Site visit inspection report on compliance with HTA minimum standards

King's College London

HTA licensing number 11023

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**

26 April 2016

Summary of inspection findings

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

Although the HTA found that King's College London (the establishment) had met the majority of the HTA standards, seven minor shortfalls were found with regard to the Governance and Quality Systems (GQS) standards. They were in relation to an absence of: (i) up to date third party agreements; (ii) internal audit system for procedures; (iii) independent audit; (iv) recorded, formalised competence training; (v) an internal audit system for records; (vi) consistent recording and follow up of incidents; and (vii) risk assessments. Advice has been given relating to the GQS and Premises, Facilities and Equipment standards, as well as to licence management.

Particular examples of 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 (DI), Licence Holder (LH), premises and practices are suitable.

The statutory duties of the DI 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 licenses 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
BM for ATMPs	**E**		**TPA**			
Other tissues/cells for ATMPs[+]	**E**	**E**	**TPA**	**E**		

[+]Other tissues/cells = leukapheresis cells, tumour tissue, whole blood.

Background to the establishment and description of inspection activities undertaken

This report refers to the activities carried out by King's College London (the establishment). Licensable activities take place in the Rayne Institute Building (Rayne Institute) as well as the private patients ward (Guthrie Wing), the apheresis unit, the operating theatre complex, the Wellcome Trust Clinical Trials Facility (CTF) and the pathology laboratory, all of which are within the main hospital building.

This was the fifth HTA site visit inspection of the establishment since it was issued an HTA

licence in January 2007 (the last inspection was in April 2014). It was a routine inspection to assess whether the establishment is continuing to meet the HTA's standards.

The establishment is licensed under the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (Q&S Regulations) for the procurement, processing, testing storage, distribution, import and export of human tissues and cells for human application. The establishment is also licensed for the storage of relevant material for use for a scheduled purpose under the Human Tissue Act 2004 (HT Act). Under the HT Act relevant material is currently stored for research in connection with disorders, or the functioning, of the human body and quality assurance (see below).

As all the cell types procured are used as starting materials for producing Advanced Therapy Medicinal Products (ATMPs) to be used in clinical trials, the establishment is also regulated by the Medicines and Healthcare products Regulatory Agency (MHRA). For ATMPs, the HTA generally regulates only the procurement and testing of the tissues and cells. However, in some instances, such as at this establishment, some processing may take place to derive the starting material for ATMP manufacture. Such processing steps are under the scope of EU Directive 2004/23/EC and consequently are regulated by the HTA.

The establishment is conducting two autologous cell therapy clinical trials.

Dendritic cell (DC) vaccine trial

In this trial, modified DCs are used to develop novel autologous immunotherapeutic treatments for specific tumours (glioblastomas). ATMP manufacture of the DC vaccine involves 'pulsing' the DCs with the patient's own tumour tissue.

Donor selection and consent for blood and tumour procurement takes place in the CTF or on the private patients ward by trained senior clinical or nursing staff. Donor selection and consent forms are ethically approved as part of the trial and participants can also consent to further research. Mandatory serology testing is conducted, under a Third Party Agreement (TPA), by the pathology laboratory. The laboratory was inspected by the HTA in 2012. Microbiological testing is also carried out by this laboratory under agreement.

Patients, who have given consent, undergo leukapheresis in the apheresis unit. Isolated leucocytes are transported to the Rayne Institute cleanroom facility by ATMP production staff. Brain tumour tissue is procured in the operating theatre complex and is similarly transported to the Rayne Institute.

Prior to being used in ATMP production the brain tumour tissue is stored in a -80°C freezer in the Rayne Institute (*see Advice items 4 and 9*).

The Rayne Institute cleanroom facility contains a grade D general laboratory and two processing laboratories, each containing an isolator which maintains an A over D grade air quality environment.

Acute adult Myeloid Leukaemia (AML) trial

In this trial, modified lymphocytes are being used in the autologous treatment of relapsed acute adult myeloid leukaemia (AML).

Donor selection and consent for both blood and bone marrow procurement, and serological testing, takes place as described above.

Heparinised venous blood is procured in the CTF or in the haematology clinic and bone marrow is procured in the operating theatre complex. Both sets of samples are transported to the Rayne Institute cleanroom facility as described above.

Peripheral blood mononuclear cells (PBMCs) are purified from the whole blood and bone marrow samples using centrifugation on a ficoll gradient. This processing step is considered part of the process by which the starting material for ATMP manufacture is produced and as

such is regulated by the HTA (*see Advice item 6*). Only one sample is processed at any one time; if two samples are received these are staggered to mitigate the risk of sample mix-up.

The ficoll-separated PBMCs are cryopreserved for 24 hours by passive freezing in a -80°C freezer in the Rayne Institute (*see Shortfall under GQ7a and Advice items 4 and 9*).

Following cryopreservation, samples are stored in the quarantine liquid nitrogen storage vessel within the Rayne Institute. Once serology and environmental monitoring data have been reviewed, along with batch manufacture records (BMRs), by the Head of Production and Head of Quality, samples are moved to the 'release' liquid nitrogen storage vessel in preparation for ATMP production.

The liquid nitrogen storage area in the Rayne Institute contains one quarantine liquid nitrogen storage vessel and one release vessel, both linked to a continuous temperature monitoring unit which feeds into a wireless callout system. Temperature excursions outside the set ranges trigger both audible alarms and the callout system and the system is tested regularly.

There are oxygen depletion monitors linked to an alarm system although staff do not carry portable monitors (*see Advice item 8*). The liquid nitrogen storage vessels are filled manually on a weekly basis.

Contingency liquid nitrogen storage vessels are available.

Research

Whole blood samples used for research are stored in -20°C freezers and leucocyte cones, purchased under a Service Level Agreement (SLA) with an HTA-licensed establishment, are stored in a -80°C freezer (see *Advice items 4 and 9*). All samples are stored for use in haematological immunology research projects which have project-specific NHS REC approval (*See Advice item 10*).

The timetable for the site visit inspection was developed after consideration of the establishment's previous inspection reports, reported cases and annual activity data. The inspection included a visual inspection of the Rayne Institute (cleanroom facilities, stock room, cryopreservation area, freezer facilities and liquid nitrogen storage area) and Cellular Therapy Unit (cleanroom facilities and liquid nitrogen storage area). Discussions and interviews were held with key staff and documentation was reviewed. Interviews were held with the DI (Professor of Molecular Medicine), the Head of Production and the Head of Quality. Audits of traceability were also carried out:

- Two samples processed and stored as part of the AML trial were selected from the 'release' liquid nitrogen tanks and label details were compared to the paper records and the electronic database. There were no discrepancies noted.
- Two tumour tissue samples, which were part of the DC vaccine trial, were selected from the -80°C freezer and label details were compared to the paper records and the electronic database. There were no discrepancies noted.
- The establishment has developed a BMR for each sample. This includes: donor selection and consent forms, donor test results and processing records – reagent/consumable batch numbers, operators involved, sample volumes, cellular yields, number of vials frozen – copies of sample labels, microbiology quality checks and environmental monitoring data. Three BMRs as part of the AML trial were reviewed. Although all three had been signed off for release, a number of discrepancies were noted (*see shortfall under GQ4b*).

Inspection findings

The HTA found the DI and the (Corporate) LH (CLH) 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

Governance and Quality Systems

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.		
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 TPA between the establishment and the testing laboratory is out of date.	**Minor**
GQ2 There is a documented system of quality management and audit.		
b) There is an internal audit system for all licensable activities.	Although there are audits against activities licensed by the MHRA the establishment has yet to develop an audit for HTA-licensed procedures, such as seeking consent, serological testing and handling of human tissue. *See Advice item 5.*	**Minor**
c) An audit is conducted in an independent manner at least every two years to verify compliance with protocols and HTA standards, and any findings and corrective actions are documented.	There is currently no independent audit against HTA standards.	**Minor**
GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills.		
e) Personnel are trained in all tasks relevant to their work and their competence is recorded.	For certain procedures, staff undergo competency assessment every six months although this was not formalised and the recording of competence was seen to be incomplete for some members of staff. *See Advice item 7.*	**Minor**
GQ4 There is a systematic and planned approach to the management 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.	During the audit the inspection team noted a number of discrepancies and missing fields in the forms that had been completed by the establishment. For example: - In one of the consent forms the donor had not indicated acceptance/refusal to allow material to be used in research involving animal experiments. There was nothing documented to indicate what action the establishment would follow for such samples. - The serology test data was not present for one of the samples. *See Advice item 5.*	**Minor**
GQ7 There are systems to ensure that all adverse events 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.	During the inspection the team noted a number of incidents which had not been recorded or followed up by the establishment. For example: - In one instance the microscope used for cellular evaluation was out of service and there was no corrective or preventative action plan in the records - In one instance a sample had been cryopreserved for 48, rather than 24, hours and there was no recording of this incident.	**Minor**
GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately.		
a) There are documented risk assessments for all practices and processes.	There are risk assessments for health and safety and for work in relation to ATMP production. There are no risk assessments covering HTA-licensed activities to ensure the quality and safety of the tissues and cells.	**Minor**

Advice

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

No.	Standard	Advice
1.	N/A	The DI is advised to appoint a Person Designated (PD) and to notify the HTA of such an appointment. Appointing a PD would not only clarify the roles and responsibilities within the group but would also bring the establishment's organisational structure in line with many of its standard operating procedures (SOPs), which assign a number of responsibilities to the PD, including

		auditing, the production of annual activity reports and the reporting of serious adverse events and adverse reactions (SAEARs) in the DI's absence.
2.	GQ1c	The DI should ensure that team meetings regularly include governance items such as standardisation of documents, changes to SOPs, audits and their findings, competence and regulatory training, management of incidents, risk assessments, the setting up of agreements with other establishments and updates from the HTA (e.g. e-newsletter items). The meetings should be governed by an agenda and minutes should be recorded and circulated. The minutes should include timelines for identified actions and there should be a standing agenda item for discussing progress against actions identified at previous meetings.
3.	GQ1d	There are inconsistencies in the format of the establishment's SOPs. The DI should ensure that all SOPs include the following key features: - Document control information, e.g. title and number, revision history and version number - Review date (at least every two-three years) - Issue date - Pagination - The names of both the author and the reviewer who has authorised the content of the document.
4.	GQ1d	Labels on all freezer doors indicate steps to be taken if the freezer audible alarms sound but these are out of date. The DI should ensure that all forms, labels and notices are included in the establishment's document control system.
5.	GQ1n, GQ2b, GQ4b, GQ5b	The DI should develop a schedule that will allow different team members to carry out selected audits. This should include horizontal audits to ensure that SOPs accurately reflect current practices and vertical traceability audits, from records of procurement to testing. The results of all audit findings, and actions taken, should be formally recorded and discussed at governance meetings, to ensure continuing improvement of processes and practices. The DI should also include audits of documentation provided by the US supplier of imported tissue, such as donor records, as part of the audit schedule.
6.	GQ2d	The establishment is currently using an established procedure for processing cells in the AML trial. If it is intended to process a new tissue type, or to modify the existing AML processing steps, the DI will need to submit a Preparation Process Dossier (PPD) to the HTA to get authorisation before the new processing procedure can begin. The DI is advised to update the establishment's change control procedures to ensure this requirement is clearly documented.
7.	GQ3e	The DI should consider ensuring the provision of a three-stage competence training process. The training could be divided into sections to fully assess progression of training: the trainee observes the trainer carrying out the activity; the trainee is observed by the trainer; and the trainee performs the activity alone.

		The training should include: the familiarity with SOPs and risk assessments, the seeking of consent and the reporting process for incidents.
8.	PFE3b	The DI should consider whether the use of portable oxygen depletion monitors would further mitigate the risks associated with working in the liquid nitrogen storage area.
9.	PFE3c	The DI should ensure that all freezers containing human tissues and cells are linked to the continuous temperature monitoring system.
10.	GQ2	The DI is advised to develop a register of the NHS REC-approved haematological immunology research projects, including dates of expiry, so that suitable arrangements can be made to store the relevant material under the HTA licence once the NHS REC approval has expired.

Concluding comments

During the inspection areas of good practice were noted:

- Paper copies of approved SOPs are printed on green paper.
- At a high level, there is a King's College London HTA Management Committee, consisting of all King's College London DIs and the CLH contact, which meets every six months.
- Bespoke inventories ensure full sample traceability from procurement to storage and end use. Additionally, the inventories have sections which allow the recording of incidents, such as freezer temperature fluctuations, alongside sample identification details.
- To mitigate against the risk of using expired reagents or consumables, the establishment uses a 'green sticker' procedure to ensure that stock has been cross-checked and is fit for use. Any reagents or consumables which have expired are labelled with 'red stickers' and are removed from the controlled storage area.

There are a number of areas of practice that require improvement, including seven minor shortfalls. The HTA has given advice to the DI with respect to the Governance and Quality Systems and Premises, Facilities and Equipment standards, as well as to licence management.

The HTA requires that the DI 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: 25 May 2016

Report returned from DI: 15 June 2016

Final report issued: 30 June 2016

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: 10 May 2018

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.
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.
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.

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.
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.

Human Tissue Act 2004 Standards

Consent standards
C1 Consent is obtained in accordance with the requirements of the Human Tissue Act 2004 (HT Act) and as set out in the code of practice
• Consent forms comply with the HTA's Code of Practice • Consent forms are in records and are made accessible to those using or releasing relevant material for a scheduled purpose • If the establishment obtains consent, a process is in place for acquiring consent in accordance with the requirements of the HT Act 2004 and the HTA's Codes of Practice • Where applicable, there are agreements with third parties to ensure that consent is obtained in accordance with the requirements of the HT Act 2004 and the HTA's Codes of Practice • Consent procedures have been ethically approved
C2 Information about the consent process is provided and in a variety of formats
• Standard operating procedures (SOPs) detail the procedure for providing information on consent • Agreements with third parties contain appropriate information • Independent interpreters are available when appropriate • Information is available in suitable formats, appropriate to the situation • Consent procedures have been ethically approved
C3 Staff involved in seeking consent receive training and support in the implications and essential requirements of taking consent
• Standard operating procedures (SOPs) detail the consent process • Evidence of suitable training of staff involved in seeking consent • Records demonstrate up-to-date staff training • Competency is assessed and maintained

Governance and quality system standards
GQ1 All aspects of the establishments work are supported by ratified documented policies and procedures as part of the overall governance process
• Policies and procedures are in place, covering all activities related to the storage of relevant material for research in connection with disorders, or the functioning, of the human body • Appropriate risk management systems are in place • Regular governance meetings are held; for example, health and safety and risk management committees, agendas and minutes • Complaints system
GQ2 There is a documented system of quality management and audit
• A document control system, covering all documented policies and standard operating procedures (SOPs). • Schedule of audits • Change control mechanisms for the implementation of new operational procedures
GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills
• Qualifications of staff and training are recorded, records showing attendance at training • Orientation and induction programmes • Documented training programme, (e.g. health and safety, fire, risk management, infection control), including developmental training • Training and reference manuals • Staff appraisal / review records and personal development plans are in place
GQ4 There is a systematic and planned approach to the management of records
• Documented procedures for the creation, amendment, retention and destruction of records • Regular audit of record content to check for completeness, legibility and accuracy • Back-up / recovery facility in the event of loss of records • Systems ensure data protection, confidentiality and public disclosure (whistle-blowing)
GQ5 There are documented procedures for distribution of body parts, tissues or cells
• A process is in place to review the release of relevant material to other organisations • An agreement is in place between the establishment and the organisation to whom relevant material is supplied regarding the tracking and use of material and eventual disposal or return

GQ6 A coding and records system facilitates traceability of bodies, body parts, tissues and cells, ensuring a robust audit trail
• There is an identification system which assigns a unique code to each donation and to each of the products associated with it • An audit trail is maintained, which includes details of when and where the relevant material was acquired, the consent obtained, the uses to which the material was put, when the material was transferred and to whom
GQ7 There are systems to ensure that all adverse events are investigated promptly
• Corrective and preventive actions are taken where necessary and improvements in practice are made • System to receive and distribute national and local information (e.g. HTA communications)
GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately
• Documented risk assessments for all practices and processes • Risk assessments are reviewed when appropriate • Staff can access risk assessments and are made aware of local hazards at training

Premises, facilities and equipment standards
PFE1 The premises are fit for purpose
• A risk assessment has been carried out of the premises to ensure that they are appropriate for the purpose • Policies in place to review and maintain the safety of staff, authorised visitors and students • The premises have sufficient space for procedures to be carried out safely and efficiently • Policies are in place to ensure that the premises are secure and confidentiality is maintained
PFE 2 Environmental controls are in place to avoid potential contamination
• Documented cleaning and decontamination procedures • Staff are provided with appropriate protective equipment and facilities that minimise risks from contamination • Appropriate health and safety controls are in place

PFE3 There are appropriate facilities for the storage of bodies, body parts, tissues and cells, consumables and records.

- Relevant material, consumables and records are stored in suitable secure environments and precautions are taken to minimise risk of damage, theft or contamination
- Contingency plans are in place in case of failure in storage area
- Critical storage conditions are monitored and recorded
- System to deal with emergencies on 24 hour basis
- Records indicating where the material is stored in the premises

PFE 4 Systems are in place to protect the quality and integrity of bodies, body parts, tissues and cells during transport and delivery to a destination

- Documented policies and procedures for the appropriate transport of relevant material, including a risk assessment of transportation
- A system is in place to ensure that traceability of relevant material is maintained during transport
- Records of transportation and delivery
- Records are kept of any agreements with recipients of relevant material
- Records are kept of any agreements with courier or transport companies

PFE5 Equipment is appropriate for use, maintained, quality assured, validated and where appropriate monitored

- Records of calibration, validation and maintenance, including any agreements with maintenance companies
- Users have access to instructions for equipment and receive training in use and maintenance where appropriate
- Staff aware of how to report an equipment problem
- Contingency plan for equipment failure

Disposal Standards

D1 There is a clear and sensitive policy for disposing of human organs and tissue

- Documented disposal policy
- Policy is made available to the public
- Compliance with health and safety recommendations

D2 The reason for disposal and the methods used are carefully documented

- Standard operating procedures (SOPs) for tracking the disposal of relevant material detail the method and reason for disposal

- Where applicable, disposal arrangements reflect specified wishes

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 Human Tissue Act 2004, Human Tissue (Quality and Safety for Human Application) Regulations 2007 or the HTA Directions.

1. **Critical shortfall:**

   A shortfall which poses a significant risk to 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 represents a systemic failure and therefore is 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 straight away.

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 the proposed action plan the establishment will be notified of the follow-up approach the HTA will take.