Site visit inspection report on performance against HTA quality standards

The Wolfson Cellular and Gene Therapy Unit
HTA licensing number 11025

Licensed for the

- **procurement, processing, testing, storage, distribution of human tissues and cells for human application under the Human Tissue (Quality and Safety for Human Application) Regulations 2007, and the**

- **storage of relevant material which has come from a human body for use for a scheduled purpose other than transplantation under the Human Tissue Act 2004**

15 – 16 November 2011 and 18 January 2012

Executive Summary

A site visit inspection of Wolfson Cellular and Gene Therapy Unit (the establishment) was carried out by the HTA on 15 and 16 November 2011. The inspection was completed on 18 January 2012, when the HTA performed a site visit inspection of the satellite premises where donor serological and microbiological testing takes place.

The establishment was found to have met all HTA standards relating to procurement, processing, storage and distribution of human tissues and cells for human application. The inspection of the satellite testing facility identified four shortfalls with respect to governance and quality.

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

All reports of HTA inspections carried out from 1 November 2010 are published on the HTA's website.

Background to the establishment and description of inspection activities undertaken

The Wolfson Cellular and Gene Therapy Unit is part of the University College London Hospital (UCLH). It comprises hub premises and three satellite sites, which are located a short walking distance from one another. The hub at Chenies Mews carries out processing and storage of peripheral blood stem cells (PBSC), donor lymphocyte infusions (DLI) and bone marrow procured at two of the satellite premises: the Haematology Day Care Unit (within the Rosenheim Building) and UCLH. The completion of a new hospital building in April 2012 will mean the Haematology Day Care Unit will move to a larger, purpose-built facility. The DI is awaiting the delivery of an additional freezer at the hub premises which will enable him to reorganise stored stem cells so that those of the highest priority will be stored in a designated freezer in line with the establishment's procedure for disaster recovery.

Two of the three satellite sites are responsible for procurement only. Procurement of PBSCs via apheresis predominantly takes place at the Haematology Day Care Unit, where the apheresis machines are housed. However, at times, PBSCs are procured from paediatric patients on the wards of University College Hospital London. In these instances, the apheresis machine is transported by staff from the Haematology Day Care Unit through a secure underground walkway to the ward so that the procedure can take place at the patient's bedside. Additionally, the theatres at UCLH are used for the procurement of bone marrow. The stem cells are then transported by trained staff from the place of procurement to the hub for processing and storage.

The Department of Virology is a third satellite site, at which donor serological and microbiological testing are performed. It has been licensed by the HTA since January 2010. Although the department relocated twice in 2011, it remains within walking distance of the other satellite and hub premises. The Inspection Team were informed that the satellite carries out Hepatitis C testing by using a nucleic acid amplification technique (NAT) and confirmatory testing. All other mandatory tests have been outsourced to a third party since October 2011. This third party testing facility is a joint venture between UCLH and a private company.

The establishment also procures stem cells on behalf of another HTA licensed establishment, which distributes them on to private hospitals for patient treatment. Consent to procure, test and store the donor's stem cells is sought by trained consultants, specialist registrars or clinical nurse specialists. Responsibilities are arranged within four donor groups:

1. Autologous adults and adolescents
2. Autologous paediatrics
3. Allogeneic adults
4. Allogeneic adolescents

Allogeneic paediatric donors are referred to another HTA licensed establishment in London.

In 2010, the establishment procured 460 units of DLI, PBSC and bone marrow. In the same year, a total of 535 units were released for patient treatment.

This was a routine inspection to assess compliance with HTA standards relating to procurement, processing, storage and distribution of human tissues and cells for human application. The wards and theatres within UCLH were not visually inspected as the DI confirmed that the premises and practices taking place there remain unchanged since the previous inspection in 2009.
A traceability audit was performed during the inspection. Three cases were selected and the

audit started at the consent taking stage through to storage of stem cells. Storage locations were confirmed using the electronic database and all associated processing and testing records were viewed. Disposal records were also audited when applicable. The audit sample was small in relation to the volume of activity but provided assurance to the inspection team that the DI is committed to ensuring there is robust traceability from donor to recipient, testing and consent requirements.

This was the establishment's third inspection. The last inspection took place in December 2009. Three conditions imposed on the establishment's licence were subsequently actioned by the Designated Individual and closed to the satisfaction of the HTA. Furthermore, the DI had proactively implemented all advice and guidance outlined in the previous report.

Meeting the HTA's licensing standards

The HTA developed its licensing standards with input from its stakeholders, in order to ensure the safe and ethical use of human tissue. The HTA expects licensed establishments to meet these standards.

This is an exception-based report: only those standards that have been assessed as not met are included. Where the HTA determines that a licensing standard is not met, the level of the shortfall will be classified as 'Critical', 'Major' or 'Minor' (see Appendix 3: Classification of the level of shortfall).

Unless otherwise advised, the establishment is required to inform the HTA within 14 days of the receipt of the final report of the corrective and preventative actions that will be taken to ensure that the improvements are addressed. A template for this purpose is provided as a separate Word document.

Please see Appendix 2: Human Application standards, to view all human application standards. Standards which do not apply to this licence are highlighted in Appendix 2.

HTA standards not met

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.		
a) There is an organisational chart clearly defining the lines of accountability and reporting relationships.	The organisational chart does not define the accountability and reporting relationships for staff employed at the satellite premises, who carry out donor and microbiological testing. When the establishment applied for a satellite licence for donor testing in January 2010, the HTA was informed that a Person Designated had been nominated to oversee licensable activities and report to the DI. However, this arrangement is no longer in place as the Person Designated has left the organisation and no one has been assigned this role. This compromises the DI's ability to oversee the licensed activity, and is contrary to HTA's guidance on licensing arrangements.	**Minor**
c) There are regular governance meetings, for example health and safety, risk management and clinical governance committees, which are recorded by agendas and minutes.	There are regular governance meetings involving staff from the hub and procurement satellite premises. However, staff from the donor testing satellite has not been brought into this arrangement. This reduces opportunities for the DI to have oversight of this element of the licensed activity.	**Minor**
p) There are written agreements with third parties whenever an activity takes place that has the potential to influence the quality and safety of human tissues and / or cells.	The Managed Facility Agreement between the donor testing satellite and its third party for additional donor testing is a commercial agreement that does not comply with the requirements of The Human Tissue (Quality and Safety for Human Application) Regulations 2007, in relation to Third Party Agreements. The purpose of	**Minor**
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.	Third Party Agreements is to make certain that the service provided by the third party ensures the quality and safety of tissues and cells, and there are specific requirements that must be included.	
s) Third party agreements specify that the third party will inform the establishment in the event of a serious adverse reaction or event.		

Advice

Below are matters which the HTA advises the DI to consider.

No.	Standard	Advice
1.	GQ1(b)	The DI is advised to make the necessary changes to its service level agreement with the Department of Virology to enhance its governance arrangements and ensure compliance with relevant HTA legislation, directions and guidance. The agreement should include: • the nomination of a Person Designated who can direct activities that are licensed there and who is accountable to the DI at the main hub site; • more specific information on who is responsible for reporting serious adverse events and reactions to the DI; • the requirement for serious adverse events and reactions to be reported to the HTA within 24 hours of discovery or determination; • the maintenance of an accurate record of tests carried out by the satellite and those that are carried out by the third party.
2.	GQ1(c)	In establishing regular governance meetings with the donor testing satellite, the DI might consider including the following agenda items: • incident reporting, to enable the DI to satisfy himself that appropriate corrective and preventative measures have been put in place to avoid reoccurrence; • the evaluation of the third party's compliance with HTA Standards and the Guide to Quality and Safety Assurance for Human Tissues and Cells for Patient Treatment (2010) • audits of licensed activity.
3.	GQ1(h)	To provide an additional level of quarantine to minimise the risk of cross contamination, the DI is advised to separate PBSCs that are bacterially contaminated from those that are awaiting test results.
4.	GQ2(b)(c)	The DI should consider performing internal audits at the donor testing satellite site to verify its compliance with protocols, the service level agreement and HTA Standards.
5.	GQ2(d)	Samples for Hepatitis C testing by using a nucleic acid amplification technique (NAT) are stored for up to seven days before testing. A validation paper submitted after the inspection demonstrates that storing for more than five days or above 25ºC increases the risk of a false negative test. The DI is advised to ensure that current practice is changed to reflect this finding.

6.	GQ3(e)	At the donor testing satellite site, staff have not received formal training from the supplier of the laboratory automation system purchased in October 2011. The acquisition of this piece of equipment enables automation of labour-intensive tasks including sample identification, decapping, recapping, sorting, and archive preparation of sample tubes. It is additionally equipped with an aliquoting unit. If the equipment fails or is not used properly, it could have a significant impact on tests carried out on samples. The DI should ensure that formal training is provided and documented. Further steps to assess competence to use the equipment should also be arranged and documented.
7.	GQ4(b)	The schedule of audits includes a paper-based audit of processing records in the laboratory. Since the data contained within these written records is manually entered onto an electronic database, and referred to on this system thereafter (written records are archived off-site), the DI may wish to extend the audit to include data entry as an additional quality assurance measure.
8.	GQ7(a)	The DI is advised to improve the written procedures for the identification, reporting, investigation and recording of serious adverse events and reactions in three ways: 1. notifying the HTA of any serious adverse event or serious adverse reaction within 24 hours of discovery or determination 2. in the interest of timely reporting, identifying another staff member to report incidents in circumstances where the DI is unavailable 3. make clear the reporting procedures when a serious adverse event or reaction relates to the procurement being carried out for another licensed establishment. The DI is advised to refer to paragraphs 171 – 187 in the Guide to Quality and Safety Assurance for Human Tissues and Cells for Patient Treatment (2010) for more information.
9.	PFE(b)	The clean room and clean air devices are routinely monitored both on a sessional basis (i.e. during processing of each specimen) and weekly post cleaning and decontamination. Results indicate that the Grade A with a Grade B background is maintained in the clean room. However, settle plates used for sessional monitoring are left for anywhere between 20 minutes and four hours, the start and end times for which are not recorded. The recommended limits in the European Guide to Good Manufacturing Practice (GMP), Annex 1 are expressed as colony forming units (CFU) per four hours. The DI therefore needs to know the duration of exposure of settle plates in order to adhere to meaningful alert and action limits and express these as CFU per 4 hours. The DI is therefore advised to consider recording start and end times when monitoring background air in any given session in order to determine that results correlate with the recommended limits as outlined in paragraph 19. The DI is also advised to monitor the clean room air quality in operation as opposed to at rest, post clean as currently per current practice. For

		instance, monitoring at the end of the week before the clean, whilst in operation and with the maximum number of operators in the clean room, may give a more accurate picture about whether Grade A is maintained.

Concluding comments

The Wolfson Cellular and Gene Therapy Unit is a long established service for patients requiring stem cell therapies. Whilst the establishment employs many staff working at multiple sites, it was evident that there are strong governance systems in place between the hub and the procurement satellite premises. Evidence of this included regular governance meetings and an effective quality management system delivered by a dedicated quality manager. Inspectors observed that where possible, the DI had implemented all advice and guidance given to the DI at the establishment's previous inspection in 2009. For example, this included significant thought and arrangement of contingency plans for disaster recovery. This is particularly important since the eight, large storage freezers are located in the basement in the hub premises.

The satellite for donor testing is a relatively new arrangement compared with the satellite arrangements for procurement of stem cells. The inspection on 18 January 2012 confirmed that there are weaker governance arrangements in place for the oversight of testing and hence the shortfalls and much of the advice outlined above.

Although the DI was previously advised to separate quarantined samples from samples for released, this has not been possible since the lack of space available to acquire a new freezer for this purpose. Despite this, the laboratory manager has separated the quarantined samples in colour-coded containers within the freezer to mitigate any risk of a mix-up. His response demonstrates responsiveness to advice and guidance previously provided by the HTA.

Lastly, inspectors considered that the arrangements in place to seek consent for testing, procuring, storage, disposal and research were robust and were in accordance with the Human Tissue Act 2004 and Code of Practice 1: Consent.

Report sent to DI for factual accuracy: 9 February 2012

Report returned from DI: 23 February 2012

Final report issued: 6 March 2012

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: 19 September 2012

Appendices

Appendix 1: HTA inspection process

The Human Tissue Authority (HTA) regulates the removal, storage, and use of human bodies, body parts, organs and tissue for activities such as research, transplantation, and education and training. The legal requirements for establishments which carry out such activities are set out in the Human Tissue Act 2004 and The Human Tissue Act 2004 (Ethical Approval, Exceptions from Licensing and Supply of Information about Transplants) Regulations 2006.

The HTA is also the designated Competent Authority for the purposes of the European Union Tissue and Cells Directives (the Directives) so far as they relate to tissues and cells for use in human application (using tissues and cells for patient treatment). On 5 July 2007 the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (the Regulations) came into force. The Regulations formally transposed the Directives into UK law. Under the Regulations the HTA regulates and licences the procurement, testing, processing, storage, distribution, import or export of tissues or cells intended for human application. The HTA has produced detailed Directions to complement the implementation of the Directives.

As part of the regulatory framework, the HTA licenses establishments and undertakes inspections to assess compliance with expected standards.

Inspections

We use the term 'inspection' to describe when we:

- visit an establishment to meet with staff, view premises and facilities, and review policies and procedures (a site-visit inspection); or
- assess written information we have requested from an establishment (a desk-based assessment / inspection).

We carry out inspections to assess if the Designated Individual (DI) is suitable to supervise the activity covered by the licence, as it is their responsibility to ensure that:

- other staff working under the licence are suitable;
- suitable practices are used when carrying out the activity;
- the conditions of the licence are met;
- the conditions of third party agreements are met; and
- the information and confidentiality requirements set down in the Regulations are complied with.

We also need to be satisfied that the licence applicant or holder, the establishment's premises, and the practices relating to licensed activities, are suitable.

To help us reach our decisions, we have developed standards under four headings: Consent; Governance and Quality; Premises, Facilities and Equipment; and Disposal.

After every site visit inspection, we write a report documenting our findings. Where we find a particular standard is not fully met, we will describe the level of the shortfall as 'Critical', 'Major' or 'Minor'. In most cases, it will be the responsibility of the DI to seek the HTA's agreement on how they will address the identified shortfalls. More information about the classification of shortfalls can be found in Appendix 3.

The majority of our site-visit inspections are announced. If we have concerns about an establishment, we can also undertake an unannounced site visit inspection.

You can find reports for site visit inspections which took place after 1 November 2010 on our website.

Appendix 2: HTA Standards

Standards which are not applicable to this establishment have been highlighted.

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 3: Classification of the level of shortfall

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, which individually do not pose a direct risk of harm to a recipient or living donor, 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 or 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/or cells.

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 at the time of the next inspection.

Follow up actions

A template corrective and preventative action plan is available as a separate Word document. 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.