Site visit inspection report on compliance with HTA minimum standards

CyteTech Limited

HTA licensing number 22671

Licensed for the

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

11 July 2019

Summary of inspection findings

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

Although the HTA found that CyteTech Limited (the establishment) had met the majority of the HTA standards, two minor shortfalls were found in relation to governance and quality, and premises facilities and equipment standards. The shortfalls relate to the back-up of raw data, and temperature monitoring. In addition, two shortfalls identified during the establishment's 2018 licence application assessment visit (LAAV) were open at the time of the inspection to which this report refers; these shortfalls remain open.

Prior to the issue of the final inspection report, the establishment confirmed that action has been taken to address the shortfalls that have been identified during both the licence assessment assessment visit and the routine 2019 inspection. This is reflected in the table of shortfalls below. Following these shortfalls being assessed as having been met, the establishment is considered to have met all applicable HTA standards.

The HTA has given advice to the Designated Individual with respect to quarantine arrangements, service level agreements, audit, routine maintenance and monitoring systems.

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.

Tissue Category; Tissue Type	Procurement	Processing	Testing	Storage	Distribution	Import	Export
Progenitor Cell, Hematopoietic, Cord Blood; Cord Blood				**E**			
Other, Cord Tissue; Cord Tissue				**E**			

Background to the establishment and description of inspection activities undertaken

The establishment is licensed for the storage of human tissues and cells for human application under the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended) (the Regulations).

The establishment has been licensed by the HTA since July 2018. This report relates to the first routine site visit inspection of the establishment, following its LAAV. Annual activity data, pre-inspection discussions with the DI and the report resulting from the LAAV were used to inform the timetable that was developed for this inspection.

The establishment stores umbilical cord blood (UCB) and cord tissue (CT) on behalf of another HTA-licensed establishment. The other licensed establishment takes responsibility for movement of UCB and CT between the two establishments and also any cell or tissue handling while UCB and CT are in storage. Cell or tissue handling includes movement of cells or tissue between tanks in order to consolidate storage and retrieval of any cells or tissue that have been requested for release.

UCB and CT are stored in vapour phase liquid nitrogen storage tanks. Each storage tank's temperature is monitored using an automated monitoring system, which also alerts establishment staff via SMS message to any deviations from the expected storage temperature range.

For security, the premises are monitored by a motion-sensing, infrared CCTV system, which establishment staff can log into remotely to view the storage area should the system be triggered. In addition, the premises are covered by separate intruder and fire alarm systems.

This inspection focussed on a detailed review of data relating to the processes around storage of UCB and CT. In addition to reviewing the establishment's procedural documents, a detailed review of tank maintenance and temperature records was undertaken.

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

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

Governance and Quality

Standard	Inspection findings	Level of shortfall
GQ4 There is a systematic and planned approach to the management of records.		
d) There is a system for back-up / recovery in the event of loss of computerised records.	Temperature monitoring data is stored on a stand-alone laptop computer within the establishment's storage facility and is not backed-up. *Following the inspection, the DI submitted evidence demonstrating that this standard is now fully met.*	**Minor**

Premises, Facilities and Equipment

Standard	Inspection findings	Level of shortfall
PFE3 There are appropriate facilities for the storage of bodies, body parts, tissues, cells, consumables and records.		
c) Tissues and / or cells are stored in controlled, monitored and recorded conditions that maintain tissue and / or cell integrity.	The temperatures of the liquid nitrogen tanks are monitored by probes which send information wirelessly to a laptop computer. If probes fail or are being serviced, they are replaced by spare probes which the establishment keeps as a contingency measure. At the time of the inspection, no records showing the locations of the temperature monitoring probes at any given time were available. The establishment has no standard operating procedure detailing how the location of monitoring probes should be recorded and how these records are updated should the location of the probes change. During a review of temperature monitoring data, examples of where temperature monitoring data had not been recorded as expected were identified. This has resulted in gaps for which no raw data relating to storage temperatures is available. Throughout these gaps in the monitoring data, the establishment had undertaken and recorded periodic manual temperature checks of the liquid nitrogen tanks. However, periods for which there is no temperature data inbetween these manual checks remain. *Prior to the publication of the final inspection report, the establishment confirmed that corrective actions have been taken to address this shortfall. This standard is now considered to be fully met.*	**Minor**

Advice

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

No.	Standard	Advice
1.	GQ1(h)	The establishment does not currently have any UCB or CT that requires quarantined storage. The DI is advised to ensure procedures for the storage of quarantine material are in place prior to the arrival of such material should the need arise.

2.	GQ1(r)	The establishment has a service level agreement (SLA) in place with the other HTA-licensed establishment who's UCB and CT samples are being stored. The SLA is based on a generic agreement, which in some areas may benefit from some clarification. The DI is advised to consider adding more detail/clarifying the following sections: • Schedule 2, section 2 should always reference CT in addition to UCB being stored. • Schedule 2, section 5 could be clarified to list the individual records referred to as 'records'. • Schedule 4, section 7 details the storage temperature that UCB and CB will be stored at. However, no lower temperature limit is defined. The expected storage temperature range is defined in the vessel acceptance paperwork which is completed upon acceptance of a storage tank at the establishment. • Schedule 4, section 5 could be expanded to state how long the establishment will store raw data and traceability data.
3.	GQ2(b)	The other HTA-licensed establishment whose UCB and CT samples are being stored is still consolidating samples within the storage tanks following their transfer. Upon the completion of this exercise, the DI is advised to liaise with the other HTA-licensed establishment to undertake an audit of stored tissue and cells to verify that they are stored in the expected location.
4.	PFE3(a)	The establishment has a procedure (CT-METH 7060) relating to the routine maintenance and observations of storage equipment undertaken by establishment staff, including periodic liquid nitrogen level checks, de-icing of storage tank lids and temperature checks. The DI is advised to create a bespoke pro-forma to record when these checks are performed on each tank. In addition, in addressing the shortfall identified against standard PFE3(a), the DI is advised to consider adding checks that the remote temperature monitoring system is receiving data from the monitoring probes to these maintenance and status inspections.
5.	PFE3(b)	The establishment's temperature monitoring system sends out alerts to establishment staff if there are issues with storage temperatures or the signal between the temperature probe and the receiver. The DI is advised to record more detailed reasons behind each alarm triggered by the system so that reviews of historic data can more easily identify the cause of the alert.

Assessment of existing conditions/shortfalls against standards

Two shortfalls identified during the establishment's 2018 LAAV remained open at the time of the inspection to which this report refers. The open shortfalls are as set out below.

Governance and Quality

Standard	Inspection findings	Level of shortfall
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.	There are no risk assessments covering licensable activities. *2019 inspection: The establishment has developed risk assessments following the LAAV. However, these do not sufficiently identify all risks associated with the licensable activity being undertaken by the establishment. Examples of risks not assessed include, but are not limited to, loss of temperature monitoring data, failure of the temperature monitoring alarm system and the risk of loss of traceability of UCB or CT samples during their transfer, consolidation or retrieval. This shortfall will remain open.* *Prior to the publication of the final inspection report, the establishment confirmed that corrective actions have been taken to address this shortfall. This standard is now considered to be fully met.*	**Minor**

Premises, Facilities and Equipment

Standard	Inspection findings	Level of shortfall
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 are no risk assessments covering premises. *2019 inspection: The establishment has developed risk assessments following the LAAV however, these do not assess all of the potential risks associated with the premises. Examples of risks not assessed include, but are not limited to, security of the premises with regards to intrusion, security of the premises with regards to fire, loss of temperature monitoring data and failure of the temperature monitoring alarm system. This shortfall will remain open.* *Prior to the publication of the final inspection report, the establishment confirmed that corrective actions have been taken to address this shortfall. This standard is now considered to be fully met.*	**Minor**

Concluding comments

There are a number of areas of practice that require improvement, including two minor shortfalls and two shortfalls that remain open from the previous LAAV. The HTA has given advice to the Designated Individual with respect to quarantine arrangements, service level agreements, audit, routine maintenance and monitoring systems.

Prior to the issue of the final inspection report, the establishment confirmed that action has been taken to address the shortfalls that have been identified during both the licence assessment assessment visit and the routine 2019 inspection. This is reflected in the table of shortfalls above. Following these shortfalls being assessed as having been met, the establishment is considered to have met all applicable HTA standards.

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

Report sent to DI for factual accuracy: 6 August 2019

Report returned from DI: 16 August 2019

Final report issued: 12 September 2019

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

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.
g) There are procedures to ensure that an authorised person verifies that tissues and / or cells received by the establishment meet required specifications.
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.
o) There is a complaints system in place.
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.
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.
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.
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.

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

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.
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.
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.

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 shortfall which poses a significant risk to human safety and/or dignity or is a breach of the Human Tissue Act 2004 (HT Act) or associated Directions,

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 breach in the relevant Codes of Practices, 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 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.