Site visit inspection report on compliance with HTA minimum standards

Future Health Technologies Ltd.

HTA licensing number 22503

Licensed for the

- **procurement, processing, testing, 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; and**

- **storage of relevant material which has come from a human body for use for a scheduled purpose**

5-6 September 2017

Summary of inspection findings

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

Although the HTA found that Future Health Technologies Ltd (the establishment) had met the majority of the HTA standards, two major and nine minor shortfalls were identified. The major shortfalls are related to the marketing of services which have not been authorised and the absence of validation studies for transport kits used. The remaining minor shortfalls are related to the absence of accurate documentation of procedures, internal and independent audits, sterility and quality checks, records of plastic consumables used during processing and risk assessments of premises.

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
Progenitor Cell, Haematopoeitic, Cord Blood; Cord Blood	**TPA**	**E**	**E/TPA**	**E**	**E**	**E**	**E**
Other; Dental Pulp	**E**	**E**	**E/TPA**	**E**	**E**	**E**	**E**
Other; Cord Tissue	**TPA**	**E**	**E/TPA**	**E**	**E**	**E**	**E**

Background to the establishment and description of inspection activities undertaken

This report refers to the activities undertaken by Future Health Technologies Ltd (the establishment). The establishment is licensed for all activities under the Human Tissue (Quality and Safety for Human Application) Regulation (Q&S Regulations) for long-term storage of umbilical cord blood (UCB), umbilical cord tissue (UCT) and dental pulp (DP) for future autologous or allogeneic use. The establishment is also licensed for storage of relevant material under the Human Tissue Act, although it is currently not undertaking this activity. This is the eighth inspection of the establishment since being licensed by the HTA in 2006.

The establishment has a second facility based in Switzerland which began operations in 2013. This site is currently commencing part of the validation work required for HTA-licensable processes in the UK.

The procurement of UCT and UCB within the UK is undertaken on behalf of the establishment by a phlebotomy agency acting under the terms of a TPA. For collection of UCT and UCB units from abroad, the establishment liaises with its international partner offices, who take responsibility for obtaining consent and providing transport kits to clients. The establishment is responsible for ensuring all client samples received for processing and storage in the UK comply with all HTA standards. For the transport of UCT and DP samples, the establishment includes a 'preservation' tablet in the kit which has validated to prevent microbial contamination in the transport media. A temperature logging device is also included in the procurement kits which provides information on the minimum and maximum temperatures reached during transit. Samples which are received outside the accepted criteria for temperature and times in transit will be still be processed, and clients will be informed based on the outcome of the quality checks to decide whether or not the samples will be banked as per the terms of their agreements.

The establishment's processing facility consists of four clean rooms for processing each tissue type separately. The microbiological safety cabinets (MSCs) in the clean rooms maintain a Grade A environment within a Grade B background for UCT and DP processing, and within a Grade C background for UCB processing. All environmental monitoring is conducted throughout in accordance with the requirements of Directions 003/2010 and Annex I of the EU Guidelines to Good Manufacturing Practice. Plates and samples for microbiological testing, and blood samples taken for mandatory serology testing, are analysed in-house. Any positive microbiology or serology samples are sent to an external private laboratory for confirmation and identification of microbial contaminants.

Following processing, the samples are cryopreserved using controlled-rate freezers. Samples are then stored in liquid nitrogen storage tanks, and corresponding pilot samples for quality checks are stored in separate cryovessels. Any sample with a positive microbial result, or a previously unknown positive serology, will be transferred out to a separate 'viral' or 'microbial' tank respectively. The liquid nitrogen vessels are linked to a continuous temperature monitoring system that alerts staff on a 24-hour basis should any deviation in temperatures occur. For quality assurance, the establishment carries out post-cryopreservation checks on all UCT, DP and whole blood UCB samples. For volume-reduced UCB samples, quality assessments are performed prior to cryopreservation.

The inspection included a visual inspection of the premises and round table discussions with key members of staff, including the DI who is also the Compliance Manager, Laboratory Manager, Quality Assurance Supervisor and Chief Operations Officer. A review of documentation, an observation of processing of a UCT sample and an assessment of ongoing validation work was also undertaken with the main attention given to quality checks throughout the procedures. Prior to the inspection, the HTA requested information on all samples received in the preceding twelve months. The data supplied included information on the tissue type, country of origin, time in transit and the minimum and maximum temperatures reached during transit. The inspection team reviewed six individual samples from this data using traceability audits looking at procurement reports, serology and microbiology results, processing records, environmental monitoring, staff training and communication with clients. Whilst no discrepancies were found in the specific records reviewed, it was noted the processing records and forms were not completed consistently.

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

Consent

Standard	Inspection findings	Level of shortfall
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 003/2010 is included.	The establishment's partner organisations, who provide marketing services for the establishment, are advertising services which are not in line with the establishment's validated processes. Although the establishment is undertaking validation studies to be able to offer these range of services to clients, this has not yet been completed.	**Major**

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.		
b) There are procedures for all licensable activities that ensure integrity of tissue and / or cells and minimise the risk of contamination.	The establishment's documents are not in line with practices. The establishment's policies for storage of serological positive samples are	**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.	inconsistent with standard operating procedures (SOP). This includes, for example, the fact that the SOP for the release of samples from the quarantine to the long term storage tanks includes storage of HIV positive samples in the viral tank; this contradicts the establishment's policy for not accepting HIV positive samples. Furthermore, the establishment's SOPs are not in line with working practices in a number of areas. For example, the SOP for controlled rate freezing does not include steps for the monitoring of the programme; the SOP for UCT processing does not include the back-up procedures in the event that a processing failure occurs; and the SOP for haematological analysis does not include instructions for staff if values do not fall within the expected ranges. The establishment also has SOPs in circulation that are not applicable to the establishment's current practices, for example SOPs for the collection, processing and storage of unlicensed tissue types.	
GQ2 There is a documented system of quality management and audit.		
b) There is an internal audit system for all licensable activities.	Although a schedule of internal audits reviewing HTA licensable activities was in place, the audits detailed had not completed.	**Minor**
c) An audit is conducted in an independent manner at least every two years to verify compliance with protocols and HTA standards, and any findings and corrective actions are documented.	The establishment's independent audit does not assess the establishment's compliance against HTA standards.	**Minor**

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.	The establishment has an SOP for the collection of client samples in the event a transport kit is not available. However, this procedure has not been validated. Although the establishment carries out post-cryopreservation checks, for example viability checks for UCT and DP samples and CD34 counts for UCB, there is no comparable tests being carried out for volume-reduced UCB. Furthermore, while samples are subjected to the post-thaw tests described above, a regular quality control programme comprising of the full range of appropriate quality checks intended to ensure all processes are meeting the required standards, is not being undertaken.	**Minor**
GQ4 There is a systematic and planned approach to the management of records.		
j) Records are kept of products and material coming into contact with the tissues and / or cells.	The establishment records batch details of plastic consumables used during the processing of volume-reduced CB products. However, there are no records of the plastic consumables used during the processing of whole UCB, UCT and DP.	**Minor**
GQ7 There are systems to ensure that all adverse events are investigated promptly.		
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.	There are no procedures to test the sterility of UCT samples prior to long term storage, although these sterility checks are performed for UCB and DP samples. While the establishment does carry out microbial tests on UCT transport media, should the media appear discoloured or if the preservation tablet is not used, this is not sufficient to exclude contamination in all UCT samples.	**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.	Although the establishment has in place risk assessments for processes relating to the quality and safety of tissue products, the risk assessments are not reviewed annually.	**Minor**
c) Staff can access risk assessments and are made aware of local hazards at training.	The risk assessments are stored within a quality system folder and are not accessible by staff.	**Minor**

Premises, Facilities and Equipment

Standard	**Inspection findings**	**Level of shortfall**
PFE1 The premises are fit for purpose.		
a) A risk assessment has been carried out of the premises to ensure that they are fit for purpose.	There are no risk assessments looking at the security of the processing and storage facilities and back-up systems for data.	**Minor**
PFE4 Systems are in place to protect the quality and integrity of bodies, body parts, tissues and cells during transport and delivery to a destination.		
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.	The establishment has not validated the transport kits used to transport samples from clients. Analysis of transit data from the data provided prior to the inspection revealed an excess of 20% of all samples received in 2016 exceeded the temperature limits set by the establishment. This issue was highlighted during the previous HTA inspection and although the establishment has commenced validation work, this is still not completed.	**Major**
h) Packaging and containers used for transportation are validated to ensure they are fit for purpose.		

Advice

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

No.	Standard	Advice
1.	GQ1g	The DI should ensure that only the most current epidemiological guidance is available to staff receiving tissue samples. Staff checking-in samples refer to printed guidance from the European Centre for Disease Prevention and Control (ECDC) website to determine if donors are at risk of communicable diseases based on recent travel history. However, the printed guidance is out of date and refers to epidemiology updates in 2015 and 2016.
2.	GQ1b/r	The DI is advised to review the procedure for release of samples to ensure tissue products are sent to authorised medical facilities. The SOP should clearly set out the checks required to ensure the receiving transplant centres are regulated by competent authorities and there are protocols to receive medical reports following transplant and to ensure the receiving centre reports SAEARs to the DI within 24 hours of discovery of the event.
3.	GQ1r	The DI should review the agreement with the external testing laboratory performing confirmatory testing to ensure the agreement refers to the correct legislation, includes the stipulation that any SAEAR should be reported to the DI within 24 hours of discovery of the event and includes suitable contact details for SAEARs reporting.
4.	GQ1p	The DI is advised to review the use of the automatic signature system for renewing agreements. The inspection team noted a TPA was recently signed by an ex-member of staff which renders the agreement void.
5.	GQ2d	While the establishment participates in external quality assurance (QA) schemes for serological testing and flow cytometry, the external QA samples are only processed by two senior staff scientists. The DI should ensure all operators process the external QA samples to ensure the results received are representative the establishment's procedures.
6.	GQ3f	Although staff training and induction programme includes an introduction to the HT Act and Q&S Regulations regulatory framework, the DI is advised to include knowledge of the scientific and ethical principles of working with human tissue.
7.	GQ4b	The establishment plans to implement a final quality control checklist prior to movement of samples to the final storage tank. The DI is advised to ensure that the final checklist is rolled out for all samples, and not only non-compliant samples. The form should be in line with current donor testing procedures and include a review of the time and temperature of samples during transit.

8.	GQ4f	The DI is advised to review the 'Phlebotomist Procurement Form'. Sections of the form are consistently not completed as the requested information in this form is completed in other forms and documents.
9.	GQ7a	The DI is advised to ensure that there are back up personnel available to review all incidents reported, which are currently only reviewed by the Quality Assurance Supervisor. This is to ensure that any incident which needs to be escalated to a SAEAR is reported to the HTA within 24 hours.
10.	PFE2b	The DI is advised to ensure decontamination of hands with aerosol spray within the safety cabinet does not affect the ongoing environmental monitoring. The DI should also ensure MSC vents are always kept clear. On inspection, the inspection team observed staff decontaminate hands close to settle plates and tube racks and air particle monitors are placed against the vents at the back of safety cabinet.
11.	PFE2b	The DI is advised to amend the form used to record daily pressure readings to clearly state the expected differential pressures required between change and clean rooms. The DI should ensure staff involved in processing are trained in the minimum differential pressures required and the accepted standard deviations. The related SOP for recording pressure readings should be amended to clearly set out the minimum differential pressures required, and remove references to pressure differentials between clean rooms and ambient.
12.	PFE2c	The DI is advised to include swabs of hatches between clean rooms in monthly environmental monitoring checks to ensure the decontamination procedures are effective.
13.	PFE3a	The DI is advised to review the temporary storage of UCB in the same refrigerator in the haematological laboratory which is used to store microbial samples and cell culture plates.
14.	PFE4e	The DI is advised to contact the manufacturer of the preservation tablet provided for use in transport medium to confirm that the storage of the tablet up to 30ºC does not affect potency of the tablet and to align future storage instructions with the manufacturer's recommendations. It was noted that the manufacturer's instruction sheet has specified storage of the preservation tablet of between 2-8ºC, which is not in line storage temperatures provided in client instructions of 2-30ºC.

Concluding comments

There are a number of areas of practice that require improvement, resulting in two major and nine minor shortfalls. These relate to a number of aspects absent in the establishment's consent procedures, governance and quality systems and premises, facilities and equipment. The HTA has given advice to the Designated Individual with respect to procedures for product receipt and release, reviewing of agreements and forms, procedures to ensure efficiency of environmental monitoring, staff performing external quality checks, temporary storage of UCB sample and confirmation of storage temperatures for the preservation tablet.

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: 4 October 2017

Report returned from DI: 12 October 2017

Final report issued: 20 October 2017

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: 07 March 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.
a) If the establishment acts as a procurer of tissues and / or cells, there is an established process for acquiring donor consent which meets the requirements of the HT Act 2004 the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (Q&S Regulations) and 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.
a) The procedure on obtaining consent details what information will be provided to donors. As a minimum, the information specified by Directions 003/2010 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 003/2010 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.
e) There are procedures for tissue and / or cell procurement, which ensure the safety of living 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.
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 003/2010.
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 003/2010.
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 003/2010, is collected and maintained.
g) There is a system to ensure records are secure and that donor confidentiality is maintained in accordance with Directions 003/2010.
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 003/2010 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 003/2010.
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 003/2010.
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 003/2010.
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.
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 003/2010.
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 003/2010.
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.

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.