Virtual Regulatory Assessment (VRA) Assessment: 02 November 2021
Site Visit: 09-10 November 2021

Addenbrooke's Hospital
HTA licensing number 11066

Licensed under the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended)

Licensable activities carried out by the establishment
Licensed activities
'E' = Establishment is licensed to carry out this activity and is currently carrying it out.
'TPA' = Third party agreement; the establishment is licensed for this activity but another establishment (not licensed by the HTA) carries out the activity on their behalf.

Site	Procurement	Processing	Testing	Storage	Distribution	Import	Export
Addenbrooke's Hospital	E	E	TPA	E	E		E

Tissue types authorised for licensed activities

Authorised = Establishment is authorised to carry out this activity and is currently carrying it out.
Authorised* = Establishment is authorised to carry out this activity but is not currently carrying it out.

Tissue Category; Tissue Type	Procurement	Processing	Testing	Storage	Distribution	Import	Export
Progenitor Cell, Haematopoietic, PBSC; PBSC	Authorised	Authorised	Authorised	Authorised	Authorised		Authorised
Progenitor Cell, Haematopoietic, Bone Marrow; Bone Marrow	Authorised	Authorised	Authorised	Authorised	Authorised		Authorised
Progenitor Cell, Haematopoietic, Bone Marrow; Bone Marrow (ATMP)	Authorised		Authorised				Authorised
Mature Cell, MNC; DLI	Authorised	Authorised	Authorised	Authorised	Authorised		Authorised
Mature Cell, MNC; PBMC	Authorised	Authorised	Authorised	Authorised			Authorised

Progenitor Cell, Hematopoietic, Cord Blood; **Cord Blood**			Authorised*	Authorised	Authorised		Authorised*
Musculoskeletal, Cartilage; Cartilage (ATMP)	Authorised*		Authorised*				Authorised*
Other; Tumour (ATMP)	Authorised		Authorised				Authorised

Summary of inspection findings

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

Although the HTA found that Addenbrooke's Hospital (the establishment) had met many of the HTA's standards that were assessed during the inspection, three major and 12 minor shortfalls were found against standards for Consent, Governance and Quality, and Premises, Facilities and Equipment.

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.

Compliance with HTA standards

Major shortfalls

Standard	VRA findings	Level of shortfall
GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills.		
k) The establishment is sufficiently staffed to carry out its activities.	Since the last inspection, activities under the licence have expanded and there have been significant changes to establishment staff at all levels, including a new DI, Quality Manager and processing staff. Staff in key roles were found to be suitable. However, the establishment was not sufficiently staffed to support the full range of activities under the licence. This was reflected in a number of shortfalls identified during the inspection, including those relating to: • the oversight of licensable activities; • delays in the undertaking of key equipment and facility maintenance activities; • the scope and completion of internal audits; • the number and similar nature of incidents; and, • the number of open corrective and preventative actions (CAPAs) arising from audits and incidents.	**Major**

GQ5 There are documented procedures for donor selection and exclusion, including donor criteria.		
b) The testing of donors by the establishment or a third party on behalf of the establishment is carried out in accordance with the requirements of Directions 001/2021.	The systems and procedures for mandatory serological testing at the third-party testing laboratory were not aligned with the requirements of Directions 001/2021. For example, frequent temperature excursions both at the upper and lower limits of the ranges were seen in temperature monitoring records for refrigerators used to store serology samples and test kits. The establishment has not provided a documented rationale that supports the suitability of storage environments that frequently fall outside specified requirements. Furthermore, laboratory procedures state that blood samples may remain at room temperature for up to 24 hours post-draw before being centrifuged. During the inspection an example was seen where a blood sample was booked into the testing laboratory for processing two days after it was collected. The establishment was unable to demonstrate that the sample had been kept under appropriate conditions prior to processing. In addition, the laboratory's procedures for the reporting of incidents did not include a requirement to ensure that the DI would be informed of potential serious adverse events related to activities under the licence within 24 hours of discovery or determination.	**Major**

PFE2 Environmental controls are in place to avoid potential contamination.		
b) Where processing of tissues and / or cells involves exposure to the environment, it occurs in an appropriate, monitored environment as required by Directions 001/2021.	As a result of difficulties with one of its contracted maintenance companies, the establishment's clean room facility has not been maintained in accordance with its biannual maintenance and requalification schedule. During the inspection, the incident record relating to the status of the clean room could not be provided. In addition, the establishment has one working particle monitor. Its calibration certificate expired in May 2021 and recalibration has not been undertaken due to the level of processing activity and lack of alternative monitors. Furthermore, the establishment collects environmental monitoring data in a spreadsheet with the intention of undertaking quarterly rolling trend reviews of the previous 15 months for discussion at the establishment's governance meetings. However, the last documented review was undertaken in December 2020.	**Major**

Minor Shortfalls

Standard	VRA 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.		
b) There are procedures for all licensable activities that ensure	During the inspection, a number of findings were identified relating to the	**Minor**

integrity of tissue and / or cells and minimise the risk of contamination.	establishment's documented procedures. For example: • the establishment's procedures relating to donor lymphocyte infusions (DLIs) and tissues and cells that are the starting material for advanced therapy medicinal products (ATMPs) are not consistently aligned with the requirement for blood samples to be collected on the day of procurement or within seven days post procurement, as defined by Directions 001/2021; • Although in practice the establishment's donor selection process met regulatory requirements, the documented procedure for allogeneic donor selection did not include all the mandatory criteria set out in Annex A of the 'Guide to Quality and Safety Assurance of Human Tissues and Cells for Patient Treatment'; • the establishment does not have a standard operating procedure (SOP) in place to define temperature monitoring procedures and the maintenance of temperature monitoring equipment in the establishment's apheresis areas; • the establishment's maximum permitted time from the addition of Dimethyl Sulfoxide (DMSO) to the start of cryopreservation is not defined in procedures; and, • the procedure describing the actions to be taken in the event of a catastrophic failure of the liquid nitrogen tank(s) was overdue for review and included emergency contact details for a member of staff no longer employed at the establishment.	

GQ2 There is a documented system of quality management and audit.		
b) There is an internal audit system for all licensable activities.	The establishment has not undertaken audits of all activities under the licence, particularly those activities undertaken by the third-party testing laboratory, activities within hospital theatres, and activities relating to ATMP starting materials. In addition, a number of audits scheduled in 2021 had not been undertaken. Furthermore, some audits had not been written up in a timely manner, leading to delays in implementing CAPAs.	**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.	Although the establishment has undertaken an independent audit since the last inspection, this was not against all the standards applicable to the licence and did not include a review of primary records and raw data such as patient records, processing records and environmental monitoring data.	**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.	The establishment was unable to demonstrate that a member of staff who had undertaken receipt and release checks in the laboratory was trained against the version of the SOP that was effective at the time. The establishment has recently implemented an apheresis competency spreadsheet, but this was not completed for all staff undertaking licensable activities.	**Minor**

GQ4 There is a systematic and planned approach to the management of records.		
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.	The third-party testing laboratory retains raw data such as temperature monitoring data for 10 years or the lifetime of the equipment, which is not aligned with the regulatory requirement to retain raw data for 10 years from use or disposal of tissues or cells.	**Minor**
GQ6 A coding and records system facilitates traceability of bodies, body parts, tissues and cells, ensuring a robust audit trail.		
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.	In June-August 2021 the establishment audited four liquid nitrogen storage tanks that were used to store older cell stocks. A number of discrepancies were identified between the documented location of the cells and their true location within the tanks. One processing file relating to a unit of cells stored within the tanks could not be located.	**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.	The establishment has systems in place to ensure incidents (referred to as quality events) are reported, documented and CAPAs identified. However, CAPAs frequently remained open for extended periods, or were closed off without being robustly addressed. In addition, several examples of the same or similar incidents were identified. The establishment has recognised the risk presented by the number and similar nature of some of the incidents. This risk has been documented and discussed in governance meetings as part of a risk-based plan to address the high frequency of incidents and prioritise the resolution of CAPAs identified. However, the number of open and similar cases has remained high, indicating that the root cause has not yet been addressed.	**Minor**
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.	During the inspection, an example was noted where an assay undertaken to demonstrate the function and potency of a procured bone marrow unit had failed. Although the unit was subsequently infused, the assay was not repeated and the rationale for the decision to use the unit was not captured in the establishment's records.	**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.	The establishment has a range of risk assessments, but these do not cover risks to the quality and safety of tissues and cells for all activities and areas that fall within the scope of the licence.	**Minor**

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.	The establishment does not have documented premises risk assessments covering all premises that fall within the scope of the licence.	**Minor**
PFE3 There are appropriate facilities for the storage of bodies, body parts, tissues, 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.	The permitted temperature range in the apheresis area is not aligned with the manufacturer's stipulated operating range for the apheresis equipment.	**Minor**
PFE5 Equipment is appropriate for use, maintained, quality assured, validated and where appropriate monitored.		
c) Equipment affecting critical processes and storage parameters is identified and monitored to detect malfunctions and defects and procedures are in place to take any corrective actions.	The establishment's liquid nitrogen storage tanks are not on a routine service schedule. The establishment has a system in place whereby a senior staff member is required to sign off the use of cell transportation shippers where the temperature as measured by the available probe was higher than a pre-defined cut off. This confirmatory sign-off was not captured on all occasions reviewed during the inspection.	**Minor**

The HTA requires the DI to submit a completed corrective and preventative action (CAPA) plan setting out how the shortfalls will be addressed, within 14 days of receipt of the final report (refer to Appendix 3 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.

Advice

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

Number	Standard	Advice
1.	General	The DI is advised to amend the establishment's quality manual to reference the relevant legislation: The Human Tissue (Quality and Safety for Human Application) Regulations, 2007 (as amended).
2.	GQ2b	The DI is encouraged to streamline the audit reporting process through the use of templates and checklists wherever possible, so that the scope and findings are captured consistently and progress towards addressing any findings identified is not unduly delayed.
3.	GQ5b	The DI is advised to nominate a PD within the third-party testing laboratory to act as a point of contact and support the DI in overseeing licensable activities at the laboratory. The DI is further advised to include the PD in the establishment's governance meetings and circulation list for meeting minutes and other applicable communications.
4.	GQ7a	The establishment has implemented a comprehensive form for documenting the details of quality events, including investigations undertaken, agreed CAPAs and their completion. The DI is advised to ensure that when a quality event is raised the reference number is included in the applicable raw data record, so that when records are reviewed and audited it is clear that there is a quality event associated with the work that was being undertaken.
5.	PFE2b	During the inspection, examples were observed in which environmental monitoring using settle plates was not undertaken according to the planned schedule for routine periodic monitoring. The DI is advised to review the schedule for routine monitoring against resource availability to ensure that work can be completed as planned.

6.	PFE3a	The DI is advised to consider challenging the temperature monitoring systems used in various cell, reagent and sample storage areas to ensure they are working effectively and that staff respond to excursions. The DI is further advised to review arrangements for responding to alarms in the testing laboratory to ensure that there are robust arrangements in place to respond to alarms when the primary person responsible for this task is not available.
7.	PFE5a	The DI is advised to ensure that the time and date settings on standalone equipment such as particle monitors are routinely checked, for example after spring and autumn clock changes, so that their records are aligned with other time recordings captured within processing records.
8.	PFE5c	During the inspection an apheresis machine was observed that had been taken out of use for stem cell procurement but was still available for other purposes which fall outside the scope of establishment's HTA licence. The DI is advised to ensure that staff promptly label any equipment that has been taken out of use or had its routine use restricted, to help ensure staff are clear on which equipment is currently available for use. The DI is further advised to ensure that, where apheresis equipment is used for more than one procedure in a single day, cleaning activities between each procedure are captured in the establishment's records in addition to the daily and monthly cleans. The DI is also advised to capture apheresis start and end times and the time at which cells are placed into liquid nitrogen storage within their records to assist with audits and investigations.

Background

Addenbrooke's Hospital is part of the Cambridge University Hospital (CUH) NHS Foundation Trust. The establishment's core team are based at the hospital's Cambridge Cellular Therapy Laboratory (CCTL), which is part of the bone marrow transplant (BMT) programme

within the Department of Haematology. Licensable activities are undertaken at the laboratory, within hospital theatres and apheresis areas, and the third-party testing laboratory, which is also located on the Addenbrooke's site.

The establishment has been licensed by the HTA since August 2006. This was the establishment's first hybrid inspection combining a VRA with a site visit inspection. Prior to this, six site visit inspections of the establishment have been conducted; the most recent previous inspection took place in June 2019.

Since the site inspection in 2019, there have been a number of changes to staffing and activities under the licence, including a new DI, quality manager and laboratory staff. Activities under the licence have expanded to include procurement, testing and (where applicable) processing of a range of tissues and cells as ATMP starting materials. In future, the establishment intends to send some older cell stocks to another HTA-licensed establishment in order to reduce pressure on storage capacity under the licence. Plans are also in progress to expand activities into a laboratory building that was newly constructed at the time of the inspection. The HTA must assess the suitability of the premises before licensable activities within the new building commence.

Description of VRA activities undertaken

The HTA's regulatory requirements are set out in Appendix 2. The following areas were covered during the inspection:

Records of consent, procurement, testing, processing, storage, release (including distribution) and export, as applicable, relating to:

- one autologous PBSC collection;
- one allogeneic PBSC collection;
- one allogeneic bone marrow collection, including communication with the accredited assessor and the HTA;
- one autologous PBMC procurement for ATMP manufacture which was exported unprocessed;
- one autologous PBMC procurement for ATMP manufacture that was processed before export; and
- one autologous tumour tissue procurement for ATMP manufacture.

The inspection also included a review of records relating to equipment and facility maintenance, environmental monitoring, incidents, audits, staff training, documented procedures, selected agreements and risk assessments.

Report sent to DI for factual accuracy: 15 February 2022

Report returned from DI: 01 March 2022

Final Report issued: 15 June 2022

Appendix 1: HTA standards

The HTA standards applicable to this establishment are shown below; those not assessed during the VRA 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
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 001/2021 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 Medical Devices Regulation 2002 (SI 2002 618, as amended) (UK MDR 2002) and United Kingdom Conformity Assessed (UKCA).
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 third countries meet the standards of quality and safety set out in Directions 001/2021.

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 001/2021.
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 001/2021, is collected and maintained.
g) There is a system to ensure records are secure and that donor confidentiality is maintained in accordance with Directions 001/2021.
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 001/2021 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 001/2021.
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 001/2021.
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 UKCA or CE marked diagnostic tests, in line with the requirements set out in Directions 001/2021.
f) Samples taken for donor testing are clearly labelled with the time and place the sample was taken and a unique donor identification code.

GQ6 A coding and records system facilitates traceability of tissues and / or cells, ensuring a robust audit trail.
a) There is a donor identification system which assigns a unique code to each donation and to each of the products associated with it.
b) An audit trail is maintained, which includes details of when the tissues and / or cells were acquired and from where, the uses to which the tissues and / or cells were put, when the tissues and / or cells were transferred elsewhere and to whom.
c) The establishment has procedures to ensure that tissues and / or cells imported, procured, processed, stored, distributed and exported are traceable from donor to recipient and vice versa.
GQ7 There are systems to ensure that all adverse events, reactions and/or incidents are investigated promptly.
a) There are procedures for the identification, reporting, investigation and recording of adverse events and reactions, including documentation of any corrective or preventative actions.
b) There is a system to receive and distribute national and local information (e.g. HTA regulatory alerts) and notify the HTA and other establishments as necessary of serious adverse events or reactions.
c) The responsibilities of personnel investigating adverse events and reactions are clearly defined.
d) There are procedures to identify and decide the fate of tissues and / or cells affected by an adverse event, reaction or deviation from the required quality and safety standards.

e) In the event of a recall, there are personnel authorised within the establishment to assess the need for a recall and if appropriate initiate and coordinate a recall.
f) There is an effective, documented recall procedure which includes a description of responsibilities and actions to be taken in the event of a recall including notification of the HTA and pre-defined times in which actions must be taken.
g) Establishments distributing tissue and / or cells provide information to end users on how to report a serious adverse event or reaction and have agreements with them specifying that they will report these events or reactions.
h) Establishments distributing tissues and / or cells have systems to receive notifications of serious adverse events and reactions from end users and notify the HTA.
GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately.
a) There are documented risk assessments for all practices and processes.
b) Risk assessments are reviewed regularly, as a minimum annually or when any changes are made that may affect the quality and safety of tissues and cells.
c) Staff can access risk assessments and are made aware of local hazards at training.
d) A documented risk assessment is carried out to decide the fate of any tissue and / or cells stored prior to the introduction of a new donor selection criteria or a new processing step, which enhances the quality and safety of tissue and / or cells.

Premises, Facilities and Equipment

Standard
PFE1 The premises are fit for purpose.
a) A risk assessment has been carried out of the premises to ensure that they are fit for purpose.
b) There are procedures to review and maintain the safety of staff, visitors and patients.
c) The premises have sufficient space for procedures to be carried out safely and efficiently.
e) There are procedures to ensure that the premises are secure, and confidentiality is maintained.
f) There is access to a nominated, registered medical practitioner and / or a scientific advisor to provide advice and oversee the establishment's medical and scientific activities.
PFE2 Environmental controls are in place to avoid potential contamination.
a) Tissues and / or cells stored in quarantine are stored separately from tissue and / or cells that have been released from quarantine.
b) Where processing of tissues and / or cells involves exposure to the environment, it occurs in an appropriate, monitored environment as required by Directions 001/2021.
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 001/2021.
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 001/2021.
j) Shipping packaging containing tissues and / or cells is labelled with the information required by Directions 001/2021.
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: The HTA's regulatory requirements

The HTA must assure itself that the DI, Licence Holder, 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 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 3: 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 and VRAs carried out from 1 November 2010 are published on the HTA's website.

Appendix 3: 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 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:

   - A notice of proposal being issued to revoke the licence
   - 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.
   - A notice of suspension of licensable activities
   - Additional conditions being proposed
   - 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 VRA 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 on-site inspection or VRA.

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 VRA report.

Follow up actions

A template corrective and preventative action plan will be sent as a separate Word document with the final VRA report. Establishments 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 routine site-visit inspection.

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