

Site visit inspection report on compliance with HTA licensing standards

Inspection date: 11-12 February 2020



Wessex Blood and Marrow Transplant Unit (Adult & Paediatric)

HTA licensing number 22526

Licensed under the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended)

Licensable activities carried out by the establishment

Licensed activities

'E' = Establishment is licensed to carry out this activity and is currently carrying it out.

Site	Procurement	Processing	Testing	Storage	Distribution	Import	Export
Wessex Blood and Marrow Transplant Unit	E		E				

Tissue types authorised for licensed activities

Authorised = Establishment is authorised to carry out this activity and is currently carrying it out.

Tissue Category; Tissue Type	Procurement	Processing	Testing	Storage	Distribution	Import	Export
Mature Cell, MNC; DLI	Authorised		Authorised				
Mature Cell, MNC; PBMC	Authorised		Authorised				

Progenitor Cell, Haematopoietic, Bone Marrow; Bone Marrow	Authorised		Authorised				
Progenitor Cell, Haematopoietic, PBSC; PBSC	Authorised		Authorised				

Summary of inspection findings

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

Although the HTA found that Wessex Blood and Marrow Transplant Unit (the establishment) had met the majority of the HTA's standards, five minor shortfalls were found against standards for Governance and Quality, and Premises, Facilities and Equipment. The shortfalls relate to the independent audit, donor exclusion criteria, the timing of blood sampling for donor serology testing, risk assessments, and temperature records.

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.

Compliance with HTA standards

Minor Shortfalls

Standard	Inspection findings	Level of shortfall
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.	Although an independent audit has been completed to verify compliance with protocols and HTA standards, not all applicable standards were included.	Minor
GQ5 There are documented procedures for donor selection and exclusion, including donor criteria.		
a) Donors are selected either by the establishment or the third party acting on its behalf in accordance with the criteria required by Directions 002/2018.	The establishment's donor medical assessment form does not include a question regarding transplantation with xenografts, as required by the donor exclusion criteria set out in Annex A of the Guide to Quality and Safety Assurance for Human Tissues and Cells for Patient Treatment.	Minor
b) The testing of donors by the establishment or a third party on behalf of the establishment is carried out in accordance with the requirements of Directions 002/2018.	During the inspection, procurement records for two donor lymphocyte infusions (DLIs), which were collected independently of any other cells, were reviewed. Patient blood samples for mandatory serology tests were not obtained within the required time frame for these DLI donors. Establishment staff indicated that previous DLI donors were also not tested according to requirements.	Minor

GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately.

a) There are documented risk assessments for all practices and processes.	The risk assessment for bone marrow harvesting does not assess the risks associated with the transport of bone marrow from theatres to the processing laboratory by establishment staff.	Minor
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PFE3 There are appropriate facilities for the storage of bodies, body parts, tissues, 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.	Daily temperature monitoring records held within different sections of the apheresis department were incomplete on multiple occasions.	Minor
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The HTA requires the DI to submit a completed corrective and preventative action (CAPA) plan setting out how the shortfalls will be addressed, 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.

Advice

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

Number	Standard	Advice
1.	GQ2b	The DI is advised to review the document used to audit the testing laboratory to ensure all applicable requirements of the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended), are considered.
2.	GQ4h	The DI is advised to review the agreement between the testing laboratory and the temperature monitoring service provider to ensure the requirements of the standard are met.
3.	GQ8d	The establishment has a documented risk assessment to decide the fate of any cells stored prior to the introduction of a new donor selection criterion. The DI is advised to consider including a reference to seeking advice from a professional advisory committee if this situation arises.
4.	PFE2c PFE5f	The DI is advised to ensure there are no blank spaces in documents used to record temperature and humidity data, as well as cleaning activities. Gaps should be struck through, and/or annotated with the reason for not recording a particular event.
5.	PFE5f	The DI is advised to review the form for recording monthly apheresis equipment cleaning to ensure the cleaning is undertaken at appropriate intervals.

Background

The establishment has been licensed by the HTA since October 2008, and is licensed for procurement and testing of DLIs, peripheral blood mononuclear cells (PBMC), bone marrow and peripheral blood stem cells (PBSC). This was the sixth site visit inspection of the establishment; the previous inspection took place in February 2018.

In May 2018, the HTA licence for the paediatric service was revoked and the licensable activities were incorporated into the HTA licence for the adult service. There were no significant changes to personnel, practices or premises.

Description of inspection activities undertaken

The HTA's regulatory requirements are set out in Appendix 1. The inspection team covered the following areas during the inspection:

Standards assessed against during inspection

Standards covered at this inspection are listed in Appendix 3. Any standards that were not applicable to the establishment have been deleted from this table. Any standards that were applicable, but were not covered during the inspection, have been highlighted in grey.

Review of governance documentation

The inspection included a review of policies and procedural documentation relevant to the establishment's licensable activities. The inspection also included a review of equipment service contracts and records of servicing, temperature monitoring records for consumables and reagents, and agreements. The review of information relating to the quality management system included meeting minutes, incidents, audits, risk assessments and staff training records.

Visual inspection

The inspection included a visual inspection of the apheresis collection facilities (adult and paediatric), areas used to store consumables and reagents, and the testing laboratory.

Audit of records

The procurement records were audited for the following donors:

- two DLI donors;
- a sibling bone marrow donor;
- two autologous paediatric PBSC donors; and
- two allogeneic PBSC donors.

The audit included a review of donor consent and medical assessment, the cell collection records and timing of blood sample collection for mandatory serology testing, and the testing results. The blood sample collection timings were correct for the bone marrow and PBSC donations; however, for the DLI donations which were collected independently of any other cells, the timing of the blood sample collection was incorrect. For one of the two DLI donations the apheresis work sheet was not signed by the member of staff responsible for the collection. This was not sufficient to amount to a shortfall but oral advice was given to the establishment at the time of the inspection.

Meetings with establishment staff

The inspection included discussions with the Collection Facility Medical Director (who is also the DI), the Quality Manager, the Associate Specialist in Blood & Marrow Transplantation, the Clinical Programme Medical Director, a Paediatric Consultant for the autologous transplant service, the Lead Apheresis Nurse, the Lead Nurse for BMT and Cellular Therapy, a Research Nurse, the BMT Data Manager, the Clinical Director for Virology and a Biomedical Scientist (BMS) from the testing laboratory.

Report sent to DI for factual accuracy: 09 March 2020

Report returned from DI: 10 March 2020

Final report issued: 24 March 2020

Appendix 1: The HTA's regulatory requirements

The HTA must assure itself that the DI, Licence Holder, 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 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.

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 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:

- A notice of proposal being issued to revoke the licence
- 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.
- A notice of suspension of licensable activities
- Additional conditions being proposed
- 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 the final inspection report. Establishments 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 routine site-visit inspection.

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

Appendix 3: HTA Standards

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

Consent
C1 Consent is obtained in accordance with the requirements of the HT Act 2004, the Human Tissue (Quality and Safety for Human Application) Regulations 2007 and as set out in the HTA's Codes of Practice.
a) If the establishment acts as a procurer of tissues and / or cells, there is an established process for acquiring donor consent which meets the requirements of the HT Act 2004 the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (Q&S Regulations) and the HTA's Codes of Practice
c) The establishment or the third party's procedure on obtaining donor consent includes how potential donors are identified and who is able to take consent.
d) Consent forms comply with the HTA Codes of Practice.
e) Completed consent forms are included in records and are made accessible to those using or releasing tissue and / or cells for a Scheduled Purpose.
C2 Information about the consent process is provided and in a variety of formats.
a) The procedure on obtaining consent details what information will be provided to donors. As a minimum, the information specified by Directions 002/2018 is included.
c) Information is available in suitable formats and there is access to independent interpreters when required.
d) There are procedures to ensure that information is provided to the donor or donor's family by trained personnel.
C3 Staff involved in seeking consent receive training and support in the implications and essential requirements of taking consent.
a) Staff involved in obtaining consent are provided with training on how to take informed consent in accordance with the requirements of the HT Act 2004 and Code of Practice on Consent.

b) Training records are kept demonstrating attendance at training on consent.

Governance and Quality

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.

l) There are procedures to ensure that in the event of termination of activities for whatever reason, stored tissues and / or cells are transferred to another licensed establishment or establishments.

m) The criteria for allocating tissues and / or cells to patients and health care institutions are documented and made available to these parties on request.

o) There is a complaints system in place.

p) There are written agreements with third parties whenever an activity takes place that has the potential to influence the quality and safety of human tissues and / or cells.

q) There is a record of agreements established with third parties.

r) Third party agreements specify the responsibilities of the third party and meet the requirements set out in Directions 002/2018.

s) Third party agreements specify that the third party will inform the establishment in the event of a serious adverse reaction or event.

t) There are procedures for the re-provision of service in an emergency.

GQ2 There is a documented system of quality management and audit.

a) There is a quality management system which ensures continuous and systematic improvement.

b) There is an internal audit system for all licensable activities.

c) An audit is conducted in an independent manner at least every two years to verify compliance with protocols and HTA standards, and any findings and corrective actions are documented.

d) Processes affecting the quality and safety of tissues and / or cells are validated and undergo regular evaluation to ensure they continue to achieve the intended results.

GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills.

a) There are clearly documented job descriptions for all staff.

b) There are orientation and induction programmes for new staff.

c) There are continuous professional development (CPD) plans for staff and attendance at training is recorded.

d) There is annual documented mandatory training (e.g. health and safety and fire).

e) Personnel are trained in all tasks relevant to their work and their competence is recorded.

f) There is a documented training programme that ensures that staff have adequate knowledge of the scientific and ethical principles relevant to their work, and the regulatory context.

g) There is a documented training programme that ensures that staff understand the organisational structure and the quality systems used within the establishment.

h) There is a system of staff appraisal.

i) Where appropriate, staff are registered with a professional or statutory body.

j) There are training and reference manuals available.

k) The establishment is sufficiently staffed to carry out its activities.

GQ4 There is a systematic and planned approach to the management of records.

a) There are procedures for the creation, identification, maintenance, access, amendment, retention and destruction of records.

b) There is a system for the regular audit of records and their content to check for completeness, legibility and accuracy and to resolve any discrepancies found.

c) Written records are legible and indelible. Records kept in other formats such as computerised records are stored on a validated system.

d) There is a system for back-up / recovery in the event of loss of computerised records.

e) The establishment keeps a register of the types and quantities of tissues and / or cells that are procured, tested, preserved, processed, stored and distributed or otherwise disposed of, and on the origin and destination of tissues and cells intended for human application.

f) There are procedures to ensure that donor documentation, as specified by Directions 002/2018, is collected and maintained.

g) There is a system to ensure records are secure and that donor confidentiality is maintained in accordance with Directions 002/2018.

h) Raw data which are critical to the safety and quality of tissues and cells are kept for 10 years after the use, expiry date or disposal of tissues and / or cells.

i) The minimum data to ensure traceability from donor to recipient as required by Directions 002/2018 are kept for 30 years after the use, expiry or disposal of tissues and / or cells.

j) Records are kept of products and material coming into contact with the tissues and / or cells.

l) The establishment records the acceptance or rejection of tissue and / or cells that it receives and in the case of rejection why this rejection occurred.

m) In the event of termination of activities of the establishment a contingency plan to ensure records of traceability are maintained for 10 or 30 years as required.

GQ5 There are documented procedures for donor selection and exclusion, including donor criteria.

a) Donors are selected either by the establishment or the third party acting on its behalf in accordance with the criteria required by Directions 002/2018.

b) The testing of donors by the establishment or a third party on behalf of the establishment is carried out in accordance with the requirements of Directions 002/2018.

c) In cases other than autologous donors, donor selection is carried out by authorised personnel and signed and reviewed by a qualified health professional.

d) There is a system in place either at the establishment or at a third party acting on its behalf to record results of donor selection and associated tests.

e) Testing of donor samples is carried out using CE marked diagnostic tests.

f) Samples taken for donor testing are clearly labelled with the time and place the sample was taken and a unique donor identification code.

GQ6 A coding and records system facilitates traceability of tissues and / or cells, ensuring a robust audit trail.

a) There is a donor identification system which assigns a unique code to each donation and to each of the products associated with it.

b) An audit trail is maintained, which includes details of when the tissues and / or cells were acquired and from where, the uses to which the

tissues and / or cells were put, when the tissues and / or cells were transferred elsewhere and to whom.

c) The establishment has procedures to ensure that tissues and / or cells imported, procured, processed, stored, distributed and exported are traceable from donor to recipient and vice versa.

d) The requirements of the Single European Code are adhered to as set out in Directions 002/2018.

GQ7 There are systems to ensure that all adverse events, reactions and/or incidents are investigated promptly.

a) There are procedures for the identification, reporting, investigation and recording of adverse events and reactions, including documentation of any corrective or preventative actions.

b) There is a system to receive and distribute national and local information (e.g. HTA regulatory alerts) and notify the HTA and other establishments as necessary of serious adverse events or reactions.

c) The responsibilities of personnel investigating adverse events and reactions are clearly defined.

d) There are procedures to identify and decide the fate of tissues and / or cells affected by an adverse event, reaction or deviation from the required quality and safety standards.

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.

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

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.

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.

b) There are procedures for the transport of tissues and / or cells which reflect identified risks associated with transport.

c) There is a system to ensure that traceability of tissues and / or cells is maintained during transport.

d) Records are kept of transportation and delivery.

e) Tissues and / or cells are packaged and transported in a manner and under conditions that minimise the risk of contamination and ensure their safety and quality.

f) There are third party agreements with courier or transport companies to ensure that any specific transport conditions required are maintained.

g) Critical transport conditions required to maintain the properties of tissue and / or cells are defined and documented.

h) Packaging and containers used for transportation are validated to ensure they are fit for purpose.

i) Primary packaging containing tissues and / or cells is labelled with the information required by Directions.

j) Shipping packaging containing tissues and / or cells is labelled with the information required by Directions.

PFE5 Equipment is appropriate for use, maintained, quality assured, validated and where appropriate monitored.

a) Critical equipment and technical devices are identified, validated, regularly inspected and records are maintained.

b) Critical equipment is maintained and serviced in accordance with the manufacturer's instructions.

c) Equipment affecting critical processes and storage parameters is identified and monitored to detect malfunctions and defects and procedures are in place to take any corrective actions.

d) New and repaired equipment is validated before use and this is documented.
e) There are documented agreements with maintenance companies.
f) Cleaning, disinfection and sanitation of critical equipment is performed regularly and this is recorded.
g) Instruments and devices used for procurement are sterile, validated and regularly maintained.
h) Users have access to instructions for equipment and receive training in the use of equipment and maintenance where appropriate.
i) Staff are aware of how to report an equipment problem.
j) For each critical process, the materials, equipment and personnel are identified and documented.
k) There are contingency plans for equipment failure.