Site visit inspection report on compliance with HTA minimum standards

Smart Cells International

HTA licensing number 22522

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**

10-12 November 2014

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 Smart Cells International (the establishment) had met the majority of the HTA standards, two major and four minor shortfalls were found in relation to Premises, Facilities and Equipment, and Governance and Quality Systems. These relate to process validation and the need for on-going performance monitoring, the approach to independent audits and donor serology testing, risk assessments and a particular aspect of the establishment's transport procedures.

Particular examples of strengths and 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 type	Procurement	Processing	Testing	Storage	Distribution	Import	Export
Umbilical cord blood	**TPA**	**E**	**TPA**	**E**	**E**	**E**	**E**
Umbilical cord tissue	**TPA**		**TPA**	**E**	**E**	**E**	**E**

Background to the establishment and description of inspection activities undertaken

This report refers to the activities carried out by Smart Cells International (SCI). The establishment is licensed for the procurement, testing, processing, storage, distribution and import/export of human tissues and cells under the Human Tissue (Quality and Safety for Human Application) Regulations 2007, and has been licensed by the HTA since October 2008. The establishment has been inspected on three previous occasions.

SCI is a private tissue bank that processes and stores umbilical cord blood and tissue for future, autologous or allogeneic use. Samples are sent to SCI from across the UK and from overseas. Donor selection and the seeking of consent are predominantly managed by a team based in the UK. However, in the case of the overseas clients, these processes may be managed by partner offices in the relevant territories according to well-defined procedures. Donor serology testing is carried out in the UK or overseas by third party laboratories under the terms of appropriate agreements. Umbilical cord blood samples are processed by the establishment in a dedicated cleanroom facility prior to being stored on site. Since the last

inspection, the establishment has entered into an agreement with a partner organisation in another EU member state which now undertakes the processing and storage of umbilical cord tissue samples on its behalf. Further background to the establishment can be found in past inspection reports, which are available on the HTA's website.

This report describes the establishment's fourth site visit inspection which took place on 10-12 November 2014. The inspection was a non-routine inspection and was scheduled in response to a number of issues that were identified at the previous inspection and which were not addressed to the HTA's satisfaction in the period thereafter. In addition to reviewing SCI's compliance with the HTA's licensing standards, the purpose of the inspection was to review the action taken by the establishment to address the findings of the previous inspection. The inspection team also conducted a thorough review of the steps taken by the establishment in response to Directions that were issued by the HTA subsequent to the previous site visit. In this regard, the inspection included an audit of client correspondence across a range of activities, together with a review of certain records to ensure that they had been labelled in accordance with HTA requirements.

The inspection also included interviews with key members of staff working under the licence, including the Scientific and Business Development Manager, who is also the Designated Individual, and the Chief Executive Office, who serves as the Corporate Licence Holder contact. A review of documentation relevant to the establishment's activities and a visual inspection of the premises where licensable activities are carried out were also conducted, as well as an audit of procurement and processing records.

Inspection findings

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

Compliance with HTA standards

Governance and Quality

Standard	Inspection findings	Level of shortfall
GQ2 There is a documented system of quality management and audit.		
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 has conducted a number of audits since the last inspection aimed at verifying compliance with protocols and HTA standards in an independent manner. However, the audits were conducted by the establishment's previous DI who left the company earlier in the year. The HTA do not consider that this individual was sufficiently independent to meet the requirements of this standard.	**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.	Since the last inspection, the establishment has conducted additional validation studies relating to the processing and storage of umbilical cord tissue. The results of these studies were submitted to the HTA for review immediately prior to the inspection. Although the data suggests that stem cells can be cryopreserved in uncontaminated samples processed within 48 hours of procurement, insufficient data has been generated to demonstrate that the same outcome can be assured if the samples are processed after 48 hours or if the samples are contaminated at the point of receipt. Without such data, and in the absence of additional quality control checks on non-conforming samples at the point of receipt, the establishment is not in a position to ensure that all samples that have entered long-term storage meet its minimum storage criteria. Furthermore, although the establishment analyses a number of umbilical cord blood samples each year to assess post-cryopreservation recovery rates, a critical review of the data obtained from these studies has not been conducted. Clear benchmarks for cell recovery have not been agreed upon or documented. As a result, the establishment has not ascertained whether the cryopreservation methodologies currently being employed continue to achieve the intended results. This issue was raised at the last inspection and has not been addressed adequately in the intervening period.	**Major**

GQ5 There are documented procedures for donor selection and exclusion, including donor criteria.		
b) The testing of donors by the establishment or a third party on behalf of the establishment is carried out in accordance with the requirements of Directions 003/2010.	The establishment's 'Statement of consent form / Maternal Health Questionnaire' ascertains whether either parent has lived in, or originates from, an area with a high prevalence of HTLV-1. However, it does not ascertain whether the donor has had sexual partners from those areas or whether the donor's parents originate from those areas. As a result, the establishment are not in a position to ensure that donor testing is carried out in accordance with the requirements of Directions 003/2010. **Following the inspection, the DI notified the HTA that the Maternal Health Questionnaire had been updated in accordance with the requirements outlined above. The HTA therefore consider this shortfall to have been addressed.**	**Minor**
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.	Although the establishment has a number of risk assessments in place relating to licensable activities, a risk assessment that addresses the risks associated with the use of the vial and quarantine freezers is not in place. This is particularly important as these tanks have limited reservoirs of liquid nitrogen and are filled manually on a daily basis to ensure that appropriate storage temperatures are maintained. The risk assessment should address issues such as a failure in the supply of liquid nitrogen supply or an inability to access the site and the impact this would have on stored samples. The risk assessment should be informed by the establishment's tank monitoring records which highlight the rate of loss of liquid nitrogen from these tanks over a 24 hour period. **Following the inspection, the establishment completed a risk assessment for this activity. The HTA therefore consider this shortfall to have been addressed.**	**Minor**

Premises, Facilities and Equipment

Standard	Inspection findings	Level of shortfall
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.		
b) There are procedures for the transport of tissues and / or cells which reflect identified risks associated with transport.	Although many of the procurement kits issued by the establishment now include data loggers so that the transport conditions can be assessed upon receipt, an SOP describing how the data will be reviewed, and deviations escalated, has not been put in place. **Following the inspection, the DI notified the HTA that documented procedures have been put in place to address this finding. The HTA therefore consider this shortfall to have been addressed.**	**Minor**
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.	Since the last inspection, the establishment has entered into an agreement with a partner organisation in another EU Member State for the processing of umbilical cord tissue. Although the third party has validated its processing methodologies, this validation extends only to those samples shipped between 2 and 22^{o}C. SCI's packaging is not validated to maintain this temperature range. As a result, the establishment is not in a position to ensure that the tissue is transported in a manner and under conditions that ensure their safety and quality.	**Major**

Advice

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

No.	Standard	Advice
1.	C2	Although many of the establishment's overseas offices use translated versions of SCI's paperwork, some partner offices use their own forms. Where this is the case, the DI is advised to have these documents translated to ensure that they are aligned with SCI's policies and procedures and the requirements of the HTA's 'Guide to Quality and Safety Assurance for Human Tissues and Cells for Patient Treatment' which forms the Annex to Directions 003/2010.
2.	GQ1	The DI is advised to review and update the establishment's standard operating procedures (SOPs) with a view to removing any references to public cord blood banking. This will help streamline certain documents and make them more relevant to the services currently being offered by the company.

3.	GQ1b	The DI is advised to review the SOP relating to the processing of umbilical cord blood units (SOP BS 004) to ensure that paragraph references contained within the document are accurate. For example, the section that deals with the collection of blood samples for HLA typing (paragraph 8.5.8) includes a link to paragraph 8.5.20, when the correct link should be to paragraph 8.5.14. The DI is also advised to update this document to include clear guidance on the environmental monitoring that should be performed during the collection of blood samples for HLA typing where such sampling takes place in a microbiological safety cabinet.
4.	GQ1b	The DI is advised to review the wording of the batch processing forms used for umbilical cord blood to ensure that the maximum time between procurement and processing is clearly defined. The current wording makes it unclear whether the upper limit that is specified relates to the time between procurement and processing, or between procurement and receipt into the lab. As the latter may precede processing by up to 24 hours the two time points are not interchangeable.
5.	GQ1b and PFE2c	The DI is advised to develop, validate and document a decontamination procedure for the transfer of materials and samples into the preparation room. This will help ensure that contamination is not introduced into the cleanrooms via the transfer hatches.
6.	GQ1g	The DI is advised to update the SOP that deals with the receipting of samples (reference SOP BS 001) to reflect current working practices. The document currently states that samples that arrive too late in the day to be processed will be stored securely until the following day when they will be processed. However, the inspection team were informed that staff would always review the time that had elapsed since the sample was procured to ensure that an additional delay prior to processing would not impact detrimentally on the sample.
7.	GQ4b	The DI is advised to audit batch processing records for umbilical cord blood to ensure that steps which relate to the collection of samples for quality control testing are being completed in line with the establishment's procedures. In particular, the DI is advised to ensure that there is a consistent, agreed upon approach to the completion of step '13' when the requisite number of pieces of tubing containing blood, as set out in step '12', cannot be collected.
8.	GQ4b	During the course of the inspection, a number of incomplete signature fields were noted on forms relating to cord blood / tissue procurement and donor testing. In light of this, the DI is advised to conduct a more comprehensive audit of such forms to establish whether these were isolated non-conformances or whether they were indicative of a more systemic failing in this regard. If the latter, the DI should consider whether additional training or guidance is needed to ensure that records are completed accurately.
9.	GQ4e	The DI advised to update batch processing records to include clear reference to the establishment's acceptance criteria for measures such a total nucleated cell counts (TNC) and CD34 counts. This will help ensure that samples that should be processed under variance are identified and treated accordingly.
10.	GQ5b	The DI is advised to revise the wording of section '3' of the establishment's cord blood / cord tissue storage agreement to make it clear that maternal blood samples for serology testing must be taken on the day of delivery, or within seven days post-donation. This will bring the document in line with the establishment's SOP on maternal blood collection which states that blood samples should be collected on the day the mother gives birth, or up to seven

		days thereafter. The DI is also advised to review any other documents that make reference to serology testing to make sure that they are similarly aligned.
11.	GQ4b and PFE1a	The DI is advised to review the approach to the completion of premises risk assessments by those involved in the collection of cord blood and cord tissue. Although the inspection team saw evidence that risk assessments were routinely carried out by phlebotomists, this was not always the case when procurement was carried out by other healthcare professionals.
12.	GQ7d	The DI is advised to review the establishment's policy on the processing and storage of samples (PD002) to ensure that the section that deals with client notification in the event of a non-conformance associated with sample transport time is aligned with current working practices. As it stands, the policy states that clients should be contacted if an umbilical cord blood unit is received outside of the validated timeframe even if that sample meets the establishment's acceptance criteria for storage. However, current practice is to only notify clients in the event that the storage criteria are not met.
13.	PFE2a	The DI is advised to review the establishment's SOPs and policy documents to ensure that they are aligned with respect to the handling and storage of HIV-positive samples.
14.	PFE2c	The DI is advised to expand the establishment's environmental monitoring within its cleanroom to include specific checks for fungal contamination. Consideration should be given to the use of additional growth media, such as sabouraud agar, and different incubation temperatures to facilitate this.
15.	PFE3a and PFE5c	The DI is advised to implement the use of min/max thermometers in fridges and storage areas where temperature-sensitive reagents and consumables are stored. Although conventional thermometers are already in use in these areas, readings are only taken once a day and so the establishment is not in a position to identify transient or periodic temperature excursions that might impact on the quality of stored products.
16.	PFE3c	The DI is advised to add alert / action limits to fridge and freezer monitoring sheets to ensure that staff remain aware of the trigger points for remedial action.
17.	PFE3c	The DI is advised to review the establishment's current approach to the monitoring of the vial freezer. Although the liquid nitrogen level in this tank is checked on a daily basis, the decision not to keep the tank's temperature sensor and alarm system on throughout the day removes an additional safeguard that would otherwise be in place to help safeguard the stored cells.
18.	PFE5d	Although the establishment's change control procedure makes reference to the need to consider whether there are any regulatory issues associated with a change request, related forms do not reflect this requirement. The DI is advised to update the establishment's change control request form accordingly. This will help ensure that significant changes to working practices, such as to a preparation process, are reported to regulatory bodies as appropriate.
19.	Licensing	The DI is advised to ensure that a Person Designated at the establishment has access to the HTA's online portal for the purposes of SAEARs reporting.

Assessment of existing conditions/shortfalls against standards

During the course of the inspection, the HTA also conducted a review of the action taken by the establishment in response to the findings of the previous inspection and the Directions that were issued thereafter. In this regard, the HTA noted that an agreement has been put in place with a third party to undertake umbilical cord tissue processing and storage whilst additional process validation is on-going at SCI. However, an audit of records associated with cord tissue samples shipped to the partner organisation for processing in the three months preceding the inspection showed that transit times for 30 of the samples were found to have exceeded the maximum 72 hour transit time that has been validated. As these samples had not been processed according to a validated procedure, SCI cannot provide any assurance about the quality of the cryopreserved tissue.

The HTA also noted that although SCI had contacted clients who were in possession of procurement kits at the time the changes were made to the umbilical cord tissue processing and storage service, the manner and content of these communications were not consistent with the requirements of Directions issued on 7 March 2014.

With regard to the samples that were identified at the last inspection that had been processed despite being shipped without the minimum specified volume of PBS, it was noted that all clients affected by this issue had been contacted and offered additional quality control checks on their samples, as per the requirements of the Directions. However, an audit of letters sent to clients in relation to this matter revealed that those with positive results were led to believe that the additional quality control tests gave a measure of the stem cell content of the sample. However, this was not measured by the viability studies that were conducted.

The HTA intends to work with the establishment to address these issues.

Concluding comments

The HTA saw a number of examples of good practice during the course of the inspection, including a robust approach to staff training and a well thought out approach to the carrying out and documenting of internal audits. Good progress has been made in updating SOPs following the last inspection, and the establishment remains an active participant in the National External Quality Assessment Service (NEQAS) scheme for its quality control testing.

Six areas of practice were identified during the inspection that require improvement, resulting in two major and four minor shortfalls. These relate to the need for appropriate validation to be in place for both sample transportation and processing, along with certain aspects of the establishment's governance and quality systems. The HTA has also given advice to the Designated Individual with respect to a range of the establishment's procedures with a view to helping the establishment further develop its working practices and governance systems. In this regard, in the weeks immediately after the inspection the establishment provided evidence demonstrating that it had taken steps to address the advice items listed in this report. The HTA is satisfied that appropriate action has been taken to address the majority of these. The HTA will review any additional actions taken by the establishment in response to the advice given in this report at the time of the next inspection.

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: 27 January 2015

Report returned from DI: 13 February 2015

Final report issued: 24 May 2015

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.
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.
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.

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.
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 number of 'major' shortfalls, none of which is critical on its own, but viewed cumulatively represent a systemic failure and therefore are considered 'critical'.

   A critical shortfall may result in one or more of the following:

   (1) A notice of proposal being issued to revoke the licence

   (2) Some or all of the licensable activity at the establishment ceasing with immediate effect until a corrective action plan is developed, agreed by the HTA and implemented.

   (3) A notice of suspension of licensable activities

   (4) Additional conditions being proposed

   (5) Directions being issued requiring specific action to be taken straightaway

2. **Major shortfall:**

   A non-critical shortfall.

   A shortfall in the carrying out of licensable activities which poses an indirect risk to the safety of a donor or a recipient

   or

   A shortfall in the establishment's quality and safety procedures which poses an indirect risk to the safety of a donor or a recipient;

   or

   A shortfall which indicates a major deviation from the **Human Tissue (Quality and Safety for Human Application) Regulations 2007** or the **HTA Directions**;

   or

   A shortfall which indicates a failure to carry out satisfactory procedures for the release of tissues and cells or a failure on the part of the designated individual to fulfil his or her legal duties;

   or

   A combination of several 'minor' shortfalls, none of which is major on its own, but which, viewed cumulatively, could constitute a major shortfall by adversely affecting the quality and safety of the tissues and cells.

In response to a major shortfall, an establishment is expected to implement corrective and preventative actions within 1-2 months of the issue of the final inspection report. Major shortfalls pose a higher level of risk and therefore a shorter deadline is given, compared to minor shortfalls, to ensure the level of risk is reduced in an appropriate timeframe.

3. **Minor shortfall:**

   A shortfall which cannot be classified as either critical or major and, which can be addressed by further development by the establishment.

   This category of shortfall requires the development of a corrective action plan, the results of which will usually be assessed by the HTA either by desk based review or at the time of the next inspection.

   In response to a minor shortfall, an establishment is expected to implement corrective and preventative actions within 3-4 months of the issue of the final inspection report.

Follow up actions

A template corrective and preventative action plan will be sent as a separate Word document with both the draft and final inspection report. You must complete this template and return it to the HTA within 14 days of the issue of the final report.

Based on the level of the shortfall, the HTA will consider the most suitable type of follow-up of the completion of the corrective and preventative action plan. This may include a combination of

- a follow-up site-visit inspection
- a request for information that shows completion of actions
- monitoring of the action plan completion
- follow up at next desk-based or site-visit inspection.

After an assessment of your proposed action plan you will be notified of the follow-up approach the HTA will take.