Site visit inspection report on compliance with HTA minimum standards

University Hospital of Wales

HTA licensing number 11094

Licensed for the

- **procurement, processing, testing, storage, distribution and export of human tissues and cells for human application under the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended)**

22 – 23 January 2019

Summary of inspection findings

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

Although the HTA found that University Hospital of Wales (the establishment) had met the majority of the HTA standards, shortfalls were found in relation to third party agreements, labelling of serological testing samples, application of the Single European Code, traceability, environmental monitoring and monitoring the storage temperatures of consumables and reagents. In addition, the HTA assessed progress towards meeting shortfalls that were identified during the previous inspection. As a result, three of the five open shortfalls were assessed as being fully met and were closed; however, the two remaining shortfalls relating to procedures around the termination of activity and the reprovision of services in an emergency remain open.

The HTA has also given advice to the DI with regards to patient information leaflets, procedural documents, audits, donor selection, clean room monitoring procedures and temperature monitoring.

The HTA's regulatory requirements

The HTA must assure itself that the Designated Individual, Licence Holder, premises and practices are suitable.

The statutory duties of the Designated Individual are set down in Section 18 of the Human Tissue Act 2004. They are to secure that:

- the other persons to whom the licence applies are suitable persons to participate in the carrying-on of the licensed activity;
- suitable practices are used in the course of carrying on that activity; and
- the conditions of the licence are complied with.

The HTA developed its licensing standards with input from its stakeholders. They are designed to ensure the safe and ethical use of human tissue and the dignified and respectful treatment of the deceased. The HTA inspects the establishments it licences against four groups of standards:

- consent
- governance and quality systems
- premises facilities and equipment
- disposal.

This is an exception-based report: only those standards that have been assessed as not met are included. Where the HTA determines that a standard is not met, the level of the shortfall is classified as 'Critical', 'Major' or 'Minor' (see Appendix 2: Classification of the level of shortfall). Where HTA standards are fully met, but the HTA has identified an area of practice that could be further improved, advice is given to the DI.

Reports of HTA inspections carried out from 1 November 2010 are published on the HTA's website.

Licensable activities carried out by the establishment

'E' = Establishment is licensed to carry out this activity.

'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.

Tissue Category; Tissue Type	Procurement	Processing	Testing	Storage	Distribution	Import	Export
Progenitor Cell, Hematopoietic, Bone Marrow; Bone Marrow	**E**	**E**	**E**	**E**	**TPA**		**E***
Progenitor Cell, Hematopoietic, PBSC; PBSC	**E**	**E**	**E**	**E**	**TPA**		**E***
Progenitor Cell, Hematopoietic, Cord Blood; Cord Blood				**E**	**TPA**		

Mature Cell, T Cell (DLI);DLI	**E**	**E**	**E**	**E**	**TPA**		**E***

Background to the establishment and description of inspection activities undertaken

The establishment is licensed for the procurement, processing, testing, storage, distribution and export of human tissues and cells for human application under the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended) (the Regulations).

The establishment has been licensed by the HTA since October 2006 and this is the seventh routine site visit inspection to assess whether or not the establishment meets the HTA's standards. Annual activity data, pre-inspection discussions with the DI, the previous inspection report and a review of open shortfalls were used to inform the timetable that was developed for this inspection.

The establishment is part of the South Wales Blood and Marrow Transplant (SWBMT) programme for South Wales. It procures peripheral blood stem cells (PBSC), bone marrow (BM) and donor lymphocytes (DLI) from adult donors for autologous and allogeneic use and from paediatric donors for autologous use. Paediatric patients requiring allogeneic treatment are referred for treatment to another hospital. The establishment can also on occasion receive PBSCs, bone marrow and umbilical cord blood from other HTA-licensed establishments which have identified suitable unrelated donors for the establishment's recipients; however, this area of activity was not reviewed during this inspection.

Procured PBSCs are taken to the establishment's clean room processing facility for cryopreservation. Following cryopreservation frozen cells are stored in vapour phase liquid nitrogen (LN2) tanks which are housed in the establishment's processing facility. The establishment releases cryopreserved cells for infusion into patients from its own Health Board and for patients from a hospital in another Health Board but which is part of the same blood and marrow transplant programme.

BM and PBSCs that require volume reduction or other processing not undertaken by the establishment are transferred to another HTA-licensed establishment for processing under a Service Level Agreement; this area of activity was not reviewed during this inspection.

Audit exercise

During the inspection audits were carried out relating to both donor selection and procurement and processing of the procured cells.

Two sets of donor records, one allogeneic and one autologous, were reviewed. The review included the pre-collection clinic checklist, consent to treatment and examination, donor medical questionnaire, final donor clearance, consent for testing, storage and disposal, apheresis worksheet (including records of kits and reagents used during procurement) and donor serological testing results. An example of a data entry which was not easily legible was identified during the audit (see advice item – 6).

Processing records were reviewed for four PBSC collections and the location recorded in the records cross-checked against the locations recorded in the inventory spreadsheets and individual racking maps. There were no anomalies in the processing records, however, the location of one of the four products had been moved and the location records not updated on either the inventory spreadsheet or processing record. On further investigation, the transfer was noted on the individual racking maps for the LN2 storage. In addition, environmental monitoring records for the Grade A and B processing environments were reviewed for a

randomly selected month in 2018. While the Grade A environment was maintained, the Grade B environment was recorded as outside the acceptable parameters on multiple occasions, for either 0.5µM, 5µM or both, particle counts.

Inspection findings

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

Compliance with HTA standards

Governance and Quality

Standard	Inspection findings	Level of shortfall
GQ1 All aspects of the establishment's work are supported by ratified documented policies and procedures as part of the overall governance process.		
r) Third party agreements specify the responsibilities of the third party and meet the requirements set out in Directions 002/2018.	The establishment's TPA with the transport provider moving cells to other organisations does not include the requirement for the provider to alert the establishment to any serious adverse events that may occur so that the incidents can be reported to the HTA within 24 hours of their discovery.	**Minor**
GQ5 There are documented procedures for donor selection and exclusion, including donor criteria.		
f) Samples taken for donor testing are clearly labelled with the time and place the sample was taken and a unique donor identification code.	Although donor serological testing samples are labelled with the date that the blood was taken, the time of the blood draw is not recorded.	**Minor**

GQ6 A coding and records system facilitates traceability of bodies, body parts, tissues and cells, ensuring a robust audit trail.		
b) An audit trail is maintained, which includes details of when the tissues and / or cells were acquired and from where, the uses to which the tissues and / or cells were put, when the tissues and / or cells were transferred elsewhere and to whom.	In the past due to storage space constraints, the establishment transferred cells to another HTA-licensed facility for off-site storage. Upon return of the cells to the establishment's new storage facility, the cells were placed into new storage tanks in re-named storage racks. Location information for processed cells is recorded in the paper processing records and in electronic spreadsheets. Following the return of cells to the establishment, the location details of the cells changed due to them being placed into the newly named storage tanks and storage racks. The paper processing records have not been updated to reflect this change in location details. Although during the inspection, traceability could be demonstrated, determining the location details required cross checking several records. In addition, in one of the four cases audited, the location details of the cells had not been updated in either the processing records or the electronic spreadsheet. The establishment is in the process of creating a new spreadsheet which will record the historical and current storage details of stored cells so that finding location information will be facilitated however, this list is not yet completed. In addition, the establishment is implementing a new electronic traceability system however again, this is not yet in use.	**Minor**
d) The requirements of the Single European Code are adhered to as set out in Directions 002/2018.	The establishment occasionally sends bone marrow aspirates to another HTA-licensed organisation for processing before cells are returned to the establishment for end use. When releasing the cells for circulation to the other licensed organisation, the establishment does not include the Single European Code (SEC) donor identification sequence with the transported cells. In addition, when sending cells to another hospital within the South Wales Blood and Marrow Transplant programme, the cells being released for end use do not have the SEC applied to them or accompanying them.	**Minor**

Premises, Facilities and Equipment

Standard	Inspection findings	Level of shortfall
PFE2 Environmental controls are in place to avoid potential contamination.		
b) Where processing of tissues and / or cells involves exposure to the environment, it occurs in an appropriate, monitored environment as required by Directions 002/2018.	The establishment has determined its operational air quality as a Grade A environment within a Grade B background. During a review of environmental monitoring records, it was found that although the establishment was achieving a Grade A environment in the processing cabinet, there were occasions where the requisite air quality for the Grade B background had not been achieved during processing. Despite the environmental monitoring findings in the Grade B, the post processing sterility test of the processed cells showed no microbiological contamination of the processed cells. The establishment also has not defined action and alert levels to facilitate the determination of appropriate responses to environmental monitoring findings so that they are recorded, followed up and actions to address the findings taken. These actions also include any risk assessment necessary to asses the quality and safety of the cells being processed at the time of the non-conforming environmental monitoring result.	**Minor**

PFE3 There are appropriate facilities for the storage of bodies, body parts, tissues, cells, consumables and records.		
a) Tissues, cells, consumables and records are stored in secure environments and precautions are taken to minimise risk of damage, theft or contamination.	The establishment stores apheresis kits, anticoagulant (ACD-A) and sodium chloride on the ward where apheresis takes place. Although the storage temperature of the ACD-A is monitored, the storage temperatures of the apheresis tubing kits and sodium chloride is not. Both the apheresis kits and sodium chloride have defined storage temperature ranges however without appropriate monitoring the establishment cannot determine if these have been exceeded. Various reagents, including environmental monitoring plates, Dimethyl sulfoxide (DMSO) and cleaning consumables, are stored in the clean room facility where the establishment undertakes processing of PBSCs. DMSO used in the cryopreservation of PBSCs and the cleaning consumables both have defined storage temperature limits, however the establishment is storing them in an environment which is not temperature monitored. Again, without appropriate monitoring the establishment cannot determine of these defined temperature limits have been exceeded. The establishment monitors the temperature of the fridge that is routinely used to store environmental monitoring plates using a data logging device which is downloaded and reviewed monthly. As a result, the shortfall against PFE3(a) that was identified at the previous inspection was considered to have been met however advice has also been given (see advice item 13).	**Major**

	During this inspection it was found that a newly installed fridge was also being used to store environmental monitoring plates. This fridge is also temperature-monitored via a recently installed remote monitoring system which will also monitor the temperature of the liquid nitrogen storage tanks. A review of the fridge's temperature monitoring records showed that on several occasions the fridge's temperature had fallen below the lower storage temperature limit defined by the manufacturer of the plates. This temperature deviation had not been identified by the establishment and poses a potential risk that the monitoring plates used to detect contamination within the clean room facility may not be as effective as they should be.	

Advice

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

No.	Standard	Advice
1.	C2(c)	The establishment's donor information leaflets state that "collected cells will be stored for a minimum of five years" before their continued storage will be reviewed and kept under review if stored for longer. There may be instances, however, where cells are not stored for this five year period, for example if the intended recipient dies. The DI is advised to review to wording of the information leaflet to reflect that cells will be stored for up to five years or until it is deemed that they are no longer needed before their continued storage will be reviewed and kept under review if stored for longer.
2.	GQ1(b)	The establishment's standard operating procedure (SOP) regarding bone marrow collection states that on occasions, bone marrow may be procured at another hospital within the same blood and marrow transplant programme. During the inspection however, the establishment stated that although this had happened very occasionally in the past, no bone marrow procurements would take place at the other hospital and all bone marrow donors would donate at the establishment. The DI is advised to update the establishment's SOP to remove reference to bone marrow collections taking place at hospitals other than the establishment.
3.	GQ1(b)	During cryopreservation of PBSC's, processing staff re-visit the controlled-rate freezer (CRF) once it has been started to verify that it continues to decrease the temperature appropriately to freeze the cells. The DI is advised to create a space in the processing records where this re-visit to the CRF can be recorded. This may also help to act as a prompt for clean room staff to re-visit the CRF and act as a subject of an audit to help assure the DI that this critical phase of cryopreservation is being undertaken and monitored as expected.
4.	GQ1(b)	Following the installation of new storage tanks, the processing lab are using an electronic temperature-monitoring system which consists of two elements. The

		storage tank's in-built alarm contacts an on-call phone and in addition, temperature probes placed in the storage tanks are linked to an alarm that emails the establishment in the event of a temperature excursion. The establishment has an SOP covering the procedure to follow in the event of a temperature excursion. However, the establishment's SOP regarding the use of the new monitoring systems and use of the monitoring system to review historic temperature records is still in draft. The DI is advised to expedite the introduction of the draft SOP as soon as possible so that staff have procedures to facilitate the review of temperature data.
5.	GQ1(b)	There are a number of steps in processes that are not formally documented in associated SOPs. These include, but are not limited to: - spraying consumables with ethanol when they are placed in the Grade A environment; and - reviewing the Grade A and Grade B environmental monitoring records.
6.	GQ2(b)	During the review of donor consent and screening records, an example of a donor that had not had infectious disease serological screening undertaken on the day of procurement as required by the establishment's procedure was identified. Serological testing of the donor had taken place within 30 days prior to procurement as required by Directions 002/2018 however, the establishment's own procedure requires an additional screen to be undertaken on the day of the procurement and this had not been undertaken. The DI is advised to include virology results in the establishment's internal audit programme so that he can assure himself that the second serological screen on the day of procurement is taking place for all donors as expected and required by the establishment's procedures.
7.	GQ2(b)	During the inspection, a review of audit activity was undertaken. During the review, reports for some of the audits could not easily be found due to where they were filed within the establishment's quality management system. Although the audit reports were eventually located, the DI is advised to maintain a list of all audits that are undertaken in both clinical and laboratory areas and to include in this list links to the audit reports so that they may easily be retrieved and reviewed.
8.	GQ4(b) GQ4(c)	During the review of donor consent and donor selection records, examples of completed consent forms were reviewed. In one case, one of the entries by the clinician who had completed the documentation was not easily legible. The DI is advised to include consent and screening documentation in the establishment's internal audit programme so that he can assure himself that all entries are being completed as expected and that they are legible.
9.	GQ5(a)	The establishment's documented donor exclusion criteria includes screening for donors that may have been exposed to poisons or heavy metals which is a mandatory screening criteria under Directions 002/2018. The establishment stated that donors are asked about such exposures during the collection of a medical history however, the donor pathway documentation has no dedicated field within the documentation to record the result of this screening question. During the inspection, the establishment indicated that including the question about possible exposure to poisons or heavy metals within the donor self-evaluation questionnaire, so that donors can identify if they think that they may have been exposed to these risks, may be helpful. This may also facilitate recording the response to this selection/exclusion criteria as it would be recorded on the questionnaire. Clinicians undertaking donor screening can

		then ensure that they follow up and ask further questions about exposure to these elements, as is the current process. The DI is advised to consider how responses to this donor selection criteria are recorded within the donor evaluation documentation.
10.	PFE2(b)	The DI is advised to consider implementing a procedure to monitor for potential contamination within the establishment's processing facility of: • hard to reach areas of the clean room such as the corners of the transfer hatches which cannot be reached using contact plates; and • areas with frequent use by multiple operators such as hatch latches and switches.
11.	PFE2(c)	The DI is advised to implement a gowning revalidation procedure at a frequency to assure himself that operators within the establishment's clean room continue to gown effectively and minimise the risk of introducing contamination into the clean room during, or as a result of, gowning.
12.	PFE3(a)	The establishment monitors the temperature of the fridge that is routinely used to store environmental monitoring plates using a data logging device which is downloaded and reviewed monthly. As a result, the shortfall against PFE3(a) that was identified at the previous inspection was considered to have been met. Using the datalogger in this way gives the establishment retrospective temperature data for the fridge. However, it is possible that plates stored in the fridge will have already been used for environmental monitoring by the time the data is downloaded. The DI is advised to consider reviewing the temperature data from the datalogger on a more frequent basis so that any deviation in the temperature of the fridge which may effect the efficacy of the monitoring plates can be detected sooner. This may help to identify plates that have been subject to any temperature excursion but not have not yet been used, so that the establishment can assess any risks posed to the plates' efficacy.
13.	PFE3(a)	The establishment has installed a remote temperature monitoring system to monitor the temperature of the liquid nitrogen storage tanks. The system is not yet fully operational and is therefore not being used. The temperature of the storage tanks is being monitored by the tank's own in-built alarm system which has been connected to an autodialer system which contacts an on-call phone if the temperature deviates from the expected range. The DI is advised to continue with the installation and implementation of the new remote temperature monitoring system as this may help to facilitate reviews of historical temperature data and provide a back-up alarm system to alert establishment staff of temperature deviations.

Assessment of existing conditions/shortfalls against standards

At the time of the 2019 inspection, five shortfalls that were identified during the previous inspection had not been closed. These were reviewed during the inspection and three shortfalls had been addressed satisfactorily and are now considered to be fully met. As a result, three of these open shortfalls will now be closed. The remaining two continue to be open and will be addressed as part of the corrective and preventative action plan for the 2019 inspection.

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.		
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.	The establishment does not have a formal agreement with another licensed establishment for the transfer and storage of cells in the event of termination of activities.	**Minor**
t) There are procedures for the re-provision of service in an emergency.	The establishment has informal agreements with a licensed establishment for the processing of cells in the event the establishment is unable to process the cells. However, in light of the proposed extension to the processing facility, these agreements have not been formalised and the procedure for transferring activities has not been documented.	**Minor**
GQ2 There is a documented system of quality management and audit.		
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.	Since the last inspection, the establishment has commissioned an independent audit. However, the audit carried out to date was limited and did not assess compliance against all the relevant HTA standards. *Since the last inspection the establishment has commissioned an independent audit by another HTA licensed establishment which is familiar with the type of activity taking place at the establishment. The independent audit was reviewed during the 2019 inspection. This standard is now considered to have been met.*	**Minor** ***Fully met***

GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills.		
e) Personnel are trained in all tasks relevant to their work and their competence is recorded. 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.	During the inspection, an example of a proposed training record was presented. However, staff training has not been formally captured in training records. *A selection of training records for staff were reviewed during the 2019 inspection. The records that were reviewed were up to date and were found to be complete. This standard is now considered to have been met.*	**Minor** ***Fully met***

Premises, Facilities and Equipment

Standard	**Inspection findings**	**Level of shortfall**
PFE3 There are appropriate facilities for the storage of bodies, body parts, tissues, cells, consumables and records.		
a) Tissues, cells, consumables and records are stored in secure environments and precautions are taken to minimise risk of damage, theft or contamination.	The establishment does not monitor the temperature of the fridge used to store plates used during environmental monitoring. *The establishment monitors the temperature of the fridge that is routinely used to store environmental monitoring plates using a data logging device which is downloaded and reviewed monthly (see advice item 13)*	**Minor** ***Fully Met***

Concluding comments

An area of good practice that was noted was the establishment's training procedures for clinicians who will seek consent for donation of PBSCs and bone marrow. The establishment continues to have a training package covering both the clinical aspect of the establishment's work and the regulatory context within which they work. This training is supplemented with a test of the trainee's understanding at which trainees must achieve a specific pass mark before being authorised to seek donor consent.

There are a number of areas of practice that require improvement, including five minor and one major shortfalls identified during the 2019 inspection and two minor shortfalls identified during the previous inspection. The HTA has also given advice to the DI with regards to

patient information leaflets, procedural documents, audit, donor selection, clean room monitoring procedures and temperature monitoring.

The HTA requires that the Designated Individual addresses the shortfalls by submitting a completed corrective and preventative action (CAPA) plan within 14 days of receipt of the final report (refer to Appendix 2 for recommended timeframes within which to complete actions). The HTA will then inform the establishment of the evidence required to demonstrate that the actions agreed in the plan have been completed.

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

Report sent to DI for factual accuracy: 18 February 2019

Report returned from DI: 28 February 2019

Final report issued: 25 March 2019

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: 19 March 2021

Appendix 1: HTA standards

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

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

Consent

Standard
C1 Consent is obtained in accordance with the requirements of the HT Act 2004, the Human Tissue (Quality and Safety for Human Application) Regulations 2007 and as set out in the HTA's Codes of Practice.
a) If the establishment acts as a procurer of tissues and / or cells, there is an established process for acquiring donor consent which meets the requirements of the HT Act 2004 the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (Q&S Regulations) and the HTA's Codes of Practice
b) If there is a third party procuring tissues and / or cells on behalf of the establishment the third party agreement ensures that consent is obtained in accordance with the requirements of the HT Act 2004, the Q&S Regulations and the HTA's Codes of Practice.
c) The establishment or the third party's procedure on obtaining donor consent includes how potential donors are identified and who is able to take consent.
d) Consent forms comply with the HTA Codes of Practice.
e) Completed consent forms are included in records and are made accessible to those using or releasing tissue and / or cells for a Scheduled Purpose.
C2 Information about the consent process is provided and in a variety of formats.
a) The procedure on obtaining consent details what information will be provided to donors. As a minimum, the information specified by Directions 002/2018 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 002/2018 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.
f) There are procedures for tissue and / or cell procurement, which ensure the dignity of deceased donors.
g) There are procedures to ensure that an authorised person verifies that tissues and / or cells received by the establishment meet required specifications.
h) There are procedures for the management and quarantine of non-conforming consignments or those with incomplete test results, to ensure no risk of cross contamination.
i) There are procedures to ensure tissues and / or cells are not released from quarantine until verification has been completed and recorded.
j) There are procedures detailing the critical materials and reagents used and where applicable, materials and reagents meet the standards laid down by the European directives on medical devices and in vitro diagnostic medical devices.
k) There is a procedure for handling returned products.
l) There are procedures to ensure that in the event of termination of activities for whatever reason, stored tissues and / or cells are transferred to another licensed establishment or establishments.
m) The criteria for allocating tissues and / or cells to patients and health care institutions are documented and made available to these parties on request.
n) The establishment ensures imports from non EEA states meet the standards of quality and safety set out in Directions 002/2018.
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 002/2018.

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 002/2018, is collected and maintained.
g) There is a system to ensure records are secure and that donor confidentiality is maintained in accordance with Directions 002/2018.
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 002/2018 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 002/2018.
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 002/2018.
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 002/2018.
c) In cases other than autologous donors, donor selection is carried out by authorised personnel and signed and reviewed by a qualified health professional.
d) There is a system in place either at the establishment or at a third party acting on its behalf to record results of donor selection and associated tests.
e) Testing of donor samples is carried out using CE marked diagnostic tests.
f) Samples taken for donor testing are clearly labelled with the time and place the sample was taken and a unique donor identification code.
GQ6 A coding and records system facilitates traceability of tissues and / or cells, ensuring a robust audit trail.
a) There is a donor identification system which assigns a unique code to each donation and to each of the products associated with it.
b) An audit trail is maintained, which includes details of when the tissues and / or cells were acquired and from where, the uses to which the tissues and / or cells were put, when the tissues and / or cells were transferred elsewhere and to whom.

c) The establishment has procedures to ensure that tissues and / or cells imported, procured, processed, stored, distributed and exported are traceable from donor to recipient and vice versa.
d) The requirements of the Single European Code are adhered to as set out in Directions 002/2018.
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.
d) Where appropriate, there are procedures to ensure that the premises are of a standard that ensures the dignity of deceased persons.
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 002/2018.
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 002/2018.
b) There are procedures for the transport of tissues and / or cells which reflect identified risks associated with transport.
c) There is a system to ensure that traceability of tissues and / or cells is maintained during transport.
d) Records are kept of transportation and delivery.
e) Tissues and / or cells are packaged and transported in a manner and under conditions that minimise the risk of contamination and ensure their safety and quality.
f) There are third party agreements with courier or transport companies to ensure that any specific transport conditions required are maintained.
g) Critical transport conditions required to maintain the properties of tissue and / or cells are defined and documented.

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

Disposal

Standard
D1 There is a clear and sensitive policy for disposing of tissues and / or cells.
a) The disposal policy complies with HTA's Codes of Practice.
b) The disposal procedure complies with Health and Safety recommendations.
c) There is a documented procedure on disposal which ensures that there is no cross contamination.
D2 The reasons for disposal and the methods used are carefully documented.
a) There is a procedure for tracking the disposal of tissue and / or cells that details the method and reason for disposal.
b) Disposal arrangements reflect (where applicable) the consent given for disposal.

Appendix 2: Classification of the level of shortfall (HA)

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

The action an establishment will be required to make following the identification of a shortfall is based on the HTA's assessment of risk of harm and/or a breach of the HT Act 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:

   (1) A notice of proposal being issued to revoke the licence

   (2) Some or all of the licensable activity at the establishment ceasing with immediate effect until a corrective action plan is developed, agreed by the HTA and implemented.

   (3) A notice of suspension of licensable activities

   (4) Additional conditions being proposed

   (5) Directions being issued requiring specific action to be taken 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 inspection report. Major shortfalls pose a higher level of risk and therefore a shorter deadline is given, compared to minor shortfalls, to ensure the level of risk is reduced in an appropriate timeframe.

3. **Minor shortfall:**

   A shortfall which cannot be classified as either critical or major and, which can be addressed by further development by the establishment.

   This category of shortfall requires the development of a corrective action plan, the results of which will usually be assessed by the HTA either by desk based review or at the time of the next inspection.

   In response to a minor shortfall, an establishment is expected to implement corrective and preventative actions within 3-4 months of the issue of the final inspection report.

Follow up actions

A template corrective and preventative action plan will be sent as a separate Word document with both the draft and final inspection report. You must complete this template and return it to the HTA within 14 days of the issue of the final report.

Based on the level of the shortfall, the HTA will consider the most suitable type of follow-up of the completion of the corrective and preventative action plan. This may include a combination of

- a follow-up site-visit inspection
- a request for information that shows completion of actions
- monitoring of the action plan completion
- follow up at next desk-based or site-visit inspection.

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