Inspection report on compliance with HTA licensing standards
Inspection dates: **20-22 August and 06 September 2024**

Tissue and Cell Technologies Ltd.

HTA licensing number 11020

Licensed under the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended)
and
Licensed under the Human Tissue Act 2004

Licensable activities carried out by the establishment
Licensed activities – Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended)
'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
Tissue & Cell Technologies Ltd.	TPA	E	TPA	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
Adipose; Adipose	Authorised	Authorised	Authorised	Authorised	Authorised		
Other; Hair Follicles	Authorised	Authorised	Authorised	Authorised	Authorised		
Skin; skin	Authorised*		Authorised*				

Licensed activities – Human Tissue Act 2004
The establishment is licensed for the storage of relevant material which has come from a human body for use for a scheduled purpose.

Summary of inspection findings

Although the HTA found that Tissue and Cell Technologies Ltd. (the establishment) had met many of the HTA's standards that were assessed during the inspection, five major and six minor shortfalls were found against standards for Governance and Quality, and Premises, Facilities and Equipment. A further six minor shortfalls were identified relating to the storage of relevant material under the Human Tissue Act 2004 (HT Act, 2004).

In addition, one major and two minor shortfalls identified during the establishment's 2022 inspection remained open at the time of this inspection. The major shortfall related to changes to the establishment's procedures that had been made without submission of validation data to the HTA and which had been implemented without the associated authorisation. The minor shortfalls related to the detection and management of samples not received within specified parameters, and the alignment of the establishment's procedures with the specifications for sample management set out by the manufacturer of the kits used for HTLV I/II testing.

The establishment works with a third party organisation to undertake activities relating to hair follicle units (HFUs). Shortly before the inspection, the establishment indicated that arrangements with the third party were to cease and requested the activities of procurement, processing, distribution and donor testing in relation to hair follicles be removed from the licence. During the inspection, it was determined that the establishment had processed and stored HFUs imported from third country suppliers (3CSs), as well as undertaking associated donor testing, without there being a suitable licence in place for the import activity.

Taking the above into account, the HTA considers that the DI and CLH have failed to meet their obligations under the Human Tissue (Quality and Safety for Human Application) Regulations 2007, as set out in the HTA's Guide to Quality and Safety Assurance for Human Tissues and Cells for Patient Treatment, and will consider the need for further regulatory action in response to these findings.

Compliance with HTA standards

Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended) standards

Major shortfalls

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.		
b) There are procedures for all licensable activities that ensure	The establishment's procedures for the microbiological testing of adipose tissue are not sufficient to minimise the risks associated with potential or actual contamination of samples intended for human application. Specifically, the testing methodology does not allow for the detection of	**Major**

integrity of tissue and / or cells and minimise the risk of contamination.	relevant anaerobic contaminants, and the establishment no longer undertakes the speciation of any contamination detected post-processing to help inform clinical decision making. Related to this, examples were identified where establishment procedures were not aligned with current practice. For example: • The DI explained that any contamination detected in adipose tissue post-processing but not detected in pre-processing samples would be speciated. This approach is not documented within the applicable procedure, training documentation or risk assessment. • Instructions within SOP QMS-74 'Procedure for In-house Bioburden and Sterility Testing' lack clarity and are not aligned with current practice as described by staff during the inspection or as set out within staff training documents. Examples were also identified where documented procedures were unclear or not aligned with authorised processes: • The establishment undertakes aseptic adipose tissue processing activities in microbiological safety cabinets (MSCs) within a cleanroom environment. The grade A background environment is described in establishment procedures as 'grade P'. Although the SOP includes reference to classification criteria set out in the European Guide to Good Manufacturing Practice, Volume 4, Annex 1, the specification for the 'grade P' area, including monitoring processes and the contamination thresholds that would trigger investigation and corrective actions, have not been documented. • SOP QMS-51 relating to adipose tissue processing instructs staff that	

	to undertake a viability test on adipose tissue processed more than 24 hours after procurement, but concessional release may be required if the tissue is not processed within 72 hours of procurement. This is not aligned with the parameters that have been authorised by the HTA, which require tissue to be processed within 24 hours of procurement.	
GQ1 All aspects of the establishment's work are supported by ratified documented policies and procedures as part of the overall governance process.		
g) There are procedures to ensure that an authorised person verifies that tissues and / or cells received by the establishment meet required specifications. n) The establishment ensures imports from third countries meet the standards of quality and safety set out in Directions 001/2021.	At the establishment's 2022 inspection it was determined that the establishment's procedures were not robust enough to identify tissue products received which did not meet required specifications. Although work was subsequently undertaken to strengthen receipt checks for HFUs procured within the UK, the shortfall remained open at the time of this inspection pending resolution of remaining actions relating to adipose tissue. During this inspection, it was determined that the establishment had processed and stored HFUs imported from suppliers outside the UK. Procedures and records associated with this activity are embedded in the establishment's governance systems and the DI has attended audits of third country suppliers. However, although the tissue was procured for the same intended purposes as tissue procured within the UK, it was not subject to equivalent specifications and controls. Samples were identified which were not received and processed within validated and authorised parameters, including examples that had been received up to 16 days after procurement. In each case, the tissue was stored and receipt documentation was completed by	**Major cumulative**

	staff and approved by the Quality Assurance team. However, associated records did not reflect the fact that samples had been subject to a deviation from authorised and validated processes. Furthermore, records did not provide assurance that samples collected for mandatory serological testing were managed in accordance with validated parameters for the relevant test kits.	
GQ2 There is a documented system of quality management and audit.		
a) There is a quality management system which ensures continuous and systematic improvement.	The establishment's quality management system (QMS) and governance arrangements do not support continuous and systematic improvement, as evidenced by: • the number and nature of open shortfalls from the last inspection and the recurrent nature of shortfalls identified during this inspection; • the identification that the establishment has routinely processed, stored and undertaken associated donor serology testing of HFUs imported from third country suppliers outside of an appropriate HTA import licence; and • examples reviewed during the inspection demonstrating that HFUs imported from third country suppliers outside of a suitable licence authorisation were not managed within the establishment's QMS in accordance with the systems and procedures applied to HFUs procured under the establishment's licence in the UK for the same intended purposes. Deviations from required standards were not reported and assessed within the establishment's incident	**Major**

	management systems.	
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.	The establishment's authorised process for the cryopreservation of HFUs includes specification of a controlled-rate freezer cycle which, following a conditioning step, freezes the HFUs at a rate of 2°C per minute to a final temperature of -100°C. Examples reviewed during the inspection indicated the current cycle freezes HFUs to a final temperature of -80°C. The HTA was not notified about this change prior to it being implemented. The classification of this shortfall as a major finding reflects the identification of similar findings at the establishment's last inspection.	**Major**
GQ5 There are documented procedures for donor selection and exclusion, including donor criteria.	During the last inspection, a minor shortfall was identified relating to the management of serology samples used for donor serological testing, as follows: *The manufacturer of the HTLV I/II testing kit used to test adipose and hair follicle donors requires blood samples to be centrifuged before shipping. This is to separate the serum or plasma from the clot, red cells or gel separator. This centrifugation step is not carried out by the establishment.* This shortfall had not been resolved at the time of the 2024 inspection and could not be resolved through information provided by the establishment and testing laboratory during the course of the inspection. This shortfall therefore remains active and has been escalated to major as the activity is ongoing without effective resolution since it was first identified. In addition to this, during the inspection it was determined that the	**Major cumulative**
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.		
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.	establishment had undertaken donor testing associated with HFUs imported from third country suppliers. An example was reviewed in which procurement was undertaken in 2023 but the follicles and associated blood for serology testing were not received by the third-party hair clinic until 16 days later. Prior to the inspection the results from serology tests undertaken on these samples had not been reviewed for any positive markers or further testing undertaken for this donor. It was further confirmed through the inspection that in three examples, serology results were unavailable because the samples had either not been received by the laboratory or had been rejected as unsuitable. These events had not been documented, reported to the HTA where applicable, investigated or followed up by the establishment prior to the inspection.	
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.		

Minor Shortfalls

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.		
r) Third party agreements specify the responsibilities of the third party and meet the requirements set out in Directions 001/2021.	The establishment's third party agreement with a laboratory contracted to undertake speciation work, when this is requested, does not specify the third party's responsibilities regarding the reporting of potential serious adverse events and retention of raw data, as specified by Directions 001/2021.	**Minor**
s) Third party agreements specify that the third party will inform the		

establishment in the event of a serious adverse reaction or event.		
GQ4 There is a systematic and planned approach to the management of records.		
j) Records are kept of products and material coming into contact with the tissues and / or cells.	Some consumables, such as sterile forceps and containers used in the procurement and processing of hair follicles, were not recorded in establishment records.	**Minor**
GQ5 There are documented procedures for donor selection and exclusion, including donor criteria.		
f) Samples taken for donor testing are clearly labelled with the time and place the sample was taken and a unique donor identification code.	During a review of records at the third party testing laboratory examples were identified where samples had been sent for testing with incomplete information, leading to the rejection of the sample and requirement to seek a further sample to complete mandatory testing. These events were not consistently captured in the establishment's incident records to help avoid a recurrence.	**Minor**
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.	Reagents coming into direct contact with HFUs during procurement and cryopreservation are prepared in a MSC at the third party's premises before being supplied to the hair clinic for use. The MSC is not monitored as required by Directions 001/2021.	**Minor**

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.	The frequency that staff are required to refill the liquid nitrogen in adipose tissue storage tanks is not defined within establishment SOPs. *The establishment submitted sufficient evidence to address this shortfall before the report was finalised.*	**Minor**
PFE5 Equipment is appropriate for use, maintained, quality assured, validated and where appropriate monitored.		
b) Critical equipment is maintained and serviced in accordance with the manufacturer's instructions.	The annual service of the controlled-rate freezer used to freeze HFUs at the third party did not take place in July 2024 in accordance with its annual service schedule. The equipment was used to freeze HFUs in August 2024. The suitability of the equipment for use outside of the service period had not been documented in establishment records.	**Minor**

Human Tissue Act 2004 standards

Minor Shortfalls

Standard	Inspection findings	Level of shortfall
C1 Consent is obtained in accordance with the requirements of the Human Tissue Act 2004 (HT Act) and as set out in the HTA's Codes of Practice		
a) Consent procedures are documented and these, along with any associated documents, comply with the HT Act and the HTA's Codes of Practice.	The documentation related to the consent procedure did not provide an assurance that the donor is made aware that they can withdraw their consent. *The establishment submitted sufficient evidence to address this shortfall before the report was finalised.*	**Minor**
c) Where applicable, there are agreements with other parties to ensure that consent is obtained in accordance with the requirements of the HT Act and the HTA's Codes of Practice.	The agreement with the third party organisation procuring HFUs did not provide an assurance that consent is obtained in accordance with the requirements of the HT Act and the HTA's Codes of Practice.	**Minor**
GQ1 All aspects of the establishments work are governed by documented policies and procedures as part of the overall governance process		

a) Ratified, documented and up-to-date policies and procedures are in place, covering all licensable activities.	The establishment did not have documented procedures in place covering the scope of activities undertaken in relation to the receipt, storage, management and release of tissue stored under the HT Act 2004.	**Minor**
GQ2 There is a documented system of audit		
a) There is a documented schedule of audits covering licensable activities.	The establishment did not have a schedule of audits covering the licensable activities undertaken under the HT Act 2004.	**Minor**
GQ6 Risk assessments of the establishment's practices and processes are completed regularly, recorded and monitored		
a) There are documented risk assessments for all practices and processes requiring compliance with the HT Act and the HTA's Codes of Practice.	The establishment's risk assessments did not cover all licensable activities and required review and updating to ensure their scope covers all practices and processes. Examples included, but were not limited to: • the processes in place for obtaining consent or assuring appropriate consent is in place; • storing or using human tissue after consent withdrawal or outside the limitations of the consent that was given; • the transfer of samples that were procured for clinical use to continued storage for research use; and, • sample mix-up or loss of traceability.	**Minor**
T1 A coding and records system facilitates the traceability of bodies and human tissue, ensuring a robust audit trail		
c) An audit trail is maintained, which includes details of: when and where	One adipose tissue research sample in the -80°C freezer was not recorded in the correct location. The establishment stores adipose tissue research	**Minor**

the bodies or tissue were acquired and received; the consent obtained; all sample storage locations; the uses to which any material was put; when and where the material was transferred, and to whom.	samples in coloured boxes that are logged as the location in its inventory system. A sample in a ‘green’ box on the bottom shelf was recorded in the records as being in a ‘clear’ box. In addition, the second adipose tissue research sample audited had no evidence of consent for research use. The sample had been imported from a third country and the agreement with that agent had lapsed several years previously, with most of the material from that country having been disposed of. The only consent documentation available was for clinical use, and it was unclear if there was consent in place for the continued storage of the material.	

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 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.

DI and CLH/LH suitability

The nature of the open shortfalls at the time of this inspection and the additional findings described in this report raise concerns that both the DI and CLH may have failed to discharge their duty to supervise the licensed activity, specifically in relation to their responsibility for ensuring that suitable practices are adopted. The HTA will review the suitability of the DI and CLH as the corrective actions are undertaken to address the shortfalls identified during the inspection.

Advice

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

Human Tissue (Quality and Safety for Human Application) Regulations 2007 Standards (as amended)

Number	Standard	Advice
1.	GQ1b	The DI is advised to update SOP QMS-47 to provide more explicit information to adipose tissue procurement centres about the information to be recorded on serology samples, to help avoid the risk of samples being rejected at the testing laboratory due to the necessary information not being present. The DI is also advised to update the establishment's environmental monitoring SOP to ensure that criteria for the grade A environment are aligned with the current version of European Guide to Good Manufacturing Practice, Volume 4, Annex 1, which came into operation in August 2023.
2.	GQ4a	The establishment manually measures the liquid nitrogen level in the dewar used for storing HFU, and tops-up as required. Whilst the activity is recorded, the DI is advised to expand the form to prompt staff to record the measured level, or amount filled, as a review of this data may provide advance warning of a failure should the dewar start to lose liquid nitrogen at an increased rate. The DI is further advised to review forms such as those used to record liquid nitrogen storage tank refills and fridge cleaning to ensure these are suitably identified and controlled within the establishment's quality management system.
3.	GQ4c,d	The establishment has developed a customised electronic record system to capture raw data relevant to licensable activities. The DI is advised to review the establishment's risk assessments and ensure risks associated with the security and maintenance of the system are suitably controlled and all records safeguarded should, for example, staff involved in the development of the system no longer work for the company.

4.	GQ5f	Within the testing laboratory, serology testing profiles used for the testing of samples sent by the establishment are named within the laboratory's SOPs according to the tissue being banked. As a result, samples are being routinely labelled as being related to skin, rather than HFU or adipose as applicable, to ensure that the correct panel of tests is carried out. The DI is advised to work with the laboratory to review the current naming conventions within the laboratory's SOP and sample labels and consider implementing a clearer naming convention for samples sent by the establishment.
5.	GQ8a	The DI is advised to formally document a risk assessment regarding the storage of quarantined samples in the same vapour phase liquid nitrogen tank as non-quarantined samples; this will provide further assurance that all potential risks have been considered and appropriate mitigating steps implemented.
6.	PFE2b	The establishment samples adipose tissue before and after processing to look for microbial contaminants. Samples are incubated in broth and if growth is detected samples are plated out in the MSCs used for routine processing activities. The DI is advised to risk assess this practice, giving consideration to the potential risk to the grade A environment for subsequent processing activities. The DI is advised to add a prompt within the establishment's maintenance schedule for staff to update stand-alone clocks within establishment equipment in March and October in line with British Summer Time (BST) and Greenwich Mean Time (GMT), respectively. This will help to ensure that establishment raw data records can be aligned with periods when work was being undertaken. For example, aligning non-viable particle monitor sampling times with documented aseptic processing times in the establishment's processing records.
7.	PFE3a	The establishment calibrates temperature probes used to monitor storage and incubation equipment using an externally calibrated reference thermometer. Measurements are compared across a range of relevant temperatures and the average temperature displayed by the probe under test must be within 1°C of the average readings provided by the reference probe. This approach allows for readings at

		some points to deviate from the reference probe by more than 1°C. The DI is advised to review this procedure giving consideration to assigning a maximum permitted deviation at each temperature that is tested.
8.	PFE3a	The establishment manually plots daily storage temperatures over time to identify trends in temperature that may indicate a potential issue with the respective storage unit before a failure occurs. The DI is advised to consider plotting the minimum and maximum daily temperatures, in addition to the average temperature, as this would allow for a review of the daily temperature range over time. This advice applies to the storage of samples under both the Q&S Regs and the HT Act 2004.
9.	PFE3c	The establishment challenges freezer alarms annually to ensure that they are working as expected. The DI is advised to consider implementing a process to challenge alarms throughout the year as this will provide an assurance that the alarm system, and response process, is functional at multiple times throughout the year rather than on a single day. This advice applies to the storage of samples under both the Q&S Regs and the HT Act 2004.
10.	PFE5a	The controlled-rate freezer used to cryopreserve HFU is serviced annually. The annual service had been due on the 7th July 2024 but had not been undertaken at the time of the inspection. The controlled-rate freezer was used to cryopreserve samples in August 2024, beyond the annual service date. The DI is advised to review maintenance schedules to ensure that equipment remains within required service schedules at all sites under the licence.
11.	PFE5k	The DI is advised to update the establishment's contingency procedures to document the procedures that the DI described would be followed in the event of a fault with the establishment's controlled-rate freezer or one of its incubators.

Human Tissue Act 2004

12.	C1a	The DI is advised to amend the consent form for HFU to document that the donor has understood that their samples may be used for research purposes. Whilst this is explained in the patient information sheet (PIS), the consent form itself indicates that the HFU are being banked for the donor's use. In addition, the DI is advised to clarify the information around research in the PIS to ensure the donor has understood that this may be laboratory-based research rather than a clinical trial where the HFU will be implanted in the donor.
13.	C1c	The DI is advised to seek assurance from the third party organisation procuring HFU under the licence that samples imported from third countries have met the requirements of the local legislation in those third countries for samples to be collected, and exported, for research purposes.
14.	T1c	The DI is advised to review and update inventory records for samples held under the HT Act 2004, to ensure that they are sufficiently detailed to allow samples to be accurately located within the establishment's freezers.
15.	PFE1c	The DI is advised to implement, and document, a procedure to clean, decontaminate, maintain and defrost the -80°C freezer used to store relevant material under the HT Act 2004, as required.
16.	PFE2a	Adipose tissue research samples are stored in a -80°C freezer in loose boxes together with racked tubes used for other purposes. The DI is advised to consider if the use of a freezer racking system would facilitate the storage of, access to, and traceability of relevant material.

Background

Tissue and Cell Technologies Ltd (the establishment) has been licensed by the HTA since August 2006. The establishment originally operated as CellTran Ltd, then became York Pharma, and subsequently Altrika Ltd. In 2013 the establishment was renamed Regenerys Limited, before becoming Tissue and Cell Technologies Ltd in 2019.

This was the establishment's ninth inspection; the last inspection took place in July and August 2022. At the time of this inspection, three shortfalls from the 2022 inspection remained open. These were a major shortfall relating to changes to the establishment's procedures outside of the scope of authorised preparation process dossiers, a minor shortfall relating to the detection and management of samples not received within specified parameters, and a minor shortfall relating to the alignment of the establishment's procedures with the specifications for sample management set out by the manufacturer of the kits used for HTLV I/II testing.

Prior to the most recent inspection the establishment requested the removal of procurement, processing, distribution and donor testing in relation to hair follicles from the licence. However, at the time of the inspection these activities remained on the licence.

In addition to the Human Application sector-related activities described above, the establishment also stores relevant material for scheduled purposes under the HT Act, 2004. Adipose tissue samples in storage for research use may be collected specifically for research purposes but may also be transferred to storage for a scheduled purpose when they are no longer required for human application if appropriate consent is in place. The establishment also stores cryopreserved HFUs that may be released for research use. Whilst the establishment has oversight of these activities, the third party organisation takes responsibility for ensuring that consent is in place for HFUs.

Description of inspection activities undertaken

The HTA's regulatory requirements are set out in Appendix 1. The following areas were covered during the inspection:

Review of governance documentation

The inspection included reviews of procedural documents relating to licensed activities, equipment servicing records, agreements with third parties and end users, audits, risk assessments, reported incidents, temperature monitoring for the storage units, and staff training records.

Visual inspection
The inspection team undertook a review of the establishment's premises including areas for tissue receipt, the processing facility, tissue and consumable storage areas, and the area and equipment used for the incubation of sterility samples. The team also undertook visits to the third party laboratory that undertakes serological testing and the third party with whom the establishment collaborates to procure and process hair follicle samples. The inspection included a review of storage arrangements for samples stored for research under the HT Act, 2004.

Audit of records
Representative records from three adipose tissue and four hair follicle donors were reviewed, including (as applicable) information provided to donors, communications with relevant clinicians, procurement dates and times, processing activities and associated environmental monitoring records, records relating to sample management, sterility testing and donor serological testing, reagent and consumable records and records documenting the release and distribution of samples for human application and research activities.

Two adipose tissue samples in frozen storage under the HT Act, 2004 were reviewed from storage location to associated records, see shortfall against T1c under the HT Act, 2004 standards. In addition, records relating to donor consent, sample traceability, storage and, where applicable, release for a further two adipose tissue samples and three examples of HFUs stored under the HT Act were also reviewed, see shortfall against the HT Act, 2004 standard C1a, and advice items C1a and C1c.

Meetings with establishment staff
The inspection team met with the Designated Individual, the Quality Manager and staff working under the licence. The inspection team also met with representatives of the laboratory that undertakes mandatory serological testing.

The inspection included a visit to the hair transplant clinic where hair follicles were procured and processed. The team met with a co-founder of the hair clinic, who is also a co-founder and Medical Director for the company with whom clients consent to the banking of hair follicles for potential use as a starting material for the manufacture of an advanced therapy medicinal product. The team also met with the Chief Executive Officer of the follicle banking company.

Report sent to DI for factual accuracy: 18 December 2024

Report returned from DI: 06 January 2025

Final report issued: 04 April 2025

Appendix 1: 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 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.

Appendix 2: Classification of the level of shortfall

Where the HTA determines that a licensing standard is not met, the improvements required will be stated and the level of the shortfall will be classified as ‘Critical’, ‘Major’ or ‘Minor’. Where the HTA is not presented with evidence that an establishment meets the requirements of an expected standard, it works on the premise that a lack of evidence indicates a shortfall.

The action an establishment will be required to make following the identification of a shortfall is based on the HTA's assessment of risk of harm and/or a breach of the Human Tissue Act 2004, Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended), 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 (as amended) 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 on-site 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 the final inspection 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 inspection
- a request for information that shows completion of actions
- monitoring of the action plan completion
- follow up at next routine inspection.

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

Appendix 3: 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 (as amended)

Consent

Standard
C1 Consent is obtained in accordance with the requirements of the Human Tissue Act 2004 (HT Act), the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended) 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 (as amended) 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 Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended) 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.
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 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.
k) There are documented agreements with end users to ensure they record and store the data required by Directions 001/2021.
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 is in place to ensure raw data and records of traceability are maintained for 10 or 30 years respectively, 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.

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.

Human Tissue Act 2004 standards

Consent

Standard
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
a) Consent procedures are documented and these, along with any associated documents, comply with the HT Act and the HTA's Codes of Practice.
b) Where applicable, there are agreements with other parties to ensure that consent is obtained in accordance with the requirements of the HT Act and the HTA's Codes of Practice.
c) Where applicable, there are agreements with other parties to ensure that consent is obtained in accordance with the requirements of the HT Act and the HTA's Codes of Practice.
d) Written information is provided to those from whom consent is sought, which reflects the requirements of the HT Act and the HTA's Codes of Practice.
e) Language translations are available when appropriate.

f) Information is available in formats appropriate to the situation.
C2 Staff involved in seeking consent receive training and support in the essential requirements of taking consent
a) There is suitable training and support of staff involved in seeking consent, which addresses the requirements of the HT Act and the HTA's Codes of Practice.
b) Records demonstrate up-to-date staff training.
c) Competency is assessed and maintained.

Governance and Quality

Standard
GQ1 All aspects of the establishments work are governed by documented policies and procedures as part of the overall governance process
a) Ratified, documented and up-to-date policies and procedures are in place, covering all licensable activities.
b) There is a document control system.
c) There are change control mechanisms for the implementation of new operational procedures.
d) Matters relating to HTA-licensed activities are discussed at regular governance meetings, involving establishment staff.
e) There is a system for managing complaints.
GQ2 There is a documented system of audit

a) There is a documented schedule of audits covering licensable activities.
b) Audit findings include who is responsible for follow-up actions and the timeframes for completing these.
GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills
a) Qualifications of staff and all training are recorded, records showing attendance at training.
b) There are documented induction training programmes for new staff.
c) Training provisions include those for visiting staff.
d) Staff have appraisals and personal development plans.
GQ4 There is a systematic and planned approach to the management of records
a) There are suitable systems for the creation, review, amendment, retention and destruction of records.
b) There are provisions for back-up / recovery in the event of loss of records.
c) Systems ensure data protection, confidentiality and public disclosure (whistleblowing).
GQ5 There are systems to ensure that all adverse events are investigated promptly
a) Staff are instructed in how to use incident reporting systems.
b) Effective corrective and preventive actions are taken where necessary and improvements in practice are made.
GQ6 Risk assessments of the establishment’s practices and processes are completed regularly, recorded and monitored

a) There are documented risk assessments for all practices and processes requiring compliance with the HT Act and the HTA's Codes of Practice.
b) Risk assessments are reviewed regularly.
c) Staff can access risk assessments and are made aware of risks during training.

Traceability

Standard
T1 A coding and records system facilitates the traceability of bodies and human tissue, ensuring a robust audit trail
a) There is an identification system which assigns a unique code to each donation and to each of the products associated with it.
b) A register of donated material, and the associated products where relevant, is maintained.
c) An audit trail is maintained, which includes details of: when and where the bodies or tissue were acquired and received; the consent obtained; all sample storage locations; the uses to which any material was put; when and where the material was transferred, and to whom.
d) A system is in place to ensure that traceability of relevant material is maintained during transport.
e) Records of transportation and delivery are kept.
f) Records of any agreements with courier or transport companies are kept.
g) Records of any agreements with recipients of relevant material are kept.

T2 Bodies and human tissue are disposed of in an appropriate manner
a) Disposal is carried out in accordance with the HTA's Codes of Practice.
b) The date, reason for disposal and the method used are documented.

Premises, facilities and equipment

Standard
PFE1 The premises are secure and fit for purpose
a) An assessment of the premises has been carried out to ensure that they are appropriate for the purpose.
b) Arrangements are in place to ensure that the premises are secure and confidentiality is maintained.
c) There are documented cleaning and decontamination procedures.
PFE2 There are appropriate facilities for the storage of bodies and human tissue
a) There is sufficient storage capacity.
c) Storage conditions are monitored, recorded and acted on when required.
d) There are documented contingency plans in place in case of failure in storage area.
PFE3 Equipment is appropriate for use, maintained, validated and where appropriate monitored
a) Equipment is subject to recommended calibration, validation, maintenance, monitoring, and records are kept.
b) Users have access to instructions for equipment and are aware of how to report an equipment problem.
c) Staff are provided with suitable personal protective equipment.