



Site visit inspection report on compliance with HTA minimum standards

Source BioScience PLC

HTA licensing number 22570

Licensed for the

- **storage, distribution and export of human tissues and cells for human application under the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended); and**
- **storage of relevant material which has come from a human body for use for a scheduled purpose**

17 July 2018

Summary of inspection findings

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

Although the HTA found that Source BioScience PLC (the establishment) had met the majority of the HTA standards, three minor shortfalls were found in relation to documentation, audit and risk assessments. The HTA has also given advice to the Designated Individual with respect to documentation, governance meetings, audits and equipment maintenance.

Particular examples of good practice are included in the concluding comments section of the report.

The HTA's regulatory requirements

The HTA must assure itself that the Designated Individual (DI), 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.

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

'TPA' = Third party agreement; the establishment is licensed for this activity but another establishment (unlicensed) carries out the activity on their behalf.

Tissue category; Tissue type	Procurement	Processing	Testing	Storage	Distribution	Import	Export
Progenitor Cell, Hematopoietic, PBSC;PBSC	-	-	-	E	E	-	E*
Progenitor Cell, Hematopoietic, Cord Blood; PBSC	-	-	-	E	E	-	E*
Other; Cord Tissue	-	-	-	E	E	-	E*

Other; Embryonic Stem Cells	-	-	-	E	E	-	E*
Other; Fibroblasts	-	-	-	E	E	-	E*
Other; Dental Pulp	-	-	-	E	E	-	E*

Background to the establishment and description of inspection activities undertaken

The establishment is licensed for the storage, distribution and export of human tissues and cells for human application under the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended) (the Regulations) and for storage of relevant material which has come from a human body for use for a scheduled purpose under the Human Tissue Act 2004. At the time of the inspection, no storage of material under the Human Tissue was being undertaken and systems were not reviewed for this activity.

The establishment's main licensable activity is storage of tissues and cells on behalf of customers who are also licensed under the Regulations. The collections are largely static, meaning that, routinely, the numbers of samples stored does not change. New samples are sent infrequently by the establishment's customers to add to their sample collections and, on rare occasions, some samples are returned to the customer upon their request.

The establishment uses a courier acting under the authority of an appropriate TPA to undertake the transport of samples as necessary. The establishment's customers may organise transport of samples using their own couriers. On such occasions, this activity is carried out under the authority of the customer's own HTA licence. Although licensed for distribution and export, the establishment is not currently undertaking these activities.

The two liquid nitrogen storage tanks currently in the establishment's storage facility consist of one main storage tank and a quarantine storage tank; both are owned by the establishment. When the establishment receives samples from clients, assurance from the customer that the samples' donors have been appropriately consented and have undergone the mandatory serology screens (which were negative) is required. When a new customer supplies a subset of samples to the establishment for integration into the larger collection of samples, the establishment requests and undertakes a review of all of the donors' mandatory serological test results and only accepts samples that are negative for all of the markers. These checks are performed and signed off by the DI.

When a customer supplies a subset of samples to the establishment for integration into the larger collection of samples, the establishment undertakes a two-person verification of all new sample tube identifiers against a manifest of samples supplied by the customer. This helps to assure the DI that an accurate record of samples that are in storage is maintained. At the time of the inspection, there was no storage of client tanks.

Both vapour phase liquid nitrogen vessels are temperature-monitored and this feeds into a wireless callout system. Temperature excursions outside the set ranges trigger the alarm and the callout system. If an alarm is triggered out of hours or at weekends, the on call site engineer attends and will inform the DI of any equipment malfunction.

The temperatures of the tanks are monitored twice daily using both the individual tank temperature gauges and the readings obtained from the remote monitoring system. Included in the daily checks is monitoring of the external main liquid nitrogen supply tank's level. The establishment also has a process where weekly and monthly cleans of the storage area and outside of the storage tanks are undertaken. Records of all of these activities are maintained on dedicated forms designed for that purpose.

The establishment's remote temperature-monitoring system is on a service contract and is maintained annually. The establishment controls the servicing of its two tanks.

The establishment has been licensed by the HTA since May 2009 and this was the fourth routine site visit inspection. The timetable was developed in consideration of the establishment's annual activity data, previous inspection reports and pre-inspection discussions with the DI. During the inspection, the storage area housing two liquid nitrogen storage tanks was visited. Reviews of the establishment's documentation were undertaken and discussions and interviews were held with key members of staff. A traceability audit of samples from two clients was undertaken from receipt documentation to the stability storage database. No discrepancies were noted.

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

Governance and Quality

Standard	Inspection findings	Level of shortfall
GQ2 There is a documented system of quality management and audit.		
b) There is an internal audit system for all licensable activities.	Although an external audit against the full range of HTA standards had been performed in the previous six months, there was no evidence that the establishment had carried out internal audits for all licensable activities since the previous inspection (see <i>Advice</i> , item 5)	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.	Raw data, such as temperature records, are being retained for at least 10 years after the use, expiry date or disposal of cells. However, this is not documented in the relevant SOP.	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.	Risk assessments are currently reviewed every two years. There is a regulatory requirement to review risk assessments annually as a minimum.	Minor

Advice

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

No.	Standard	Advice
1.	N/A	The establishment is no longer licensed for import. The DI is advised to ensure all documents within the quality management system (QMS) have been updated to reflect this change of activity and that reference is made to the updated 'Guide to Quality and Safety Assurance for Human Tissues and Cells for Patient Treatment, version 2' (April 2018), as implemented by Directions 002/2018. This also includes updating SEC labelling requirements in BIO-SOP-01 (7.1.4).
2.	GQ1(c)	Regular governance meetings, covering quality management issues, take place monthly. The DI is advised to ensure information discussed at these meetings is disseminated to all staff carrying out licensable activities.
3.	GQ1(m)	Although licensed for distribution, the establishment is not currently undertaking this activity, but may do so in the future. In this event, the DI is advised to contact the HTA to ensure all requirements under the Q&S Regulations, such as application of the Single European Code, have been met prior to commencing this activity.
4.	GQ2(c)	The DI should ensure that independent audits maintain impartiality; for example, staff performing the independent audit are not directly involved in the audited procedures, including the review of quality management systems.
5.	GQ2(b), (c)	The DI is advised to expand the scope of the audits to include loss of traceability.
6.	PFE5(b)	The DI is advised that all equipment that might be used is listed in the maintenance schedule in the electronic QMS, such as the portable workbench used for transporting samples from one tank to another in the storage facility. This will ensure all maintenance is carried out regularly and equipment remains fit for purpose.

Concluding comments

Some areas of good practice were identified during the inspection and an example of these is included below.

The establishment uses appropriate visual aids to ensure there is a clear understanding of procedures such as in SOP 'Cryogenic Suite Technical Operations' and in the visual instructions on the temperature control panels to reset the alarm system. The latter ensures that all staff are able to respond to deviations in temperature quickly and effectively.

There are a number of areas of practice that require improvement, including three minor shortfalls against governance and quality standards. The HTA requires that the Designated Individual addresses the shortfalls by submitting a completed corrective and preventative action (CAPA) plan 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.

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.

Report sent to DI for factual accuracy: 20 August 2018

Report returned from DI: 3 September 2018

Final report issued: 4 September 2018

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.
h) There are procedures for the management and quarantine of non-conforming consignments or those with incomplete test results, to ensure no risk of cross contamination.
i) There are procedures to ensure tissues and / or cells are not released from quarantine until verification has been completed and recorded.
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.
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.
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.
k) There are documented agreements with end users to ensure they record and store the data

required by Directions 002/2018.
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.
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.
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

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.
PFE2 Environmental controls are in place to avoid potential contamination.
a) Tissues and / or cells stored in quarantine are stored separately from tissue and / or cells that have been released from quarantine.
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.

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.
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.

Disposal

Standard
D1 There is a clear and sensitive policy for disposing of tissues and / or cells.
a) The disposal policy complies with HTA's Codes of Practice.
b) The disposal procedure complies with Health and Safety recommendations.
c) There is a documented procedure on disposal which ensures that there is no cross contamination.
D2 The reasons for disposal and the methods used are carefully documented.
a) There is a procedure for tracking the disposal of tissue and / or cells that details the method and reason for disposal.

Human Tissue Act (2004) standards

Governance and quality system standards
GQ1 All aspects of the establishments work are governed by documented policies and procedures as part of the overall governance process
<p>a) Ratified, documented and up-to-date policies and procedures are in place, covering all licensable activities.</p> <p>b) There is a document control system.</p> <p>c) There are change control mechanisms for the implementation of new operational procedures.</p> <p>d) Matters relating to HTA-licensed activities are discussed at regular governance meetings, involving establishment staff.</p> <p>e) There is a system for managing complaints.</p>
GQ2 There is a documented system of audit
<p>a) There is a documented schedule of audits covering licensable activities.</p> <p>b) Audit findings include who is responsible for follow-up actions and the timeframes for completing these.</p>
GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills
<p>a) Qualifications of staff and all training are recorded, records showing attendance at training.</p> <p>b) There are documented induction training programmes for new staff.</p> <p>c) Training provisions include those for visiting staff.</p> <p>d) Staff have appraisals and personal development plans.</p>
GQ4 There is a systematic and planned approach to the management of records
<p>a) There are suitable systems for the creation, review, amendment, retention and destruction of records.</p> <p>b) There are provisions for back-up / recovery in the event of loss of records.</p> <p>c) Systems ensure data protection, confidentiality and public disclosure (whistleblowing).</p>
GQ5 There are systems to ensure that all adverse events are investigated promptly
<p>a) Staff are instructed in how to use incident reporting systems.</p> <p>b) Effective corrective and preventive actions are taken where necessary and improvements in practice are made.</p>
GQ6 Risk assessments of the establishment's practices and processes are completed regularly, recorded and monitored
<p>a) There are documented risk assessments for all practices and processes requiring compliance with</p>

the HT Act and the HTA's Codes of Practice.

b) Risk assessments are reviewed regularly.

c) Staff can access risk assessments and are made aware of risks during training.

Traceability standards

T1 A coding and records system facilitates the traceability of bodies and human tissue, ensuring a robust audit trail

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

b) A register of donated material, and the associated products where relevant, is maintained.

c) An audit trail is maintained, which includes details of: when and where the bodies or tissue were acquired and received; the consent obtained; all sample storage locations; the uses to which any material was put; when and where the material was transferred, and to whom.

d) A system is in place to ensure that traceability of relevant material is maintained during transport.

e) Records of transportation and delivery are kept.

f) Records of any agreements with courier or transport companies are kept.

T2 Bodies and human tissue are disposed of in an appropriate manner

a) Disposal is carried out in accordance with the HTA's Codes of Practice.

b) The date, reason for disposal and the method used are documented.

Premises, facilities and equipment standards

PFE1 The premises are secure and fit for purpose

a) An assessment of the premises has been carried out to ensure that they are appropriate for the purpose.

b) Arrangements are in place to ensure that the premises are secure and confidentiality is maintained.

c) There are documented cleaning and decontamination procedures.

PFE2 There are appropriate facilities for the storage of bodies and human tissue

a) There is sufficient storage capacity.

b) Where relevant, storage arrangements ensure the dignity of the deceased.

c) Storage conditions are monitored, recorded and acted on when required.

d) There are documented contingency plans in place in case of failure in storage area.

PFE3 Equipment is appropriate for use, maintained, validated and where appropriate monitored

- a) Equipment is subject to recommended calibration, validation, maintenance, monitoring, and records are kept.
- b) Users have access to instructions for equipment and are aware of how to report an equipment problem.
- c) Staff are provided with suitable personal protective equipment.

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 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 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 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.