Site visit inspection report on compliance with HTA minimum standards

The Royal London Hospital

HTA licensing number 22638

Licensed for the

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

26 and 27 July 2016

Summary of inspection findings

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

Although the HTA found that the Royal London Hospital (the establishment) had met the majority of the HTA standards, one major and five minor shortfalls were found with regard to the Governance and Quality Systems (GQS) standards. The major shortfall was in relation to weaknesses in the incident reporting system. The minor shortfalls were in relation to an absence of: (i) governance meetings; (ii) up-to-date finalised third party and service level agreements; (iii) an independent audit; (iv) appropriate serological sampling protocols; and (v) acceptance criteria for serology test results. Advice has been given relating to the Consent, GQS and Premises, Facilities and Equipment and Disposal standards, as well as to licence management.

In addition, there was no Designated Individual in place at the time of the inspection. The absence of a DI is in breach of paragraph 5(a) of Schedule 1 of the Human Tissue (Quality and Safety for Human Application) Regulations 2007: 'It shall be a condition of a licence under this Schedule that the licensed activities shall be carried on only under the supervision of the Designated Individual'.

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 (DI), Licence Holder (LH), premises and practices are suitable.

The statutory duties of the DI 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 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.

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

Tissue type	Procurement	Processing	Testing	Storage	Distribution	Import	Export
DLI	**E**		**E**		**TPA**		
PBSC	**E**		**E**		**TPA**		
Other tissues/cells for ATMPs*	**E**		**E**				**E/TPA**

DLI = cells for donor lymphocyte infusion.

PBSC = peripheral blood stem cells.

*Other tissues/cells = skeletal muscle tissue.

Background to the establishment and description of inspection activities undertaken

This report refers to the activities carried out by the Royal London Hospital (the establishment). The establishment's licensing arrangements cover the Royal London Hospital - the hub site - and the satellite site (St. Bartholomew's Hospital).

The Royal London and St. Bartholomew's Hospitals are part of Bart's Health NHS Trust. The Trust was formed in 2012 and consists of the following five hospitals: The Royal London Hospital; St. Bartholomew's Hospital; Mile End Hospital; Newham University Hospital; and Whipps Cross University Hospital.

The establishment was issued an HTA licence in February 2007. The first two routine inspections were conducted under the previous licensing arrangement (HTA licensing number 11099), which consisted of a single site at St. Bartholomew's Hospital. A new facility was established at the Royal London Hospital in 2011 and processing, testing and storage were transferred there. This resulted in the current hub and satellite licensing arrangement (HTA licensing number 22638). This was the third HTA site visit inspection of the establishment under this arrangement since the current HTA licence was issued in December 2011. The last routine inspection was in January 2014, although the HTA also undertook a site visit in October 2015 to review progress on actions taken following a serious adverse event (SAE) that was reported in April 2015.

The current inspection was a routine one to assess whether the establishment is continuing to meet the HTA's standards. The action points and recommendations made by the HTA during the site visit conducted in October 2015 were also reviewed during this inspection.

The establishment no longer processes tissues and cells for human application. The establishment is currently licensed under the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (Q&S Regulations) for the procurement, testing, storage, distribution and export of tissues and cells for human application. The establishment is also licensed for the storage of relevant material for use for a scheduled purpose under the Human Tissue Act 2004 (HT Act). Although licensed for this activity, the establishment does not currently store tissues and cells for human application. The organisation is also accredited by the Joint Accreditation Committee - European Society for Blood and Marrow Transplantation (EBMT) and the International Society for Cellular Therapy (ISCT) (JACIE) and was last inspected by this organisation in November 2015.

There is currently no DI in post (see below). The Corporate LH (CLH) is Bart's Health NHS Trust and the CLH Contact (CLHC) is the Trust Clinical Director of Pathology. There is one Person Designated (PD) on the licence, the Haematopoietic Stem Cell Transplant (HSCT) Clinical Programme Director (based at the satellite site).

<u>The satellite site</u>

The HSCT Unit provides an adult stem cell collection and allogeneic and autologous stem cell transplantation service for patients at Bart's Health NHS Trust. Approximately 145 autologous peripheral blood stem cell (PBSC) collections are carried out annually, along with 25 allogeneic (related directed) PBSC collections and five allogeneic collections of cells for donor lymphocyte infusion (DLI).

Transplanted cells include those from directed related and autologous donations within the hospital, as well as from tissue-typed ('matched') unrelated donations. Matched unrelated PBSC donations are managed by the Anthony Nolan and NHS Stem Cell Registry under service level agreement (SLA). In total, approximately 50 allogeneic and 85 autologous transplants are carried out annually.

Donor selection and consent for PBSC and DLI collections, as well as for mandatory serology tests, take place in the HSCT Unit (*see Advice item 10*). Patients are consented at both initial

consultation and on the day of collection by trained staff working to well-defined procedures. A Trust consent form is used, along with a separate HSCT consent form which records consent for cell mobilisation, collection, processing, testing, storage and disposal, as well as for research (*see Advice items 2 and 3*). Donors give their consent for a maximum five-year storage period.

Samples for mandatory serology testing are taken up to 30 days prior to cell collection and are transported by courier under third party agreement (TPA) to the Department of Virology at the hub site (*see Shortfall under GQ1p*).

The HSCT Unit contains three apheresis machines. Following collection, cells are packaged in preparation for distribution. Reagents and consumables for apheresis are stored in a secure, temperature-monitored storage area. At the present time sample labels are handwritten (*see Advice item 9*).

Cellular processing and (if required) cryopreservation and storage are carried out at a separate HTA-licensed establishment ('processing centre') under SLA (*see Shortfall under GQ1p*). Collections are transported by courier using well-defined, validated procedures under TPA (*see Shortfall under GQ1p*). Staff make use of an online facility where the courier can be tracked from the initiation of the collection request to courier arrival, collection and delivery at the processing centre. The system ensures that the samples are fully traceable and that transport times are monitored.

A variety of tests to ensure cellular quality and safety are carried out at both the hub site and at the processing centre. Total nucleated cell count (TNCC), CD34 immunophenotype, haemoglobin levels and blood group analysis of pre-apheresis samples are determined in the Department of Haematology and Blood Transfusion at the hub site. Human leukocyte antigen (HLA) tissue typing is carried out in the Department of Clinical Transplantation at the hub site. Serology testing is carried out in the Department of Virology at the hub site (see below).

The processing centre carries out sterility analysis (for both bacteria and fungi), pre-processing TNCC and pre-cryopreservation analysis for CD34/CD45 immunophenotype, cell viability and colony-forming unit biological function.

The establishment has acceptance criteria for cell transplantation based on the above set of markers. Cells which do not meet these thresholds are stored for research or, for samples with minimal cell counts, are disposed of.

Appropriate records are kept at all stages from procurement through to end use to ensure sample traceability (*see Advice item 11*).

The hub site

Procurement. The Colorectal Surgery Unit at the hub site is involved in a clinical trial using autologous muscle derived cell (AMDC) transplants to treat faecal incontinence. To date, nine patients have taken part in the UK arm of the trial. In this procedure, needle biopsies of the patient's thigh skeletal muscle are taken and these are used as a starting material for a cell-based Advanced Therapy Medicinal Product (ATMP). They are cultured (processed) and, in a second surgical procedure, the processed product ('autologous muscle derived cells for anal sphincter repair': AMDC-ASR) is injected into the external anal sphincter using a small needle.

Consent to tissue donation, ATMP implantation and serological testing is sought by clinicians in the Day Surgery Unit within the hospital (*see Advice item 4*). A blood sample for donor testing is taken at the time of consenting (up to 30 days prior to procurement) and serological testing is carried out in the Department of Virology at the hub site (*see Shortfall under GQ5b*). Tissue procurement (harvesting) takes place in the Colorectal Surgery Unit.

Tissue is processed by a US company under agreement. The company provides muscle biopsy kits up to four weeks in advance of the procedure and these are stored in a refrigerator linked to a continuous temperature monitoring unit in the Department of Immunology at the hub site. Samples are taken away on the same day as the procurement by courier (under TPA) and are exported to the US. The manufactured product is returned for implantation 6-9 weeks later.

Testing. The Department of Virology laboratories at the hub site are accredited by the United Kingdom Accreditation Service (UKAS) to International Organization for Standardization (ISO) standard 15189 (2012). Samples are tested using CE-marked diagnostic kits on automated testing equipment according to manufacturer's instructions. Tests for HTLV-1 and 2, HIV-1 and 2, HBV, HCV and *T. pallidum* are carried out. Confirmatory serology and Nucleic Acid Amplification Technique (NAT) testing is also carried out this Department.

The Department routinely takes part in external quality assessment schemes for the above tests.

Storage. There are no cells for human application currently stored at this site. Following the HTA site visit in October 2015 the two liquid nitrogen storage vessels (cryovessels) containing cells for human application, along with the two mobile quarantine cryovessels containing cells from virology positive donors, were transported to a separate HTA-licensed storage establishment under SLA.

There is one -80°C freezer remaining in the liquid nitrogen storage area which contains reagents and samples previously used for validation studies (*see Advice item 7*).

The timetable for the current site visit inspection was developed after consideration of the establishment's previous inspection reports, communications with the HTA since the last inspection and annual activity data. The inspection included a visual inspection of the satellite (HSCT Unit) and hub sites (Virology Department, previous processing laboratory, liquid nitrogen storage area and Department of Immunology refrigerator). Discussions and interviews were held with key staff and documentation was reviewed. Interviews were held with the CLHC, the PD, the Apheresis Charge Nurse, the satellite Quality Manager, the Lead Biomedical Scientist in the Department of Virology and a Clinical Trials Research Nurse. Audits of traceability were also carried out:

- The paper and electronic records of six PBSC donations were reviewed (four autologous, two paired directed donations and corresponding transplants). They included: donor assessment and donor/recipient consent forms; apheresis care plans and procedure records; results of serological and microbiological analysis; sample labelling, packaging and transport documentation. There were no discrepancies noted.

Inspection findings

The HTA found the CLH to be suitable in accordance with the requirements of the legislation. The DI was appointed in August 2015 but has since left the organisation and was not available during the current inspection. The absence of a DI is in breach of paragraph 5(a) of Schedule 1 of the Q&S Regulations: 'It shall be a condition of a licence under this Schedule that the licensed activities shall be carried on only under the supervision of the Designated Individual'. After the inspection the HTA issued Directions to require the establishment to appoint a DI.

Following this action, the HTA received and approved an application for a new DI at the Royal London Hospital. The HTA therefore considers this issue to have been addressed.

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.		
c) There are regular governance meetings, for example health and safety, risk management and clinical governance committees, which are recorded by agendas and minutes.	During the site visit conducted in October 2015 the HTA notified the establishment that governance arrangements must be strengthened and clarified so that individual staff members are clear about their responsibilities in relation to licensed activities. Although regular meetings of the collection and transplant team take place at the satellite site, there are no regular governance meetings taking place where all staff working under the licence can discuss matters relating to HTA-licensed activities. *See Advice item 5.*	**Minor**
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.	The TPA between the establishment and the courier is out of date. The SLA with the processing centre has yet to be finalised.	**Minor**
GQ2 There is a documented system of quality management and audit.		
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.	There is currently no independent audit to verify compliance with protocols and HTA standards.	**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.	Annex B of the HTA's 'Guide to Quality and Safety Assurance for Human Tissues and Cells for Patient Treatment' sets out that, in the case of living donors (except allogeneic bone marrow stem-cell and peripheral blood stem-cell donors), blood samples for donor testing must be obtained at the time of donation or within seven days post donation (this is the 'donation sample') unless the tissues and cells are being stored for long periods and provision is made for donor re-sampling and testing after 180 days. In relation to the AMDC work that is being carried out, the establishment takes blood samples for serological testing up to 30 days prior to the donation. This approach does not satisfy the mandatory testing requirements of Annex B.	**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 Department of Virology releases results to the computerised record system so that they can be accessed by the clinical staff who requested them. These results are released from the analysers used in the Department based on the results of Quality Control (QC) checks that are run on the machine twice daily. The acceptance criteria for the QC tests and the process of releasing results were not available at the time of the inspection.	**Minor**
GQ7 There are systems to ensure that all adverse events 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.	There are still severe weaknesses in the establishment's incident reporting system: During the inspection the team noted that an incident concerning the mis-reporting of CD34 results to staff in the HSCT Unit had resulted in a failed procurement of stem cells. The incident had not been recorded on the Trust's incident reporting system by staff working under the licence. The establishment has two separate standard operating procedures (SOPs)	**Major**
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.	relating to adverse events: (i) 'Clinical incident reporting' (SOP/QM/004) - ratified. (ii) 'Critical incident and emergency plan' (SOP/SO86) - in draft. Neither document gives clear instructions to staff working under the licence for identifying and reporting serious adverse events and adverse reactions (SAEARs). Discussions with various members of staff during the inspection confirmed that they were not aware of SAEAR reporting requirements. There are no identified personnel who are able to report SAEARs in the DI's absence. *See Advice item 12.*	

Advice

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

No.	Standard	Advice
1.	N/A	The DI is advised to appoint PDs in the Department of Virology and in the Colorectal Surgery Unit at the hub site and to notify the HTA of such appointments. Appointing PDs will clarify roles and responsibilities under the licence, will ensure that all licensed activities fall under the DI's supervision and will ensure that certain activities, such as the reporting of SAEARs, can take place in the DI's absence.
2.	C1d	The DI is advised to consider adding a line to the HSCT consent form acknowledging agreement to the giving of a blood sample for mandatory serology marker analysis.
3.	C1d, GQ2b	There are inconsistencies between the Trust and HSCT consent forms relating to the use of donated samples for research. The HSCT form often has a ticked box confirming that the patient has consented for this use, but the Trust form research section is consistently left blank and unsigned. The DI is advised to consider including completed Trust and HSCT consent forms within the audit schedule.
4.	C3a, b GQ3g	The DI is advised to ensure that staff in the Colorectal Surgery Unit who seek consent are included in the consent and regulatory training programme given by the satellite Quality Manager. The satellite Quality Manager is advised to ensure that records are kept of all staff who attend this training and that refresher training is provided when required.
5.	GQ1c	The DI is advised to ensure that governance meetings identified in the shortfall regularly include items such as standardisation of documents, changes to SOPs, audits and their findings, competence and regulatory training, management of incidents, risk assessments, equipment maintenance, the setting up of agreements with other establishments and updates from the HTA (e.g. e-newsletter items).

		The meetings should be governed by an agenda and minutes should be recorded and circulated. The minutes should include timelines for identified actions and there should be a standing agenda item for discussing progress against actions identified at previous meetings. The DI is advised to ensure that the PDs from the Department of Virology and the Colorectal Surgery Unit attend the meetings. The DI may also wish to consider whether to include representatives from other departments, such as those of Clinical Governance and Information Technology, to help develop the establishment's working practices.
6.	GQ2b, 4b	The DI is advised to consider extending the current audit schedule to include relevant audits in the Department of Virology and Colorectal Surgery Unit at the hub site.
7.	GQ2b	The DI is advised to ensure that all samples in the -80°C freezer are catalogued and managed as a matter of urgency.
8.	GQ3e	The DI is advised to consider reviewing and recording training to ensure that all staff are familiar with the relevant SOPs and risk assessments.
9.	GQ4c	The DI is advised to ensure that a robust sample labelling system is used which minimises error.
10.	GQ5a	The DI is advised to consider adding more detail to the SOP on donor selection under the section which covers recent travel abroad. The SOP currently includes references to HTA alerts covering issues such as Ebola virus but has not been updated to include Zika virus. The DI is advised to consider including a link to the Joint United Kingdom Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee (JPAC) Donor Selection Guidelines and to the Geographical Disease Risk Index rather than including a list of individual infections.
11.	GQ6c	The DI is advised to consider reviewing the current method of communicating donor information to the processing centre. The current system of scanning and sending information from the hub site is not sufficiently controlled or captured in an SOP. It may be more advisable for staff in the HSCT Unit to perform this procedure.
12.	GQ7a-c	The DI is advised to ensure that a stand-alone SOP is created for the identification and reporting of SAEARs. The SOP should contain: • The types of incidents which are classified as SAEARs. • The reporting obligations to the HTA (within 24 hours of discovery or confirmation). • The receipt and dissemination of HTA regulatory alerts. • The personnel who should report SAEARs in the DI's absence. • The requirement to submit a follow-up report to the HTA within 90 days. The DI is advised to ensure that all staff working under the licence are familiar with this SOP. The DI is referred to the HTA's website page for further information: https://www.hta.gov.uk/policies/serious-adverse-event-or-reaction-saears

13.	PFE5a	The DI may wish to keep copies within the Department of all maintenance visits and maintenance agreements relating to critical equipment.
14.	D2a	The DI is advised to ensure that the disposal procedure is updated to include recording the date of disposal. The date of disposal should also be included on the relevant forms and on the establishment's electronic records.

Concluding comments

During the inspection areas of good practice were noted:

- The satellite site has robust procedures for document control, in line with JACIE requirements. The Virology Department at the hub site has also introduced a robust document control system.
- The satellite site has a robust system for audit, including regular dissemination of audit findings and corrective and preventative action plans, in line with JACIE requirements.
- The satellite Quality Manager has introduced 'quizzes' to assess staff familiarity with different SOPs, in line with JACIE requirements.
- There is a detailed panel of risk assessments covering all licensed activities.

There are a number of areas of practice that require improvement, including one major and five minor shortfalls. The HTA has given advice to the DI with respect to the Consent, Governance and Quality Systems, Premises, Facilities and Equipment and Disposal standards, as well as to licence management.

The HTA requires that the DI 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: 05 September 2016

Report returned from DI: 28 September 2016

Final report issued: 14 November 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: 15 May 2018

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
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.
c) Information is available in suitable formats and there is access to independent interpreters when required.
d) There are procedures to ensure that information is provided to the donor or donor's family by trained personnel.
C3 Staff involved in seeking consent receive training and support in the implications and essential requirements of taking consent.
a) Staff involved in obtaining consent are provided with training on how to take informed consent in accordance with the requirements of the HT Act 2004 and Code of Practice on Consent.
b) Training records are kept demonstrating attendance at training on consent.

Governance and Quality

Standard
GQ1 All aspects of the establishment's work are supported by ratified documented policies and procedures as part of the overall governance process.
a) There is an organisational chart clearly defining the lines of accountability and reporting relationships.

b) There are procedures for all licensable activities that ensure integrity of tissue and / or cells and minimise the risk of contamination.
c) There are regular governance meetings, for example health and safety, risk management and clinical governance committees, which are recorded by agendas and minutes.
d) There is a document control system to ensure that changes to documents are reviewed, approved, dated and documented by an authorised person and only current documents are in use.
e) There are procedures for tissue and / or cell procurement, which ensure the safety of living donors.
g) There are procedures to ensure that an authorised person verifies that tissues and / or cells received by the establishment meet required specifications.
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.
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.
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.
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.
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.
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.
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

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 Human Tissue Act 2004, Human Tissue (Quality and Safety for Human Application) Regulations 2007 or the HTA Directions.

1. **Critical shortfall:**

   A shortfall which poses a significant risk to causing harm to a recipient patient or to a living donor,

   or

   A number of 'major' shortfalls, none of which is critical on its own, but viewed cumulatively represents a systemic failure and therefore is 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 straight away.

2. **Major shortfall:**

   A non-critical shortfall.

   A shortfall in the carrying out of licensable activities which poses an indirect risk to the safety of a donor or a recipient

   or

   A shortfall in the establishment's quality and safety procedures which poses an indirect risk to the safety of a donor or a recipient;

   or

   A shortfall which indicates a major deviation from the Human Tissue (Quality and Safety for Human Application) Regulations 2007 or the HTA Directions;

   or

   A shortfall which indicates a failure to carry out satisfactory procedures for the release of tissues and cells or a failure on the part of the designated individual to fulfil his or her legal duties;

   or

   A combination of several 'minor' shortfalls, none of which is major on its own, but which, viewed cumulatively, could constitute a major shortfall by adversely affecting the quality and safety of the tissues and cells.

   In response to a major shortfall, an establishment is expected to implement corrective and

preventative actions within 1-2 months of the issue of the final inspection report. Major shortfalls pose a higher level of risk and therefore a shorter deadline is given, compared to minor shortfalls, to ensure the level of risk is reduced in an appropriate timeframe.

3. **Minor shortfall:**

   A shortfall which cannot be classified as either critical or major and which can be addressed by further development by the establishment.

   This category of shortfall requires the development of a corrective action plan, the results of which will usually be assessed by the HTA either by desk based review or at the time of the next inspection.

   In response to a minor shortfall, an establishment is expected to implement corrective and preventative actions within 3-4 months of the issue of the final inspection report.

Follow up actions

A template corrective and preventative action plan will be sent as a separate Word document with both the draft and final inspection report. You must complete this template and return it to the HTA within 14 days of the issue of the final report.

Based on the level of the shortfall, the HTA will consider the most suitable type of follow-up of the completion of the corrective and preventative action plan. This may include a combination of

- a follow-up site visit inspection
- a request for information that shows completion of actions
- monitoring of the action plan completion
- follow up at next desk-based or site-visit inspection.

After an assessment of the proposed action plan the establishment will be notified of the follow-up approach the HTA will take.