



Site visit inspection report on compliance with HTA minimum standards

Southampton General Hospital Wessex Blood and Marrow Transplantation Unit

HTA licensing number 22526

Licensed for the

- **procurement and testing of human tissues and cells for human application under the Human Tissue (Quality and Safety for Human Application) Regulations 2007**

25 May 2016

Summary of inspection findings

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

The Wessex Blood and Marrow Transplant Unit, Southampton General Hospital (the establishment) was found to have met all HTA standards.

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

The HTA's regulatory requirements

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

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

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

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

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

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

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

Licensable activities carried out by the establishment

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

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

'SLA' = Service Level Agreement; another licensed establishment carries out this activity

Tissue type	Procurement	Processing	Testing	Storage	Distribution	Import	Export
PBSC	E	SLA	TPA	SLA	SLA		
Bone Marrow	E	SLA	TPA	SLA	SLA		

Background to the establishment and description of inspection activities undertaken

The Wessex Blood and Marrow Transplant Unit at Southampton General Hospital is licensed by the HTA for procurement of peripheral blood stem cells (PBSCs) and bone marrow, and donor testing from donors over 17 years of age. The corporate licence holder is the University Hospital Southampton NHS Foundation Trust and the corporate licence holder contact is the Medical Director of the Trust. The stem cell transplant programme has been accredited by JACIE (Joint Accreditation Committee ISCT; International Society for Cellular Therapy and EMBT; European Society for Blood and Marrow Transplantation) for collection of PBSCs from adult donors for autologous and allogeneic use, and treatment of recipients since 2008.

All activities relating to the transplant programme (other than procurement of bone marrow) take place on Ward C7. The ward has consultation rooms, isolation areas, recovery rooms and day rooms. Transplant co-ordinators are responsible for liaising with referring hospitals, scheduling appointments with donors and accompany the donor when consent is sought. The DI who is the Medical Director of the Collection Facility, provides information and seeks consent from autologous donors; the Associate Specialist Consultant seeks consent and undertakes donor evaluation of sibling and related donors. Consent discussions cover risks

relating to the procurement of stem cells and in the case of autologous donors, reinfusion of stem cells and loss of fertility following myoablative chemotherapy. Consent is sought for donor testing, storage of stem cells and research; donors are informed that cells will be stored for five years. Transplant co-ordinators support donors during stem cell mobilisation and donors are monitored to ensure that the target CD34 counts are reached before they are scheduled for apheresis.

Blood samples for donor testing are taken within 30 days before procurement of stem cells and sent to the testing laboratory in the Hospital. The testing laboratory works under a Third party agreement (TPA) and holds Clinical Pathology Accreditation (CPA).

The unit has three apheresis machines; apheresis kits and kits for bone marrow procurement are stored in a dedicated storage area. Acid Citrate Dextrose Solution A is stored in a fridge which is temperature controlled and monitored. Monthly checks are undertaken to ensure that sufficient stock is available and that consumables are within date. Trained staff are responsible for procurement and set up and monitor apheresis machines. Bone marrow harvests take place infrequently; the most recent harvest took place in October 2014. This inspection did not cover the premises where bone marrow procurement takes place.

The Hospital has a service level agreement (SLA) with another HTA licensed establishment located within the Hospital grounds which is responsible for transporting, processing, cryopreserving and storing stem cells for human application. That establishment also provides the Information Standard for Blood and Transplant (ISBT) 128 labels used to label bags containing PBSCs. Staff from the establishment which processes stem cells attend the ward and transports the cells for processing and storage.

The establishment also participates in a multicentre randomised phase II study to evaluate the impact of infusing CD4 lymphocytes on the recovery of the recipient's immune system. Donors (an HLA identical sibling donor) donate lymphocytes three to four months after the recipient received stem cells from the same donor. Clinicians seek consent from donors and procurement takes place at this establishment; all other activities relating to this study including processing and transportation of CD4 lymphocytes takes place at another HTA licensed establishment.

This is the fourth routine inspection of the establishment and included a visual inspection of the premises, discussions with the DI, the Associate Specialist Consultant, Lead Nurse Apheresis team, Lead Nurse for blood and marrow transplantation, Transplant co-ordinators and trainee apheresis nurses.

A document review was carried out. Documents reviewed included: the Quality Management Plan document, standard operating procedures (SOPs) and policies which cover licensable activities. Training records, meeting minutes, donor test records on the hospital electronic records system, equipment maintenance records, agreements with third parties, risk assessments, audit schedule and report of an audit of compliance with HTA standards undertaken by the DI of another HTA licensed facility were also reviewed. Reports of near misses and incidents and the investigation into these incidents, corrective and preventative actions taken and closure of these incidents were also reviewed.

An audit trail of four stem cell harvests – two autologous PBSC procurements, an allogeneic PBSC procurement and a bone marrow harvest and subsequent re-infusion were carried out. The audit covered the consent forms, consent forms for donor virology testing, storage and discard of stem cells, harvest report, report of donation and processing which accompany frozen stem cells for re-infusion. The hospital uses name, date of birth and hospital number as well as a unique ISBT number for traceability. There were no discrepancies.

Inspection findings

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

Compliance with HTA standards

All applicable HTA standards have been assessed as fully met.

Advice

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

No.	Standard	Advice
1.	GQ1	<p>During the inspection, the inspection team was informed that there are plans to merge two HTA licences currently held by Southampton General Hospital which cover apheresis and bone marrow procurement and testing activities relating to paediatric and adult donors/patients. The DI is advised to inform the HTA once the plan is finalised.</p> <p>The SLA between the establishment and the HTA licensed establishment responsible for selection and transportation of CD4 lymphocytes used in the multicentre randomised phase II study is out of date. The DI is advised to update the SLA in order to ensure that the next procurement is carried out under a valid legal agreement.</p>
2.	GQ3e	<p>Some members of staff who undertake apheresis completed their training several years ago. The DI is advised to consider arranging for the apheresis equipment manufacturer to provide refresher training in order to ensure that staff are aware of new software and other developments relating to apheresis equipment.</p> <p>The DI is advised to consider arranging for staff involved in bone marrow procurements to attend other centres where procurement takes place in order to maintain competency and exchange ideas on best practice.</p>
3.	GQ7	<p>The incident and near miss event policy (GP-2 version 2.3) describes the procedure for reporting incidents within the Trust and to the HTA. The DI is advised to consider including the definition of HTA reportable serious adverse events and serious adverse reactions within this policy. The HTA definition of reportable incidents differs from the types of incidents which should be reported to the Trust incident management system.</p>

4.	GQ8a	The DI is advised to risk assess the bone marrow procurement procedure in order to identify risks relating to the availability of trained competent staff, availability of theatres and transporting bone marrow harvests to the HTA licensed establishment which processes bone marrow, so that appropriate action can be taken to minimise identified risks.
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Concluding comments

There were several areas of good practice. The programme is well supported by senior management. There are effective systems of communication between staff who work in the transplant programme, key members of staff at the establishment where processing and storage takes place, and staff based in the donor testing laboratory. Professionals, including oncologists, haematologists, paediatricians, Clinical Nurse Specialists, Lead Nurse (Blood and Marrow Transplantation), apheresis nurses, transplant co-ordinators and laboratory staff attend regular scheduled meetings which cover quality management, planning and operational issues and patient outcomes. Each year the establishment organises a haematopoietic transplantation educational forum for clinicians and other professionals based in the Wessex region, who refer patients to the hospital.

Quality indicators for the collection of stem cells and the effectiveness of the clinical programme such as engraftment data are reviewed during regular meetings. There are regular infection control audits; the temperature of the room where apheresis takes place is monitored and recorded. There are effective systems in place to manage incidents and near misses.

The unit implemented a new electronic database to help with management and scheduling of donors and maintaining donor records. There are additional resources and systems in place for on-going auditing of information recorded in the electronic database in order to ensure accuracy of records.

The HTA has given advice to the Designated Individual with respect to updating an SLA, risk assessing bone marrow procurement as this activity is being undertaken infrequently, and updating the incident and near miss reporting policy.

The HTA has assessed the establishment as suitable to be licensed for the activities specified.

Report sent to DI for factual accuracy: 20 June 2016

Report returned from DI: 28 June 2016

Final report issued: 12 July 2016

Appendix 1: HTA standards

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

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

Consent

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

Governance and Quality

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

b) There are procedures for all licensable activities that ensure integrity of tissue and / or cells and minimise the risk of contamination.
c) There are regular governance meetings, for example health and safety, risk management and clinical governance committees, which are recorded by agendas and minutes.
d) There is a document control system to ensure that changes to documents are reviewed, approved, dated and documented by an authorised person and only current documents are in use.
e) There are procedures for tissue and / or cell procurement, which ensure the safety of living donors.
g) There are procedures to ensure that an authorised person verifies that tissues and / or cells received by the establishment meet required specifications.
j) There are procedures detailing the critical materials and reagents used and where applicable, materials and reagents meet the standards laid down by the European directives on medical devices and in vitro diagnostic medical devices.
m) The criteria for allocating tissues and / or cells to patients and health care institutions are documented and made available to these parties on request.
o) There is a complaints system in place.
p) There are written agreements with third parties whenever an activity takes place that has the potential to influence the quality and safety of human tissues and / or cells.
q) There is a record of agreements established with third parties.
r) Third party agreements specify the responsibilities of the third party and meet the requirements set out in Directions 003/2010.
s) Third party agreements specify that the third party will inform the establishment in the event of a serious adverse reaction or event.
t) There are procedures for the re-provision of service in an emergency.
GQ2 There is a documented system of quality management and audit.
a) There is a quality management system which ensures continuous and systematic improvement.
b) There is an internal audit system for all licensable activities.
c) An audit is conducted in an independent manner at least every two years to verify compliance with protocols and HTA standards, and any findings and corrective actions are documented.
d) Processes affecting the quality and safety of tissues and / or cells are validated and undergo regular evaluation to ensure they continue to achieve the intended results.
GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills.
a) There are clearly documented job descriptions for all staff.
b) There are orientation and induction programmes for new staff.
c) There are continuous professional development (CPD) plans for staff and attendance at training is recorded.

d) There is annual documented mandatory training (e.g. health and safety and fire).
e) Personnel are trained in all tasks relevant to their work and their competence is recorded.
f) There is a documented training programme that ensures that staff have adequate knowledge of the scientific and ethical principles relevant to their work, and the regulatory context.
g) There is a documented training programme that ensures that staff understand the organisational structure and the quality systems used within the establishment.
h) There is a system of staff appraisal.
i) Where appropriate, staff are registered with a professional or statutory body.
j) There are training and reference manuals available.
k) The establishment is sufficiently staffed to carry out its activities.
GQ4 There is a systematic and planned approach to the management of records.
a) There are procedures for the creation, identification, maintenance, access, amendment, retention and destruction of records.
b) There is a system for the regular audit of records and their content to check for completeness, legibility and accuracy and to resolve any discrepancies found.
c) Written records are legible and indelible. Records kept in other formats such as computerised records are stored on a validated system.
d) There is a system for back-up / recovery in the event of loss of computerised records.
e) The establishment keeps a register of the types and quantities of tissues and / or cells that are procured, tested, preserved, processed, stored and distributed or otherwise disposed of, and on the origin and destination of tissues and cells intended for human application.
f) There are procedures to ensure that donor documentation, as specified by Directions 003/2010, is collected and maintained.
g) There is a system to ensure records are secure and that donor confidentiality is maintained in accordance with Directions 003/2010.
h) Raw data which are critical to the safety and quality of tissues and cells are kept for 10 years after the use, expiry date or disposal of tissues and / or cells.
i) The minimum data to ensure traceability from donor to recipient as required by Directions 003/2010 are kept for 30 years after the use, expiry or disposal of tissues and / or cells.
j) Records are kept of products and material coming into contact with the tissues and / or cells.
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.
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.
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.
g) Critical transport conditions required to maintain the properties of tissue and / or cells are defined and documented.
i) Primary packaging containing tissues and / or cells is labelled with the information required by Directions.

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

Disposal

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

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

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

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

1. Critical shortfall:

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

Or

A number of 'major' shortfalls, none of which is critical on its own, but viewed cumulatively represent a systemic failure and therefore are considered 'critical'.

A critical shortfall may result in one or more of the following:

- (1) A notice of proposal being issued to revoke the licence
- (2) Some or all of the licensable activity at the establishment ceasing with immediate effect until a corrective action plan is developed, agreed by the HTA and implemented.
- (3) A notice of suspension of licensable activities
- (4) Additional conditions being proposed
- (5) Directions being issued requiring specific action to be taken straightaway

2. Major shortfall:

A non-critical shortfall.

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

or

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

or

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

or

A shortfall which indicates a 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 your proposed action plan you will be notified of the follow-up approach the HTA will take.