Site visit inspection report on compliance with HTA minimum standards

WideCells Ltd

HTA licensing number 22665

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); and**

- **storage of relevant material which has come from a human body for use for a scheduled purpose**

23-24 October 2018

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 WideCells Ltd (the establishment) had met the some of the HTA standards, three major and 12 minor shortfalls were found in relation to Governance and Quality Systems and to Premises, Facilities and Equipment. The first major shortfall relates to the content of the standard operating procedures (SOPs) not reflecting current working practices. The second major shortfall related to the need for processes that could affect the quality and safety of tissues and/or cells to be regularly evaluated to ensure that they continue to achieve the intended result. The final major shortfall was in relation to ensuring that environmental controls are in place to avoid potential contamination and to ensure that practices in the clean room were consistent with the formal designation of this area The minor shortfalls were found in relation to the monitoring of the temperature of the fridges; the absence of some risk assessments; donor selection criteria; internal audits being limited to processing activities and audits being undertaken by the same member of staff undertaking the processing activity; the time in transit of blood samples prior to testing and how this relates to the validation of the testing kits; the limited staff resource; staff training and completion of training records; recording of sufficient data to maintain traceability; absence of contingency arrangements for the failure of the controlled-rate freezer; the absence of

suitable procedures in the event of termination of activities and the requirement to maintain and service critical equipment.

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.

'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, Cord Blood; Cord Blood	**TPA**	**E**	**TPA**	**E**	**E**		**E**
Other; Cord tissue	**TPA**	**E**	**TPA**	**E**	**E**		**E**

Background to the establishment and description of inspection activities undertaken

WideCells Ltd (the establishment), is a private tissue bank licensed under the Human Tissue

(Quality and Safety for Human Application) Regulations 2007(as amended) for the procurement, processing, testing, storage, distribution and export of umbilical cord tissue (UCT) and umbilical cord blood (UCB) for future autologous or allogeneic use. This is the first inspection since the establishment was licensed in February 2018.

UCB and UCT are procured, from UK-based clients, by a third party under the terms of appropriate agreements using kits supplied by the establishment. The establishment is responsible for the courier arrangements but the organisation of the collection is undertaken by the client. On receipt, the data from the temperature logging device is downloaded and recorded into a database. In addition, other information such as the date and time the UCB and UCT were collected and received, whether any maternal blood samples were received and the weight of the cord blood unit are recorded onto the database. UCB processing only takes place if samples are over a set minimum volume. The cord blood sample is allocated a unique reference number and the Single European Code Donor Identification Sequence (SEC-DI) is also allocated.

The maternal blood is couriered to another HTA-licensed establishment for mandatory serology testing. Processing of tissues and cells takes place within a dedicated clean room facility comprising of two Grade B clean rooms, each containing microbiological safety cabinets capable of providing a Grade A environment. The establishment uses only one of the Grade B clean rooms for the processing of UCB and UCT. The second clean room is not monitored to the same extent to ensure it meets Grade B requirements, and is primarily used for conducting research activity. The UCB undergoes volume reduction in the Grade B area of the clean room using a closed processing system. A grade A cabinet is used for the setup of the UCB processing kits. Open processing of UCT is carried out within a grade A cabinet with a grade B background.

Environmental monitoring in the form of settle plates, finger dabs and non-viable particle monitoring are undertaken during the processing procedures. The plates are sent to another HTA-licensed establishment for incubation and contamination assessment.

The inspection included a visual inspection of the sample receipt, processing and cryostorage areas as well as a visit to the testing laboratory. Roundtable discussions were held with members of staff involved with processing of cord blood and cord tissue, customer operations, quality systems, audits and incident reporting. Records for three client samples were audited and this also included a review of the flow cytometry data used to assess the quality of the samples.

The establishment is also licensed for the storage of relevant material which has come from a human body for use for a scheduled purpose under the Human Tissue Act 2004 (HT Act). The current research work being undertaken is under recognised research ethics committee approval and is therefore exempt from the licensing requirements of the HT Act.

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.		
b) There are procedures for all licensable activities that ensure integrity of tissue and / or cells and minimise the risk of contamination	A number of discrepancies between the standard operating procedures (SOPs) and the actual practices were noted. Examples of these include, but are not limited to: • the minimum acceptable volume of cord blood was different in the sample receipt SOP in comparison to the validation protocol; • the SOP for processing cord tissue requires 2g of tissue to be stored. The establishment's practices do not observe this requirement; and • the SOP for receipt of samples stipulates that any serology positive samples will be disposed off whereas the risk assessment states that positive samples will be stored in a quarantine liquid nitrogen tank. • In addition, some of the SOPs were absent or lacked sufficient detail to ensure consistency with practices. Examples of these include, but are not limited to: • there was no SOP detailing how the establishment would be able to verify that trained phlebotomists were made aware of, and received appropriate training, whenever changes to procurement practices were implemented; • the time limit from the addition of cryoprotectant to the cord blood or cord tissue to the commencement of cryopreservation has not been defined and documented; • the SOP for the clean room did not specify the minimum number of steps an operative should take on the sticky mat before entry to the Grade B clean	**Major**

	room; and • the SOP for the receipt of UCT and UCB does not detail all the documents that have to be reviewed during the receipt 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. m) The criteria for allocating tissue and/ or cells to patient and health care institutions are documented and made available to these parties on request.	The current arrangements, in the event of termination of activities, have not taken into consideration whether the storage establishment has suitable procedures and the personnel in place to facilitate the release of tissues and cells.	**Minor**
GQ2 There is a documented system of quality management and audit.		
b) There is an internal audit system for all licensable activities.	The audits were limited to reviewing the processing records and were conducted by the same member of staff who undertook the processing.	**Minor**
d) Processes affecting the quality and safety of tissues and / or cells are validated and undergo regular evaluation to ensure they continue to achieve the intended results.	The establishment reports the levels of CD34 and total nucleated cell counts in the banked UCB to clients. However, from discussions with the staff it is unclear if the data being collected are CD45 or total nucleated cell counts. Staff were unable to explain the gating strategy for the flow cytometry data and confirm if the data obtained related to CD45 cells or all events. As a result, data being provided to clients may not be accurate.	**Major**
GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills.		
e) Personnel are trained in all tasks relevant to their work and their competence is recorded.	The training records do not contain sufficient detail of what part of each activity staff are deemed competent to undertake. The training record for one member of staff was incomplete.	**Minor**
k) The establishment is sufficiently staffed to carry out its activities.	To date, all the processing of UCB and UCT has been undertaken by one member of staff who is also currently responsible for reviewing and signing off the processing records.	**Minor**

GQ4 There is a systematic and planned approach to the management of 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.	The establishment records details such as the weight of the cord blood and allocates a unique reference number and a SEC-DI to the sample. However, the establishment does not record whether the cord tissue met the receipt criteria, i.e. length, nor is a unique reference number allocated to enable traceability.	**Minor**
GQ5 There are documented procedures for donor selection and exclusion, including donor criteria.		
a) Donors are selected either by the establishment or by the third party acting on its behalf in accordance with the criteria required by Directions 003/2010	The donor selection does not include questions regarding “Ingestion of, or exposure to, a substance (such as cyanide, lead, mercury) that may be transmitted to recipients in a dose that could endanger their health”.	**Minor**
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.	On receipt of the blood samples at the testing laboratory, the samples are sent to the hub and then subsequently to an overseas laboratory for analysis. The establishment was not aware that only one of the mandatory serology tests was conducted in the UK. The establishment has not taken the necessary step to assure themselves that the blood sample testing times stipulated in serology testing kits used by the third party are being met.	**Minor**
c) In cases other than autologous donors, donor selection is carried out by authorised personnel and signed and reviewed by a qualified health professional.	The establishment stores UCB and UCT for possible autologous or allogenic use. However, there was no evidence that the donor selection had been reviewed and signed off by a qualified health professional.	**Minor**
GQ8 Risk assessments of the establishment’s practices and processes are completed regularly and are recorded and monitored appropriately.		
a) There are documented risk assessments for all practices and processes.	The establishment has not considered the risk associated with procurement resulting from multiple births or the same suite being used by two different patients.	**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 does not undertake fungal monitoring during the processing of cord tissue. Other aspects of the establishment's procedures were not consistent with the requirement to monitor the environment within the clean room and to have appropriate procedures in place for cleaning and decontamination. For example: • waste tips are left in a bottle containing disinfectant solution. The bottle is not removed between processing runs and will only be disposed of when the bottle is full; • the establishment has made no provision within its procedures for the routine monitoring of the transfer hatch between the tissue reception area and the clean room, and of the instruments such as the volume reduction device or heat sealers used within the clean room. For two out of three of the processing	**Major (cumulative)**

	records that were reviewed, it was noted that the pressure readings for the clean room were not checked prior to the processing of the tissue samples.	
GQ4 There is a systematic and planned approach to the management of records.		
h) Raw data which are critical to the safety and quality of tissues and cells are kept for 10 years after the use, expiry date or disposal of tissues and / or cells	Due to the omission of checking the pressure readings there is an absence of data necessary to demonstrate the quality and safety of tissue and cells.	
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.	On receipt, the cord blood units are weighed to determine their volume and hence the volume of cryoprotectant required. Prior to use, the balance is checked against a calibrated weight. The balance has not been serviced nor has the weight been calibrated to ensure that it remains accurate.	**Minor**
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.	A temperature monitoring device is used to monitor the temperature of the fridges used to store reagents. If a temperature excursion occurs designated members of staff receive an email alert. During the inspection, it was noted that the temperature probes were surrounded by cold-packs. Therefore, there would be a considerable delay before staff at the establishment received an alert. In addition, this form of alert could easily be missed if the individuals do not have access to emails. The establishment has not challenged the monitoring system to ensure that an alert message is sent and received by the designated staff members.	**Minor**

k) There are contingency plans for equipment failure.	The establishment has two controlled-rate freezers. Each instrument is used simultaneously for the cryopreservation of cord blood and cord tissue respectively. There is no contingency in the event one or both of the instruments fails, including a rationale for selecting the cord blood or tissue as priority for cryopreservation should only one controlled-rate freezer be available.	**Minor**

Advice

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

No.	Standard	Advice
1.	C1d	The customer service team may have to discuss a potential client's medical query or seek advice from the establishment's medical advisor. The DI is advised that such conversations should be documented in the client's notes.
2.	GQ1g	The establishment uses a database to record receipt of the UCB and UCT. The DI is advised to include the time the products were processed in order to ensure that the time in transit criteria from procurement to processing is met. In addition, the DI is advised to add additional fields to record whether the samples were deemed non-conforming.
3.	GQ2d	Every month, the establishment purchases and processes one UCB and UCT as part of their ongoing evaluation of their processes. However, this does not take into account factors such as the time and temperature in transit that client samples are subjected to nor the impact of long term storage on client samples. The DI is advised to review this strategy and for the evaluation to reflect these additional factors.
4.	GQ4f	The medical questionnaire asks clients whether they have visited or originate from a specific list of countries. The DI is advised to make this more of an open question and allow the client to specify the country (ies). This will allow the establishment to make a more informed decision whether, for example, the client should be tested for HTLV-1.
5.	GQ4j	The establishment maintains a list of the lot numbers for the solution used to transport UCT. The DI is advised to record the specific lot number associated with the processing of each UCT sample.
6.	PFE2b	The establishment processes UCB and UCT in morning and afternoon sessions. The DI is advised to review and risk assesses the practice of only removing the sharps bin at the end of the morning or afternoon session and not after each client sample.
7.	PFE2b	The establishment does not currently record the pressure reading for the clean rooms. Staff check whether the specification is met by ensuring that needles on the pressure gauges are in the green zone and place a tick on the log sheet. The DI is advised to record the actual pressure readings and then assess whether the pressure differentials are being met as the needles may be on the margins of acceptability. The data should also be trended to identify potential drifts and

		therefore pressure issues within the clean room.
8.	PFE2c	Prior to entry into the Grade B clean room, staff walk over a sticky mat. This mat is replaced when staff exit the clean room. The DI is advised to create a log to record that the mat has been removed and replaced.
9.	PFE2c	There is a non-clinical waste bin in the clean room which is not cleared between processing runs. The DI is advised to determine whether this bin is required and if so risk assess this practice.
10.	PFE3a	The DI is advised to contact the manufacturers of the disinfectant reagents to establish what the expiry dates, after opening, should be and to note these on the bottles. In addition, the DI is also advised to avoid storing the reagent in direct sunlight.
11.	PFE5a	The DI is advised to review the data from the temperature loggers, on a regular basis, to look for trends and to ensure there are no temperature drifts.
12.	PFE5a	The establishment uses ultra-violet lamps in the biological safety cabinets. The DI is advised to maintain a record of when the lamps were installed and when they should be replaced.
13.	PFE5a	The DI is advised to record and trend the laser voltages when performing the daily flow cytometer calibration, to identify potential drifts in the performance of the machine's laser.
14.	PFE5a	The temperature of the liquid nitrogen tanks, used for long term storage of UCB and UCT, are checked to ensure the contents remain within temperature. The DI is advised to maintain a record of the actual temperature readings rather than placing a tick in the log sheet. The temperature readings should be trended to monitor any temperature drifts and therefore possible issues with the tank or temperature monitoring device.
15.	PFE5b	The DI is advised to review and sign off maintenance records to ensure that all instruments and services meet specification, and, if not, to take remedial action.
16.	PFE5k	The establishment has an uninterruptible power supply (UPS), connected through the electrical system, as part of their contingency planning. However, the DI is advised to make other arrangements in case there is a complete electrical failure lasting longer than the time supplied by the UPS.
17.	-	The DI should ensure all documents and policies refer to the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (as amended) where appropriate, and not the Human Tissue Act 2004.

Concluding comments

Although the HTA found that the WideCells Ltd had met the majority of the HTA standards, three major and 12 minor shortfalls were found in relation to Governance and Quality and Premises, Facilities and Equipment. The first major shortfall relates to the content of the standard operating procedures (SOPs) not reflecting current working practices. The second major shortfall related to the need for processes that could affect the quality and safety of tissues and/or cells to be regularly evaluated to ensure that they continue to achieve the intended result. The final major shortfall was in relation to ensuring that environmental

controls are in place to avoid potential contamination and to ensure that practices in the clean room were consistent with the formal designation of this area The minor shortfalls were found in relation to the monitoring of the temperature of the fridges; the absence of some risk assessments; donor selection criteria; internal audits being limited to processing activities and audits being undertaken by the same member of staff undertaking the processing activity; the time in transit of blood samples prior to testing and how this relates to the validation of the testing kits; the limited staff resource; staff training and completion of training records; recording of sufficient data to maintain traceability; absence of contingency arrangements for the failure of the controlled-rate freezer; the absence of suitable procedures in the event of termination of activities and the requirement to maintain and service critical equipment.
In addition, the HTA has given advice to the Designated Individual with a view to helping the establishment further develop its working practices.

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: 21 November 2018

Report returned from DI: 3 December 2018

Final report issued: 27 December 2018

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.
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.
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.
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.
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.

Human Tissue Act 2004 Standards

Consent standards
C1 Consent is obtained in accordance with the requirements of the Human Tissue Act 2004 (HT Act) and as set out in the code of practice
a) Consent procedures are documented and these, along with any associated documents, comply with the HT Act and the HTA's Codes of Practice. b) Consent forms are available to those using or releasing relevant material for a scheduled purpose. c) Where applicable, there are agreements with other parties to ensure that consent is obtained in accordance with the requirements of the HT Act and the HTA's Codes of Practice. d) Written information is provided to those from whom consent is sought, which reflects the requirements of the HT Act and the HTA's Codes of Practice. e) Language translations are available when appropriate. f) Information is available in formats appropriate to the situation.
C2 Staff involved in seeking consent receive training and support in the essential requirements of taking consent
a) There is suitable training and support of staff involved in seeking consent, which addresses the requirements of the HT Act and the HTA's Codes of Practice. b) Records demonstrate up-to-date staff training. c) Competency is assessed and maintained.

Governance and quality system standards
GQ1 All aspects of the establishments work are governed by documented policies and procedures as part of the overall governance process
a) Ratified, documented and up-to-date policies and procedures are in place, covering all licensable activities. b) There is a document control system. c) There are change control mechanisms for the implementation of new operational procedures. d) Matters relating to HTA-licensed activities are discussed at regular governance meetings, involving establishment staff. e) There is a system for managing complaints.
GQ2 There is a documented system of audit
a) There is a documented schedule of audits covering licensable activities. b) Audit findings include who is responsible for follow-up actions and the timeframes for completing these.
GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills
a) Qualifications of staff and all training are recorded, records showing attendance at training. b) There are documented induction training programmes for new staff.

c) Training provisions include those for visiting staff.

d) Staff have appraisals and personal development plans.

GQ4 There is a systematic and planned approach to the management of records

a) There are suitable systems for the creation, review, amendment, retention and destruction of records.

b) There are provisions for back-up / recovery in the event of loss of records.

c) Systems ensure data protection, confidentiality and public disclosure (whistleblowing).

GQ5 There are systems to ensure that all adverse events are investigated promptly

a) Staff are instructed in how to use incident reporting systems.

b) Effective corrective and preventive actions are taken where necessary and improvements in practice are made.

GQ6 Risk assessments of the establishment's practices and processes are completed regularly, recorded and monitored

a) There are documented risk assessments for all practices and processes requiring compliance with the HT Act and the HTA's Codes of Practice.

b) Risk assessments are reviewed regularly.

c) Staff can access risk assessments and are made aware of risks during training.

Traceability standards

T1 A coding and records system facilitates the traceability of bodies and human tissue, ensuring a robust audit trail

a) There is an identification system which assigns a unique code to each donation and to each of the products associated with it.

b) A register of donated material, and the associated products where relevant, is maintained.

c) An audit trail is maintained, which includes details of: when and where the bodies or tissue were acquired and received; the consent obtained; all sample storage locations; the uses to which any material was put; when and where the material was transferred, and to whom.

d) A system is in place to ensure that traceability of relevant material is maintained during transport.

e) Records of transportation and delivery are kept.

f) Records of any agreements with courier or transport companies are kept.

g) Records of any agreements with recipients of relevant material are kept.

T2 Bodies and human tissue are disposed of in an appropriate manner

a) Disposal is carried out in accordance with the HTA's Codes of Practice.

b) The date, reason for disposal and the method used are documented.

Premises, facilities and equipment standards
PFE1 The premises are secure and fit for purpose
a) An assessment of the premises has been carried out to ensure that they are appropriate for the purpose. b) Arrangements are in place to ensure that the premises are secure and confidentiality is maintained. c) There are documented cleaning and decontamination procedures.
PFE2 There are appropriate facilities for the storage of bodies and human tissue
a) There is sufficient storage capacity. b) Where relevant, storage arrangements ensure the dignity of the deceased. 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: 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.