Site visit inspection report on compliance with HTA minimum standards

Edge Medical (Biologics) Ltd.

HTA licensing number 22646

Licensed for the

- **import, 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)**

31 July- 01 August 2018

Summary of inspection findings

The HTA found the Licence Holder suitable in accordance with the requirements of the legislation, but is concerned over suitability of the DI due to the number and recurrent nature of the shortfalls identified as part of this site visit inspection.

Although the HTA found that Edge Medical (Biologics) Ltd. (the establishment) had met many of the HTA standards, four major and eight minor shortfalls were found in relation to the Governance and Quality Systems (GQS) and the Premises, Facilities and Equipment (PFE) standards.

The four major shortfalls were in relation to the requirement for the establishment to ensure imports from third country suppliers meet the standards of quality and safety as set out in Directions 002/2018, the document control system, the application and recording of the Single European Code (SEC) and the establishment's risk assessments. The eight minor shortfalls were in relation to governance meetings, third party agreements, training of members of staff working under the licence, internal audits, the storage and backup of electronic records, the recording of raw data and quarantine arrangements for tissue and cell (T&C) products.

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

Tissue category; Tissue type	Procurement	Processing	Testing	Storage	Distribution	Import	Export
Musculoskeletal, Bone; Demineralised Bone Matrix (DBM)				**E**	**E**	**E**	**E***
Musculoskeletal, Bone; DBM Putty				**E**	**E**	**E**	**E***
Musculoskeletal, Bone; Cancellous Bone Particles				**E**	**E**	**E**	**E***
Musculoskeletal, Bone; Acellular Bone				**E**	**E**	**E**	**E***
Muscoskeletal, Tendons and Ligament; Tendons				**E**	**E**	**E**	**E***
Musculoskeletal, Bone; Bone				**E**	**E**	**E**	**E***
Muscoskeletal, Bone; Bone Strut				**E**	**E**	**E**	**E***
Muscoskeletal, Tendons and Ligament; Menisci				**E**	**E**	**E**	**E***
Skin; Skin				**E**	**E**	**E**	**E***

‘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.

Background to the establishment and description of inspection activities undertaken

Edge Medical (Biologics) Ltd. (the establishment) is licensed for the import, storage, distribution and export of human tissues and cells under the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended). The establishment is not currently undertaking any export activity.

The establishment imports a range of products including fresh bone, tendons, ligaments, skin and acellular T&C products. All the material is procured from deceased donors and processed in three tissue banks based in the USA. The three tissue banks are third country suppliers (3CS) of the establishment. The three 3CS undertake the processing of the T&C products and oversee the mandatory serology testing for infectious diseases of all the donors. The tests are carried out under agreement with clinical laboratory improvement amendments (CLIA)-accredited laboratories. The establishment imports the T&C products directly from the three 3CS in the USA.

The establishment receives ambient temperature and frozen products. Upon receipt of the products, staff at the establishment undertake visual checks of the packaging and the inventory is updated with all the required information. Ambient temperature T&C products are stored between 15-30°C and the ambient temperature tissue cupboard is continuously temperature-monitored. For frozen products, if there is no dry ice, the T&C product is placed in quarantine to be returned to the 3CS (*see Shortfall, under standard* PFE2 (a)). Frozen products suitable for release are placed in the relevant section of the freezer. The -80°C freezer is temperature-monitored and is connected to a wireless callout system. Temperature excursions outside the set ranges (above -74°C and below -85°C) trigger the callout system and the DI is informed by text message (*see advice item 10*). The establishment will allocate and apply the SEC on the products prior to release to end users.

The establishment has been licensed by the HTA since August 2013. This report describes the establishment's third routine inspection, which took place on 31 July and 01 August 2018. Discussions were held with the DI and key members of staff involved in the licensable activities. A review of documentation, including the processing records of six imported T&C products and a visual inspection of the premises, were also undertaken as part of the inspection. The processing records were reviewed for evidence of appropriate serology and sterility testing and the results of environmental monitoring or terminal sterilisation. No discrepancies were noted.

Audits of traceability were carried out on T&C products which included:

- six T&C products cross-checked against the inventory. No discrepancies were noted.
- four T&C products distributed to end users were cross-checked against the inventory and the packing slips. Three out of the four products were distributed without the Single European Code (SEC) applied (see Shortfall, under standards GQ4 (b) and GQ6 (d)).

Inspection findings

The HTA found the Licence Holder to be suitable in accordance with the requirements of the legislation but has concerns over suitability of the DI.

Prior to the inspection the DI was asked to supply a range of information regarding the establishment and its 3CS. Not all the requested information was provided either in advance of the inspection or during the site visit. The DI was granted an extension of an additional week following the inspection to supply the information required on the 3CS. However, the DI has not been able to supply all the information requested. During the inspection, the DI was also initially unable to access standard operating procedures (SOPs) and there was overall difficulty in supplying the information requested.

The HTA is concerned that the DI has not taken appropriate steps to ensure that the establishment is operating under a robust governance system that is underpinned by accurate and accessible procedures. The HTA is also concerned that a number of issues identified in previous inspections appear to be recurring. These include the scope of the internal audits, document control, the retention and storage of raw data, the absence of minuted governance meetings, and the establishment demonstrating appropriate due diligence in ensuring the quality and safety of imported T&C products.

The number and recurrent nature of the shortfalls identified as part of the most recent site visit inspection is of concern to the HTA. The HTA consider them indicative of the fact that the DI has not taken adequate steps to ensure that there are suitable practices in place for the conduct of licensable activities.

The HTA will be maintaining oversight of the actions taken to address these shortfalls and as part of this process will make a final assessment of the suitability of the DI.

Compliance with HTA standards

Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended).

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.		

c) There are regular governance meetings, for example health and safety, risk management and clinical governance committees, which are recorded by agendas and minutes.	Although the DI meets with staff working under the licence, there are no minuted governance meetings. *(see Advice, item 2)*	**Minor**
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.	The establishment does not have a sufficiently robust and centralised document control system to ensure all documents are reviewed, approved, dated and that only current documents are in use. For example: • during the inspection, the DI was unable to locate current electronic versions of all of the establishment's SOPs; • staff engaged in activities under the licence were unable to access the establishment's SOPs; • the inspection team was presented with two copies of SOP EMB023 for rejected goods. Both were labelled as 'version one', but contained different content; • the SOP on the SEC was written on the first day of the inspection and was not document controlled. *(see Advice, item 3)*	**Major**

n) The establishment ensures imports from non EEA states meet the standards of quality and safety set out in Directions 002/2018.	Information required to determine if one of the 3CS of the importing establishment meet the standards of quality and safety set out in Directions 002/2018 was requested a month prior to the inspection. As this information was not made available prior to, or during, the inspection, the establishment was given a further one week's extension following the site visit. To date, the inspection team has not been provided with all the requested information. Also, this 3CS did not meet the requisite air particle monitoring requirements for measurements at rest and in operation as set out in Directions 002/18. The establishment has decided to suspend the import of T&Cs from this supplier. Furthermore, the documented procedures for donor testing of the other two 3CS does not include the requirement for blood samples to be collected within seven days before tissue recovery, or if not possible, within 24 hours following tissue recovery. In addition, the documented procedures for donor selection and exclusion of the 3CS do not include all of the donor exclusion criteria as set out in Annex A of the Guide to Quality and Safety Assurance for Human Tissues and Cells for Patient Treatment. For example, the donor eligibility procedure of two of the 3CS does not screen for: • Previous history of malignant disease. • Transplantation with xenografts, including acellular grafts, such as pig heart valve. • Ingestion or exposure to, a substance (such as cyanide, mercury, gold) that may be transmitted to recipients in a dose that could endanger their health.	**Major**
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.	The establishment has no written agreements with third parties distributing T&C products to end users. Furthermore, there are no formal arrangements in place that include the	**Minor**

s) Third party agreements specify that the third party will inform the establishment in the event of a serious adverse reaction or event.	requirement for third parties to report serious adverse events and reactions (SAEARs) to the establishment within 24 hours of discovery. *Prior to the draft report being issued the DI submitted evidence of the actions taken in relation to the above shortfall. The HTA has assessed this evidence as satisfactory and considers this standard to be met.*	
GQ2 There is a documented system of quality management and audit.		
b) There is an internal audit system for all licensable activities.	The scope of the audits was limited, and did not cover the full range of activities carried out under the licence and are not against all applicable standards. There is no documented procedure detailing the frequency and how audits will be undertaken. (see Advice, item 4)	**Minor**
GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills.		
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.	The training records for members of staff working under the licence, does not include the regulatory context and ethical requirements relevant to their work. *Prior to the final report being issued the DI submitted evidence of the actions taken in relation to the above shortfall. The HTA has assessed this evidence as satisfactory and considers this standard to be met.*	**Minor**
GQ4 There is a systematic and planned approach to the management of records.		
c) Written records are legible and indelible. Records kept in other formats such as computerised records are stored on a validated system.	Although the establishment keeps electronic records these are not stored on a validated system. For example, the DI was not able to locate the most recent SOPs on the system and no other member of staff working under the licence had access to them.	**Minor**

d) There is a system for back-up / recovery in the event of loss of computerised records.	The establishment's practice is for computerised records to be backed up bi-weekly on a hard drive. However, the DI was not able to retrieve the most current SOPs from the back-up system.	**Minor**
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.	Failure of the battery in the freezer temperature probe resulted in the loss of temperature monitoring data over a period of time. The establishment's procedures did not ensure that raw data critical to the safety and quality of tissues in storage was collected and maintained.	**Minor**
GQ6 A coding and records system facilitates traceability of bodies, body parts, tissues and cells, ensuring a robust audit trail.		
d) The requirements of the Single European Code are adhered to as set out in Directions 002/2018.	The establishment's practice is to allocate and apply the SEC on T&C products prior to distribution to end users and record it on the packing slip, a copy of which is retained both electronically and on paper. It was noted during the inspection that the establishment distributed a number of T&C products to end users, during April and May 2018, without retaining a record of the SEC. Furthermore, the inspection team was not sufficiently assured that the establishment had allocated and applied the SEC on these T&C products.	**Major**
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.	Although the establishment has documented risk assessments, these do not capture all the risks associated with the activities being carried out under the licence and the full range of control measures in place, which help to mitigate identified risks. In addition, the risk assessments had not been reviewed since the previous inspection and were not accessible to staff working under the licence.	**Major (Cumulative)**

Premises, Facilities and Equipment

Standard	Inspection findings	Level of shortfall
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.	The establishment's procedures refer to quarantine of T&C products, however, the establishment has not allocated a quarantine section within the freezer or the ambient temperature storeroom. *Prior to the draft report being issued the DI submitted evidence of the actions taken in relation to the above shortfall. The HTA has assessed this evidence as satisfactory and considers this standard to be met.*	**Minor**

Advice

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

No.	Standard	Advice
1.	GQ1 (b)	The DI is advised to update the establishment's procedures to reflect the fact that the SEC is allocated and applied on T&C products prior to distribution to end users and this is recorded on the packing slip, a copy of which is retained both electronically and on paper.

		The establishment regularly tests the alarm of the freezer and checks the back-up CO2 cylinder, which is supposed to serve as a contingency in the event of freezer failure. The DI is advised to document these procedures in an SOP.
2.	GQ1 (c)	In addressing the shortfall above against GQ1c, the DI is advised to include in the agenda for the governance meetings the work undertaken by the establishment, any updates from the HTA, incidents, and issues that may have arisen. Also, the results of all audit findings, and actions taken, should be formally recorded and discussed at governance meetings, to ensure continuing improvement of processes and practices. This will help raise awareness among staff involved in this work of the associated regulatory requirements, and facilitate the integration of the licensable activities into the governance and quality management system used by the establishment.
3.	GQ1 (d)	The DI is advised to ensure that documents include revision histories, when the document is due for review, and the names of both the author and reviewer as relevant. The DI should also consider the use of a document management system, to enable a more efficient document control.
4.	GQ3 (f)	The DI is advised to formalise the process of training of staff on HTA matters and include the content of the material provided to staff as part of the training.
5.	GQ2 (b) (c)	The DI is advised to review the audit template used to carry out the internal and independent audit and include the content of what was audited for all licensable activities. Currently, the internal audit report does not provide any context for the results. Clarity on how each audit is performed will assure the DI of its rigour, and enable other staff to perform such audits in the future. The DI could consider dividing the internal audits into small, manageable tasks and nominating it to the PD(s) under the licence. The DI is also advised to expand the scope of the audits of the 3CS to also include horizontal audits of batch processing records for each of the tissue types imported by the establishment. This will help ensure that the products supplied by the 3CS meet the requirements of the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended).
6.	GQ4 (d)	The DI is advised to finalise his plans for cloud storage of the establishment's documentation, raw and traceability data. This will help ensure that, should the computer or hard drive be damaged, there will also be an electronic copy of these data.
7.	GQ8 (a)	With reference to the above shortfall against GQ8(a) the DI is advised to expand the scope of the risk assessments to include: • loss of traceability / the risk of sending out products without the SEC; • back-up of records and loss of raw and traceability data. The establishment is using a third party to monitor and retain electronically the raw data. However, the establishment was not aware that these data are only stored by the third party for two years. Previously, the

		establishment's procedure was to print off weekly and retain the temperature raw data. Recently, there was a decision to only retain the electronic data. • the practice of importing T&C products from the 3CS to end users. The DI is advised to ensure there is clarity on what the risks are and the full range of existing control measures are documented, which help to mitigate identified risks. Prior to the implementation of a new management system the DI is advised to go through an appropriate and robust change control process, including formal risk assessment. The DI is also advised to consider the way risk assessments are used as part of staff induction and training.
8.	GQ7 (a); PFE2 (a)	The establishment's procedure on control of a non-conforming product describes that records of non-conformities and action taken, including concessional releases shall be maintained. The DI is advised to formalise a non-conformity / incident log to ensure that in the future the following information is included for each non-conformity / incident: • details of the non-conformity/ incident; • any action taken; • the impact of the non-conformity / incident; • details of the investigation undertaken and when the incident was closed; and • whether or not the incident was reported to the HTA and the rationale for this decision. The DI is also advised to formalise the process for the management of non-reportable incidents in an SOP to ensure that all members of staff understand the process and what it involves.
9.	PFE3 (a)	The DI is advised to test and record the response to unannounced freezer alarms to ensure that the correct notification procedures are being followed.
10.	PFE3 (b)	The DI is advised to consider including additional members of staff as points of contact via text on the wireless callout system to ensure the quality and safety of the tissues in the DI's absence.

Concluding comments

There are a number of areas of practice that require improvement, including four major and eight minor shortfalls. The HTA will be maintaining oversight of the actions taken to address the shortfalls to ensure that they are rectified promptly and appropriately and that the DI is able to fulfil their statutory responsibilities.

The HTA requires that the Designated Individual addresses the major and minor 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: 2018/ 08/ 25

Report returned from DI: 2018/ 11/ 02

Final report issued: 2018/ 11/ 15

Completion of corrective and preventative actions (CAPA) plan

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

Date: 2020/ 10/ 01

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.
b) If there is a third party procuring tissues and / or cells on behalf of the establishment the third party agreement ensures that consent is obtained in accordance with the requirements of the HT Act 2004, the Q&S Regulations and 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.
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 002/2018 is included.

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.
f) There are procedures for tissue and / or cell procurement, which ensure the dignity of deceased donors.

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.
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.
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.
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.
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.
d) Where appropriate, there are procedures to ensure that the premises are of a standard that ensures the dignity of deceased persons.
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.
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.
h) Users have access to instructions for equipment and receive training in the use of equipment and maintenance where appropriate.

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.

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.

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.