Site visit inspection report on compliance with HTA licensing standards
Inspection date: **16-17 January 2020**

BCH Stem Cell Bank

HTA licensing number 11024

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.

Site	Procurement	Processing	Testing	Storage	Distribution	Import	Export
Hub **BCH Stem Cell Bank**	E	E	E	E			
Satellite **The Royal Hospitals**	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.

Tissue Category; Tissue Type	Procurement	Processing	Testing	Storage	Distribution	Import	Export
Progenitor Cell, Haematopoietic, PBSC; PBSC	Authorised	Authorised	Authorised	Authorised			
Progenitor Cell, Hematopoietic, Bone Marrow; Bone Marrow	Authorised	Authorised	Authorised	Authorised			
Mature Cell, T Cell (DLI); DLI	Authorised	Authorised	Authorised	Authorised			

Licensed activities – Human Tissue Act 2004

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

Area	Storage of relevant material which has come from a human body for use for a scheduled purpose
Hub site **BCH Stem Cell Bank**	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 BCH Stem Cell Bank (the establishment) had met the majority of the HTA's standards, seven minor shortfalls were found against the HTA's standards for Governance and Quality. These shortfalls relate to third party agreements, internal and independent audits, donor selection and testing, risk assessments and temperature monitoring.

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.		
s) Third party agreements specify that the third party will inform the establishment in the event of a serious adverse reaction or event.	The third party agreement between the establishment and the microbiology laboratory, used in environmental monitoring, requires that serious adverse events and serious adverse reactions (SAEARs) are reported 'promptly'. This wording does not reflect the requirement to report SAEARs within 24 hours from the point of discovery, as set out in Directions 002/2018.	**Minor**

GQ2 There is a documented system of quality management and audit.	Internal audits undertaken by the establishment do not review all associated records relating to licensable activity, for example, environmental monitoring data.	**Minor**
b) There is an internal audit system for all licensable activities.		
GQ4 There is a systematic and planned approach to the management 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.		

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.	The establishment's independent audit activity includes a review of the HTA standards and verifies that procedures relating to the standards are in place. However, the independent audits do not include reviews of records or data generated by the establishment when undertaking licensable activity, for example, original copies of donor testing results.	**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 donor exclusion criteria included in the establishment's procedural documentation does not include all of the criteria required by Directions 002/2018.	**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.	Donors of cells intended only for use as a donor lymphocyte infusion (DLI) are not tested in accordance with the requirements of Directions 002/2018.	**Minor**

GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately.		
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.	The establishment reviews risk assessments regularly during governance meetings. However, a formal documented review of risk assessments takes place only every two years and not annually, as required.	**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.	During a review of the temperature monitoring data relating to the area where the testing laboratory stores its reagents, two minor temperature deviations were identified. On review of the laboratory's governance records, there was no evidence that these deviations had been identified and their impact upon the reagents being stored in the area assessed.	**Minor**

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.	C1(a)	On occasions, consent for mandatory serological testing may be sought by clinical staff during a visit that takes place prior to the donor meeting with consultant staff when formal consent for testing, procurement, storage and discard is sought. The DI is advised to put in place a procedure to record within the donor's clinical notes that consent has been verbally sought for the serological testing by clinical staff in order to maintain a record of that process.
2.	GQ1(b)	The establishment uses cool packs when transporting plasma and donated cells the short distance from the apheresis department to the processing laboratory. Cool packs are cleaned in between each use; however, the cleaning of the packs is not detailed within the establishment's standard operating procedure (SOP). The DI is advised to document the use of the cool packs and their cleaning within the appropriate SOP.
3.	GQ1(b)	In addition to the check carried out by laboratory staff, apheresis staff verify that the mandatory serological testing of donors has been undertaken and that the timeframe between testing and procurement has not been exceeded. The DI is advised to document these checks performed by the apheresis staff within the appropriate SOP.
4.	PFE2(b)	The DI is advised to consider implementing a procedure to monitor for contamination within the establishment's processing facilities in hard to reach areas, such as the corners of the transfer hatches, which cannot be monitored by using contact plates.

5.	PFE3(b)	The establishment's temperature monitoring system is tested regularly by another hospital department to verify that the alarm triggers if the temperature of a specific area exceeds the pre-determined limits. The DI is advised to also undertake periodic tests of the alarm system, without notifying the department which monitors it, to assure themselves that establishment staff are contacted in the event of am unexpected temperature excursion.
6.	PFE3(c)	The DI is advised to review and revise the upper-temperature alarm limits for an ambient storage area within the processing laboratory area. A review of the consumables stored in this area identified an item with an upper storage temperature limit of 22ºC. The establishment's temperature monitoring system's upper alarm exceeds this figure and is set at 24ºC. A review of the temperature monitoring data provided by the establishment, however, showed that the temperature over that period had not exceeded 22ºC.

Background

The establishment procures peripheral blood stem cells (PBSCs), bone marrow and DLIs from adult donors and PBSCs from paediatric donors. Donor selection is undertaken by the establishment with mandatory serological testing taking place under the authority of a third party agreement. Procured cells are processed at the establishment's clean room facility and stored on site, in vapour phase liquid nitrogen tanks prior to being released for end-use within the establishment.

BCH stem cell bank has been licensed by the HTA since August 2006. This was the sixth routine site visit inspection of the establishment; the most recent previous inspection took place in January 2018. At the time of the 2020 inspection, there was one shortfall from the previous inspection that remained open. This shortfall related to the reprovision of service in the event of an emergency, specifically the location of the liquid nitrogen storage tanks if the current facility was not available. The establishment has been working towards locating a suitable back-up storage facility where the storage tanks could be moved if needed. The back-up facility will have liquid nitrogen supplied to it and will be wired to allow the temperature monitoring of the tanks and monitoring of the oxygen levels within the facility. The proposed facility is not yet complete; however, work has started on installing wiring for the temperature and oxygen monitoring systems. The proposed facility was visited during the 2020 inspection so that the suitability of the premises could be assessed. This shortfall will remain open under the original CAPA plan until the DI has confirmed that the work being undertaken has been completed and the facility is ready for potential use.

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

Standards C1(b), C2(b), GQ1(f), GQ1(n), GQ4(k), GQ4(l), GQ6(d), GQ7(g), GQ7(h), PFE1(d), PFE4(a), PFE4(f), and PfE4(j) were not assessed as they are not applicable to the establishment's activity. Standards GQ1(k), GQ1(l), GQ3(a), GQ3(c), GQ3(h), GQ3(j), GQ4(i), GQ4(m), GQ7(e), and GQ7(f) were also not assessed during this inspection.

This inspection focussed on the human application activity and none of the standards relating to the Human Tissue Act 2004 were assessed during this inspection.

Review of governance documentation

Service or maintenance contracts were reviewed for all apheresis machines and the establishment's non-viable particle counters. Various procedural documents were reviewed including those relating to consent, donor selection, procurement of cells, processing and controlled-rate freezing. In addition, agreements with other departments, examples of risk assessments, examples of incident reports and records relating to processed cells were reviewed.

Visual inspection

The inspection team visited the apheresis area, the clean room processing facility, areas where consumables and reagents are stored, the liquid nitrogen storage area, the paediatric procurement area and the testing laboratory. In addition, the back-up facility that is being completed and that will be used to store the establishment's liquid nitrogen tanks if their current storage area is not usable was also visited.

Audit of records
An audit of records relating to seven donors was undertaken and included one allogeneic bone marrow donor, three autologous adult PBSC donors, two autologous paediatric PBSC donors and an adult DLI donor.

The review of the records included the consultant's request to collect, consent for testing, collection and storage, laboratory serological testing results, environmental monitoring results, cryopreservation calculations, records of consumables and reagents used, microbiological contamination testing results, controlled-rate freezer records, apheresis worksheets and the checklist that is completed prior to release of cells. In addition, liquid nitrogen storage locations were cross-checked between three separate logs where the location is recorded.

One error was identified in a cryopreservation calculation; however, the establishment stated that this would not have affected the quality and safety of the cells.

Meetings with establishment staff
Various members of staff were spoken with as part of the inspection including medical consultant staff (both adult and paediatric), apheresis staff, processing laboratory staff, testing laboratory staff and quality management staff.

Report sent to DI for factual accuracy: 13 February 2020

Report returned from DI: 4 March 2020

Final report issued: 13 March 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 August 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.