Site visit inspection report on compliance with HTA licensing standards
Inspection date: **04-05 December 2019**

University College London Hospitals

HTA licensing number 11025

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

and

Licensed under the Human Tissue Act 2004

Licensable activities carried out by the establishment

Licensed activities – Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended)

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

'E*' = Establishment is licensed to carry out this activity but is not currently carrying it out.

Site	Procurement	Processing	Testing	Storage	Distribution	Import	Export
University College London Hospitals	E	E		E	E		E*

Tissue types authorised for licensed activities – Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended)

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

'Authorised*' = Establishment is authorised to carry out this activity but is not currently carrying it out.

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

Mature Cell, MNC; PBMC	Authorised				Authorised*		Authorised*
Progenitor Cell, Haematopoietic, Bone Marrow; Bone Marrow	Authorised	Authorised		Authorised	Authorised		
Progenitor Cell, Hematopoietic, Cord Blood; Cord Blood	Authorised*	Authorised*		Authorised*	Authorised*		
Progenitor Cell, Haematopoietic, PBSC; PBSC	Authorised	Authorised		Authorised	Authorised		

Licensed activities – Human Tissue Act 2004

'Licensed*' = Establishment is licensed to carry out this activity but is not currently carrying it out.

Area	Storage of relevant material which has come from a human body for use for a scheduled purpose
University College London Hospitals	Licensed*

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 University College London Hospitals (the establishment) had met the majority of the HTA's standards, eleven minor shortfalls were found against standards for Governance and Quality, and Premises, Facilities and Equipment. The shortfalls relate to documented procedures for licensable activities, recording raw data, donor exclusion criteria, the timing of blood sampling for donor

serology testing, risk assessments, environmental monitoring, temperature and cleaning records and the validation for the transport container.

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

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

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.		
b) There are procedures for all licensable activities that ensure integrity of tissue and / or cells and minimise the risk of contamination.	The documented procedure for apheresis equipment maintenance states the incubator used to store reagents for procurement (ACD-A and saline) must operate below 29°C. This exceeds the manufacturer's recommended maximum storage temperature for ACD-A. The establishment does not have procedures for monitoring the temperature of all areas in which apheresis and bone marrow reagents are stored. Although establishment staff described the maximum permitted time between the addition of DMSO and the commencement of cryopreservation, this was not specified in the documented procedure for the activity. The documented guidance describing the timings to obtain donor blood samples for mandatory serological tests states incorrect time frames.	**Minor**

GQ4 There is a systematic and planned approach to the management of records.		
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.	Although documented procedures describe steps for recording temperature data, temperatures for the incubator used to store apheresis reagents have not been logged since June 2018.	**Minor**
GQ5 There are documented procedures for donor selection and exclusion, including donor criteria.		
a) Donors are selected either by the establishment or the third party acting on its behalf in accordance with the criteria required by Directions 002/2018.	The establishment's donor selection procedure does not include all of the donor exclusion criteria as set out in Annex A of the Guide to Quality and Safety Assurance for Human Tissues and Cells for Patient Treatment. For example, the donors are not asked about ingestion of, or exposure to, a substance (such as cyanide, lead, mercury, gold) that may be transmitted to recipients in a dose that could endanger their health or transplantation with xenografts.	**Minor**
b) The testing of donors by the establishment or a third party on behalf of the establishment is carried out in accordance with the requirements of Directions 002/2018.	The establishment procures peripheral blood lymphocytes for donor lymphocyte infusion (DLI), and peripheral blood mononuclear cells (PBMCs) as starting material for an Advanced Therapy Medicinal Product (ATMP). Patient blood samples for mandatory serology tests were not obtained within the required time frame for a DLI and PBMC donor. In addition, a PBMC donor was not tested for all of the mandatory tests.	**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 establishment does not have documented risk assessments for all practices and processes relating to procurement of apheresis products and bone marrow.	**Minor**

c) Staff can access risk assessments and are made aware of local hazards at training.	Risk assessments are not made accessible to staff carrying out licensable activities.	**Minor**
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.	There is no risk assessment for the apheresis collection facility or the storage facility used to store reagents used for bone marrow procurement.	**Minor**
PFE2 Environmental controls are in place to avoid potential contamination.		
b) Where processing of tissues and / or cells involves exposure to the environment, it occurs in an appropriate, monitored environment as required by Directions 002/2018.	The establishment does not undertake appropriate monitoring of the Grade A environment during the preparation of cryoprotectant, which is a step carried out during the processing of cells. The documented procedure for environmental monitoring states the Grade B environment is monitored with an air sampler during processing, and as part of weekly monitoring. Environmental monitoring records showed no monitoring took place during the period of time the air sampler was undergoing servicing.	**Minor**
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.	Apheresis reagents and kits are stored in a separate room within the apheresis collection facility which is not currently temperature monitored. During the inspection it was noted the room, which is located in a publicly accessible area, was not secured in line with local requirements. Reagents used for bone marrow procurement are stored in a fridge located within an office area. There are no documented temperature records for the fridge.	**Minor**

PFE4 Systems are in place to protect the quality and integrity of bodies, body parts, tissues and cells during transport and delivery to a destination.		
h) Packaging and containers used for transportation are validated to ensure they are fit for purpose.	The establishment has recently started transporting PBMCs to another HTA-licensed establishment for cryopreservation. The current transport container validation does not reflect the new time frame for which the container is required to maintain the temperature for.	**Minor**
PFE5 Equipment is appropriate for use, maintained, quality assured, validated and where appropriate monitored.		
f) Cleaning, disinfection and sanitation of critical equipment is performed regularly and this is recorded.	Weekly cleaning records for apheresis equipment were incomplete for a number of different machines on multiple occasions.	**Minor**

The establishment is also licensed for the storage of relevant material for use for a scheduled purpose under the Human Tissue Act 2004. The establishment does not currently store relevant material. Therefore, the applicable HTA standards were not audited during this inspection.

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.	GQ1b	A number of documented references to legislation, HTA Codes of Practice and the organisational structure were not up to date. In addition, there is no reference to the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended) in the Clinical Trial consent procedure. The DI is advised to review all procedures and policies and update the references as required to ensure staff carrying out licensable activities are adhering to the appropriate regulatory legislation.
2.	GQ2c	The DI should ensure that information relating to the evidence audited for the independent audit is appropriately documented.
3.	PFE2b	The DI should consider protecting the power supply to the computer which stores non-viable particle monitoring data, in order to prevent accidental disruption of the power supply and loss of data.
4.	PFE2c	The DI is advised to review procedures for the retention of the same hand sanitising gel bottle in the Grade A hood for multiple processing sessions, and to include steps for decontamination of the bottle in documented procedures, if appropriate.
5.	PFE3a	Reagents for apheresis are stored in an incubator within the ward area which is unlocked during working hours. The DI is advised to risk assess this arrangement because reagents are potentially accessible to patients and visitors.
6.	PFE5c	As part of the ‘at rest’ environmental monitoring programme, settle plates are used to monitor the transfer hatch for contamination. The DI is advised to consider including swabs of the transfer hatch in the environmental monitoring programme, in order to monitor the effectiveness of cleaning procedures.

Background

University College London Hospitals (UCLH) has been licensed by the HTA since November 2006. The establishment is licensed for procurement, processing, storage and distribution of DLIs, bone marrow, peripheral blood stem cells (PBSC) and cord blood, although the establishment has not procured cord blood since the previous inspection. The establishment is also licensed for procurement, distribution and export of PBMCs. In addition to undertaking procurement for its own patients, the establishment also procures for a UK registry under the terms of a Service Level Agreement (SLA).

This was the seventh site visit inspection of the establishment; the most recent previous inspection took place in November 2017. Since the previous inspection, there have been no significant changes to the licence arrangements or the activities carried out under the licence.

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

There are 121 standards in the Human Application sector of which 114 were assessed. Standards C1(b), C2(b), GQ1(f)(n), GQ5(e) and PFE1(d) were not applicable, and standard GQ3(a) was not assessed.

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 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 facility, the theatres department, the fridge used to store reagents used during bone marrow procurement, the stem cell processing laboratory and the cryostore.

Audit of records

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 PBSC and bone marrow donations, however for the DLI donation, the timing of the blood sample collection was incorrect. This was also the case for one of the three PBMC donations. In addition, a second PBMC donor was not tested for all of the mandatory serology tests.

The procurement and processing records (where applicable) were audited for the following cells/tissue donors:

- a sibling DLI donor;
- two PBSC donors (one related and one unrelated collected on behalf of a registry under the terms of a SLA);
- an autologous PBSC donor;
- a sibling bone marrow donor; and
- three PBMC donors (to be used as starting material for an ATMP).

Meetings with establishment staff

The inspection included discussions with the Processing Facility Director (who is also the DI), the Quality and Service Improvement Manager, the Quality Manager for the Haematopoietic Stem Cell Transplantation (HSCT) Programme, the Apheresis trainer, Clinical Nurse Specialists (CNSs) from the Bone Marrow Transplant Team, the Laboratory Manager, the Processing Facility Medical Director and Senior Clinical Trial staff.

Report sent to DI for factual accuracy: 02 January 2020

Report returned from DI: 08 January 2020

Final report issued: 14 January 2020

Completion of corrective and preventative actions (CAPA) plan

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

Date: 27 April 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 (HT Act), 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 shortfall which poses a significant risk to human safety and/or dignity or is a breach of the HT Act or associated Directions,

   Or

   A number of ‘major’ shortfalls, none of which are 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 breach in the relevant Codes of Practice, the HT Act and other relevant professional and statutory guidelines;

or

A shortfall which indicates a failure to carry out satisfactory procedures 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.

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 the proposed action plan establishments will be notified of the follow-up approach the HTA will take.