Site visit inspection report on compliance with HTA licensing standards
Inspection date: **30-31 October 2019**

The London Clinic
HTA licensing number 11052

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

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

'TPA' = Third party agreement; the establishment is licensed for this activity but another establishment (not licensed by the HTA) carries out the activity on their behalf.

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

Site	Procurement	Processing	Testing	Storage	Distribution	Import	Export
Hub **The London Clinic** **Harley Street**		E	E TPA	E	E		E
Satellite **The London Clinic** **Devonshire Place**	E			E	E	E	

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

Tissue Category; Tissue Type	Procurement	Processing	Testing	Storage	Distribution	Import	Export
Mature Cell, MNC; DLI	Authorised	Authorised	Authorised TPA	Authorised	Authorised		Authorised
Mature Cell, MNC; PBMC	Authorised		Authorised TPA		Authorised		Authorised
Ocular, Cornea; Cornea						Authorised	
Other; Tumour (ATMP)	Authorised		Authorised TPA				
Progenitor Cell, Haematopoietic, Bone Marrow; Bone Marrow	Authorised	Authorised	Authorised TPA	Authorised	Authorised		Authorised
Progenitor Cell, Haematopoietic, PBSC; PBSC	Authorised	Authorised	Authorised TPA	Authorised	Authorised		Authorised

Licensed activities – Human Tissue Act 2004

Area	Storage of relevant material which has come from a human body for use for a scheduled purpose
The London Clinic	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 The London Clinic (the establishment) had met the majority of the HTA's standards, eight minor shortfalls were found against standards for Governance and Quality and Premises, Facilities and Equipment. The shortfalls relate to documented procedures for licensable activities, internal and independent audits, donor exclusion criteria, the timing of blood sampling for donor serology testing, risk assessments, environmental monitoring and the storage of consumables for apheresis.

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 establishment releases tumour tissue as starting material for an Advanced Therapy Medicinal Product (ATMP). Although staff use a checklist, there is currently no documented procedure for carrying out these release checks, including who can authorise the release. Although establishment staff described the maximum permitted time between the addition of DMSO and the commencement of cryopreservation, this was not	**Minor**

	specified in the documented procedure for the activity. *Following the inspection, the establishment provided evidence to the HTA demonstrating that measures have been put in place to meet the standard prior to the release of the final report. The HTA now considers this standard to be fully met.*	***Fully met***
GQ2 There is a documented system of quality management and audit.		
b) There is an internal audit system for all licensable activities.	The internal audits do not cover the full range of licensable activities carried out by the establishment.	**Minor**
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 licensable activities 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 history questionnaire 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.	As part of a clinical trial, the establishment procures tumour tissue as starting material for an ATMP. Patient blood samples for mandatory serology tests were not obtained within the required time frame.	**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 assessments do not assess all risks associated with the procedures for licensable activities. For example: • the risk assessment for storage does not assess the risks associated with passive freezing and the use of the same freezer shelf for storage of uncontaminated units alongside contaminated units; and • the risk assessment for procuring starting material does not assess the risks associated with donor serology testing or release procedures.	**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.	Staff do not follow the documented procedure when undertaking finger dabs during processing. Finger dabs are taken before the procedure is completed, following the aliquoting of cells into the bags. The establishment's procedure sets out that this step should be performed at the end of the procedure.	**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.	Consumables for apheresis are stored in an unsecured room adjacent to the patient and family waiting area.	**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.

DI and LH suitability

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

Advice

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

Number	Standard	Advice
1.	GQ1b	The DI is advised to ensure that the documented procedure for business continuity is consistent with practices. For example, the contingency arrangement for a freezer malfunction refers to an old practice of transferring to a LN2 tank, rather than transfer to their current back-up freezer.
2.	GQ1l	In the event of termination of licensable activities at the establishment, documented procedures described that the establishment will identify a HA licensed establishment to transfer tissue and cells to, and will fund the storage of these for five years. After this time, donors would be contacted by the establishment to advise them of their options for ongoing storage. The DI is advised to review the procedure, and include who would be responsible for contacting the donors in the event the establishment is no longer operating.
3.	GQ4b	The review of records identified three instances where mandatory serology results were missing from patient's folders, although these results were available electronically. The DI is advised to review procedures for the

		retention of this information within the patient record. If the establishment continues to retain copies of serology results in the patient record, the DI is advised to regularly audit these records to ensure consistency of record keeping.
4.	GQ7a	The DI is advised to review the definition of a serious adverse event and reaction (SAEAR) to ensure all applicable incidents are reported to the HTA.
5.	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

The establishment has been licensed by the HTA since August 2006, and was re-licensed in December 2009 following a move to new premises. The establishment is licensed for procurement, testing, processing, storage, distribution and export of peripheral blood lymphocytes for donor lymphocyte infusions (DLI), bone marrow and peripheral blood stem cells (PBSC). The majority of collections are performed on behalf of registries in the UK and the EU under the terms of appropriate agreements.

This was the seventh site visit inspection of the establishment; the most recent previous inspection took place in October 2017. Since the previous inspection, the establishment has started to carry out the following new activities:

- procurement, testing, distribution and export of PBMCs as starting material for ATMP manufacture;
- procurement and testing of tumour tissue, also as starting material for ATMP manufacture; and
- import of corneas.

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 GQ1f and PFE1d were not applicable, and standards GQ1(n)(o), GQ3(d), PFE1(a) and PFE4(f) were 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 equipment service contracts and records of servicing, temperature monitoring records for consumables, reagents and product storage areas and agreements with third parties. 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 suite and clinical consent areas, the day surgery unit, the stem cell processing laboratory and cryostore, and the in-house virology and microbiology testing laboratory.

Audit of records

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

- a DLI sibling donor;
- two PBSC sibling donors;
- two autologous PBSC donors;
- six bone marrow and two PBSC donors (collected on behalf of three registries under the terms of SLAs and a TPA); and
- tumour tissue donated as starting material for an ATMP, for a clinical trial.

The audit included a review of donor consent, 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 DLI, PBSC and bone marrow donations, however for the tumour tissue donation, the timing of the blood sample collection was incorrect. Whilst some minor discrepancies were found in relation to the completeness of the records, these were 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 Processing Medical Director (who is a Consultant Haematologist and the DI), the Cellular Therapies and Transplant Services Quality Manager, the Transplant Services Coordinator, the lead for Apheresis, a Consultant Haematologist, the Senior Clinical Trials Co-ordinator, the Head of Clinical Governance, Clinical Audit Lead, the Pathology Quality Manager, the Theatre Manager and the lead for Virology.

Report sent to DI for factual accuracy: 28 November 2019

Report returned from DI: 03 December 2019

Final report issued: 30 December 2019

Completion of corrective and preventative actions (CAPA) plan

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

Date: 28 May 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.