q&S Regulations and the HTA's Codes of Practice.
c) The establishment or the third party's procedure on obtaining donor consent includes how potential donors are identified and who is able to take consent.
d) Consent forms comply with the HTA Codes of Practice.
e) Completed consent forms are included in records and are made accessible to those using or releasing tissue and / or cells for a Scheduled Purpose.
C2 Information about the consent process is provided and in a variety of formats.
a) The procedure on obtaining consent details what information will be provided to donors. As a minimum, the information specified by Directions 003/2010 is included.
b) If third parties act as procurers of tissues and / or cells, the third party agreement details what information will be provided to donors. As a minimum, the information specified by Directions 003/2010 is included.

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.
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 003/2010.
s) Third party agreements specify that the third party will inform the establishment in the event of a serious adverse reaction or event.
t) There are procedures for the re-provision of service in an emergency.

GQ2 There is a documented system of quality management and audit.
a) There is a quality management system which ensures continuous and systematic improvement.
b) There is an internal audit system for all licensable activities.
c) An audit is conducted in an independent manner at least every two years to verify compliance with protocols and HTA standards, and any findings and corrective actions are documented.
d) Processes affecting the quality and safety of tissues and / or cells are validated and undergo regular evaluation to ensure they continue to achieve the intended results.
GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills.
a) There are clearly documented job descriptions for all staff.
b) There are orientation and induction programmes for new staff.
c) There are continuous professional development (CPD) plans for staff and attendance at training is recorded.
d) There is annual documented mandatory training (e.g. health and safety and fire).
e) Personnel are trained in all tasks relevant to their work and their competence is recorded.
f) There is a documented training programme that ensures that staff have adequate knowledge of the scientific and ethical principles relevant to their work, and the regulatory context.
g) There is a documented training programme that ensures that staff understand the organisational structure and the quality systems used within the establishment.
h) There is a system of staff appraisal.
i) Where appropriate, staff are registered with a professional or statutory body.
j) There are training and reference manuals available.
k) The establishment is sufficiently staffed to carry out its activities.
GQ4 There is a systematic and planned approach to the management of records.
a) There are procedures for the creation, identification, maintenance, access, amendment, retention and destruction of records.
b) There is a system for the regular audit of records and their content to check for completeness, legibility and accuracy and to resolve any discrepancies found.
c) Written records are legible and indelible. Records kept in other formats such as computerised records are stored on a validated system.
d) There is a system for back-up / recovery in the event of loss of computerised records.
e) The establishment keeps a register of the types and quantities of tissues and / or cells that are procured, tested, preserved, processed, stored and distributed or otherwise disposed of, and on the origin and destination of tissues and cells intended for human application.

f) There are procedures to ensure that donor documentation, as specified by Directions 003/2010, is collected and maintained.
g) There is a system to ensure records are secure and that donor confidentiality is maintained in accordance with Directions 003/2010.
h) Raw data which are critical to the safety and quality of tissues and cells are kept for 10 years after the use, expiry date or disposal of tissues and / or cells.
i) The minimum data to ensure traceability from donor to recipient as required by Directions 003/2010 are kept for 30 years after the use, expiry or disposal of tissues and / or cells.
j) Records are kept of products and material coming into contact with the tissues and / or cells.
k) There are documented agreements with end users to ensure they record and store the data required by Directions 003/2010.
l) The establishment records the acceptance or rejection of tissue and / or cells that it receives and in the case of rejection why this rejection occurred.
m) In the event of termination of activities of the establishment a contingency plan to ensure records of traceability are maintained for 10 or 30 years as required.
GQ5 There are documented procedures for donor selection and exclusion, including donor criteria.
a) Donors are selected either by the establishment or the third party acting on its behalf in accordance with the criteria required by Directions 003/2010.
b) The testing of donors by the establishment or a third party on behalf of the establishment is carried out in accordance with the requirements of Directions 003/2010.
c) In cases other than autologous donors, donor selection is carried out by authorised personnel and signed and reviewed by a qualified health professional.
d) There is a system in place either at the establishment or at a third party acting on its behalf to record results of donor selection and associated tests.
GQ6 A coding and records system facilitates traceability of tissues and / or cells, ensuring a robust audit trail.
a) There is a donor identification system which assigns a unique code to each donation and to each of the products associated with it.
b) An audit trail is maintained, which includes details of when the tissues and / or cells were acquired and from where, the uses to which the tissues and / or cells were put, when the tissues and / or cells were transferred elsewhere and to whom.
c) The establishment has procedures to ensure that tissues and / or cells imported, procured, processed, stored, distributed and exported are traceable from donor to recipient and vice versa.
GQ7 There are systems to ensure that all adverse events, reactions and/or incidents are investigated promptly.
a) There are procedures for the identification, reporting, investigation and recording of adverse events and reactions, including documentation of any corrective or preventative actions.

b) There is a system to receive and distribute national and local information (e.g. HTA regulatory alerts) and notify the HTA and other establishments as necessary of serious adverse events or reactions.
c) The responsibilities of personnel investigating adverse events and reactions are clearly defined.
d) There are procedures to identify and decide the fate of tissues and / or cells affected by an adverse event, reaction or deviation from the required quality and safety standards.
e) In the event of a recall, there are personnel authorised within the establishment to assess the need for a recall and if appropriate initiate and coordinate a recall.
f) There is an effective, documented recall procedure which includes a description of responsibilities and actions to be taken in the event of a recall including notification of the HTA and pre-defined times in which actions must be taken.
g) Establishments distributing tissue and / or cells provide information to end users on how to report a serious adverse event or reaction and have agreements with them specifying that they will report these events or reactions.
h) Establishments distributing tissues and / or cells have systems to receive notifications of serious adverse events and reactions from end users and notify the HTA.
GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately.
a) There are documented risk assessments for all practices and processes.
b) Risk assessments are reviewed regularly, as a minimum annually or when any changes are made that may affect the quality and safety of tissues and cells.
c) Staff can access risk assessments and are made aware of local hazards at training.
d) A documented risk assessment is carried out to decide the fate of any tissue and / or cells stored prior to the introduction of a new donor selection criteria or a new processing step, which enhances the quality and safety of tissue and / or cells.

Premises, Facilities and Equipment

Standard
PFE1 The premises are fit for purpose.
a) A risk assessment has been carried out of the premises to ensure that they are fit for purpose.
b) There are procedures to review and maintain the safety of staff, visitors and patients.
c) The premises have sufficient space for procedures to be carried out safely and efficiently.
d) Where appropriate, there are procedures to ensure that the premises are of a standard that ensures the dignity of deceased persons.
e) There are procedures to ensure that the premises are secure and confidentiality is maintained.
f) There is access to a nominated, registered medical practitioner and / or a scientific advisor to provide advice and oversee the establishment's medical and scientific activities.

PFE2 Environmental controls are in place to avoid potential contamination.
a) Tissues and / or cells stored in quarantine are stored separately from tissue and / or cells that have been released from quarantine.
b) Where processing of tissues and / or cells involves exposure to the environment, it occurs in an appropriate, monitored environment as required by Directions 003/2010.
c) There are procedures for cleaning and decontamination.
d) Staff are provided with appropriate protective clothing and equipment that minimise the risk of contamination of tissue and / or cells and the risk of infection to themselves.
PFE3 There are appropriate facilities for the storage of tissues and / or cells, consumables and records.
a) Tissues, cells, consumables and records are stored in secure environments and precautions are taken to minimise risk of damage, theft or contamination.
b) There are systems to deal with emergencies on a 24 hour basis.
c) Tissues and / or cells are stored in controlled, monitored and recorded conditions that maintain tissue and / or cell integrity.
d) There is a documented, specified maximum storage period for tissues and / or cells.
PFE4 Systems are in place to protect the quality and integrity of tissues and / or cells during transport and delivery to its destination.
a) There is a system to ensure tissue and / or cells are not distributed until they meet the standards laid down by Directions 003/2010.
b) There are procedures for the transport of tissues and / or cells which reflect identified risks associated with transport.
c) There is a system to ensure that traceability of tissues and / or cells is maintained during transport.
d) Records are kept of transportation and delivery.
e) Tissues and / or cells are packaged and transported in a manner and under conditions that minimise the risk of contamination and ensure their safety and quality.
f) There are third party agreements with courier or transport companies to ensure that any specific transport conditions required are maintained.
g) Critical transport conditions required to maintain the properties of tissue and / or cells are defined and documented.
h) Packaging and containers used for transportation are validated to ensure they are fit for purpose.
i) Primary packaging containing tissues and / or cells is labelled with the information required by Directions.

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.

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
• Consent forms comply with the HTA's Code of Practice • Consent forms are in records and are made accessible to those using or releasing relevant material for a scheduled purpose • If the establishment obtains consent, a process is in place for acquiring consent in accordance with the requirements of the HT Act 2004 and the HTA's Codes of Practice • Where applicable, there are agreements with third parties to ensure that consent is obtained in accordance with the requirements of the HT Act 2004 and the HTA's Codes of Practice • Consent procedures have been ethically approved
C2 Information about the consent process is provided and in a variety of formats
• Standard operating procedures (SOPs) detail the procedure for providing information on consent • Agreements with third parties contain appropriate information • Independent interpreters are available when appropriate • Information is available in suitable formats, appropriate to the situation • Consent procedures have been ethically approved
C3 Staff involved in seeking consent receive training and support in the implications and essential requirements of taking consent
• Standard operating procedures (SOPs) detail the consent process • Evidence of suitable training of staff involved in seeking consent • Records demonstrate up-to-date staff training • Competency is assessed and maintained

Governance and quality system standards
GQ1 All aspects of the establishments work are supported by ratified documented policies and procedures as part of the overall governance process
• Policies and procedures are in place, covering all activities related to the storage of relevant material for research in connection with disorders, or the functioning, of the human body • Appropriate risk management systems are in place • Regular governance meetings are held; for example, health and safety and risk management committees, agendas and minutes • Complaints system

GQ2 There is a documented system of quality management and audit
• A document control system, covering all documented policies and standard operating procedures (SOPs). • Schedule of audits • Change control mechanisms for the implementation of new operational procedures
GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills
• Qualifications of staff and training are recorded, records showing attendance at training • Orientation and induction programmes • Documented training programme, (e.g. health and safety, fire, risk management, infection control), including developmental training • Training and reference manuals • Staff appraisal / review records and personal development plans are in place
GQ4 There is a systematic and planned approach to the management of records
• Documented procedures for the creation, amendment, retention and destruction of records • Regular audit of record content to check for completeness, legibility and accuracy • Back-up / recovery facility in the event of loss of records • Systems ensure data protection, confidentiality and public disclosure (whistle-blowing)
GQ5 There are documented procedures for distribution of body parts, tissues or cells
• A process is in place to review the release of relevant material to other organisations • An agreement is in place between the establishment and the organisation to whom relevant material is supplied regarding the tracking and use of material and eventual disposal or return
GQ6 A coding and records system facilitates traceability of bodies, body parts, tissues and cells, ensuring a robust audit trail
• There is an identification system which assigns a unique code to each donation and to each of the products associated with it • An audit trail is maintained, which includes details of when and where the relevant material was acquired, the consent obtained, the uses to which the material was put, when the material was transferred and to whom
GQ7 There are systems to ensure that all adverse events are investigated promptly
• Corrective and preventive actions are taken where necessary and improvements in practice are made • System to receive and distribute national and local information (e.g. HTA communications)

GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately
• Documented risk assessments for all practices and processes • Risk assessments are reviewed when appropriate • Staff can access risk assessments and are made aware of local hazards at training

Premises, facilities and equipment standards
PFE1 The premises are fit for purpose
• A risk assessment has been carried out of the premises to ensure that they are appropriate for the purpose • Policies in place to review and maintain the safety of staff, authorised visitors and students • The premises have sufficient space for procedures to be carried out safely and efficiently • Policies are in place to ensure that the premises are secure and confidentiality is maintained
PFE 2 Environmental controls are in place to avoid potential contamination
• Documented cleaning and decontamination procedures • Staff are provided with appropriate protective equipment and facilities that minimise risks from contamination • Appropriate health and safety controls are in place
PFE3 There are appropriate facilities for the storage of bodies, body parts, tissues and cells, consumables and records.
• Relevant material, consumables and records are stored in suitable secure environments and precautions are taken to minimise risk of damage, theft or contamination • Contingency plans are in place in case of failure in storage area • Critical storage conditions are monitored and recorded • System to deal with emergencies on 24 hour basis • Records indicating where the material is stored in the premises
PFE 4 Systems are in place to protect the quality and integrity of bodies, body parts, tissues and cells during transport and delivery to a destination
• Documented policies and procedures for the appropriate transport of relevant material, including a risk assessment of transportation • A system is in place to ensure that traceability of relevant material is maintained during transport • Records of transportation and delivery • Records are kept of any agreements with recipients of relevant material

- Records are kept of any agreements with courier or transport companies

PFE5 Equipment is appropriate for use, maintained, quality assured, validated and where appropriate monitored

- Records of calibration, validation and maintenance, including any agreements with maintenance companies
- Users have access to instructions for equipment and receive training in use and maintenance where appropriate
- Staff aware of how to report an equipment problem
- Contingency plan for equipment failure

Disposal Standards

D1 There is a clear and sensitive policy for disposing of human organs and tissue

- Documented disposal policy
- Policy is made available to the public
- Compliance with health and safety recommendations

D2 The reason for disposal and the methods used are carefully documented

- Standard operating procedures (SOPs) for tracking the disposal of relevant material detail the method and reason for disposal
- Where applicable, disposal arrangements reflect specified wishes

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.