Site visit inspection report on compliance with HTA minimum standards

Queen Elizabeth Hospital Birmingham

HTA licensing number 11100

Licensed for the

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

7 and 8 December 2016

Summary of inspection findings

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

Although the HTA found that Queen Elizabeth Hospital Birmingham (the establishment) had met the majority of the HTA standards, seven minor shortfalls were found: one with regard to the Consent (C) standards, five with regard to the Governance and Quality Systems (GQS) standards and one with regard to the Disposal (D) standards. The minor shortfalls were in relation to: (i) the consent training process; (ii) a contingency plan for stored tissue and cells in the event of licence revocation; (iii) written agreements with third parties; (iv) an independent audit; (v) competence training; (vi) testing requirements for liver vessel donors; and (vii) records of disposal. Advice has been given relating to the C, GQS and Premises, Facilities and Equipment standards, as well as to licence management.

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.

'SLA' = Service level agreement; another establishment (licensed) carries out the activity on behalf of the establishment.

Tissue type	Procurement	Testing	Storage	Distribution
Bone			**E**	
DLI	**E**	**E**		
Keratinocytes	**E**	**E**		**SLA**
Liver vessels		**E**	**E**	**E**
Nerve grafts			**E**	
PBSC	**E**	**E**		
Tendons/ ligaments			**E**	
Whole skin	**E**	**E**	**E**	

DLI = cells for donor lymphocyte infusion.

PBSC = peripheral blood stem cells.

Background to the establishment and description of inspection activities undertaken

This report refers to the activities carried out by Queen Elizabeth Hospital Birmingham (the establishment). The establishment was issued an HTA licence in July 2006. This was the third HTA site visit inspection of the establishment at its current site since its relocation from Selly Oak Hospital, Birmingham (the last inspection was in April 2014). The current inspection was a routine one to assess whether the establishment is continuing to meet the HTA's standards.

Queen Elizabeth Hospital Birmingham is part of University Hospitals Birmingham NHS Foundation Trust (FT).

The establishment is licensed under the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (Q&S Regulations) for the procurement, testing, storage and distribution 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 relevant material for use for a scheduled purpose (see *Advice*, item 1). 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 as part of its ongoing accreditation in December 2012.

The DI is the Lead Biomedical Scientist for the Clinical Laboratory Services (CLS) Directorate. The Corporate LH (CLH) is University Hospitals Birmingham NHS FT and the CLH Contact (CLHC) is the Director of Operations in the Division containing CLS. There are five Persons Designated (PDs) on the licence: a Consultant Burns and Plastics Surgeon, the Liver Unit Theatre Team Leader, the Bone Marrow Transplant/Apheresis Team Leader, the Apheresis Charge Nurse and the Tissue Services Manager.

Licensed activities at the establishment relate to a wide range of tissue and cell types, as shown in the table above.

Whole Skin and Keratinocyte Cells

Skin tissue is used in both the autologous and allogeneic treatment of adult patients who have suffered major burns and/or scalds. In 2015, the establishment performed 305 skin allografts and eight autografts.

Keratinocyte expansion and advanced therapy medicinal product (ATMP) production for autologous treatment. In selected patients, keratinocyte cells derived from skin biopsies are expanded, cultured and processed into an ATMP, which is used in autologous treatment. A separate company manufactures the ATMP under the terms of a service level agreement (SLA).

For patients who have capacity to consent, donor selection and consent take place in the operating theatres (see shortfall against standard C3(b) and *Advice,* item 5). The establishment uses its own donor selection, donor information and consent forms, along with the Trust Consent Form A. For patients who do not have capacity, the consenting process takes place through a person with lasting power of attorney or through an Independent Mental Capacity Advocate. If neither of these is present, two separate consultants will act directly in the best interests of the patient by performing the procedure. In this case, donor selection, donor information and consent forms, along with the Trust Consent Form C, are completed by the consultants and the patient completes them retrospectively, when possible (see *Advice*, item 3).

Serology sampling and skin biopsy procurement occur in the operating theatres. The establishment makes up its own 'skin procurement pack'. Swabs of the wound and biopsy site, along with samples for mandatory serology testing, are sent to the Department of Clinical

Microbiology (see below). The skin biopsy is double-potted in validated, sterile containers and stored in the lockable 4ºC 'skin' refrigerator (in medication room 2 between Theatres 15 and 16) for up to four hours pending transport to the ATMP manufacturer. The manufacturer has an agreement with a courier company for transport of the biopsy.

The ATMP is returned usually after a period several weeks.

The skin refrigerator is labelled to indicate that it contains human tissue. It is linked to a continuous temperature-monitoring unit that feeds into a wireless callout system. Temperature excursions outside the set ranges trigger both audible alarms and the callout system but the system is not tested routinely (see *Advice*, item 19). The skin refrigerator is subject to an annual service and calibration under contract. A back-up refrigerator is available for contingency storage and emergency off-site storage has been arranged with a separate HTA-licensed establishment.

Occasionally, skin for ATMP manufacture is procured under the terms of an SLA at Birmingham Children's Hospital NHS FT and is transferred by courier to the establishment pending transport to the ATMP manufacturer.

Whole skin patches for autologous treatment. In a separate procedure, the establishment procures and stores skin tissue from patients for a period of up to two weeks in the skin refrigerator before use. The stored skin is used as an autologous treatment to assist the natural healing and repair process. Units pending mandatory serology test results are stored on a separate shelf in the refrigerator.

Whole skin for allogeneic treatment. The establishment stores packaged, cryopreserved split skin from cadaveric donors. The skin is purchased from a HTA-licensed supplier under the terms of an SLA. The supplier is responsible for donor selection, consent, procurement, serological testing and transportation.

The skin is received into the Tissue Services Department by authorised personnel. All allograft details are entered onto a requisitions and deliveries file and paper copies of dispatch sheets are kept separately. The details from the requisitions and deliveries file are transferred onto a Tissue Services database and an Excel spreadsheet, which are backed up as part of the Trust Information Teshnology (IT) system.

The skin is stored securely at -80ºC in a labelled, lockable 'tissue bank' freezer in medication room 2. Non-conforming units are stored on a separate shelf. The freezer is linked to the continuous temperature-monitoring unit. Arrangements are in place for service, calibration and contingency.

When required for engraftment, the units of skin are removed and taken to the operating theatres for thawing before use. The date of removal and patient number of the recipient are entered onto the Excel spreadsheet (see *Advice*, item 9).

Details of tissue disposed are entered into the Excel spreadsheet. Tissue disposal is by incineration and the tissue is bagged separately from other clinical waste, although the reason for disposal is not recorded (see shortfall against standard D2(a)).

Bone, Tendons/Ligaments and Nerve Allografts

The establishment also stores cryopreserved bone, tendons, ligaments and peripheral nerve from cadaveric donors. The tissue is purchased from two HTA-licensed suppliers as described above.

Bone, tendons and ligaments are used in adult hip replacement and hip revision procedures, as well as in knee revision and reconstructive foot and ankle surgery. Peripheral nerve allografts are used in the reconstruction of adult peripheral nerve discontinuities caused by traumatic injury or surgical intervention.

In 2015, the establishment performed one bone, 33 tendon/ligament and three peripheral nerve allografts.

The tissue is received into the Tissue Services Department by authorised personnel, who keep paper and electronic records as described above. Storage is at -80ºC in a freezer in either the Clinical Room of the Burns Centre or in medication room 2. The freezer is linked to the continuous temperature-monitoring unit.

When required for engraftment, the tissue is removed and taken to the operating theatres as described above.

Demineralised Bone Matrix

The establishment purchases demineralised bone matrix from two HTA-licensed suppliers. A comprehensive log is maintained of the quantities, batch numbers and expiry dates of the packs received and used. The material is stored securely at room temperature but the temperature is not monitored (see *Advice*, item 17).

Liver Vessels

The establishment receives and stores liver vessels retrieved during the organ retrieval process. The organ and associated vessels (mainly iliac arteries and veins) are retrieved within the Trust, or at other hospitals as part of the National Organ Retrieval Service (NORS). The Trust holds an organ donation and transplant (ODT) licence (HTA licensing number 40042) for organ retrieval and transplant.

The liver vessels may be used at the time of organ transplant or during an additional revision procedure following transplant. Liver vessels stored for more than 48 hours for use in a patient other than the primary recipient are subject to the Q&S Regulations and fall under the current licence. The establishment stores liver vessels for up to 14 days pending use in a different recipient and occasionally distributes vessels to other HTA-licensed ODT organisations for transplant. There are no agreements with such organisations (see shortfall against standard GQ1(p)).

In 2015, the establishment received 420 units of liver vessels; 30 of these were used in transplants and 30 units were distributed to other HTA-licensed ODT organisations.

Serological testing of cadaveric donors is carried out under the Quality and Safety of Organs Intended for Transplantation Regulations 2012 and test results are uploaded onto the NHS Blood and Transplant Electronic Offering System (EOS) so that they can be reviewed by the transplanting establishment. For vessels stored under the Q&S Regulations, a serology test for mandatory serological markers in accordance with the requirements of the Q&S Regulations must be performed. Liver vessel donor blood samples for mandatory testing are sent to the Trust's Department of Clinical Microbiology (see below).

The liver vessels are received into the Transplant Room in vessel storage solution in validated, sterile containers by authorised personnel, who keep paper and electronic records as described above. A sample of vessel storage solution is sent to the Department of Clinical Microbiology for microbiological analysis when the vessels are used.

The liver vessels are stored securely in a labelled, lockable refrigerator within a defined area in the Transplant Room. Non-conforming units and those pending mandatory serology test results are stored on a separate shelf. The refrigerator is linked to the continuous temperature-monitoring unit. Arrangements are in place for service, calibration and contingency.

When required for transplant after storage, the liver vessels are removed and taken to the operating theatres as described above.

Liver vessels for distribution are packaged pending transport by courier.

Peripheral Blood Stem Cells (PBSC) and Cells for Donor Lymphocyte Infusion (DLI)

The establishment provides an adult stem cell collection and allogeneic and autologous stem cell transplantation service for patients.

In 2015, the establishment performed 195 autologous PBSC collections, along with 30 allogeneic (directed related) PBSC collections and five allogeneic collections of cells for DLI.

In 2015, the establishment performed 70 allogeneic and 100 autologous PBSC transplants. Allogeneic transplants include those from directed, related donations within the hospital and those from tissue-typed ('matched') unrelated donations managed by the Anthony Nolan and NHS Stem Cell Registry under the terms of an SLA. There are occasional umbilical cord blood transplants using donations managed by this registry.

Collection takes place in the Department of Haematology and Oncology and processing, cryopreservation and storage are carried out at a separate HTA-licensed establishment ('processing centre') under the terms of an SLA.

Donor selection (medical assessment) and consent for PBSC and DLI collections, as well as for mandatory serology tests, take place within the Department. Patients are consented by consultants or apheresis staff (see shortfall against standard C3(b) and *Advice,* item 5). In the case of directed, related donations, medical assessments are conducted by an independent qualified medical practitioner. A single consent form is used, which records consent for cell mobilisation, collection, processing, testing and storage.

Duplicate samples for mandatory serology testing are taken up to 30 days prior to cell collection and on the day of collection. Samples are tested separately by the Department of Clinical Microbiology and the processing centre.

The apheresis unit contains four apheresis machines. Following collection, cells are packaged and transported to the processing centre using validated procedures. Transplant products are returned by processing centre staff using similar validated procedures. Reagents and consumables for apheresis are stored in a secure, temperature-monitored storage area.

The processing centre performs total nucleated cell count, immunophenotype, cell viability and biological function assays for all collections, as well as human leukocyte antigen tissue typing and sterility analysis. Haematocrit levels, blood group and chimerism analysis are performed in the Department of Laboratory Haematology within CLS.

Tests on pre-apheresis, pre-processed and pre-cryopreserved product are performed, as appropriate, as well as tests on the product prior to transplant. The establishment has acceptance and release criteria for cell transplant based on the above set of markers. Products with minimal cell counts are disposed of by the processing centre.

Testing

The Department of Clinical Microbiology within the establishment is 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, HIV-1 and 2, HBsAg, HBc, 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.

Samples intended for certain serological tests (e.g. HTLV-1) are kept in a refrigerator for several days prior to analysis. The temperature of this refrigerator is monitored manually during the working week but not at weekends (see *Advice*, item 18).

The Department performs liver vessel donor testing for vessels stored under the Q&S Regulations. A proportion of donor samples are supplied to the Department in EDTA tubes. The Department does not have validated tests for these samples (see shortfall against standard GQ5(b)).

The Inspection Process

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 site [Burns Centre, Transplant Room (Shared Retrieval Room), operating theatre complex, Department of Clinical Microbiology, Department of Haematology and Oncology]. Discussions and interviews were held with key staff and documentation was reviewed. Interviews were held with the DI, the CLHC, all five PDs, the Clinical Haematology Quality Manager and the Department of Clinical Microbiology Laboratory Manager.

Audits of traceability were carried out:

Whole Skin and Keratinocyte Cells. Consent documentation, results of serological and microbiological analysis and engraftment documentation for one procured skin biopsy were reviewed in the paper and electronic records, and clinical notes. There were no discrepancies noted.

Two units of skin were selected at random from the freezer and labelling details were compared to the records in the tissue register, on the dispatch sheets and on the electronic spreadsheet. There were no discrepancies noted.

Four sets of clinical notes for patients who had received allograft skin were reviewed and the labelling details of the units of skin in the notes were compared to the records in the tissue register and on the electronic spreadsheet. There were no discrepancies noted.

Tendons. Three units of tendon were selected at random from the freezer and labelling details were compared to the records in the tissue register, on the dispatch sheets and on the electronic spreadsheet. There were no discrepancies noted.

Liver Vessels. Six sets of liver vessels were selected at random from the refrigerator and labelling details were compared to the records in the tissue register and on the electronic spreadsheet. Consent documentation and results of serological and microbiological analysis were also reviewed. There were no discrepancies noted.

The electronic and paper records of four sets of liver vessels retrieved during the organ retrieval process, stored and then allocated for use in patients were reviewed (two from the Trust, two from other hospitals). The records included consent documentation and results of serological and microbiological analysis. There were no discrepancies noted.

PBSCs. The electronic and paper records of six PBSC donations were reviewed (four autologous, two directed, related donations) along with the corresponding transplants. The records included: medical assessment and donor/recipient consent forms, apheresis care plans, processing worksheets and results of serological and microbiological analysis. There were no discrepancies noted.

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

Consent

Standard	Inspection findings	Level of shortfall
C3 Staff involved in seeking consent receive training and support in the implications and essential requirements of taking consent.		
b) Training records are kept demonstrating attendance at training on consent.	All relevant staff have been trained in how to take informed consent for tissue/cell procurement and serological testing. However, the documentation recording the attendance at training, and refresher training, is incomplete.	**Minor**

Governance and Quality

Standard	Inspection findings	Level of shortfall
GQ1 All aspects of the establishment's work are supported by ratified documented policies and procedures as part of the overall governance process.		
l) There are procedures to ensure that in the event of termination of activities for whatever reason, stored tissues and / or cells are transferred to another licensed establishment or establishments.	The DI has discussed contingency plans for the termination of activities with other licensed establishments but no final plan and agreement is in place. See *Advice*, item 12.	**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.	There are no agreements with any of the organisations receiving liver vessels for end use. See *Advice*, item 7.	**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**
GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills.		
e) Personnel are trained in all tasks relevant to their work and their competence is recorded.	During the inspection, it was noted that staff other than authorised personnel were removing stored allografts from the freezers for end use. See *Advice*, item 8.	**Minor**
GQ5 There are documented procedures for donor selection and exclusion, including donor criteria.		
b) The testing of donors by the establishment or a third party on behalf of the establishment is carried out in accordance with the requirements of Directions 003/2010.	Where liver vessels are being stored under the Q&S Regulations, donor blood samples for mandatory testing must be tested in a HTA-licensed testing laboratory. The establishment's Department of Clinical Microbiology is the HTA-licensed testing laboratory. A proportion of liver vessel donor blood samples are received into the Department from retrieval centres in EDTA tubes. The Department does not have validated tests for these samples. As a result, the establishment relies on the EOS data alone to provide serology results. It is unclear if all the laboratories associated with retrieval centres providing EOS data to the establishment are licensed by the HTA for testing.	**Minor**

Disposal

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.	The establishment records the date and method of disposal of each tissue and cellular sample but not the reason.	**Minor**

Advice

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

No.	Standard	Advice
1.	N/A	The DI is advised to consider revoking the establishment's licence held under the HT Act from its portfolio of HTA licences as this licence is not being used.
2.	N/A	The DI is advised to consider appointing a PD in the Department of Clinical Microbiology and to notify the HTA of such an appointment. Appointing such a PD 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.
3.	C1(a), (e), GQ2(b)	The establishment has recently conducted an internal self-assessment against HTA standards. This identified discrepancies in the consenting process for two Burns Centre patients who did not have capacity, where consent forms were incorrectly completed. The DI is advised to consider including an audit of consent forms in the audit schedule.
4.	C1(c), GQ1(b), GQ2(a), (b)	The licence covers a wide range of tissue types over different clinical areas. Although there is progress in unifying governance procedures, duplications and inconsistencies in documentation still exist. The DI is advised to consider including in the schedule an audit of the establishment's policies and standard operating procedures (SOPs) to identify duplication and repetition and to inform the development of concise documents.
5.	C3(a)	There are inconsistencies in the consent training requirements for Burns Centre and Haematology Consultants. Burns Centre Consultants are required to attend a Trust Consent Training Session whereas this is not mandatory for Haematology Consultants. The DI is advised to ensure that consent training is uniform across all departments.
6.	GQ1(c)	Several meetings were set up by the previous DI; these included meetings of the HTA Governance Committee, the Cellular Pathology Quality Management Committee and individual meetings with other PDs. It is important that such governance meetings continue, under the chair of the new DI, where appropriate. Additional attendees may include: members of the Haematology and Oncology Stem Cell Transplantation Quality Management Committee, staff from the Department of Clinical Microbiology, and Clinical Governance and IT staff. Attendance of such staff would help develop the establishment's working practices.
7.	GQ1(p)	The DI is advised to ensure that agreements with organisations receiving liver vessels for end use include: • Responsibilities for SAEARs reporting between the organisations. • Maintenance of traceability during transport and confirmation of receipt.

		• Validation of transport conditions. • Responsibilities to store traceability data relating to the vessels and their use for 30 years and raw data for 10 years.
8.	GQ3(e)	The DI is advised to consider formalising a competence training process for all staff receiving and removing allograft tissue. This could be of the form of a three-stage process where: the trainee observes the trainer carrying out the activity, the trainer observes the trainee and the trainee performs the activity alone.
9.	GQ4(e)	The DI is advised consider using a two-person checking system to cover allograft placement into storage, retrieval from storage and confirmation of identity prior to thawing.
10.	GQ4(e)	The DI is advised to consider adding the following to the allograft tissue database and electronic spreadsheet: • The time from release by the supplier to deposit in the freezer. • The expiry date and shelf location of the allograft. • The time of removal of the allograft.
11.	GQ4(i)	For allograft recipients, the DI is advised to consider highlighting that the patient file needs to be retained for 30 years from the date of tissue engraftment.
12.	GQ4(m)	As part of the contingency plan for termination, the DI is advised to be aware of the arrangements for contingency storage of records of traceability (for 30 years) and raw data (10 years). The records need to be labelled appropriately and stored in the Trust archives.
13.	GQ5(a)	The DI is advised to consider adding more detail to the SOP on donor selection (medical assessment) under the section that covers recent travel abroad. The SOP 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.
14.	GQ7(a), (b)	The DI is advised to consider creating a single SOP to cover the reporting of SAEARs alone. The current document covers both SAEARs and the reporting of incidents in the Post Mortem sector.
15.	PFE1(a)	The DI is advised to consider collating the risk assessments for the separate areas where licensed activities take place to provide an overall risk assessment of the premises.
16.	PFE3(b)	The DI is advised to consider hard-wiring refrigerators and freezers into the Trust power supply to prevent accidental disconnection of the plug from the socket.
17.	PFE3(c)	The DI is advised to consider monitoring the storage temperature of the demineralised bone matrix on a regular basis.
18.	PFE3(c)	The DI is advised to consider risk assessing the storage of serology samples in the Clinical Microbiology refrigerator to ensure that recommended

		temperature ranges are not exceeded.
19.	PFE3(c)	The DI is advised to consider carrying out regular testing of the continuous temperature-monitoring system to ensure that the callout procedure is functioning correctly.
20.	PFE3(c)	The DI is advised to consider initiating a programme by which, at suitable timeframes, the temperature plots from the monitoring system are reviewed. This may help to identify a potential failure of the system before it occurs.

Concluding comments

During the inspection, areas of good practice were noted:

- There is a wide range of comprehensive governance processes, including SOPs, meetings and risk assessments, which have been set up by the previous DI and which are now being taken over by the current DI.
- The establishment makes widespread use of the document management system in all relevant departments to ensure consistency. This covers: SOPs and document control, audit schedules and audit findings ('non-conformances'), adverse events ('error logs'), risk assessments and 'asset lists' (maintenance contracts and maintenance visits).
- Audit findings and root causes/corrective and preventative actions related to adverse events are discussed regularly at governance meetings.
- Staff from the Haematology and Oncology Department regularly attend the annual meeting of the 'Stem Cell User Group', held by the processing centre.

There are a number of areas of practice that require improvement, including seven 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 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: 7 March 2017

Report returned from DI: 25 April 2017

Final report issued: 25 January 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
b) If there is a third party procuring tissues and / or cells on behalf of the establishment the third party agreement ensures that consent is obtained in accordance with the requirements of the HT Act 2004, the Q&S Regulations and the HTA's Codes of Practice.
c) The establishment or the third party's procedure on obtaining donor consent includes how potential donors are identified and who is able to take consent.
d) Consent forms comply with the HTA Codes of Practice.
e) Completed consent forms are included in records and are made accessible to those using or releasing tissue and / or cells for a Scheduled Purpose.
C2 Information about the consent process is provided and in a variety of formats.
a) The procedure on obtaining consent details what information will be provided to donors. As a minimum, the information specified by Directions 003/2010 is included.
b) If third parties act as procurers of tissues and / or cells, the third party agreement details what information will be provided to donors. As a minimum, the information specified by Directions 003/2010 is included.
c) Information is available in suitable formats and there is access to independent interpreters when required.
d) There are procedures to ensure that information is provided to the donor or donor's family by trained personnel.
C3 Staff involved in seeking consent receive training and support in the implications and essential requirements of taking consent.
a) Staff involved in obtaining consent are provided with training on how to take informed consent in accordance with the requirements of the HT Act 2004 and Code of Practice on Consent.
b) Training records are kept demonstrating attendance at training on consent.

Governance and Quality

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

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

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

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

Premises, Facilities and Equipment

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

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

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