Site visit inspection report on compliance with HTA minimum standards

Royal Victoria Infirmary

HTA licensing number 11122

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

24-26 November 2015

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.

The HTA found that Royal Victoria Infirmary ('the establishment') had met the majority of the HTA standards. Minor shortfalls were found regarding: documented procedures for the autologous pancreatic islet transplantation programme; documented procedures for receipt, storage and distribution of cardiac valves, iliac vessels and bone; serology testing arrangements for donors of pancreatic islets and iliac vessels; documented procedures for recall of distributed tissues; assessment of risks associated with pancreatic islet transplantation, and; continuous monitoring of non-viable airborne particulates during stem cell processing procedures.

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

The HTA's regulatory requirements

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

The statutory duties of the Designated Individual (DI) are set out in Section 18 of the Human Tissue Act 2004 ('the HT Act'). 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 licenses against four groups of standards:

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

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

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

Licensable activities carried out by the establishment

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

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

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

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

Tissue type	Procurement	Processing	Testing	Storage	Distribution
Bone	**-**	**-**	**-**	**E**	**E**
Peripheral blood stem cells (PBSCs)	**E**	**E**	**E**	**E**	**E**
Bone marrow (BM)	**E**	**E**	**E**	**E**	**E**

Donor lymphocyte infusions (DLIs)	**E**	**E**	**E**	**E**	**E**
Umbilical cord blood (UCB)	**E and SLA**	**E**	**E**	**E**	**E**
Human embryonic stem cells (hESCs)	**-**	**-**	**-**	**E**	**-**
Heart valves	**-**	**-**	**-**	**E**	**E**
Iliac vessels	**-**	**-**	**-**	**E**	**E**
Amniotic membrane	**-**	**E**	**-**	**E**	**-**
Limbal stem cells	**E**	**E**	**E**	**-**	**-**
Pancreatic islets	**E**	**E**	**E**	**-**	**-**

Background to the establishment and description of inspection activities undertaken

Royal Victoria Infirmary ('the establishment') is licensed under the Human Tissue (Quality and Safety for Human Application) Regulations 2007 ('the Quality and Safety Regulations 2007') for the procurement, processing, storage, donor serology testing and distribution of tissues and cells for human application. The establishment is also licensed under the HT Act for the storage of relevant material for use for scheduled purposes. Licensable activities take place at Royal Victoria Infirmary ('the hub') and two satellite sites (the Freeman Hospital and the Newcastle Bio-Manufacturing Facility).

- Activities at Royal Victoria Infirmary are: the procurement of PBSCs from paediatric donors by apheresis; BM procurement from adult and paediatric donors; directed UCB procurements, and; processing, cryopreservation and storage of UCB, PBSCs, BM and DLIs. Storage of stem cells is in the vapour phase of liquid nitrogen.
- Activities at Freeman Hospital are: the storage of bone, iliac vessels and cardiac valves; donor serology testing; procurement of PBSCs and DLIs from adult donors by apheresis for autologous and allogeneic use; and; procurement of pancreata for autologous pancreatic islet transplantation. Bone is purchased from National Health Service Blood and Transplant (NHSBT), cardiac valves are received from HTA-licensed tissue banks, and iliac vessels are received with cadaveric donor livers accepted for transplantation. The iliac vessels may be used in the recipient of the associated liver or for another recipient, or could be distributed to another centre. Bone is also distributed to the hub or to other hospitals according to surgical need. Procurement of autologous cells for clinical trials, leading to advanced therapy investigational medicinal products (ATIMPs), also takes place at this site. ATIMP manufacture is under a Medicines and Healthcare products Regulatory Agency (MHRA) licence. Cells procured for ATIMP manufacture include: autologous limbal stem cells; peripheral blood mononuclear cells, and; dendritic tumours.
- Activities at Newcastle Bio-Manufacturing Facility are: the processing of autologous pancreatic islets, and: storage of hESCs in the vapour phase of liquid nitrogen (refer to

Advice, item 9). Islet processing takes place within a dedicated cleanroom at this site.

Following authorisation of a Preparation Processing Dossier in 2013, the establishment began an autologous pancreatic islet transplantation programme. Donors are patients suffering from chronic pancreatitis or who had received a traumatic injury to their pancreas. Donor consent is sought by the consultant surgeon who performs the pancreatectomy. A blood sample for serological testing is taken several days before the pancreatectomy. Pancreata are resected at Freeman Hospital and transported by the surgeon to the Newcastle Bio-Manufacturing Facility for islet isolation. Processed islets are returned by the surgeon to Freeman Hospital for re-infusion. This transplantation programme is performed by a highly experienced team of core staff and is currently on hold pending a decision on further funding. Review of processes and documentation for this programme at the inspection identified some shortfalls which will need to be addressed should this transplantation programme resume in the future.

The establishment has performed a small number of autologous limbal stem cell transplantation procedures in recent years. A biopsy of corneoscleral disc is cultured between amniotic membranes that were purchased from NHSBT to generate an ATIMP whose manufacture takes place under the establishment's MHRA licence. This transplantation programme ended in 2015.

The establishment has been licensed by the HTA since April 2006. Four previous site visit inspections have taken place (May 2008, April 2010, November 2011 and November 2013). This report describes the fifth, routine, site visit inspection of the establishment in November 2015. During the inspection, the inspectors met with staff involved with licensable activities, visually inspected areas where licensable activities are carried out and reviewed documentation. Traceability records were audited for:

- two autologous limbal stem cell transplants;
- two cardiac valves used for surgery and one cardiac valve in storage;
- one autologous pancreatic islet transplant;
- three adult stem cell transplants;
- one iliac vessel in storage;
- three paediatric stem cell transplants;
- four femoral heads in storage.

One anomaly was found. A donor had not written their initials in two boxes on an adult stem cell consent form. No other anomalies were identified in other traceability audits.

Newcastle upon Tyne Hospitals NHS Foundation Trust holds other HTA licences under the HT Act and the Human Tissue (Quality and Safety of Organs Intended for Transplantation) Regulations 2012 (licensing numbers 12341 and 40045 respectively). Activities under these other licences were not reviewed at this inspection.

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.		
b) There are procedures for all licensable activities that ensure integrity of tissue and / or cells and minimise the risk of contamination. 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.	The processing of pancreata at Newcastle Bio-Manufacturing Facility and distribution of pancreatic islets to Freeman Hospital for re-infusion are set out in a comprehensive standard operating procedure (SOP). There is, however, no SOP describing: • donor selection and exclusion criteria; • seeking of donor consent for pancreatic islet processing and mandatory serology testing, including the use of consent forms and patient information leaflets; • how reagents and consumables that come into contact with the pancreas during the pancreatectomy are recorded; • how a pancreas is preserved following retrieval; • packaging of a pancreas for transportation to Newcastle Bio-Manufacturing Facility; • labelling of the transportation box; • what information about the pancreas will accompany the organ; • transportation of the pancreas from Freeman Hospital to Newcastle Bio-Manufacturing Facility. Should this transplantation programme resume in the future, documented procedures that, at a minimum, address these points will need to be in place.	**Minor**
b) There are procedures for all licensable activities that ensure integrity of tissue and / or cells and minimise the risk of contamination.	SOPs for receipt, storage and distribution of bone, cardiac valves and iliac vessels do not fully describe local procedures as were explained at the inspection. For example;	**Minor**

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.	• the 'Storage and recording of bone products' SOP does not describe the checks undertaken of the pot and paperwork upon receipt on bone from NHSBT, how units of bone are selected for use based on expiry date, or how bone is distributed to other centres. This SOP also states the temperature range of the storage freezer is -28 °C to -34 °C, whereas its operational range is -30 °C to -36 °C; • the SOP for receipt and storage of cardiac valves does not describe what visual checks are made when tissues are receipted, how release and use of tissue is recorded, and processes for managing valves that reach their expiry date. To meet this shortfall, the establishment should review all SOPs relating to bone, cardiac valves and iliac vessels to ensure they contain an appropriate level of detail.	
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.	For the autologous pancreatic islet transplantation programme, a donor blood sample for serology testing for mandatory markers is taken several days prior to the procurement. However, there is no blood sample for serology testing taken at the time of procurement. It is a requirement under the European Union (EU) Tissues and Cells Directives that for autologous donors a blood sample for serology testing must be taken at the time of procurement or, if this is not possible, within seven days following procurement. The current serology testing approach is therefore not compliant with the Quality and Safety Regulations 2007.	**Minor**

	Serology testing of cadaveric liver donors is carried out under the licensing framework of The Quality and Safety of Organs Intended for Transplantation 2012, and test results are uploaded to NHSBT's Electronic Offering System (EOS). Iliac vessels that are procured with the liver may be used in the patient who received that liver or could, potentially, be used instead in another recipient. Where iliac vessels are being stored for more than 48 hours for use in a patient other than the recipient of the associated liver, repeat donor serology testing of the donor's blood sample must be performed in accordance with the requirements of the Quality and Safety Regulations 2007. However, such repeat serology testing of the donor blood sample is not routinely being performed by the establishment.	**Minor**
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.	For iliac vessels, cardiac valves and femoral heads there are no documented procedures for the management of: • a recall of tissues distributed to the establishment, or; • the initiation of a recall of tissues that have been distributed by this establishment to end users.	**Minor**

GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately.		
a) There are documented risk assessments for all practices and processes.	Potential risks associated with the autologous pancreatic islet transplantation programme have not been formally assessed. Risks could arise from, for example: • inappropriate donor selection; • inappropriate donor consent; • donor serology testing not being conducted in line with the requirements of the Quality and Safety Regulations 2007; • the pancreatectomy procedure; • transportation of a pancreas from Freeman Hospital to Newcastle Bio-Manufacturing Facility; • the processing procedure; • transportation of pancreatic islets from Newcastle Bio-Manufacturing Facility to Freeman Hospital for re-infusion; Documented risk assessments should set out: the existing control measures for each risk identified; any measures which can be taken to further reduce risk; identified deadlines for completion of these additional risk control measures, and; should be subject to regular review.	**Minor**

Premises, Facilities and Equipment

Standard	**Inspection findings**	**Level of shortfall**
PFE2 Environmental controls are in place to avoid potential contamination.		
b) Where processing of tissues and / or cells involves exposure to the environment, it occurs in an appropriate, monitored environment as required by Directions 003/2010.	Under Annex One of the EU Guidelines to Good Manufacturing Practice, it is a requirement that monitoring of non-viable airborne particulates is undertaken for the full duration of critical processing in a Grade A environment. However, continuous monitoring of non-viable airborne particulates in the Grade A safety cabinet is not being performed during stem cell processing procedures.	**Minor**

Advice

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

No.	Standard	Advice
1.	C2c	While a donor information leaflet is available for the autologous pancreatic islet transplantation programme, it does not appear this is always used during the seeking of consent. The DI is advised to ensure the donor information leaflet is always available when consent is being sought for this procedure.
2.	GQ1a	The establishment undertakes a diverse range of activities under its HTA and MHRA licences, across three licensed premises. The establishment has identified the appointment of a dedicated member of staff to oversee all aspects of clinical and laboratory activity taking place under the HTA and MHRA licences, who would report directly to the Director for Cellular Therapies Facility, as a means to further reinforce the establishment's governance framework. The DI is advised that the HTA is supportive of this proposal.
3.	GQ2b	The DI is advised to develop a more structured approach to the auditing of tissues stored in theatres at Freeman Hospital. This may include, for example: • developing a specific audit checklist for each tissue type; • considering an appropriate frequency and sample size for each tissue type, based on levels of storage and activity; • the review and dissemination of audit findings; • the management of non-conformances identified; • cross-auditing by staff from different clinical areas.
4.	GQ1h, PFE2a	The DI is advised to consider quarantine arrangements for iliac vessels from a donor with a known positive virology status, to minimise any potential risk to vessels from serology negative donors that are stored in the same fridge. For example, vessels from a serology positive donor could be placed in a dedicated sealed container in the storage fridge, or be clearly labelled to highlight their status.
5.	PFE2c	At Royal Victoria Infirmary, microbiological safety cabinets used for stem cell processing have a sharps bin affixed to the external frame of the cabinet for used consumables to be placed in. The positioning of the sharps bin could, potentially, obstruct the person working in the safety cabinet. Moreover, if the bin is not emptied immediately after processing is complete, it is a potential source of contamination within the cleanroom. The DI is advised to consider whether the sharps bin could be moved from its position at the front of the cabinet, and how often it is emptied.
6.	PFE3a	Regarding temperature monitoring of reagent storage areas at Royal Victoria Infirmary, the DI is advised: • the data logger in the ACD-A storage area for paediatric apheresis is not functioning and needs to be replaced, and; • the heparin used in bone marrow procurement is being stored in an area within theatres that is not temperature monitored. The storage temperature of this reagent should be monitored so that the DI could be made aware if the temperature has deviated from the required range.

7.	PFE3a	The DI is advised to seek written advice from NHSBT on whether storage of femoral heads at temperatures between -30 °C to -36 °C changes the maximum storage time printed on the bone pot labels compared to when such tissues are being stored at temperature at -40 °C or below.
8.	PFE5f	The establishment has clearly documented cleaning protocols for the apheresis machines used to apherese adult donors which detail the routine, weekly and monthly cleaning protocols. However, it is not stated in cleaning records which of those protocols had been employed. The DI is advised to consider whether the cleaning protocol followed could be more clearly recorded, for example by writing 'R', 'W' or 'M' next to each entry to denote routine, weekly or monthly cleaning respectively. This would allow the DI to confirm that weekly and monthly cleans are being performed as expected.
9.	N/A	At the time of the inspection it was not clear whether hESCs were being stored for use in human application or for research under a Human Fertilisation and Embryology Authority (HFEA) licence. As a result, the storage and traceability details of these cells were not reviewed during this inspection. The DI is advised to confirm with colleagues whether the hESCs at Newcastle Bio-Manufacturing Facility are being stored under the authority of the establishment's HFEA licence for *in vitro* research or are being stored under the HTA licence and therefore must come under the governance of the establishment's licence.

Concluding comments

Despite the shortfalls identified during the inspection, several aspects of strength were seen. All staff were very knowledgeable about local practice, and were receptive to the inspection team's findings. A clear and comprehensive Trust-wide form is used to record donor consent for serology testing, storage and discard of tissues and cells for human application. The establishment has robust tissue traceability systems in all areas. Premises at all sites are clean, well maintained and generally appropriately monitored. As an example of good practice, there is enhanced training planned for staff in the specific maintenance and use of the freezer for storage of cardiac valves.

A number of areas of practice require improvement, including seven minor shortfalls. The HTA has given advice to the DI with respect to some consent, governance and quality, and premises, facilities and equipment standards.

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: 22 December 2015

Report returned from DI: 11 January 2016

Final report issued: 12 January 2016

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 March 2017

Appendix 1: HTA standards

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

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

Consent

Standard
C1 Consent is obtained in accordance with the requirements of the HT Act 2004, the Human Tissue (Quality and Safety for Human Application) Regulations 2007 and as set out in the HTA's Codes of Practice.
a) If the establishment acts as a procurer of tissues and / or cells, there is an established process for acquiring donor consent which meets the requirements of the HT Act 2004 the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (Q&S Regulations) and the HTA's Codes of Practice
b) If there is a third party procuring tissues and / or cells on behalf of the establishment the third party agreement ensures that consent is obtained in accordance with the requirements of the HT Act 2004, the Q&S Regulations and the HTA's Codes of Practice.
c) The establishment or the third party's procedure on obtaining donor consent includes how potential donors are identified and who is able to take consent.
d) Consent forms comply with the HTA Codes of Practice.
e) Completed consent forms are included in records and are made accessible to those using or releasing tissue and / or cells for a Scheduled Purpose.
C2 Information about the consent process is provided and in a variety of formats.
a) The procedure on obtaining consent details what information will be provided to donors. As a minimum, the information specified by Directions 003/2010 is included.
b) If third parties act as procurers of tissues and / or cells, the third party agreement details what information will be provided to donors. As a minimum, the information specified by Directions 003/2010 is included.
c) Information is available in suitable formats and there is access to independent interpreters when required.
d) There are procedures to ensure that information is provided to the donor or donor's family by trained personnel.
C3 Staff involved in seeking consent receive training and support in the implications and essential requirements of taking consent.
a) Staff involved in obtaining consent are provided with training on how to take informed consent in accordance with the requirements of the HT Act 2004 and Code of Practice on Consent.
b) Training records are kept demonstrating attendance at training on consent.

Governance and Quality

Standard
GQ1 All aspects of the establishment's work are supported by ratified documented policies and procedures as part of the overall governance process.
a) There is an organisational chart clearly defining the lines of accountability and reporting relationships.
b) There are procedures for all licensable activities that ensure integrity of tissue and / or cells and minimise the risk of contamination.
c) There are regular governance meetings, for example health and safety, risk management and clinical governance committees, which are recorded by agendas and minutes.
d) There is a document control system to ensure that changes to documents are reviewed, approved, dated and documented by an authorised person and only current documents are in use.
e) There are procedures for tissue and / or cell procurement, which ensure the safety of living donors.
f) There are procedures for tissue and / or cell procurement, which ensure the dignity of deceased donors.
g) There are procedures to ensure that an authorised person verifies that tissues and / or cells received by the establishment meet required specifications.
h) There are procedures for the management and quarantine of non-conforming consignments or those with incomplete test results, to ensure no risk of cross contamination.
i) There are procedures to ensure tissues and / or cells are not released from quarantine until verification has been completed and recorded.
j) There are procedures detailing the critical materials and reagents used and where applicable, materials and reagents meet the standards laid down by the European directives on medical devices and in vitro diagnostic medical devices.
k) There is a procedure for handling returned products.
l) There are procedures to ensure that in the event of termination of activities for whatever reason, stored tissues and / or cells are transferred to another licensed establishment or establishments.
m) The criteria for allocating tissues and / or cells to patients and health care institutions are documented and made available to these parties on request.
o) There is a complaints system in place.
p) There are written agreements with third parties whenever an activity takes place that has the potential to influence the quality and safety of human tissues and / or cells.
q) There is a record of agreements established with third parties.
r) Third party agreements specify the responsibilities of the third party and meet the requirements set out in Directions 003/2010.
s) Third party agreements specify that the third party will inform the establishment in the event of a serious adverse reaction or event.

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

e) The establishment keeps a register of the types and quantities of tissues and / or cells that are procured, tested, preserved, processed, stored and distributed or otherwise disposed of, and on the origin and destination of tissues and cells intended for human application.
f) There are procedures to ensure that donor documentation, as specified by Directions 003/2010, is collected and maintained.
g) There is a system to ensure records are secure and that donor confidentiality is maintained in accordance with Directions 003/2010.
h) Raw data which are critical to the safety and quality of tissues and cells are kept for 10 years after the use, expiry date or disposal of tissues and / or cells.
i) The minimum data to ensure traceability from donor to recipient as required by Directions 003/2010 are kept for 30 years after the use, expiry or disposal of tissues and / or cells.
j) Records are kept of products and material coming into contact with the tissues and / or cells.
k) There are documented agreements with end users to ensure they record and store the data required by Directions 003/2010.
l) The establishment records the acceptance or rejection of tissue and / or cells that it receives and in the case of rejection why this rejection occurred.
m) In the event of termination of activities of the establishment a contingency plan to ensure records of traceability are maintained for 10 or 30 years as required.
GQ5 There are documented procedures for donor selection and exclusion, including donor criteria.
a) Donors are selected either by the establishment or the third party acting on its behalf in accordance with the criteria required by Directions 003/2010.
b) The testing of donors by the establishment or a third party on behalf of the establishment is carried out in accordance with the requirements of Directions 003/2010.
c) In cases other than autologous donors, donor selection is carried out by authorised personnel and signed and reviewed by a qualified health professional.
d) There is a system in place either at the establishment or at a third party acting on its behalf to record results of donor selection and associated tests.
e) Testing of donor samples is carried out using CE marked diagnostic tests.
f) Samples taken for donor testing are clearly labelled with the time and place the sample was taken and a unique donor identification code.
GQ6 A coding and records system facilitates traceability of tissues and / or cells, ensuring a robust audit trail.
a) There is a donor identification system which assigns a unique code to each donation and to each of the products associated with it.
b) An audit trail is maintained, which includes details of when the tissues and / or cells were acquired and from where, the uses to which the tissues and / or cells were put, when the tissues and / or cells were transferred elsewhere and to whom.

c) The establishment has procedures to ensure that tissues and / or cells imported, procured, processed, stored, distributed and exported are traceable from donor to recipient and vice versa.
GQ7 There are systems to ensure that all adverse events, reactions and/or incidents are investigated promptly.
a) There are procedures for the identification, reporting, investigation and recording of adverse events and reactions, including documentation of any corrective or preventative actions.
b) There is a system to receive and distribute national and local information (e.g. HTA regulatory alerts) and notify the HTA and other establishments as necessary of serious adverse events or reactions.
c) The responsibilities of personnel investigating adverse events and reactions are clearly defined.
d) There are procedures to identify and decide the fate of tissues and / or cells affected by an adverse event, reaction or deviation from the required quality and safety standards.
e) In the event of a recall, there are personnel authorised within the establishment to assess the need for a recall and if appropriate initiate and coordinate a recall.
f) There is an effective, documented recall procedure which includes a description of responsibilities and actions to be taken in the event of a recall including notification of the HTA and pre-defined times in which actions must be taken.
g) Establishments distributing tissue and / or cells provide information to end users on how to report a serious adverse event or reaction and have agreements with them specifying that they will report these events or reactions.
h) Establishments distributing tissues and / or cells have systems to receive notifications of serious adverse events and reactions from end users and notify the HTA.
GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately.
a) There are documented risk assessments for all practices and processes.
b) Risk assessments are reviewed regularly, as a minimum annually or when any changes are made that may affect the quality and safety of tissues and cells.
c) Staff can access risk assessments and are made aware of local hazards at training.
d) A documented risk assessment is carried out to decide the fate of any tissue and / or cells stored prior to the introduction of a new donor selection criteria or a new processing step, which enhances the quality and safety of tissue and / or cells.

Premises, Facilities and Equipment

Standard
PFE1 The premises are fit for purpose.
a) A risk assessment has been carried out of the premises to ensure that they are fit for purpose.
b) There are procedures to review and maintain the safety of staff, visitors and patients.
c) The premises have sufficient space for procedures to be carried out safely and efficiently.

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

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

Disposal

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

Human Tissue Act 2004 Standards

Consent standards
C1 Consent is obtained in accordance with the requirements of the Human Tissue Act 2004 (HT Act) and as set out in the code of practice
• 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
PFE2 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
PFE4 Systems are in place to protect the quality and integrity of bodies, body parts, tissues and cells during transport and delivery to a destination
• 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.