Site visit inspection report on compliance with HTA minimum standards

King's Cell Isolation Unit

HTA licensing number 11062

Licensed for the

- **processing, storage and distribution of human tissues and cells for human application under the Human Tissue (Quality and Safety for Human Application) Regulations 2007**
- **storage of relevant material which has come from a human body for use for Scheduled Purposes other than transplantation under the Human Tissue Act 2004**

3 April 2013

Summary of inspection findings

The King's Cell Isolation Unit (the establishment) was found to have met the majority of HTA standards. However, three shortfalls were identified, one minor shortfall in relation to governance and quality; and two in relation to premises, facilities and equipment, one major and one minor. The major shortfall relates to the need for non-viable particulate monitoring during processing.

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

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 Paragraph 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.

'SLA' = Service Level Agreement; the establishment is licensed for this activity but another establishment (licensed) carries out the activity on their behalf.

Tissue type	Procurement	Processing	Testing	Storage	Distribution	Import	Export
Pancreatic islet cells	**SLA**	**E**	**-**	**E**	**E**	**-**	**-**
Hepatocytes	**SLA**	**E**	**-**	**E**	**E**	**-**	**-**

Background to the establishment and description of inspection activities undertaken

The King's Cell Isolation Unit (CIU), set up jointly by the Institute of Liver Studies and Department of Diabetes and Endocrinology, incorporates a free-standing unit (portacabin) acting as a clean room facility, cryogenic storage area and related store rooms. The CIU undertakes processing, storage and distribution activities for two cell types (as summarised above) for therapeutic use. Microbiological and serological testing is conducted in the hospital Microbiology laboratory.

All donated organs are screened in accordance with criteria specified for whole organ transplantation. Liver blood vessels are cannulated, perfused and purified according to established protocols. The final product for clinical hepatocyte transplantation is only released once it has been determined that there is no evidence of microbiological contamination. Hepatocytes are then infused into patients with liver-based metabolic disease or acute liver failure. Hepatocytes that do not meet established criteria for clinical use are used for related research in liver disease, subject to appropriate consent for use of relevant material for a scheduled purpose under the Human Tissue Act 2004.

Additionally, the CIU are working under a MHRA licence to purify and encapsulate hepatocytes which are then used for related clinical applications (as an Advanced Therapy Medicinal Product (ATMP)).

Following equivalent procedures relating to pancreatic processing, islet cells deemed suitable for release and use are infused into patients with intractable diabetes in order to stimulate the production of insulin. If deemed unsuitable for clinical purposes, consented material is used for research related to diabetes.

In the clean room environment, both harvested hepatocytes and pancreatic islet cells are isolated under controlled aseptic conditions for use in autologous and allogeneic transplantation in paediatric and adult patients. In the cryogenic facility, processed hepatocytes are cryopreserved and stored under monitored conditions in the vapour phase of dedicated liquid nitrogen tanks.

The King's CIU has service level agreements (SLAs) in place for hepatocyte and islet cell procurement. On-site procurement of donor livers and pancreata unused for transplantation takes places via a Service Level Agreement (SLA) with the Liver Transplant Service at King's College Hospital (KCH) and, externally, there are SLAs with the NHS Blood and Transplant Service for the referral of donated pancreas for islet isolation and a number of SLAs with Islet Transplant Centres across the UK (e.g. Manchester, Oxford) for the provision of isolated pancreatic islet cells. These establishments are licensed under the Organ Donation and Transplantation (ODT) framework.

The establishment was previously inspected in October 2009. This site visit, undertaken on 3rd April 2013, was a routine inspection and again provided an opportunity for the HTA to review governance arrangements. Under statutory requirements, inspections of licensed establishments under the Human Application (patient treatment) sector are normally undertaken at 2-year intervals. However, given the original proposal to move to a new GMP facility (KCH Cell Therapy Unit) by late 2011, the scheduled HTA inspection had been postponed over the last 18 months to allow this transition to occur. However, given local delays in the proposed move, a decision was recently taken by the HTA to schedule this inspection ahead of the now imminent move.

The site visit included a visual inspection of the premises (sample receipt and preparation areas, clean room, cryostorage facilities (in the KCH Stem Cell Laboratory) and consumables store) and formal interviews with the Designated Individual, Quality Manager/Senior Lecturer, respective Heads of Liver and Pancreas Processing, Medical Advisor (islet cells) and the Corporate Licence Holder Contact.

The DI is Director of the Cell Isolation Unit, Clinical Director (Child Health) and Professor of Paediatric Hepatology. The LH is King's College Hospital NHS FT with the Associate Director of Governance and Assurance acting as the named contact.

A traceability audit was carried out on five sets of donor records for autologous and allogenic products, three sets of records relating to hepatocytes and two records relating to islet cells. Each included: donor consent, evidence of procurement, transport to King's Cell Isolation Unit, receipt, processing, testing and storage. No anomalies or discrepancies were found on the selected examples during the traceability audits.

A document review of the establishment's policies and operational procedures was also conducted. This included review of consent forms and supporting information, serology test results, audit schedules for 2012, clean room environmental monitoring data, examples of incident reports, risk assessments, service level agreements and the quality manual.

Inspection findings

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

HTA standards not met:

Governance and Quality

Standard	Inspection findings	Level of shortfall
GQ1b There are procedures for all licensable activities that ensure integrity of tissue and / or cells and minimise the risk of contamination. & GQ5b 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 SLAs currently in place within internal services and external procurement organisations do not indicate the mandatory testing requirements for HTLV-1 in accordance with the criteria required by Directions 003/2010 . Additionally, this testing requirement is not appropriately reflected in a local SOP although testing arrangements for HTLV-1 are in place and recorded as part of donor test results.	**Minor**

Premises, Facilities and Equipment

Standard	Inspection findings	Level of shortfall
PFE2b 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.	The establishment has a system of in-process monitoring of viable particulates using various environmental monitoring control measures such as the use of finger dabs, settle plates and contact plates. However, at present, non-viable particulate monitoring is not currently conducted during processing. The establishment should extend in-process non-viable particulate monitoring to the full duration	**Major**

	of critical processing to bring working practices in line with Annex I of the EU Guidelines to Good Manufacturing Practice and the requirements of Directions 003/2010. Additionally, exposure times for weekly settle plates varies between 2 and 4 hours for environmental monitoring of the clean room facility. Although this is consistent with local formal procedures, the levels required by Directions 003/2010 are for a four hour exposure period (or accordingly, calculations which extrapolate to this exposure time). Although colony-forming unit (CFU) counts rarely approach warning or action levels, the shorter (uncorrected) exposure period presents a potential risk in terms of an under-recording of CFUs. Processing records for one of the hepatocyte samples reviewed indicated that the finger dabs performed had reached defined action levels during one stage of processing. However, this was not recorded as a quality exception on the associated form.	
PFE3a Tissues, cells, consumables and records are stored in secure environments and precautions are taken to minimise risk of damage, theft or contamination. & PFE3c Tissues and / or cells are stored in controlled, monitored and recorded conditions that maintain tissue and / or cell integrity.	A number of media and reagents (e.g. perfusion and decontamination solutions) are stored within refrigeration units outside of the manufacturer's recommended temperature ranges. BacT/Alert broth bottles are stored at room temperature. However, room temperature within the clean room facility is not sufficiently well controlled. Logs confirm that the room temperature has deviated outside the recommended storage conditions on a number of occasions without this being appropriately addressed.	**Minor**

Advice

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

No.	Standard	Advice
1.	GQ1r, GQ2b	Evidence of audits was seen during the inspection. The frequency and scope of completed audits could be further developed to support and enhance working practices and aid traceability. In particular, the DI is advised to set out and implement a clearly defined schedule of audits in relation to a wider variety of licensable activities e.g. periodic reviews of SOPs in relation to existing cleaning, monitoring and processing practices and review of quality exception records post-audit.
2.	GQ1p, GQ1r, GQ7b, GQ7c	The establishment has a SOP – CIU_A.14 (Adverse Event Procedures) - which indicates that serious adverse incidents or reactions (SAEARs) should be reported to the HTA within 24 hours and the specific procedure to be followed for reporting SAEARs. However, the DI should be able to equally assure himself that external establishments procuring relevant material on behalf of the CIU are aware of these requirements. It is not sufficiently clear from existing SLAs whether the respective organisations are fully aware of the specific HTA requirements in this regard. The DI is advised to update the TPAs accordingly and may wish to refer to the HTA website for further information: http://www.hta.gov.uk/licensingandinspections/reportingtothehta/adverseeventandreactionreporting.cfm
3.	GQ2a, GQ3f	The DI is advised to amend and update the existing Quality Manual (version 6, February 2013) to ensure it fully reflects regulatory requirements relating to Directions 003/2010 in particular. Subsequently, staff are made aware of and trained on the updated Quality Manual.
4.	GQ3c, GQ3f	As part of their CPD, the DI may wish to consider identifying other staff working under the licence to undertake the HTA e-learning training package to further develop an understanding of HTA requirements relating to the sector.
5.	GQ7a, GQ7c	The establishment has a robust internal mechanism for escalation and investigation of SAEARs and/or incidents, and an operating procedure that clearly states the HTA requirements for reporting of events or reactions. The DI should ensure that all SAEARs are reported to the HTA within required timescales in parallel with internal management processes.
6.	GQ8a	Risk assessments reviewed during the inspection include assessments of both health & safety and quality & safety issues. The DI is advised to additionally base a set of risk assessments on common reportable categories for SAEARs. Please refer to the HTA website for further information: http://www.hta.gov.uk/licensingandinspections/reportingtothehta/adverseeventandreactionreporting.cfm
7.	PFE1a	Prior to the new GMP facility becoming fully operational, the DI is advised to undertake appropriate risk assessments of the current clean room facility to ensure that transition arrangements have been suitably highlighted and risks sufficiently mitigated for processing activities that will continue in parallel within the existing facilities during this interim period.

		If existing equipment is to be moved across to the new facility, the DI is advised to ensure that this is done so under appropriately documented change control procedures.
8.	GQ4b, PFE2b	The DI is recommended to review the existing approach to incubation of EM plates. Standard practice would be to expose SAB and TSA plates and then incubate immediately at respective defined temperature ranges of 20 - 25C and 30 - 35C.
9.	PFE2b	There appears to be an inconsistent approach to the performance of and recording of finger dabs during hepatocyte processing. Formal procedures suggest that finger dabs and glove changes should be performed at specified points during processing activities. However, completed operational records suggest there is inconsistency in practice in relation to these established procedures. Additionally, the daily Microbiology Monitoring Log records finger dab results. However, individual batch numbers are not currently identified on this form. The DI is advised to record this information moving forwards in order to minimise the risk of confusion between different batches of hepatocyte preparations. The DI is also advised to undertake a sample review of quality exception records to determine whether there are any specific training requirements identified as a result. It was also noted that processing records for hepatocytes did not include a field for the microbiology results for the 'product'. This information was hand written onto respective forms. Forms should be updated to include this field and ensure that this information is routinely recorded.
10.	PFE2c	Cleaning of the clean room takes place on a regular basis and is recorded; however the DI is advised to ensure there are detailed instructions for how this should be carried out. Details such as whether the balance can be regularly moved to permit cleaning underneath should be included.

Concluding comments

The DI leads a committed and motivated team undertaking scientific and clinical work which significantly impacts on the care of patients with typically very acute illness. Staff at the establishment work collaboratively across clinical and laboratory areas. They demonstrate a clear commitment to meeting HTA requirements and to the on-going development of a culture of continuous improvement. The senior level appointment of a Quality Director for the new GMP facility is fully endorsed by the HTA and will potentially further develop a robust Quality Management System (QMS) and provide support to existing staff who are managing systems and processes relating to issues of quality.

Environmental monitoring data indicate that the specifications relating to the design and build of the existing facilities have resulted in an existing clean room which can routinely meet operational requirements of microbiological and viable particulate control.

Areas of strength and good practice were seen. For example: a detailed and extensive set of validation reports exist for both equipment and critical processing steps; robust traceability within the King's CIU for samples in cryopreservation and also the audit trail from clinical records and paperwork related to external establishments procuring relevant material on behalf of the Unit. The Quality Manual is generally well considered and constructed and is underpinned by an effective QMS.

The capital works for the KCH CTU build are now close to completion and the new GMP facility will shortly be ready for use. As the HTA understands, the exact details for the

proposed move will be mapped out over the next few months in conjunction with other groups moving into the new facility. Currently, the facility is completing a period of performance qualifications and a validation plan for aseptic processing. The new facility contains clean room production areas for the Hepatocyte and Islet groups and an isolated clean room suite with dedicated air handling (HVAC) for hepatocyte and islet processing. Initial processing activities will follow current working practices using Microbiological Safety Cabinets in a Grade C environment, however remaining activities will in future be conducted in a Grade A isolator with continuous monitoring of both viable and non-viable particulates.

As highlighted above, there are some areas of practice that require improvement and the HTA has given advice to the DI with respect to these.

The HTA requires that the DI addresses the three identified 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 shortfalls identified during the inspection.

Report sent to DI for factual accuracy: 30 April 2013

Report returned from DI: 10 May 2013

Final report issued: 23 May 2013

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: 12 August 2013

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.