Inspection report on compliance with HTA licensing standards
Inspection dates: 16-18 January 2024

Royal Free Hospital

HTA licensing number 11016

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.
E*= Establishment is licensed to carry out this activity but is not currently carrying it out
TPA = Third party agreement; the establishment is licensed for this activity but another establishment (unlicensed) carries out the activity on their behalf.

Site	Procurement	Processing	Testing	Storage	Distribution	Import	Export
Royal Free Hospital	E	E	TPA	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.
Authorised* = Establishment is authorised to carry out this activity but is currently not carrying it out

Tissue Category; Tissue Type	Procurement	Processing	Testing	Storage	Distribution	Import	Export
Progenitor Cell, Hematopoietic, Bone Marrow; Bone Marrow	Authorised*	Authorised*		Authorised*	Authorised*		Authorised*
Progenitor Cell, Hematopoietic; Peripheral Blood Stem Cells (PBSC)	Authorised*	Authorised		Authorised	Authorised		Authorised*
Mature Cell, T Cell (DLI); DLI**	Authorised*	Authorised*		Authorised*	Authorised*		Authorised*
Progenitor Cell, Hematopoietic, Unspecified; Peripheral Blood Mononuclear Cells (PBMC)	Authorised*	Authorised*		Authorised*	Authorised*		Authorised*
Reproductive, Ovarian; Ovarian Tissue	Authorised*	Authorised*	Authorised*	Authorised	Authorised		
Progenitor Cell, Hematopoietic, Bone Marrow; Bone Marrow (ATMP)	Authorised						
Other; Tumour (ATMP)						Authorised	

**DLI - donor lymphocytes for infusion

Licensed activities – Human Tissue Act 2004

Licensed = Establishment is licensed to carry out this activity and is currently carrying it out.

Area	Storage of relevant material which has come from a human body for use for a scheduled purpose
Royal Free Hospital	Licensed

Summary of inspection findings

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

Although the HTA found that Royal Free Hospital (the establishment) had met the majority of the HTA's standards under the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended) that were assessed during the site visit, three minor shortfalls were found against standards for Governance and Quality, and Premises, Facilities and Equipment. An additional five minor shortfalls were found against the standards assessed for activities that are carried out under the Human Tissue Act 2004 (HT Act). The shortfalls were against standards for Consent, Governance and Quality Systems, and Traceability. These related to standard operating procedures, audits, staff training records, risk assessments and traceability.

In addition, one major shortfall identified during the establishment's 2022 inspection remained open at the time of this inspection. This shortfall related to the absence of ongoing evaluation of the ovarian tissue cryopreservation programme to demonstrate that the critical quality attributes for this process were being met.

The HTA has assessed the establishment as suitable to be licensed for the activities specified, subject to corrective and preventative actions being implemented to meet the shortfalls identified during the inspection.

Compliance with HTA standards

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

Minor Shortfalls

Standard	Inspection findings	Level of shortfall
GQ2 There is a documented system of quality management and audit.		
b) There is an internal audit system for all licensable activities.	Although the establishment has undertaken a number of internal audits since the last inspection, its import activity and the work of the third party procurement centre have not been audited.	**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.	An independent audit was undertaken in 2023. However, as with the internal audits, this was limited in scope and did not review the establishment's import activity.	**Minor**

PFE2 environmental controls are in place to avoid potential contamination		Level of shortfall
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.	Kits for the procurement of bone marrow (ATMP) and tumour (ATMP) are prepared in laminar flow cabinets designed to maintain a grade A environment. The cabinets are located within a grade B background as designated by the establishment. The establishment does not undertake non-viable particulate monitoring of the Grade B environment at suitable frequencies or sessional viable microbiological monitoring to demonstrate that a Grade B background is maintained during the preparation of procurement kits.	**Minor**

Human Tissue Act 2004 standards

Minor Shortfalls

Standard	Inspection findings	Level of shortfall
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's documents did not cover all licensable activities and several standard operating procedures (SOPs) did not provide sufficient detail to allow staff to follow the procedure from beginning to end and ensure uniformity between staff undertaking the process. For example: • There was no SOP detailing the staff training requirements related to RTB-specific activities. • There was no SOP outlining the process for notifying Principal Investigators (PIs) of sample release requests or lists of authorised sample requestors. • The RTB stores samples for several different studies. There was no SOP available outlining the process for determining shipping requirements, or couriers to be used, for samples from different studies. • The "Aliquot release procedure" SOP does not outline a process for continued storage of samples at the RTB once they have been removed from the electronic system, prior to collection.	**Minor**

GQ2 There is a documented system of audit		
a) There is a documented schedule of audits covering licensable activities.	The establishment has not followed the schedule of audits outlined in the Biobank's audit SOP.	**Minor**

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.	The establishment was unable to provide evidence demonstrating that staff had been trained against the RTB-specific SOPs.	**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.	Establishment risk assessments related to activities at the RTB do not include all risks connected to the licensed activities, including: • Receiving and/or storing specimens without appropriate consent documentation. • Storing or using human tissue after consent withdrawal. • Storing or using human tissue outside of any limitations specified by the donor during consent. • Sample mix-up or loss of traceability. • Risks associated with non-RTB staff accessing the shared storage facility. • Receiving samples outside of normal working hours.	**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 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.	Reviewed processes did not ensure a full audit trail for samples, meaning that storage locations may not be recorded and presenting a risk that samples are not maintained under suitable conditions. Samples are logged into a commercially available Laboratory Information Management System (LIMS). When samples are requested, a list is generated in the LIMS, and the samples physically placed into a new container which is stored in the -80 freezer until it is collected by the investigator or delivered by courier. The samples are then removed from the LIMS system. During the sample traceability audit, one occasion was noted where samples were placed in a box and removed from the LIMS but were not collected by the investigator for five days. During this time there was no record of the samples retained in the LIMS system, despite the samples still being held by the RTB. Samples are normally hand delivered, or couriered, to the sample reception in the processing laboratory. Samples from some older academic studies are delivered to the Trust post room, and then transferred to an academic research office before being collected by RTB staff. Samples may remain in the post room overnight if they are received after 5pm. During the sample audit it was identified that one sample was received into the post room over a recent holiday period, but not received into the RTB until four days later. It is unclear where the sample was stored during this time.	**Minor**

The HTA requires the DI to submit a completed corrective and preventative action (CAPA) plan setting out how the shortfall will be addressed, within 14 days of receipt of the final report (refer to Appendix 3 for recommended timeframes within which to complete actions). The HTA will then inform the establishment of the evidence required to demonstrate that the actions agreed in the plan have

been completed.

Advice

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

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

Number	Standard	Advice
1.	GQ1b	The DI is advised to review all relevant SOPs to: • Remove reference to the HT Act for the requirement to report serious adverse events and reactions and replace this with the Human Tissue (Quality and Safety for Human Application) Regulations 2007. • Remove reference to unused controlled-rate freezer (CRF) profiles. • Ensure that the maximum permitted time between the addition of dimethyl sulfoxide and freezing is captured in all the relevant SOPs. • Correct the timings for taking blood samples for the mandatory serology tests from “within 30 days of procurement” to reflect the requirement of 30 days prior and up to seven days post procurement.
2.	GQ3e	The establishment occasionally undertakes colony-forming unit-granulocyte-macrophage (CFU-GM) assays on processed PBSCs if the required cell dose has not been achieved. As these assays are infrequently conducted, the DI is advised to put in place procedures through which assurance can be gained that staff continue to maintain their competency.
3	GQ7a	In one of the incidents reviewed during the inspection, it was unclear whether all or only one of the three bags containing stem cells was damaged. This incident was closed by the establishment, but the DI could not confirm whether the damage may have been related to the batch of bags. To aid future investigations, the DI is advised to ensure a more detailed account of incidents are documented. This will help in establishing the root cause and identifying the appropriate corrective and preventative actions.

4.	PFE4h	A printout of the pressure reading in the grade A area is saved in the batch manufacturing records (BMR) whenever a procurement kit is prepared. This does not provide information about whether the pressure cascades to the adjoining grade B change, or the grade C areas were within specification. For completeness, the DI is advised to consider capturing this additional information in the BMR.
5	PFE5a	The establishment's CRFs have several freezing profiles saved to them. Some procedures which used specific freezing profiles on the CRFs no longer take place at the establishment. However, the freezing profile remains on the equipment. The DI is advised to consider removing obsolete freezing profiles from the CRFs which may help to lower the risk of an operator selecting an inappropriate freezing profile in error.
7.	PFE5c	The DI is advised to consider implementing a procedure to monitor for contamination in hard-to-reach areas of the processing facility, such as the corners of the transfer hatches which cannot be reached using contact plates.

Human Tissue Act 2004

8.	C1(a)	During the sample audit it was identified that there were samples in the RTB that were collected more than 25 years ago. The DI is advised to review the sample collection and the suitability of the ongoing storage of samples with respect to any consent that may have been provided at the time of collection.
9.	C1(c)	The Service Level Agreement with the depositor of samples requires the depositor to ensure appropriate consent has been documented for the banking of samples at the RTB. The DI is advised to implement a process to ensure that any limitations placed on the storage or use of the samples during the consent process are communicated to the establishment.
10.	GQ1(a)	The DI is advised to review all relevant policies, SOPs and documentation relevant to activities undertaken under the remit of the HT Act, to ensure they:

		• Refer to requirements under the HT Act rather than the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended). • Reflect the current HTA Codes of Practice. • Accurately describe the activities undertaken at the RTB, including where samples may be sourced and the types of samples that may be stored.
11.	GQ1(c)	The RTB is in the process of moving (and generating new) SOPs/documents, training records, and risk assessments to new electronic systems. The DI as advised to manage this transfer through a robust change control process.
12.	GQ2(a)	The DI is advised to consider expanding the scope of the internal audit programme to include procedural, horizontal audits in addition to the vertical audits currently planned. This may help to ensure that SOPs accurately reflect all steps in the procedure, and that there are no steps missing between different SOPs.
13.	GQ2(a)	The establishment currently undertakes audits of a subset of samples that have been deposited into the RTB during the previous 12 months and seeks confirmation from the depositor that appropriate consent is in place. The DI is advised to also audit samples that have been held at the RTB for longer periods of time as samples are accessed and released on an ongoing basis. This will provide an assurance that the LIMS accurately reflects the samples held within the RTB, provide an assurance that the establishment is aware of the age and types of samples within the RTB, and allow the establishment to seek confirmation from the depositor that the continued storage of the samples is appropriate and covered by the consent that may have been provided.
14.	T1(b)	The Biobank Management Protocol refers to existing holdings that were collected prior to 2006. During the inspection staff were unaware of the age of older samples in the collection. The DI is advised to consider modifying the current use of the LIMS, so that staff can easily access a full register of samples, rather than utilising the current approach of reviewing samples within specific projects. In addition, the DI is advised to record any limitations, such as the time the sample may be kept in storage for research use

		and the expiry date of any recognised Research Ethics Committee (rREC) approvals, within the LIMS. This will ensure that all information relevant to a sample is readily available in a single location.

Background

Royal Free Hospital has been licensed by the HTA since July 2006. This was the establishment's eight inspection; the most recent previous inspection took place in January 2022. The establishment is also licensed by the Medicines and Healthcare products Regulatory Agency (MHRA) as a manufacturer of ATMPs and for the production of Specials.

Since the previous inspection, staff from a different organisation have been responsible for processing PBSCs using the establishment's facilities and equipment. These staff undertake processing in accordance with well-defined procedures and only after completion of appropriate training. Honorary contracts are also given to the staff to help ensure that there is appropriate oversight of this work through the establishment's governance systems. It is envisaged that, in time, these staff will be responsible for training future colleagues. In 2023, the establishment elected to pause the ovarian tissue cryopreservation program until the outstanding shortfall from the previous inspection is addressed.

In addition to the Human Application sector related activities described above, the establishment also maintains a RTB storing relevant material under the HT Act. Samples in the RTB are primarily obtained from studies with project-specific Research Ethics approval from a rREC. In these cases, the Principal Investigator takes responsibility for ensuring informed consent is in place, using documentation that has been reviewed by the respective rREC granting authorisation for the study. In addition to samples obtained from rREC-approved studies, the RTB also contains historical samples, including a number of existing holdings from before 1 September 2006, and samples that would not be considered relevant material. Since the last inspection, the establishment's RTB is now managed under the establishment's Trust's Research and Tissue Directorate. Plans are being developed to apply for a separate licence for the RTB.

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
A review of documentation relevant to the establishment's licensable activities was undertaken. This included the establishment's receipt and relevant procurement and processing procedures, engraftment outcomes, risk assessments, training records, internal and independent audits.

Visual inspection
A visual inspection of areas where licensable activity is carried out was undertaken. This included areas where samples are received, processed and stored. The areas where consumables and reagents are stored was also inspected.

Audit of records and other documentation
Relevant records for the tissue types listed below were reviewed in conjunction with establishment staff:

- Three PBSCs that were procured by another licensed establishment and sent to the establishment for processing, storage and distribution. In addition, the disposal records for one PBSC unit were also reviewed.

- Two PBMCs that were procured from adult donors at another HTA-licensed organisation and sent to the establishment for processing and storage. The cryopreserved cells were subsequently distributed for end-use.

- A total of four bone marrow samples that were procured under a third party agreement for the manufacturer of ATMPs.

- One tumour sample that was imported under the establishment's licence and a second sample procured under another establishment's licence for the manufacture of ATMPs for the treatment of two different types of malignancies.

- Two ovarian tissues that were procured under the establishment's licence and processed by its staff.

The records reviewed included: donor consent forms, mandatory donor serological testing results, consumables and reagents used during procurement and processing, storage records and, where applicable, records of release for end-use or disposal. Selected equipment maintenance records, storage temperature records of consumables and reagents and staff training were also reviewed.

The establishment is also licensed for the storage of relevant material for use in a Scheduled Purpose. This activity was reviewed as part of this inspection. The following areas were covered during this aspect of the inspection:

Standards assessed against during inspection
Human Application sector establishments storing relevant material for a scheduled purpose under the remit of the HT Act are assessed against the Research sector standards for this activity. There are 47 standards in the Research sector, of which 38 were assessed. Standards C1(a), C1(b), C1(d), C1(e), C1(f), C2(a), C2(b), C2(c), and PFE2(b) could not be assessed as staff working under the licence do not directly seek consent for storage for a scheduled purpose.

Review of governance documentation
The assessment included a review of documentation relevant to the establishment's licensed activities. This included policies and procedural documents relating to licensed activities, equipment maintenance records, risk assessments, arrangements for temperature monitoring for the storage units, staff training records, a review of the LIMS used to record and track relevant material, audits, and incidents.

Visual inspection
The site visit included a visual inspection of the area where samples are received into the establishment, receipted, logged into the establishment's systems, and stored.

Audit of records and other documentation
During the visual inspection, records for 13 different samples were reviewed as part of a traceability audit. This included several aliquots of normal and tumour tissue that had been dissected from a single piece of donated tissue. Electronic records were reviewed for individual samples from the LIMS and matched to the corresponding sample location, and vice versa. No discrepancies were found.

In addition, three internal audits undertaken in 2023 were reviewed and discussed during the site visit.

Meetings with establishment staff
The inspection of the activities related to the RTB and activities under the HT Act included discussions with the DI, the Head of Quality and Licensing, the Biobank Manager and the Director of Tissue Access for Patient Benefit, and other staff working under the licence.

Report sent to DI for factual accuracy: 15 February 2024

Report returned from DI: 27 February 2024 No factual accuracy or request for redaction comments were made by the DI.

Final Report issued: 28 February 2024

Appendix 1: HTA standards
The HTA standards applicable to this establishment are shown below; those not assessed during the inspection are shown in grey text. Individual standards which are not applicable to this establishment have been excluded.

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

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.

d) The requirements of the Single European Code are adhered to as set out in Directions 001/2021 (Northern Ireland only).
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.
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.
j) Shipping packaging containing tissues and / or cells is labelled with the information required by Directions.

PFE5 Equipment is appropriate for use, maintained, quality assured, validated and where appropriate monitored.
a) Critical equipment and technical devices are identified, validated, regularly inspected and records are maintained.
b) Critical equipment is maintained and serviced in accordance with the manufacturer’s instructions.
c) Equipment affecting critical processes and storage parameters is identified and monitored to detect malfunctions and defects and procedures are in place to take any corrective actions.
d) New and repaired equipment is validated before use and this is documented.
e) There are documented agreements with maintenance companies.
f) Cleaning, disinfection and sanitation of critical equipment is performed regularly and this is recorded.
g) Instruments and devices used for procurement are sterile, validated and regularly maintained.
h) Users have access to instructions for equipment and receive training in the use of equipment and maintenance where appropriate.
i) Staff are aware of how to report an equipment problem.
j) For each critical process, the materials, equipment and personnel are identified and documented.
k) There are contingency plans for equipment failure.

Human Tissue Act 2004 (HT Act) 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
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.
C2 Staff involved in seeking consent receive training and support in the essential requirements of taking consent

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.

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.