Virtual Regulatory Assessment (VRA) Assessment: 13-14 October 2021
Site Visit Inspection: 2 November 2021

Future Health Technologies Ltd

HTA licensing number 22503

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

'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
Hub **Future Health Technologies Ltd**	TPA	E	E	E	E	E	E

Tissue types authorised for licensed activities

Authorised = Establishment is authorised to carry out this activity and is currently carrying it out.

Tissue Category; Tissue Type	Procurement	Processing	Testing	Storage	Distribution	Import	Export
Cardiovascular, Valves; Heart Valves				Authorised			
Progenitor Cell, Haematopoeitic, Cord Blood; Cord Blood	Authorised	Authorised	Authorised	Authorised	Authorised	Authorised	Authorised
Progenitor Cell, Haematopoietic, PBSC; PBSC				Authorised			
Progenitor Cell, Haematopoietic, Bone Marrow; Bone Marrow				Authorised			
Mature Cell, T Cell (DLI); DLI				Authorised			
Other; Dental Pulp	Authorised	Authorised	Authorised	Authorised	Authorised	Authorised	Authorised
Other; Cord Tissue	Authorised	Authorised	Authorised	Authorised	Authorised	Authorised	Authorised
Reproductive, Ovarian; Ovarian tissue				Authorised			
Reproductive,				Authorised			

Testicular; Testicular tissue							
Skin; Skin				Authorised			

Summary of inspection findings

Although the HTA found that Future Health Technologies Ltd (the establishment) had met the majority of the HTA's standards that were assessed, five major and eight minor shortfalls were found against standards for Governance and Quality, and Premises, Facilities and Equipment.

In addition, three major and two minor shortfalls identified during the establishment's 2019 inspection remained open at the time of this inspection.

The HTA is concerned about the suitability of the Licence Holder (LH) and the Designated Individual (DI) due to the number and recurrent nature of the shortfalls referred to in this report.

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 and the shortfalls that remained open from the previous inspection. The HTA intends to conduct a non-routine inspection to assess the progress that has been made.

Compliance with HTA 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 integrity of tissue and / or cells and minimise the risk of contamination.	The establishment uses flow cytometry analysis as their primary quality check prior to the acceptance of tissue and cells for banking. However, there is an absence of assay-specific controls and sufficiently regular operational controls (such as assay compensation controls) to provide an assurance that the assay has been performed correctly and that the results obtained are accurate. In addition, the establishment has no schedule in place for either the monthly compensation control or equipment maintenance checks.	**Major**

	Incidents were noted where the monthly compensation was missed, and where the absence of compensation was only noted several months later during an audit. In the interim period, there was no assurance as to the ongoing suitability of the results. Furthermore, the establishment has omitted cell surface markers from the antibody panels described in their authorised Preparation Process Dossier (PPD) resulting in changes to the establishment's acceptance criteria. The establishment did not notify the HTA regarding the amendment to the panel. In addition, documented procedures for the other activities do not contain sufficient detail. For example, • the standard operating procedure (SOP) for cord blood cryopreservation do not include the maximum time allowed from the addition of DMSO to the start of cryopreservation, one of the critical processing parameters; • the SOP for flow cytometry analysis does not include details of reagents used, such as supplier and catalogue number of antibodies and viability stains; and • the SOP for downloading temperature data does not include timings as to when the download must be completed and reviewed.	

GQ2 There is a documented system of quality management and audit.		
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 is not carrying out the biannual programme of ongoing evaluation of its preparation processes, as set out in its procedures. This non-conformance was identified in the 2019 HTA inspection and actions were taken to commence the programme of evaluation resulting in the shortfall being closed. However, during the inspection the establishment was not able to provide subsequent evaluation reports to demonstrate the programme has been implemented in accordance with documented procedures.	**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 establishment has performed in-house validations for commercially available testing kits setting out the acceptable timeframes and temperature ranges for maternal blood samples during shipment. A review of transportation data identified a significant proportion of maternal blood samples are received out-of-specification, both in terms of time and temperature in transit. The establishment staff described verbally that corrective measures should include a request for a second blood sample or a review from the medical director regarding the suitability of the blood sample for testing. There is no evidence that steps were taken to ensure a second sample is obtained for the samples audited during the inspection, nor are the corrective measures described stated in any of the documented procedures. In addition, the establishment does not have procedures in place to identify blood samples that have deviated from the validated temperature ranges during shipment; therefore, it is not possible to determine if the results obtained are accurate.	**Major**

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 does not report incidents that are considered potential Serious Adverse Events and Reactions (SAEARs) to the HTA, even though such a process is described in their documented procedures. These incidents include cases where the tissues and cells had not met the establishment's acceptance criteria following processing and therefore were not banked. This could be due to samples that had either been transported outside of the pre-defined shipping conditions or which lacked temperature monitoring data related to the shipping. This non-conformance was identified in the 2019 inspection and corrective actions are still outstanding. Additional examples of SAEARs that should have been reported included an incident where a sample was not banked as it did not meet the establishment acceptance criteria, potentially as a result of a proportion of the sample being lost during processing. In addition, the establishment's incident reports do not include sufficient detail of the incident, such as whether the quality and safety of the tissues and cells were impacted by the incident, whether the incident had wider implications on the work carried out under the licence, or whether the corrective measures were sufficient to address the root cause of the incident. Furthermore, the SOP for incident reporting is not sufficiently detailed to allow staff to determine if the incident is a Serious Adverse Event (SAE), nor do procedures ensure that incidents are reviewed by managers in a timely manner to allow for escalation to the HTA if required.	**Major**

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.	If the establishment receives tissues and cells out of validated parameters, it will perform a limited amount of control checks. These control checks do not provide sufficient information on the potential impact of the deviation on the quality of the tissues and cells. During the inspection it was noted that current correspondence with clients is inadequate to enable them to make an informed decision about the banking of their tissue and cells. Where samples were subject to deviations, regardless of whether the samples are banked or not, the clients are only informed that the samples have been 'successfully banked' or 'deemed not viable'. The limited number of quality control checks carried out does not enable the establishment to definitively state that the sample has been successfully banked, and the clients are not informed of issues that may have resulted in their sample not being suitable for storage. As such communications to clients do not provide sufficient clarity on the possible consequences of the sample having been subject to non-conformances.	**Major**

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.		
c) There are regular governance meetings, for example health and safety, risk management and clinical governance committees, which are recorded by agendas and minutes.	The establishment does not have regular governance meetings.	**Minor**
n) The establishment ensures imports from third countries meet the standards of quality and safety set out in Directions 001/2021.	The establishment has not performed an audit of their third country supplier.	**Minor**
r) Third party agreements specify the responsibilities of the third party and meet the requirements set out in Directions 001/2021.	The agreement with the courier company does not stipulate the required timeframe for reporting SAEARs to the establishment to allow onward reporting to the HTA, as set out in Directions 001/ 2021.	**Minor**

GQ2 There is a documented system of quality management and audit.		
b) There is an internal audit system for all licensable activities.	During the last inspection, issues were identified with the establishment's internal audit programme. Whilst the establishment has taken steps to address this, the programme still lacks sufficient depth to adequately cover licensable activities, as reflected in a number of the findings from this inspection. For example, the establishment does not currently conduct audits linked to the receipt of donor blood samples to ensure they are received within validated temperature ranges, or conduct audits of weekly and monthly quality control and maintenance checks for the flow cytometers. Audits are also not performed to ensure that working practices are aligned with documented and authorised procedures as set out in the establishment's PPDs.	**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.	The establishment has not carried out an independent audit.	**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 offers a contingency storage service to other organisations. Depending on circumstances, the establishment may take responsibility for the transport of the samples, either in liquid nitrogen dewars or freezers, to and from the other organisations. There is no documented risk assessment to cover the transport of these samples.	**Minor**

PFE2 Environmental controls are in place to avoid potential contamination.		
c) There are procedures for cleaning and decontamination.	The establishment has no process to ensure the weekly cleaning of the flow cytometry machine has been performed.	**Minor**

PFE4 Systems are in place to protect the quality and integrity of bodies, body parts, tissues and cells during transport and delivery to a destination.		
d) Records are kept of transportation and delivery.	Whilst the establishment records airway bill reference numbers, the information linked to these numbers is only accessible for six months following receipt.	**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.

DI and CLH/LH suitability

The HTA is concerned about the number and recurrent nature of the shortfalls referred to in this report and by some of the information that was provided to the inspection team during the latest inspection as evidence of compliance with regulatory requirements.

Whilst the establishment responded to a number of the issues raised during the previous inspection, it was noted that many of the corrective actions that the establishment committed to have not been embedded into working practices. For example, in addressing shortfalls from the previous inspection, the establishment provided an assurance that SOPs and processes had been amended to ensure that deviations are raised and reportable as SAEs where samples are transported out of validated conditions, transported without temperature data, or deemed unsuitable for storage following quality control testing. This process would ensure that these incidents are investigated and trended. These deviations continue to not be reported to the HTA, indicating that these changes have not been successfully embedded into working practices.

In addition, as part of the assessment of the establishment's programme of ongoing evaluation of its preparation processes, the establishment confirmed that the programme had been undertaken and provided the signed-off report for the evaluation undertaken after closure of the CAPA from the last inspection. On review it was noted that the report included data that was previously submitted as part of the evaluation reports submitted to allow closure of the CAPA, with the modified data set being presented as new data. This suggests a lack of sufficient oversight and management of the ongoing evaluation programme, and that it had not been implemented as indicated by the establishment.

Further, prior to the inspection, the HTA contacted the establishment requesting information on the numbers of blood samples intended for mandatory serological testing that had been shipped outside of the validated shipping criteria. Through this inspection, it is apparent that the actual number of samples that shipped outside of the validated criteria was significantly higher than was reported at the time due to the absence of procedures at the establishment to identify samples shipped outside validated temperature ranges. This speaks to the absence of oversight and a lack of understanding of the regulatory requirements to identify samples that should potentially be deemed as concessional due to an absence of valid donor test results.

During the CAPA process following the previous inspection, the HTA raised concerns about the suitability of the DI. The establishment addressed this concern by reviewing the role of the DI and restructuring the reporting lines within the organisation. However, due to the recurrent issues noted during

this inspection, the HTA does not feel that this corrective action is sufficient.

As set out in Directions 001/2021, both the LH and DI have a set of responsibilities to ensure that the requirements of the Regulations are complied with, including ensuring that human tissues and cells are procured, tested, processed, stored, distributed and imported/exported in accordance with the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended). Based on this inspection, the HTA does not believe they are currently meeting these requirements.

In light of this, the HTA is concerned about the suitability of the LH and the DI, and is of the view that there is currently insufficient oversight of licensable activities at the establishment to ensure that documented procedures and regulatory requirements are adhered to. The HTA will continue to maintain oversight of the actions taken to address the shortfalls identified during this inspection, and those remaining open from the previous inspection, and will conduct a non-routine inspection to assess the progress that has been made.

Advice

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

Number	Standard	Advice
1.	GQ1b	The DI is advised to review all SOPs to ensure there is sufficient detail for staff to perform the tasks consistently. For example, the SOP describing steps to take when a processed cord blood sample fails to meet the accepted white blood cell count does not have sufficient detail on pooling of the leftover fractions for re-analysis.
2.	GQ1d	The DI is advised to update documents to ensure they reflect current working practices. For example, the SOP for release refers to adipose tissue. The establishment is no longer authorised to procure and store this tissue type.
3.	GQ5b	Where additional serology tests are required based on the donor's travel history, these additional tests are flagged on the donor's records. The establishment does not carry out these tests on the donor's blood sample but has procedures in place to alert the clinical team of the need for the tests upon release of the unit. The DI is

		advised to review these procedures to ensure all required tests are carried out prior to banking to ensure quality and safety of the unit is maintained.
4.	PFE1a	The DI is advised to incorporate the IT contingency policy for preventing data loss and maintenance of traceability into the risk assessment considering the risk related to IT security.
5.	PFE5e	The establishment currently has two flow cytometers. At the time of the inspection one had been non-functional for five days. The DI is advised to review maintenance contracts to ensure they have the right level of emergency maintenance cover.
6.	PFE5k	Although the establishment has a back-up generator this does not constitute a continuous power supply. The DI is advised to risk assess whether a system needs to be implemented to ensure that all necessary equipment can operate continuously during critical processes.
7.	Human Tissue Act 2004 C1b	The establishment offers storage facilities to organisations wishing to store relevant material for a scheduled purpose under the Human Tissue Act 2004. While the current agreements indicate that the client is responsible for ensuring that all material meets current regulatory and legislative requirements, the DI is advised to ensure the agreement with clients specifies the client's obligation to ensure that all material stored, and released at the request of the clients, has appropriate consent in place.
8.	Human Tissue Act 2004 C1b	The DI is advised to reference the Human Tissue Act 2004 and the HTA Codes of Practice in client agreements to provide an assurance that clients are aware of the appropriate regulatory requirements, particularly for any material released for use for a scheduled purpose.

Assessment of existing shortfalls against standards

Three major and two minor shortfalls that were identified during the establishment's 2019 inspection remained open at the time of the inspection to which this report refers. The major shortfalls include the transport of tissues and cells that deviated from validated parameters. These deviations were not reported as incidents nor were there additional quality control checks performed on the samples as stipulated in the establishment's authorised PPD.

The HTA will continue to assess the actions taken by the establishment to address these shortfalls as part of the CAPA process for this inspection.

Background

Future Health Technologies Ltd has been licensed by the HTA since 2006. This was the tenth site visit of the establishment; the most recent previous inspection took place in September 2019.

The establishment's activities include the procurement of tissues and cells at hospitals in the UK under third party agreements. Tissues and cells are also imported from outside the UK, which have been procured by individuals trained in the establishment's procurement and shipping procedures.

Since the site inspection in 2019, the establishment has commenced the storage of heart valves, ovarian tissue, testicular tissue and skin on behalf of other organisations. There have been no other changes in terms of licence arrangements or other activities carried out under the licence.

Description of inspection activities undertaken

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

Audit of records and other documentation

The traceability audit included a review of eight client records during the VRA and three at the on-site visit. The records included samples received from abroad and procured within the UK. Records for a sample that was released for clinical use were also reviewed.

The audit included a review of the client consent, donor selection criteria, maternal serology results and processing records, including environmental monitoring and quality control checks such as flow cytometry data. As part of the audit, related SOPs, agreements with third parties and client communications were reviewed.

Six non-conformances were selected for review. The incident and the root cause of each incident were discussed, along with corrective and preventative actions undertaken.

Review of governance documentation

The establishment also acts as a contingency storage facility for tissues and cells intended for human application and research. The governance documents for this service were also reviewed and discussed. Documents covered included risk assessments for the premises and the service, procedures for manual handling, temperature monitoring systems, back-up arrangements, alarms, alerts and security measures. In addition, the management of tissue intended for use for a scheduled purpose was also reviewed.

Report sent to DI for factual accuracy: 1 December 2021

Report returned from DI: 15 December 2021

Final Report issued: 16 December 2021

Completion of corrective and preventative actions (CAPA) plan

Based on information provided, the HTA is satisfied that the establishment has completed the agreed actions in the CAPA plan and in doing so has taken sufficient action to correct all shortfalls addressed in the Inspection Report.

Date: 25 August 2023

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
b) If there is a third party procuring tissues and / or cells on behalf of the establishment the third party agreement ensures that consent is obtained in accordance with the requirements of the HT Act 2004, the Q&S Regulations and the HTA's Codes of Practice.
c) The establishment or the third party's procedure on obtaining donor consent includes how potential donors are identified and who is able to take consent.
d) Consent forms comply with the HTA Codes of Practice.
e) Completed consent forms are included in records and are made accessible to those using or releasing tissue and / or cells for a Scheduled Purpose.
C2 Information about the consent process is provided and in a variety of formats.
a) The procedure on obtaining consent details what information will be provided to donors. As a minimum, the information specified by Directions 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 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.

Human Tissue Act 2004 Standards

Consent standards
C1 Consent is obtained in accordance with the requirements of the Human Tissue Act 2004 (HT Act) and as set out in the code of practice
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.

Governance and quality system standards
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 standards
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 standards
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.

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.