**Site visit inspection report on compliance with HTA minimum standards**

**The Royal London Hospital**

**HTA licensing number 22638**

**Licensed for the**

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

**11-13 December 2018**

**Summary of inspection findings**

The HTA found the Designated Individual (DI), the Licence Holder (LH) 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 many of the HTA's standards, five minor shortfalls were found in relation to: the absence of a documented plan for contingency storage of records; insufficient detail in donor medical assessments; inappropriate timing of blood sampling for donor lymphocyte patients; incomplete donor testing for clinical trial patients and; the absence of procedures for applying the Single European Code (SEC) to clinical trial samples.

Advice has been given relating to the Consent, Governance and Quality, and Premises, Facilities and Equipment standards, as well as advice on licence management.

A particular example of strength is 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 Category; Tissue Type | Procurement | Testing | Distribution | Export |
|---|---|---|---|---|
| **Progenitor Cell, Hematopoietic, PBSC; PBSC** | **E** | **E** | **TPA** | |
| **Mature Cell, T Cell (DLI); DLI** | **E** | **E** | **TPA** | |
| **Other; Skeletal Muscle (ATMP)** | **E** | **E** | | **E** |

**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 St. Bartholomew's Hospital (the satellite site).

The current hub and satellite licensing arrangement was set up in December 2011. This was the fifth HTA site visit inspection under this arrangement (the last inspection was in July 2016) and the first since the amended Human Tissue (Quality and Safety for Human Application) Regulations 2007 came into force on 1 April 2018 [Q&S Regulations (as amended)]. The current inspection was a routine one to assess whether the establishment is continuing to meet the HTA's standards.

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 is licensed under the Q&S Regulations (as amended) for the procurement, testing, distribution and export of tissues and cells for human application.

The establishment is also licensed under the Human Tissue Act 2004 (HT Act) for the storage of relevant material for use for a scheduled purpose but it does not currently store any relevant material for use for a scheduled purpose under this licence (see *Advice*, item 1). Relevant material consented and stored for research comes under the governance of the Queen Mary University of London research licence (HTA licensing number 12199).

The DI is a consultant haematological oncologist, the Corporate Licence Holder (CLH) is Bart's Health NHS Trust and the CLH Contact (CLHC) is the Trust Clinical Director of Pathology. There are currently five Persons Designated (PDs) working under the licence (see *Advice*, item 2).

The satellite site

Licensed activities take place in the Department of Haematological Oncology, which is part of the Bart's Cancer Centre. The Department treats a wide range of haematological malignancies, including leukaemia, lymphoma and myeloma.

The Haematopoietic Stem Cell transplant (HSCT) Unit within the department currently undertakes the collection of peripheral blood stem cells (PBSC) and donor lymphocytes (for donor lymphocyte infusion, DLI). Collections are for adult autologous transplantation or are from directed, related adult donors for transplantation at the establishment. The establishment previously undertook the collection of bone marrow (BM) but has not done this for over two years.

Tissue-typed ('matched') unrelated BM, PBSC, donor lymphocyte and umbilical cord blood donations for transplantation at the establishment are managed by the 'Anthony Nolan and NHS Stem Cell Registry' under the terms of a service level agreement (SLA) and such collections take place at other centres.

The HSCT Unit is accredited by the Joint Accreditation Committee - International Society for Cellular Therapy (ISCT-Europe) and European Society for Blood and Marrow Transplantation (EBMT) (JACIE) and was last assessed by this organisation in November 2015.

Procurement

Donor selection and the seeking of consent for PBSC and donor lymphocyte procurement, as

well as for mandatory serology tests, take place in the Haematology Day Unit. Patients are consented at both initial consultation and on the day of collection by trained staff working to specific procedures (see *Advice*, item 4). Those patients who are not suitable for autologous transplantation may receive directed, related PBSC donations. In these cases, donor selection is conducted by an independent qualified medical practitioner using HSCT donor selection forms, although the donor selection process does not include questions to exclude risk of prion disease or exposure to toxic substances [see shortfall against standard GQ5(a)] or questions related to potential HEV transmission (see *Advice*, item 11). Published information from haematological charities is provided about the donation process. A Trust consent form is used, along with a separate HSCT consent form which records consent for cell mobilisation, collection, processing, testing and storage, but not disposal (see *Advice*, item 5). A separate consent form, rather than the Trust form, is used for research donations (see *Advice*, item 6).

Human leukocyte antigen tissue typing is carried out in the Department of Clinical Transplantation at the hub site.

Blood samples for serology testing from PBSC donors are taken up to 30 days prior to cell collection and are transported by courier under the terms of a third party agreement (TPA) to the Department of Virology at the hub site. Blood samples from DLI donors are also taken up to 30 days prior to cell collection [see shortfall against standard GQ5(b)].

The procurement of cells from allogeneic donors under the age of 18 years for transplantation at the establishment is carried out at a separate HTA-licensed NHS Trust. This Trust also receives occasional collections from adult donors at the establishment for paediatric transplantation. These activities are carried out under the terms of a SLA.

The HSCT Unit contains three apheresis machines. Following collection, cells are packaged and transported by courier under the terms of a TPA using well-defined, validated procedures to a separate HTA-licensed hospital (the ‘processing and storage facility’). The PBSC and donor lymphocyte collection bags are labelled at the establishment using labels which contain the Single European Code Donation Identification Sequence (SEC-DI). Transplant products (containing both the SEC-DI and the SEC Product Identification Sequence, SEC-PI) are returned to the establishment by courier using similar procedures.

Consumables for apheresis are kept in two secure storage areas in the HSCT Unit but there are inconsistencies in the temperature monitoring of these rooms (see *Advice*, item 16).

### Processing and storage

Processing and (if required) cryopreservation and storage are carried out by the processing and storage facility under the terms of a SLA. The facility performs total nucleated cell count and CD34 immunophenotype of pre-apheresis samples, and CD34/CD45 immunophenotype and cell viability assays of post-processed samples, as well as sterility analysis (for both bacteria and fungi). Haematocrit levels, blood group and chimerism analyses are performed separately in the Department of Haematology and Blood Transfusion at the hub site.

The establishment has acceptance criteria for cell transplantation based on the above set of markers. Cells with minimal counts are disposed of by the processing and storage facility.

## The hub site

### Procurement

The Colorectal Surgery Unit in the Department of General Surgery at the hub site is involved in a clinical trial using autologous muscle derived cell (AMDC) transplants to treat faecal

incontinence. To date, twelve 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 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.

Donor selection and the seeking of consent for tissue procurement, as well as for mandatory serology tests, take place in the Clinical Sciences Research Centre at the hub site. Patients are consented at both initial consultation and on the day of collection by staff working to specific procedures (see *Advice*, item 7). An ethically-approved donor information sheet is used, along with both Trust and separate ethically-approved consent forms. The ethically-approved form records consent for procurement, processing, testing and transplantation.

A pre-operative blood sample for mandatory serology testing is taken on the day of procurement and serological testing is carried out in the Department of Virology at the hub site but the full range of mandatory tests is not carried out [see shortfall against standard GQ5(b)]. Tissue procurement takes place in the operating theatre complex at the hub site.

Tissue is processed by a US company under agreement. The company provides muscle biopsy kits and accompanying labels 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. The labels do not conform to the SEC requirement [see shortfall against standard GQ6(d)]. Biopsies are taken away on the same day as the procurement by courier (under TPA with the US manufacturer) and are exported to the US. The manufactured product is returned for transplantation 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. The last UKAS inspection was in October 2015. Samples are tested using CE-marked diagnostic kits on automated testing equipment according to manufacturers' instructions. Antibody tests for a range of viruses and bacteria are carried out, including HTLV-1, HIV-1 and 2, HBsAg, HBc, HCV and *T. pallidum*, as well as confirmatory serology and Nucleic Acid Amplification Technique (NAT) testing.

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

The timetable for the 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 site (Haematology Day Unit, HSCT Unit) and hub site (Clinical Sciences Research Centre, operating theatre complex, Department of Virology). Discussions and interviews were held with key staff and documentation was reviewed. Interviews were held with the DI, the CLHC, two consultant haematological oncologists, the Virology Quality Manager and a Professor of Surgery.

Audits of traceability were carried out:

- The electronic and paper records of four haematological donations were reviewed (two autologous PBSC; two directed, related PBSC) along with the corresponding transplants. The following information was cross-referenced: donor selection and donor/recipient consent forms, apheresis care plans and worksheets, SEC product

labels, packaging and transport documentation, and serological and microbiological test results. There were no discrepancies noted.

- The electronic and paper records of two clinical trial donations were reviewed. The following information was cross-referenced: donor selection and donor consent forms, product labels, packaging and transport documentation, and serological test results. There were incomplete serological test results and inappropriate labels used, as discussed above.

## Inspection findings

The HTA found the DI and the CLH 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 |
|---|---|---|
| GQ4 There is a systematic and planned approach to the management of records. | | |
| 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. | The establishment has a contingency plan for the re-provision of service (SOP/GEN/004) but this does not include a plan for the contingency storage of records of traceability and raw data in the event of termination of licensed activities. | **Minor** |
| GQ5 There are documented procedures for donor selection and exclusion, including donor criteria. | | |
| a) Donors are selected either by the establishment or the third party acting on its behalf in accordance with the criteria required by Directions 002/2018. | The establishment's donor selection procedure does not include questions to exclude risk of prion disease and donors who have ingested, or had an exposure to, a substance (such as cyanide, lead, mercury, gold) that may be transmitted to recipients in a dose that could endanger their health. | **Minor** |
| b) The testing of donors by the establishment or a third party on behalf of the establishment is carried out in accordance with the requirements of Directions 002/2018. | The establishment's testing procedures for donors of cells for DLI, collected independently of PBSCs, are not in in line with the Directions 002/2018 where blood samples should be obtained on the day of collection, or if not possible within seven days post donation. | **Minor** |

| | | |
|---|---|---|
| b) The testing of donors by the establishment or a third party on behalf of the establishment is carried out in accordance with the requirements of Directions 002/2018. | The full range of mandatory tests is not carried out for the blood samples taken as part of the clinical trial (the HTLV-1 test is not performed). | **Minor** |
| GQ6 A coding and records system facilitates traceability of bodies, body parts, tissues and cells, ensuring a robust audit trail. | | |
| d) The requirements of the Single European Code are adhered to as set out in Directions 002/2018. | The labels used for the muscle biopsy collections as part of the clinical trial do not have the SEC-DI applied and therefore do not meet the coding requirements as set out in Directions 002/2018.<br>See *Advice*, item 12. | **Minor** |

### Advice

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

| No. | Standard | Advice |
|---|---|---|
| 1. | N/A | The DI is also advised to consider revoking the licence held under the HT Act from the establishment's portfolio of HTA licences as this licence is not being used. |
| 2. | N/A | The DI is advised to consider rationalising the number of PDs in relation to the different licensed activities taking place across the establishment as there is duplication and some of the registered PDs are no longer involved in such activities. |
| 3. | 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 serious adverse events and adverse reactions (SAEARs), can take place in the DI's absence.<br>See *Advice*, items 8 and 13. |
| 4. | C1(a) | The standard operating procedures (SOPs) for the seeking of consent from both autologous and allogeneic donors (SOP/GEN/001, SOPO/GEN/016) do not contain any information about the timing of the serological tests and the types of test, although this information is included in the consent forms. The DI is advised to consider updating the SOPs accordingly. |
| 5. | C1(d) | The SOP for disposal of cellular therapy products by the production and storage facility (SOP/CLIN/039) states that autologous and related donors are consented for the storage of products for a minimum of 5 years. However, this is not stated on the HSCT consent form. The DI is advised to ensure that this is in included on the form |

| | | |
|---|---|---|
| | | so that valid consent has been obtained for this procedure. |
| 6. | C1(d) | The DI is advised to ensure that sections of forms which are not applicable (e.g. the research section of the Trust consent form, which refers to samples taken for clinical use and then to be used for research if not clinically acceptable) are marked as 'N/A' and are not left blank. |
| 7. | C3(a) | 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. |
| 8. | GQ1(c) | Although regular meetings of the collection and transplant teams at take place at the satellite site, there have not been any quality governance meetings since September 2017.<br>The DI is advised to ensure that such meetings re-commence and 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).<br>The meetings should be governed by an agenda and minutes should be recorded and circulated. The minutes should include timelines for identified actions and the responsible person for each action.<br>The DI is advised to ensure that the PDs from the Department of Virology and the Colorectal Surgery Unit (once appointed) attend the meetings. The DI may also wish to consider including representatives from other departments (e.g. Clinical Governance, Information Technology) to help develop the establishment's working practices. |
| 9. | GQ1(c) | Joint governance meetings, involving DIs across the different sectors, are a feature of several other organisations holding multiple HTA licences.<br>The Trust is the CLH on three HTA licences and the University (Queen Mary University of London) is CLH on three additional HTA licences partly based within the Trust.<br>There are currently no meetings between DIs and individuals named on these licences.<br>The DI and CLHCs are advised to consider setting up joint governance meetings involving staff on all of these licences as an opportunity for shared learning. |
| 10. | GQ3(f) | The DI is advised to consider incorporating the relevant parts of the 'Guide to Quality and Safety Assurance of Human Tissues and Cells for Patient Treatment' in its regulatory training programme for new staff and as part of refresher training. |
| 11. | GQ5(a) | The DI is advised to consider adding a risk assessment of HEV transmission to the SOP on donor selection. |
| 12. | GQ6(d) | The DI is advised to refer to the 'HTA guidance on coding and import regulations for tissues and cells in the human application sector' for the different SEC requirements to assist in producing a label which conforms to requirements. |

| | | |
|---|---|---|
| 13. | GQ7(a) | The establishment has two separate SOPs relating to adverse events: (i) 'Clinical incident reporting' (SOP/QM/004) and (ii) 'Critical incident and emergency plan' (SOP/SO86), both of which give the timeline for reporting SAEARs to the HTA.<br><br>The DI is advised to consider creating a stand-alone SOP for the identification and reporting of SAEARs. The SOP should additionally contain:<br><br>• The types of incidents which are classified as SAEARs (not 'HTA reportable incidents', as erroneously indicated in the current SOPs).<br><br>• The personnel who should report SAEARs in the DI's absence.<br><br>• The requirement to submit a follow-up report to the HTA within 90 days.<br><br>• References to the Q&S Regulations (as emended) (not the HT Act, as erroneously indicated).<br><br>The DI is advised to ensure that all staff working under the licence are familiar with this SOP, including the relevant staff in the Department of Virology and Colorectal Surgery Unit. |
| 14. | GQ8(a) | The DI is advised to consider adding the following to the suite of apheresis risk assessments: cell collection when multiple donors are present; product labelling and; packaging and transport. |
| 15. | PFE2(c) | The DI is advised to consider updating the apheresis machine cleaning log to record the working practice of both pre- and post-collection cleaning, and to update the SOP accordingly. |
| 16. | PFE3(a) | The DI is advised to consider aligning the temperature probes in the separate store rooms so that both probes have the facility to download temperature data. |

## Concluding comments

During the inspection, an area of strength was noted:

- There is a good working relationship, and a comprehensive and effective system of communication, between the staff.

There are a number of areas of practice that require improvement, including five minor shortfalls. The HTA has given advice to the DI with respect to the Consent, Governance and Quality, and Premises, Facilities and Equipment standards, as well as advice on 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: 16 January 2019**

**Report returned from DI: 4 February 2019**

**Final report issued: 18 February 2019**

## Completion of corrective and preventative actions (CAPA) plan

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

**Date: 31 March 2020**

## Appendix 1: HTA standards

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

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

**Consent**

| **Standard** |
|---|
| C1 Consent is obtained in accordance with the requirements of the HT Act 2004, the Human Tissue (Quality and Safety for Human Application) Regulations 2007 and as set out in the HTA's Codes of Practice. |
| 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 002/2018 is included. |
| c) Information is available in suitable formats and there is access to independent interpreters when required. |
| d) There are procedures to ensure that information is provided to the donor or donor's family by trained personnel. |
| C3 Staff involved in seeking consent receive training and support in the implications and essential requirements of taking consent. |
| a) Staff involved in obtaining consent are provided with training on how to take informed consent in accordance with the requirements of the HT Act 2004 and Code of Practice on Consent. |
| b) Training records are kept demonstrating attendance at training on consent. |

**Governance and Quality**

| **Standard** |
|---|
| GQ1 All aspects of the establishment's work are supported by ratified documented policies and procedures as part of the overall governance process. |
| a) There is an organisational chart clearly defining the lines of accountability and reporting relationships. |
| b) There are procedures for all licensable activities that ensure integrity of tissue and / or cells and |

| |
|---|
| minimise the risk of contamination. |
| c) There are regular governance meetings, for example health and safety, risk management and clinical governance committees, which are recorded by agendas and minutes. |
| d) There is a document control system to ensure that changes to documents are reviewed, approved, dated and documented by an authorised person and only current documents are in use. |
| e) There are procedures for tissue and / or cell procurement, which ensure the safety of living donors. |
| g) There are procedures to ensure that an authorised person verifies that tissues and / or cells received by the establishment meet required specifications. |
| h) There are procedures for the management and quarantine of non-conforming consignments or those with incomplete test results, to ensure no risk of cross contamination. |
| i) There are procedures to ensure tissues and / or cells are not released from quarantine until verification has been completed and recorded. |
| j) There are procedures detailing the critical materials and reagents used and where applicable, materials and reagents meet the standards laid down by the European directives on medical devices and in vitro diagnostic medical devices. |
| k) There is a procedure for handling returned products. |
| m) The criteria for allocating tissues and / or cells to patients and health care institutions are documented and made available to these parties on request. |
| o) There is a complaints system in place. |
| p) There are written agreements with third parties whenever an activity takes place that has the potential to influence the quality and safety of human tissues and / or cells. |
| q) There is a record of agreements established with third parties. |
| r) Third party agreements specify the responsibilities of the third party and meet the requirements set out in Directions 002/2018. |
| s) Third party agreements specify that the third party will inform the establishment in the event of a serious adverse reaction or event. |
| t) There are procedures for the re-provision of service in an emergency. |
| GQ2 There is a documented system of quality management and audit. |
| a) There is a quality management system which ensures continuous and systematic improvement. |
| b) There is an internal audit system for all licensable activities. |
| c) An audit is conducted in an independent manner at least every two years to verify compliance with protocols and HTA standards, and any findings and corrective actions are documented. |
| d) Processes affecting the quality and safety of tissues and / or cells are validated and undergo regular evaluation to ensure they continue to achieve the intended results. |

| |
|---|
| GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills. |
| a) There are clearly documented job descriptions for all staff. |
| b) There are orientation and induction programmes for new staff. |
| c) There are continuous professional development (CPD) plans for staff and attendance at training is recorded. |
| d) There is annual documented mandatory training (e.g. health and safety and fire). |
| e) Personnel are trained in all tasks relevant to their work and their competence is recorded. |
| f) There is a documented training programme that ensures that staff have adequate knowledge of the scientific and ethical principles relevant to their work, and the regulatory context. |
| g) There is a documented training programme that ensures that staff understand the organisational structure and the quality systems used within the establishment. |
| h) There is a system of staff appraisal. |
| i) Where appropriate, staff are registered with a professional or statutory body. |
| j) There are training and reference manuals available. |
| k) The establishment is sufficiently staffed to carry out its activities. |
| GQ4 There is a systematic and planned approach to the management of records. |
| a) There are procedures for the creation, identification, maintenance, access, amendment, retention and destruction of records. |
| b) There is a system for the regular audit of records and their content to check for completeness, legibility and accuracy and to resolve any discrepancies found. |
| c) Written records are legible and indelible. Records kept in other formats such as computerised records are stored on a validated system. |
| d) There is a system for back-up / recovery in the event of loss of computerised records. |
| e) The establishment keeps a register of the types and quantities of tissues and / or cells that are procured, tested, preserved, processed, stored and distributed or otherwise disposed of, and on the origin and destination of tissues and cells intended for human application. |
| f) There are procedures to ensure that donor documentation, as specified by Directions 002/2018, is collected and maintained. |
| g) There is a system to ensure records are secure and that donor confidentiality is maintained in accordance with Directions 002/2018. |
| h) Raw data which are critical to the safety and quality of tissues and cells are kept for 10 years after the use, expiry date or disposal of tissues and / or cells. |
| i) The minimum data to ensure traceability from donor to recipient as required by Directions 002/2018 are kept for 30 years after the use, expiry or disposal of tissues and / or cells. |

| |
|---|
| j) Records are kept of products and material coming into contact with the tissues and / or cells. |
| l) The establishment records the acceptance or rejection of tissue and / or cells that it receives and in the case of rejection why this rejection occurred. |
| m) In the event of termination of activities of the establishment a contingency plan to ensure records of traceability are maintained for 10 or 30 years as required. |
| GQ5 There are documented procedures for donor selection and exclusion, including donor criteria. |
| a) Donors are selected either by the establishment or the third party acting on its behalf in accordance with the criteria required by Directions 002/2018. |
| b) The testing of donors by the establishment or a third party on behalf of the establishment is carried out in accordance with the requirements of Directions 002/2018. |
| c) In cases other than autologous donors, donor selection is carried out by authorised personnel and signed and reviewed by a qualified health professional. |
| d) There is a system in place either at the establishment or at a third party acting on its behalf to record results of donor selection and associated tests. |
| e) Testing of donor samples is carried out using CE marked diagnostic tests. |
| f) Samples taken for donor testing are clearly labelled with the time and place the sample was taken and a unique donor identification code. |
| GQ6 A coding and records system facilitates traceability of tissues and / or cells, ensuring a robust audit trail. |
| a) There is a donor identification system which assigns a unique code to each donation and to each of the products associated with it. |
| b) An audit trail is maintained, which includes details of when the tissues and / or cells were acquired and from where, the uses to which the tissues and / or cells were put, when the tissues and / or cells were transferred elsewhere and to whom. |
| c) The establishment has procedures to ensure that tissues and / or cells imported, procured, processed, stored, distributed and exported are traceable from donor to recipient and vice versa. |
| d) The requirements of the Single European Code are adhered to as set out in Directions 002/2018. |
| GQ7 There are systems to ensure that all adverse events, reactions and/or incidents are investigated promptly. |
| a) There are procedures for the identification, reporting, investigation and recording of adverse events and reactions, including documentation of any corrective or preventative actions. |
| b) There is a system to receive and distribute national and local information (e.g. HTA regulatory alerts) and notify the HTA and other establishments as necessary of serious adverse events or reactions. |
| c) The responsibilities of personnel investigating adverse events and reactions are clearly defined. |
| d) There are procedures to identify and decide the fate of tissues and / or cells affected by an adverse event, reaction or deviation from the required quality and safety standards. |

| |
|---|
| 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. |
| b) There are procedures for the transport of tissues and / or cells which reflect identified risks associated with transport. |
| c) There is a system to ensure that traceability of tissues and / or cells is maintained during transport. |
| d) Records are kept of transportation and delivery. |

| |
|---|
| e) Tissues and / or cells are packaged and transported in a manner and under conditions that minimise the risk of contamination and ensure their safety and quality. |
| f) There are third party agreements with courier or transport companies to ensure that any specific transport conditions required are maintained. |
| g) Critical transport conditions required to maintain the properties of tissue and / or cells are defined and documented. |
| h) Packaging and containers used for transportation are validated to ensure they are fit for purpose. |
| i) Primary packaging containing tissues and / or cells is labelled with the information required by Directions. |
| j) Shipping packaging containing tissues and / or cells is labelled with the information required by Directions. |
| PFE5 Equipment is appropriate for use, maintained, quality assured, validated and where appropriate monitored. |
| a) Critical equipment and technical devices are identified, validated, regularly inspected and records are maintained. |
| b) Critical equipment is maintained and serviced in accordance with the manufacturer's instructions. |
| c) Equipment affecting critical processes and storage parameters is identified and monitored to detect malfunctions and defects and procedures are in place to take any corrective actions. |
| d) New and repaired equipment is validated before use and this is documented. |
| e) There are documented agreements with maintenance companies. |
| f) Cleaning, disinfection and sanitation of critical equipment is performed regularly and this is recorded. |
| g) Instruments and devices used for procurement are sterile, validated and regularly maintained. |
| h) Users have access to instructions for equipment and receive training in the use of equipment and maintenance where appropriate. |
| i) Staff are aware of how to report an equipment problem. |
| j) For each critical process, the materials, equipment and personnel are identified and documented. |
| k) There are contingency plans for equipment failure. |

**Disposal**

| **Standard** |
|---|
| D1 There is a clear and sensitive policy for disposing of tissues and / or cells. |
| a) The disposal policy complies with HTA's Codes of Practice. |
| b) The disposal procedure complies with Health and Safety recommendations. |
| c) There is a documented procedure on disposal which ensures that there is no cross contamination. |

| D2 The reasons for disposal and the methods used are carefully documented. |
| --- |
| a) There is a procedure for tracking the disposal of tissue and / or cells that details the method and reason for disposal. |
| b) Disposal arrangements reflect (where applicable) the consent given for disposal. |

**Human Tissue Act 2004 Standards**

| Consent standards |
| --- |
| **C1 Consent is obtained in accordance with the requirements of the Human Tissue Act 2004 (HT Act) and as set out in the code of practice** |
| a) Consent procedures are documented and these, along with any associated documents, comply with the HT Act and the HTA's Codes of Practice.<br>b) Consent forms are available to those using or releasing relevant material for a scheduled purpose.<br>c) Where applicable, there are agreements with other parties to ensure that consent is obtained in accordance with the requirements of the HT Act and the HTA's Codes of Practice.<br>d) Written information is provided to those from whom consent is sought, which reflects the requirements of the HT Act and the HTA's Codes of Practice.<br>e) Language translations are available when appropriate.<br>f) Information is available in formats appropriate to the situation. |
| **C2 Staff involved in seeking consent receive training and support in the essential requirements of taking consent** |
| a) There is suitable training and support of staff involved in seeking consent, which addresses the requirements of the HT Act and the HTA's Codes of Practice.<br>b) Records demonstrate up-to-date staff training.<br>c) Competency is assessed and maintained. |

| Governance and quality system standards |
| --- |
| **GQ1 All aspects of the establishments work are governed by documented policies and procedures as part of the overall governance process** |
| a) Ratified, documented and up-to-date policies and procedures are in place, covering all licensable activities.<br>b) There is a document control system.<br>c) There are change control mechanisms for the implementation of new operational procedures.<br>d) Matters relating to HTA-licensed activities are discussed at regular governance meetings, involving establishment staff.<br>e) There is a system for managing complaints. |
| **GQ2 There is a documented system of audit** |
| a) There is a documented schedule of audits covering licensable activities.<br>b) Audit findings include who is responsible for follow-up actions and the timeframes for completing these. |

| GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills |
|---|
| a) Qualifications of staff and all training are recorded, records showing attendance at training. |
| b) There are documented induction training programmes for new staff. |
| c) Training provisions include those for visiting staff. |
| d) Staff have appraisals and personal development plans. |
| **GQ4 There is a systematic and planned approach to the management of records** |
| a) There are suitable systems for the creation, review, amendment, retention and destruction of records. |
| b) There are provisions for back-up / recovery in the event of loss of records. |
| c) Systems ensure data protection, confidentiality and public disclosure (whistleblowing). |
| **GQ5 There are systems to ensure that all adverse events are investigated promptly** |
| a) Staff are instructed in how to use incident reporting systems. |
| b) Effective corrective and preventive actions are taken where necessary and improvements in practice are made. |
| **GQ6 Risk assessments of the establishment's practices and processes are completed regularly, recorded and monitored** |
| a) There are documented risk assessments for all practices and processes requiring compliance with the HT Act and the HTA's Codes of Practice. |
| b) Risk assessments are reviewed regularly. |
| c) Staff can access risk assessments and are made aware of risks during training. |

| Traceability standards |
|---|
| **T1 A coding and records system facilitates the traceability of bodies and human tissue, ensuring a robust audit trail** |
| a) There is an identification system which assigns a unique code to each donation and to each of the products associated with it. |
| b) A register of donated material, and the associated products where relevant, is maintained. |
| c) An audit trail is maintained, which includes details of: when and where the bodies or tissue were acquired and received; the consent obtained; all sample storage locations; the uses to which any material was put; when and where the material was transferred, and to whom. |
| d) A system is in place to ensure that traceability of relevant material is maintained during transport. |
| e) Records of transportation and delivery are kept. |
| f) Records of any agreements with courier or transport companies are kept. |
| g) Records of any agreements with recipients of relevant material are kept. |

| T2 Bodies and human tissue are disposed of in an appropriate manner |
| --- |
| a) Disposal is carried out in accordance with the HTA's Codes of Practice. |
| b) The date, reason for disposal and the method used are documented. |

| Premises, facilities and equipment standards |
| --- |
| **PFE1 The premises are secure and fit for purpose** |
| a) An assessment of the premises has been carried out to ensure that they are appropriate for the purpose. |
| b) Arrangements are in place to ensure that the premises are secure and confidentiality is maintained. |
| c) There are documented cleaning and decontamination procedures. |
| **PFE2 There are appropriate facilities for the storage of bodies and human tissue** |
| a) There is sufficient storage capacity. |
| b) Where relevant, storage arrangements ensure the dignity of the deceased. |
| c) Storage conditions are monitored, recorded and acted on when required. |
| d) There are documented contingency plans in place in case of failure in storage area. |
| **PFE3 Equipment is appropriate for use, maintained, validated and where appropriate monitored** |
| a) Equipment is subject to recommended calibration, validation, maintenance, monitoring, and records are kept. |
| b) Users have access to instructions for equipment and are aware of how to report an equipment problem. |
| c) Staff are provided with suitable personal protective equipment. |

## Appendix 2: Classification of the level of shortfall (HA)

Where the HTA determines that a licensing standard is not met, the improvements required will be stated and the level of the shortfall will be classified as 'Critical', 'Major' or 'Minor'. Where the HTA is not presented with evidence that an establishment meets the requirements of an expected standard, it works on the premise that a lack of evidence indicates a shortfall.

The action an establishment will be required to make following the identification of a shortfall is based on the HTA's assessment of risk of harm and/or a breach of the 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.