Site visit inspection report on compliance with HTA minimum standards

John Goldman Centre for Cellular Therapy

HTA licensing number 11118

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**

11-12 February 2014

Summary of inspection findings

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

Although the HTA found that the John Goldman Centre for Cellular Therapy (the establishment) had met the majority of the HTA standards, two minor shortfalls were found in relation to Premises, Facilities and Equipment. These relate to the procedures associated with the storage of temperature-sensitive reagents and to the analysis of non-viable particulate monitoring data obtained during critical processing of tissues and cells.

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
PBSCs	**E**	**E**	**E**	**E**	**E**		
Bone Marrow	**E**	**E**	**E**	**E**	**E**		
Cells for DLIs	**E**	**E**	**E**	**E**	**E**		
Umbilical cord blood				**E**			
Mesenchymal stromal cells	**E**	**E**					

Background to the establishment and description of inspection activities undertaken

This report refers to the activities carried out by the John Goldman Centre for Cellular Therapy (JGCCT). The establishment operates as part of Imperial College Healthcare NHS Trust's Clinical Haematology Transplant service, and is situated within the Catherine Lewis Centre in the Hammersmith Hospital. 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. It is also licensed for the storage of relevant material which has come from a human body for use for a scheduled purpose under the Human Tissue Act 2004. The establishment has been licensed by the HTA since August 2006 and has been inspected on three previous occasions. The

establishment is also licensed by the Medicines and Healthcare Products Regulatory Agency (MHRA) for the manufacture of Investigational Medicinal Products (IMPs) and Specials.

The JGCCT provides a range of services to support haematopoietic stem cell transplantation in routine and clinical trial settings. It currently processes approximately 400 samples a year, the majority of which are peripheral blood stem cells (PBSCs). However, the establishment also routinely processes bone marrow and donor lymphocytes, the latter for adoptive lymphocyte immunotherapy (DLIs) for post-transplant patients in relapse. It also handles a small number of cord blood samples for end use. The establishment also expands mesenchymal stromal cells from bone marrow aspirates for use in clinical trials. The procurement and donor testing associated with this work falls under the scope of the establishment's HTA licence. However, the subsequent storage, processing and distribution of this material is conducted under the authority of the establishment's MHRA licence.

Processing of tissues and cells takes place within a dedicated cleanroom facility according to well-defined procedures. There are two independent suites each having primary and secondary change rooms to two grade B clean rooms and a grade C support areas. Cellular Therapy Suite 1 is designed primarily for routine work including the processing of tissues and cells under the authority of the establishment's HTA licence; Suite 2, which can be used for tissue/cell processing as a contingency, is additionally designed to provide containment to level 2 for clinical gene transfer work or other procedures deemed by 'risk analysis' to require containment. Environmental monitoring of the Grade A microbiological safety cabinets is performed throughout processing, and includes provision for the assessment of levels of both viable and non-viable particulates. Samples requiring long-term storage are stored in the vapour-phase in liquid nitrogen storage tanks located on site. The storage facility includes provision for separate, temporary storage of samples that are awaiting test results, as well as dedicated tanks for samples requiring long-term quarantine storage.

The licence held by the JGCCT includes two satellite sites, the Department of Paediatrics in St Mary's Hospital, and the Charing Cross Hospital. The former undertakes the procurement of bone marrow and PBSCs from paediatric donors, which are subsequently transported to the JGCCT processing facility using the organisation's own couriers accordingly to well-defined, validated procedures. The Charing Cross Hospital carries out the analysis of bacteriology samples taken from tissues and cells processed at the JGCCT. Samples taken for donor serology testing are also sent to the Charing Cross Hospital where they are analysed in accordance with the requirements of Annex II of Directive 2006/17/EC.

The JGCCT also receives samples of umbilical cord blood from other HTA-licensed establishments within the UK under appropriate agreements. Such samples are transported directly to the processing facility for temporary storage prior to end use.

This report describes the establishment's fourth routine site visit inspection which took place on 11-12 February 2014. The inspection included interviews with key members of staff working under the licence, including the Director of the JGCCT, who is also the Designated Individual, the Quality Assurance Manager, the Head of the Processing Department, and a Senior Sister. A review of documentation relevant to the establishment's activities and a visual inspection of the areas of the hub and satellite sites where licensable activities are carried out were also conducted as part of the inspection.

An audit of two samples held in storage was performed. Storage locations were cross-checked with appropriate records and the donor files were reviewed to ensure that they contained all relevant documentation, including consent forms, serology and microbiology test results, and the results of environmental monitoring. No discrepancies were found. Additional records representative of the range of relevant material procured, processed and stored by the establishment, were also reviewed. This exercise identified a number of minor inconsistencies in working practices and areas for possible future development which are described in the Advice section below.

At the time of the inspection, relevant material was not being stored under this licence for use in a scheduled purpose as defined by the Human Tissue Act 2004. Consequently, the establishment's systems relating to the storage and use of such material were not assessed during this inspection.

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

Premises, Facilities and Equipment

Standard	Inspection findings	Level of shortfall
PFE2 Environmental controls are in place to avoid potential contamination.		
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.	Although the establishment performs non-viable particulate monitoring for the full duration of critical processing, only the counts immediately pre- and post-processing are reviewed and documented as part of the batch processing record.	**Minor**

PFE5 Equipment is appropriate for use, maintained, quality assured, validated and where appropriate monitored.		
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.	Although staff at St Mary's Hospital perform routine temperature monitoring of the room where reagents are stored prior to bone marrow harvests, recent excursions from the defined temperature limits for the room had not been reported or investigated in a manner consistent with the establishment's procedures. As a result, the root cause of the temperature deviations had not been identified or addressed and the impact of these events on reagents stored in the room had not been assessed. Similarly, analysis of the temperature logs associated with one of the reagent storage fridges at Charing Cross Hospital indicated that the temperature had deviated from prescribed limits for sustained periods during working hours on several days in the lead up to the inspection. Despite this, the establishment was unable to provide any evidence of anyone having been alerted to the deviations, as required by the establishment's SOPs, nor any corrective action having been taken.	**Minor**

Advice

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

No.	Standard	Advice
1.	C2a	The DI is advised to update the consent SOP at St Mary's Hospital so that it clearly sets out the principal risks that will be discussed with potential donors of tissues/cells. The DI should also consider whether the inclusion of a checklist in the relevant section of the establishment's consent forms would help ensure that all relevant side effects or complications associated with a particular procedure are consistently discussed with potential donors.
2.	GQ1b	The DI is advised to review the establishment's SOP relating to viability testing to ensure that it clearly sets out when both pre- *and* post-processing trypan blue assays are required. The DI should also consider whether updating the associated processing form to include dedicated space for both sets of results, along with a brief reminder of when both tests are needed, would help ensure that this test consistently performed.
3.	GQ1g and PFE4g	Although the establishment has well-developed systems to manage the receipt of the majority of samples into the processing laboratory, the DI is advised to review current practices with respect to those samples arriving from overseas that have been procured and distributed by third parties to ensure that it is clear who is responsible for reviewing the information contained on data loggers. This will help ensure that staff at the establishment are aware of any deviations from

		the critical transport requirements that may have occurred during transit.
4.	GQ1h	The DI is advised to review and risk assess the establishment's current approach to the storage of tissues/cells that have been classified as 'non-conforming' due to an out of specification environmental monitoring event during processing. Following this exercise, the DI should, if needed, update the relevant SOP to reflect agreed upon working practices.
5.	GQ1j and GQ4b	The DI is advised to remind staff of the need to use cryoprotectant within 24 hours of preparation as stipulated in the establishment's SOPs. Personnel involved in the review and sign off of processing records should also be reminded of the need to ascertain whether any critical timings associated with the processing of tissues/cells have been adhered to.
6.	GQ1p	The DI is advised to review the agreements that the establishment has with third parties to ensure that all those that remain relevant to the group's current activities have not expired. Any that have should be updated at the earliest opportunity to help ensure that there are no unexpected interruptions or changes to the services being provided.
7.	GQ7d	The DI is advised to consider additional ways of identifying any tissues/cells that have been classified as 'non-conforming' to ensure that they are only released for end use through the establishment's concessional release process. For example, the DI could consider attaching stickers/labels to the front cover of associated processing records as a clear, visual reminder of the need for concessional release for such products.
8.	PFE3	The DI is advised to review the current storage arrangements for stocks of DMSO to ensure that staff would be made aware of any deviations from the manufacturer's specified storage requirements. The DI is also advised to consider the use of "min/max" thermometers in the room where ACD-A is stored at the Hammersmith Hospital. Although the establishment has discussed the storage requirements of this product with the manufacturer in the past, the use of such devices would provide the DI with greater assurance the room is operating within defined temperature limits throughout the day.

Concluding comments

The HTA saw numerous examples of good practice during the course of the inspection.

The premises and equipment at each site are of a high standard and the governance and quality systems underpinning the work that takes place under the authority of this licence are well-developed and effective. Staff are supported in their roles by a comprehensive and well thought out approach to induction, training, and performance review. A wide range of governance meetings are held involving staff at all levels of the organisation. Together, these practices help ensure that tissue and cells intended for human application are procured, processed, tested, stored and distributed in such a way that safeguards their quality and safety.

The establishment has a robust approach to internal audit and has developed a wide-ranging audit schedule covering licensable activities. Audit findings are well-documented and effective systems are in place to implement corrective measures if needed. The establishment's approach to risk assessment is similarly comprehensive, with the risks associated with the

carrying out of licensable activities clearly defined at each site.

Although some advice has been given to the DI with respect to aspects of the consent process, the establishment has clearly given a lot of thought to consent and procurement practices. Paediatric donors and their families in particular are very well supported, both in terms of the information and material they are given in the lead up to a procedure, but also with respect to the personal support they receive from staff at the establishment along their care pathway.

Two areas of practice were identified during the inspection that require improvement, both resulting in minor shortfalls. These relate to the establishment's current approach to the analysis of non-viable particulate monitoring data obtained during critical processing of tissues and cells, and to the need for robust systems to be in place to investigate and address any deviations associated with the storage of temperature sensitive reagents.

The HTA has given advice to the Designated Individual in relation to a number of practices and procedures with a view to helping the establishment further develop their working practices and governance systems. This includes advice relating to agreements with third parties and several of the procedures used in relation to the management of non-confirming products. The HTA has also advised the DI to review the establishment's procedures for receipting samples from overseas, particularly with respect to the reviewing of information contained on data loggers, and to remind staff of the establishment's procedures pertaining to the preparation and use of cryoprotectant.

The HTA requires that the Designated Individual addresses the shortfalls by submitting a completed corrective and preventative action (CAPA) plan within 14 days of receipt of the final report (refer to Appendix 2 for recommended timeframes within which to complete actions). The HTA will then inform the establishment of the evidence required to demonstrate that the actions agreed in the plan have been completed.

The HTA has assessed the establishment as suitable to be licensed for the activities specified subject to corrective and preventative actions being implemented to meet the shortfalls identified during the inspection.

Report sent to DI for factual accuracy: 11 March 2014

Report returned from DI: 24 March 2014

Final report issued: 25 April 2014

Inspection CAPA Plan Closure Statement:

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: 22 October 2014

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.