Site visit inspection report on compliance with HTA minimum standards

CenoBiologics Ltd

HTA licensing number 22640

Licensed for the

- **processing, storage, distribution and import/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**

13 & 14 March 2019

Summary of inspection findings

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

Although the HTA found that CenoBiologics Ltd (the establishment) had met the majority of the HTA standards, shortfalls were found in relation to governance and quality standards specifically in relation to ensuring that imported tissue meets the same quality and safety standards required by the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended), procedures in the event that the establishment terminates activity, ensuring that traceability data is maintained by end users and the review of risk assessments.

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, 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.

'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
Musculoskeletal, Bone; Bone		**E**		**E**	**TPA**	**E**	**E**
Musculoskeletal, Bone; Acellular Bone		**E**		**E**	**TPA**	**E**	**E**
Musculoskeletal, Bone; Cancellous Bone Particles		**E**		**E**	**TPA**	**E**	**E**
Musculoskeletal, Bone; DBM		**E**		**E**	**TPA**	**E**	**E**
Musculoskeletal, Bone; Rib		**E**		**E**	**TPA**	**E**	**E**
Musculoskeletal, Bone; Skeletal Tissue		**E**		**E**	**TPA**	**E**	**E**

Other							
Musculoskeletal, Bone; Bone Strut		**E**		**E**	**TPA**	**E**	**E**
Musculoskeletal, Cartilage; Cartilage		**E**		**E**	**TPA**	**E**	**E**
Skin; Skin		**E**		**E**	**TPA**	**E**	**E**
Membrane, Amniotic; Amniotic Membrane		**E**		**E**	**TPA**	**E**	**E**
Membrane, Fascia Lata; Fascia Lata		**E**		**E**	**TPA**	**E**	**E**
Membrane, Pericardium; Pericardium		**E**		**E**	**TPA**	**E**	**E**
Cardiovascular, Valves; Heart Valves				**E**	**TPA**	**E**	**E**
Cardiovascular, Vessels; Vessels (Including Iliac)				**E**	**TPA**	**E**	**E**
Musculoskeletal, Tendon & Ligament; Tendons				**E**	**TPA**	**E**	**E**
Musculoskeletal, Tendon & Ligament; Ligaments				**E**	**TPA**	**E**	**E**

Background to the establishment and description of inspection activities undertaken

The establishment is licensed for the processing, storage, distribution, import 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). The establishment is also licensed for the storage of relevant material for use in a scheduled purpose under the Human Tissue Act 2004 (HT Act); however, activity taking place under the HT Act's legislation was not reviewed during this inspection.

The establishment has been licensed by the HTA since June 2012 and this report relates to a routine site visit inspection to assess whether or not the establishment meets the HTA's standards. Annual activity data, pre-inspection discussions with the DI and the previous inspection report were used to inform the timetable that was developed for this inspection.

The establishment receives and imports various tissues from procurement organisations both within and outside of the EEA. Tissue supplied by a tissue organisation within the EU, which is licensed by its relevant competent authority, consists of bone which is then subject to processing by the establishment before undergoing terminal sterilisation.

Tissue imported from a tissue retrieval organisation outside of the EU, a third country supplier, falls into three categories. The first category are tissues that are freeze dried before being terminally sterilised and includes bone, cartilage and membrane. The second category are tissues that are received as processed (by the third country supplier), cryopreserved products and include tendons, heart valves, conduits (iliac, veins, arteries), pericardium patches and pulmonary patches. The third and final category are tissues that are processed aseptically by the establishment before being distributed without terminal sterilisation. This third category consists of bone putty products produced from bone mixed with a carrier to produce a 'putty' product for use in orthopaedic procedures.

The freeze dried and terminally sterilised products are generated from tissue received by the establishment which is then processed before being freeze dried and terminally sterilised or in the case of cartilage, cut to size and terminally sterilised. These products are then distributed and exported for end use.

The cryopreserved products are all supplied by the third country supplier. They are imported into the establishment as a processed and cryopreserved product which is then packaged (secondary packaging) by the establishment before being distributed and exported for end use.

The establishment's bone putty product is derived from bone tissue supplied to the establishment by one of the supplying tissue establishments. In a monitored environment with a Grade A air quality, bone is processed and mixed with a carrier to create the putty product which is then distributed and exported for end use.

At the time of the inspection, the establishment had an application to import tissue from a second third country supplier. This proposed activity was not reviewed during the inspection as this will be assessed as part of the import application process.

At the time of the inspection, the establishment was also considering commencing a new procedure relating to the products which are currently in the cryopreserved category above. The establishment is considering importing tissue from third country suppliers and then processing the tissue themselves before cryopreserving them and distributing and exporting them for end use. Although discussed at high level during the inspection, the establishment will need to alert the HTA to this new activity and to submit a preparation process dossier regarding the new activity prior to it commencing.

Audit Exercise

During the inspection, audits were carried out on some of the products distributed and exported by the establishment as set out below.

Donor medical histories and lifestyle questionnaires were reviewed for one donor from each of the current two supplying organisations to verify that testing and donor selection as defined by the Regulations was being undertaken appropriately. Advice has been given to the establishment regarding the recoding of the donor selection assessments for donors from the third country supplier (see advice item 2).

The Single European Code (SEC) for a bone product in storage at the establishment was chosen at random. Records for the product were reviewed, including records of processing and sterilisation.

Records relating to two filler products (bone putty) were reviewed including processing and environmental monitoring records. In addition, records of the reagents used during the processing of the tissue were included in the review.

Records relating to the processing of five cryopreserved products (two conduits, two heart valves and one tendon) at the third country supplier's organisation were also reviewed. Environmental monitoring data, including operator finger dabs, settle plate data and post processing sterility test data, were reviewed. For the tendon, donor records were also reviewed. Infectious disease marker serological testing data for this sample were reviewed to verify that the required tests had been undertaken and the blood used for testing was taken from the donor within the required timeframe. Records relating to cryopreserved products identified that continuous non-viable particulate monitoring was not being undertaken during the processing of these tissues (see shortfall against GQ1(n)).

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
GQ1 All aspects of the establishment's work are supported by ratified documented policies and procedures as part of the overall governance process.		
n) The establishment ensures imports from non-EEA states meet the standards of quality and safety set out in Directions 002/2018.	An audit of cryopreserved tissue that is processed by the third country supplier prior to its import by the establishment was undertaken during the inspection. The audit showed that operator finger dabs and settle plates were being used during critical processing events and post process microbiological sterility testing was being undertaken on all processed products. In addition, the processing environment was monitored on a monthly basis to assure the processing establishment that the processing environment met the Grade A air quality requirements. Although the above environmental and process monitoring was being undertaken, the audit highlighted that in-process, non-viable particulate monitoring, as required by the Regulations, was not being undertaken.	**Minor**
GQ4 There is a systematic and planned approach to the management of records.		
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.	The establishment has agreements in place with distributors of tissue products which require the distributor to maintain records of traceability for 30 years as required by the Regulations. Each tissue product also has a product information document within the packaging which implies a responsibility onto the end user of the product to maintain traceability records. However, the product information leaflet does not specify the time period, 30 years from use, expiry or disposal of the product, required by the Regulations.	**Minor**
k) There are documented agreements with end users to ensure they record and store the data required by Directions 002/2018.		

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.	The establishment has a procedure in place with regards to stored tissue products in the event that it ceases to undertake licensable activity. The procedure sets out that any tissue stored at the establishment at the time of activity ceasing would be returned to the supplying organisation. The procedure, however, does not include what would happen to records and traceability data.	**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 has a range of risk assessments in place. During the inspection, some examples of risk assessments that had not been reviewed on an annual basis were found.	**Minor**

Advice

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

No.	Standard	Advice
1.	GQ4(h)	The establishment maintains environmental monitoring data regarding its facility. In the case of the building's environmental monitoring system, which records temperatures and pressures of different areas, this data is automatically downloaded to the establishment's server. However, data from the active air sampler is manually transferred to the server via a USB device. During the audit, examples were found where the data from the active air sampler had not been transferred from the sampling device to the server, although it had been maintained on the device itself. Additionally, during the review of environmental monitoring by the building's automated system, it was found that for a period of six months the automated download file had become corrupted and had not accurately recorded the data as expected. Although over this period there was no data on the server, a communication from the manufacturer of the monitoring system confirmed that the data was not lost and that it would be possible to retrieve it from the system. In addition, the manufacturer also confirmed that over this period, all of the alarms to detect out of range temperatures or pressure differentials would have been functioning as expected. Since the DI had not had any alarms over this period, the manufacturer's statement helped to assure the DI that there had been no excursions from the required temperatures or pressures over this period. The DI is advised to include regular audits of data such as this during the establishment's programme of audits to help assure himself that automated and manual data downloads are being undertaken as expected and the data is correct and appropriately archived.

2.	GQ5(d)	All tissue donor details are reviewed at the establishment to help assure the DI that donors have been appropriately selected and that the selection is in accordance with the requirements of the Regulations. The establishment, however, uses different documentation to record the results of these donor reviews depending upon the organisation from which the tissue was supplied. Although the same donor selection criteria are reviewed in both cases, the DI is advised to consider using a standardised form as this will help to facilitate donor selection reviews and audit activity as the data will be in a unified format.
3.	PFE3(c)	A storage room at the establishment used to store both raw materials and processed product is temperature monitored and has an upper temperature limit of 25^{o}C based on the upper limits of the materials being stored within it. A review of the temperature monitoring data for this room, including summer periods, demonstrated that no excursions above to maximum temperature had occurred. However, the room's temperature did rise towards the upper limit on several occasions for extended periods. With this in mind, the DI is advised to keep the temperature of this room under review in order to risk assess the need for additional cooling to maintain an appropriate temperature, especially if more equipment or refrigerators are added to this room in the future.

Concluding comments

Areas of good practice were observed during the inspection and some examples of these have been listed below:-

- The establishment continues to select various products over a one year period and sends these to an external organisation for colony forming unit analysis to assay for any potential contamination. In addition, an archive sample of every production run of the filler product that is processed by the establishment aseptically is retained so that it is available for future testing if any issues are identified at a later date. These measure help to assure the DI that aseptic processing and terminal sterilisation are performing as expected.

There are a number of areas of practice that require improvement, including four minor shortfalls. The HTA has given advice to the Designated Individual with respect to auditing of the process for archiving environmental monitoring data, standardising the use of forms to record the donor assessment criteria, automated alarms for environmental condition deviations and continuing to ensure that operational areas remain at the correct temperature to maintain the raw materials and products stored within.

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: 11 April 2019

Report returned from DI: 23 April 2019

Final report issued: 17 May 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

Consent

Standard
C1 Consent is obtained in accordance with the requirements of the HT Act 2004, the Human Tissue (Quality and Safety for Human Application) Regulations 2007 and as set out in the HTA's Codes of Practice.
c) The establishment or the third party's procedure on obtaining donor consent includes how potential donors are identified and who is able to take consent.
d) Consent forms comply with the HTA Codes of Practice.
e) Completed consent forms are included in records and are made accessible to those using or releasing tissue and / or cells for a Scheduled Purpose.
C2 Information about the consent process is provided and in a variety of formats.
a) The procedure on obtaining consent details what information will be provided to donors. As a minimum, the information specified by Directions 002/2018 is included.
b) If third parties act as procurers of tissues and / or cells, the third party agreement details what information will be provided to donors. As a minimum, the information specified by Directions Directions 002/2018 is included.
c) Information is available in suitable formats and there is access to independent interpreters when required.
d) There are procedures to ensure that information is provided to the donor or donor's family by trained personnel.
C3 Staff involved in seeking consent receive training and support in the implications and essential requirements of taking consent.
a) Staff involved in obtaining consent are provided with training on how to take informed consent in accordance with the requirements of the HT Act 2004 and Code of Practice on Consent.
b) Training records are kept demonstrating attendance at training on consent.

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.
j) There are procedures detailing the critical materials and reagents used and where applicable, materials and reagents meet the standards laid down by the European directives on medical devices and in vitro diagnostic medical devices.
k) There is a procedure for handling returned products.
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.
m) The criteria for allocating tissues and / or cells to patients and health care institutions are documented and made available to these parties on request.
n) The establishment ensures imports from non EEA states meet the standards of quality and safety set out in Directions 002/2018.
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.
f) There are procedures to ensure that donor documentation, as specified by Directions 002/2018, is collected and maintained.
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.
j) Records are kept of products and material coming into contact with the 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.
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.
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.
c) In cases other than autologous donors, donor selection is carried out by authorised personnel and signed and reviewed by a qualified health professional.
d) There is a system in place either at the establishment or at a third party acting on its behalf to record results of donor selection and associated tests.
e) Testing of donor samples is carried out using CE marked diagnostic tests.
f) Samples taken for donor testing are clearly labelled with the time and place the sample was taken and a unique donor identification code.
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.
e) In the event of a recall, there are personnel authorised within the establishment to assess the need for a recall and if appropriate initiate and coordinate a recall.
f) There is an effective, documented recall procedure which includes a description of responsibilities and actions to be taken in the event of a recall including notification of the HTA and pre-defined times in which actions must be taken.
g) Establishments distributing tissue and / or cells provide information to end users on how to report a serious adverse event or reaction and have agreements with them specifying that they will report these events or reactions.
h) Establishments distributing tissues and / or cells have systems to receive notifications of serious adverse events and reactions from end users and notify the HTA.
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.
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.
a) Tissues and / or cells stored in quarantine are stored separately from tissue and / or cells that have been released from quarantine.
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.

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.
a) There is a system to ensure tissue and / or cells are not distributed until they meet the standards laid down by Directions 002/2018.
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.
i) Primary packaging containing tissues and / or cells is labelled with the information required by Directions.
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.
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.
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.
b) Disposal arrangements reflect (where applicable) the consent given for disposal.

Human Tissue Act 2004 Standards

Consent standards
C1 Consent is obtained in accordance with the requirements of the Human Tissue Act 2004 (HT Act) and as set out in the code of practice
a) Consent procedures are documented and these, along with any associated documents, comply with the HT Act and the HTA's Codes of Practice.
b) Consent forms are available to those using or releasing relevant material for a scheduled purpose.
c) Where applicable, there are agreements with other parties to ensure that consent is obtained in

accordance with the requirements of the HT Act and the HTA's Codes of Practice.

d) Written information is provided to those from whom consent is sought, which reflects the requirements of the HT Act and the HTA's Codes of Practice.

e) Language translations are available when appropriate.

f) Information is available in formats appropriate to the situation.

C2 Staff involved in seeking consent receive training and support in the essential requirements of taking consent

a) There is suitable training and support of staff involved in seeking consent, which addresses the requirements of the HT Act and the HTA's Codes of Practice.

b) Records demonstrate up-to-date staff training.

c) Competency is assessed and maintained.

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

a) Ratified, documented and up-to-date policies and procedures are in place, covering all licensable activities.

b) There is a document control system.

c) There are change control mechanisms for the implementation of new operational procedures.

d) Matters relating to HTA-licensed activities are discussed at regular governance meetings, involving establishment staff.

e) There is a system for managing complaints.

GQ2 There is a documented system of audit

a) There is a documented schedule of audits covering licensable activities.

b) Audit findings include who is responsible for follow-up actions and the timeframes for completing these.

GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills

a) Qualifications of staff and all training are recorded, records showing attendance at training.

b) There are documented induction training programmes for new staff.

c) Training provisions include those for visiting staff.

d) Staff have appraisals and personal development plans.

GQ4 There is a systematic and planned approach to the management of records
a) There are suitable systems for the creation, review, amendment, retention and destruction of records.
b) There are provisions for back-up / recovery in the event of loss of records.
c) Systems ensure data protection, confidentiality and public disclosure (whistleblowing).
GQ5 There are systems to ensure that all adverse events are investigated promptly
a) Staff are instructed in how to use incident reporting systems.
b) Effective corrective and preventive actions are taken where necessary and improvements in practice are made.
GQ6 Risk assessments of the establishment's practices and processes are completed regularly, recorded and monitored
a) There are documented risk assessments for all practices and processes requiring compliance with 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.
g) Records of any agreements with recipients of relevant material 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 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.