Site visit inspection report on compliance with HTA minimum standards

Royal Bournemouth Hospital

HTA licensing number 11129

Licensed for the

- **procurement, testing and distribution of human tissues and cells for human application under the Human Tissue (Quality and Safety for Human Application) Regulations 2007**
- **storage of relevant material which has come from a human body for use for a scheduled purpose**

21 February 2017
and
17 March 2017

Summary of inspection findings

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

Although the HTA found that the Royal Bournemouth Hospital (the establishment) had met some of the HTA standards, five minor shortfalls were identified for activities taking place under the Human Tissue (Quality and Safety for Human Application) Regulations 2007. These were in relation to third party agreements, quality management and audit, donor testing, incident reporting and temperature monitoring records. Seven shortfalls, including four major shortfalls, were identified for activities taking place under the Human Tissue Act 2004. These were in relation to consent, documented procedures, system of audit, staff training and risk assessments.

Particular examples of strengths and good practice are included in the concluding comments section of the report.

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 licenses 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

Under the Human Tissue (Quality and Safety for Human Application) Regulations 2007, the establishment undertakes the following activities.

'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 type	Procurement	Testing	Distribution
PBSC	**E**	**E* (SLA)**	**TPA**

Under the Human Tissue Act 2004 (HT Act), the establishment stores relevant material which has come from a human body for use for a scheduled purpose, which is research.

Background to the establishment and description of inspection activities undertaken

Royal Bournemouth Hospital (the establishment) has been licensed by the HTA since September 2006. The establishment is licensed under the Human Tissue (Quality and Safety

for Human Application) Regulations 2007 (the Q&S Regulations) for procurement, testing and distribution of autologous peripheral blood stem cells (PBSC). The establishment is also licensed under the Human Tissue Act 2004 (the HT Act) for storage of relevant material for use for scheduled purposes.

This report describes the fifth routine site visit inspection of the establishment which took place on 21 February 2017 and 17 March 2017. During the inspection on 21 February 2017, a number of concerns were identified relating to the establishment's activities under the HT Act and an additional site visit inspection took place on the 17 March 2017.

Activities conducted under the Human Tissue (Quality and Safety for Human Application) Regulations 2007 Standards

The Advanced Stem Cell Transplant (SCT) Nurse Specialist seek consent from autologous donors which incorporates consent for treatment and examination as well as consent specifically for mobilisation and processing. Possible side effects associated with the procedure and use of the cells is also discussed during the process of seeking consent. On the day of the harvest a verbal consent is also confirmed by the Apheresis Nurse before proceeding to procurement. Donor blood samples are taken between 7-30 days prior to the day of harvest. Donor testing is undertaken by another HTA-licensed establishment.

Following the last site visit inspection of the establishment in 2015, the apheresis unit has moved into a new facility with a dedicated room to conduct PBSC harvests. PBSC procurement is undertaken by apheresis nurses who confirm the identity of the patient by checking the wrist band against their medical records. The PBSC, once collected, are delivered by the apheresis nurses to the transfusion laboratory at the establishment.

The transfusion laboratory is responsible for organising the transportation of the harvests using a dedicated courier company, under a third party agreement, to another HTA-licensed establishment for processing. The harvests are transported in validated shippers, which are primed before transportation using cool packs. Processed stem cells are then returned by the processing facility to the transfusion laboratory in temperature-controlled shippers. The transfusion laboratory reviews the temperature data to ensure that the quality and safety of the cells has been maintained during transport.

The Advanced SCT Nurse Specialist nurses are also responsible for the infusion of the PBSC and undertake the thawing of the PBSC (*Advice item, 4).* Prior to the infusion of PBSCs, the apheresis nurses confirm the identity of the patient by checking the wrist band containing the patient's identification against their medical records.

The ACD-A is stored in the apheresis unit in a temperature-controlled cabinet which has a minimum and maximum thermometer to record the respective readings. The apheresis nurses undertake daily temperature monitoring and record these details Monday-Friday and the thermometer only stores the temperatures for a 24 hour period (*Minor shortfall, PFE3(a)*). A contingency fridge is also available in the event that the ambient temperature exceeds the upper limit, however this is not subject to testing to ensure it is functioning optimally (*Advice item, 3*).

The inspection included a visual inspection of the premises, including the apheresis room and storage areas containing the ACD-A, interviews with key members of staff involved in activities under HA licence and a document review.

A traceability audit of six autologous donor medical records was carried out. The consent records, serology results and infusion records for each donor were reviewed. No discrepancies were identified.

Activities conducted under the HT Act

The establishment stores relevant material under its HTA licence for use for research studies. The HTA was informed in advance of the inspection that no relevant material subject to the provisions of the HT Act was being stored. However, during the course of the site visit inspection, the HTA identified that four collections that are subject to the licensing requirements of the HT Act. Staff at the establishment involved in overseeing these sample collections had not been aware of the licensing requirements of the HT Act so had not brought these to the attention of the DI (*Minor shortfall, GQ3*).

Three of the four sample collections originate from studies with expired project-specific research ethics committee (REC) or clinical trials approval. These samples are from the living and include blood, plasma (not relevant material for the purpose of the HT Act) and peripheral blood mononuclear cell samples. Some, but not all of these samples, are existing holdings (held prior to the HT Act coming into force on 1 September 2006). Consent for the storage and use of these samples had been sought by clinical staff at the establishment or by staff at the organisation from which the samples were obtained (*Advice, items 5 and 6*).

A fourth collection comprises tissue samples from the deceased. These samples were obtained during hospital (consented) post mortem (PM) examinations of three patients who had participated in a longitudinal research study. Consent for the PM examinations was sought by a clinician with responsibility for these patients during their medical care at the hospital *(Major shortfalls C1, C2 and C3)*. The PM examinations were undertaken at another HTA-licensed facility and the tissue samples were transferred to this establishment for storage. At the time of the inspection, the samples were being stored for research, but had not been used.

The establishment is also storing a large collection of samples for a research study with project-specific ethical approval from a recognised REC; thereby exempting the storage of this sample collection from the licensing requirements of the HT Act. Samples in this collection are all from the living. The collection includes approximately 3,700 sample aliquots that were uncatalogued at the time of the inspection (*Advice, item 13*). These uncatalogued samples are all existing holdings held under the governance of the project specific REC approval.

Samples are stored in three -80°C freezers, one -20°C freezer and four liquid nitrogen storage tanks, all of which are subject to continuous temperature monitoring with local and external alarms. However, the alarm system is not subject to regular testing to ensure that it is functioning correctly (*Advice, item 10*)*.*

The establishment uses a series of traceability records and databases for samples stored under the licence. Establishment staff are in the process of ensuring that records of all human samples stored in the laboratory, including those not stored under the HTA licence, are included on a central electronic sample inventory. Samples not yet recorded on this inventory are stored in a dedicated area of one of the -80°C freezers pending their inclusion in the central sample inventory.

The inspection of activities conducted under the HT Act licence comprised a visual inspection of the premises, including areas where samples are stored under the licence, interviews and a round table discussion with staff, and a review of documentation.

A traceability audit of nine samples was carried out. All samples were fully traceable against the paper records and the electronic sample traceability system. No discrepancies were found.

Consent forms for the three hospital PM examinations from which tissue samples are being stored for research were reviewed. Several discrepancies in the completion of two of the three consent forms were identified *(major shortfall, C1)*, which are set out as follows:

- On one consent form, the relevant sections that confirm that the person giving consent had been given the opportunity to read the information booklet and to have any questions about the PM examination answered, had not been completed. The timeframe and contact details for withdrawing consent for the PM examination had not been documented on the form. During the inspection, the establishment was able to confirm that consent had been given by the appropriate person in accordance with the requirements of the HT Act; however, the completed consent form did not reflect this and interviews with staff indicated a lack of understanding about the hierarchy of qualifying relationships set out in the HT Act.
- On the other consent form, as in the first case, the sections had not been completed to confirm that the person giving consent had been given the opportunity to have any questions about the PM examination answered, nor had the details of the timeframe and full contact details for withdrawing consent been provided. Furthermore, consent had been given for use of the samples for quality, teaching, public health surveillance and clinical audit; however, consent had not been given for use of the tissue samples for research. Although the samples from this donor had not been used for research, the establishment had not noted that consent had not been given for use of the samples for this purpose and had not put in place procedures to ensure that the samples were not used for research without consent.

The establishment's staff are involved in seeking consent for the retention of tissue for research, and therefore, it is for the establishment to ensure that any storage of samples is in line with the consent given and not to proceed, if there is any concern about the status or scope of the consent recorded on the consent form accompanied with the samples.

Inspection findings

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

Although the DI has appropriate oversight of activities conducted in respect of the Human Tissue (Quality and Safety for Human Application) Regulations 2007, they do not currently have sufficient oversight of the activities conducted in respect storage of tissue for use in research. Furthermore, staff lacked an awareness of the consent and licensing requirements under the HT Act. In addition, the DI was not aware that staff working under the licence were involved in storing tissue for research from the deceased without valid consent.

As a result, the HTA will continue to assess the suitability of the DI using the HTA corrective and preventative action plan (CAPA) process. The HTA considers that, as a minimum, Persons Designated (PDs) should be identified to assist the DI in being able to deliver adequate oversight of activities taking place under the HT Act licence.

However, the HTA is aware that the establishment plans to set up an ethically approved Research Tissue Bank, which will be subject to licensing by the HTA. The establishment should consider whether this resource, and other tissue stored for research, should fall under the governance of a separate HTA research licence with a separate DI providing oversight for this activity.

Compliance with HTA standards

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

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.		
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.	Although the establishment has in place a third party agreement with a courier company, the third party agreement does not contain information about the courier's responsibility for notifying the establishment about serious adverse events affecting the quality and safety of the tissue, that may occur during transport.	**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.	The establishment has not conducted an independent audit to verify compliance with HTA standards since the last site visit. *Following the inspection, satisfactory information has been received from the establishment and the HTA considers the shortfall to have been met.*	**Minor**
GQ5 There are documented procedures for donor selection and exclusion, including donor criteria		
b) The testing of donors by the establishment or a third party on behalf of the establishment is carried out in accordance with the requirements of Directions 003/2010.	The establishment staff were unaware about the timeframes in which HTLV I/II samples are received by the third party laboratory responsible for processing them and whether any possible delays in transport could have an impact on sample stability.	**Minor**

GQ7 There are systems to ensure that all adverse events are investigated promptly.		
a) There are procedures for the identification, reporting, investigation and recording of adverse events and reactions, including documentation of any corrective or preventative actions.	Although the establishment has a number of documents that make reference to the reporting requirements associated with Serious Adverse Events and Reactions (SAEARs), these do not include the requirement to report SAEARs to the HTA within 24 hours as set out in the "Guide to Quality and Safety Assurance for Human Tissues and Cells for Patient Treatment" which forms the Annex to Directions 003/2010.	**Minor**

Premises, Facilities and Equipment

Standard	**Inspection findings**	**Level of shortfall**
PFE3 There are appropriate facilities for the storage of tissues and / or cells, consumables and records.		
a) Tissues, cells, consumables and records are stored in secure environments and precautions are taken to minimise risk of damage, theft or contamination.	The ACD-A is stored in the Chemotherapy room in the jigsaw Building in a temperature-controlled cabinet, with a minimum and maximum thermometer that stores the temperature data for a period of 24 hours only. Establishment staff monitor and document the temperature during working hours on Monday to Friday only. There is no provision for reviewing and recording temperatures over the weekend and bank holidays and as a result there is a risk that any deviations that take place over the weekend may go unnoticed. *Please see advice item, 3.*	**Minor**

Human Tissue Act 2004

Consent

Standard	Inspection findings	Level of shortfall
C1 Consent is obtained in accordance with the requirements of the Human Tissue Act 2004 (HT Act) and as set out in the Code of Practice.	During the traceability audits, discrepancies were identified in the completion of two consent forms for hospital PM examination and the establishment was storing tissue samples for research without appropriate consent (see details of the consent form audit on page 6 of the report). The consent form used to seek consent for these PM examinations (see details of consent form audit on page 6 of the report) had been obtained from another HTA licensed establishment. The consent form does not include information about seeking consent from the person ranked highest in the hierarchy of qualifying relationships. This issue is being followed up separately with the establishment responsible for this form. Nevertheless, it is the responsibility of the establishment seeking consent to ensure that it is documented in line with statutory and regulatory requirements. The failures to demonstrate that consent complies with statutory requirements, in relation to tissue from the deceased, poses a risk that tissue may be stored without consent and therefore represents a major shortfall against this standard.	**Major**
C2 Information about the consent process is provided and in a variety of formats.	In relation to the issues identified in the completion of the two hospital PM consent forms (see details of the consent form audit on page 6 of the report), the establishment is not able to provide evidence that adequate information was provided to those giving consent to enable them to make a fully informed decision.	**Major**
C3 Staff involved in seeking consent receive training and support in the implications and essential requirements of taking consent.	Staff who have been involved in seeking consent for hospital PM examination, and where tissue samples have been subsequently stored for use in research, have not received training in seeking consent for PM examination and the HT Act and do not have appropriate knowledge of the requirements of the HT Act, including the hierarchy of qualifying relationships.	**Major**

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.	The establishment does not have documented procedures governing the activities relating to the samples stored under the licence for research. This includes sample receipt, storage and release and anonymisation procedures.	**Major**
GQ2 There is a documented system of quality management and audit.	Although research staff audit the tissue samples held under the governance of ethically approved studies, there is no evidence of an audit schedule or audits in relation to the samples that are stored under the HT Act, including audit of consent records.	**Minor**
GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills.	Research staff working under the licence have not received training in the requirements of the HT Act. During the inspection, it was evident that research staff members working under the licence had a poor awareness of the requirements of the HT Act as well its licensing requirements. They were unclear about which samples are subject to the consent and licensing requirements of the HT Act.	**Minor**
GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately.	Although a range of risk assessments are in place considering health and safety risks, there are no risk assessments of activities taking place under the HT Act licence. *Please see Advice, item 8.*	**Minor**

Advice

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

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

No.	Standard	Advice
1.	GQ1(p)	The DI is advised to review the content of the agreement between the HTA licensed establishment undertaking the serology testing and the third party laboratory that undertakes HTLV I & II testing to ensure that the arrangements in line with the donor testing requirements as set out in the Human Tissue (Quality and Safety for Human Application) Regulations 2007. This is particularly important in light of the fact that staff were not familiar with these arrangements.

2.	GQ4(h)	The establishment's documented procedures specify that raw data is kept for 30 years after the use, expiry or disposal of tissues and cells. Under the Human Tissue (Quality and Safety for Human Application) Regulations 2007, raw data should be kept for a period of 10 years. The DI may wish to consider revising the procedure to reflect this and also consider reviewing procedures that link to termination of activities to ensure it appropriately reflects these data storage requirements under the Human Tissue (Quality and Safety for Human Application) Regulations 2007.
3.	PFE3(a)	In the event that the temperature in the room where the ACD-A is stored exceeds the upper limit for its storage, the establishment has access to contingency fridge controlled by Pharmacy. Although this fridge is temperature-monitored, the alarm system is not tested. The DI is advised to develop a process by which the alarm is tested prior to the transfer of samples into the fridge.
4.	PFE5(a)	Although contingency arrangements are in place, the DI is advised to consider putting in place a maintenance contract for the equipment used to thaw cells prior to infusion. This will help ensure that faulty equipment is repaired promptly, thus, potentially avoiding the need to implement changes to working practices.

Human Tissue Act 2004

No.	Standard	Advice
5.	C1	The DI should consider setting up formal agreements with third party organisations responsible for supplying tissue samples for use in research. Such agreements should provide confirmation that consent for the storage and use of those tissue samples has been obtained in accordance with the requirements of the HT Act.
6.	C3	Research Nurses involved in seeking consent for ethically approved research studies are provided with extensive consent training, which focuses on the common law requirements for seeking consent, including the assessment of mental capacity. The training does not include consent requirements under the HT Act and the DI is advised to incorporate this. This will help to further raise the awareness of the HT Act, especially as these samples may be stored under the HTA licence subsequently.
7.	GQ7	The establishment has a formal procedure for reporting incidents; however, this procedure does not include specific reference to incidents involving human tissue samples and the activities conducted under the HT Act. The DI is advised to document a procedure which includes how to identify and report incidents involving human tissue samples. Examples of incidents can be found in Advice item 8 of this report.

8.	GQ8	The DI should ensure that documented risk assessments cover the premises, practices and procedures connected with licensed activities, including: • receiving and/or storing specimens without appropriate consent documentation; • storing or using human tissue after consent withdrawal; • storage failure or other damage affecting human tissue quality for useful research; • loss of human tissue; • sample mix-up or loss of traceability; • transport of specimens to and from the establishment; • security arrangements; • incorrect disposal.
9.	D2	The DI should consider extending the local disposal policy to include the management of tissue from deceased donors and the methods by which this tissue can be disposed of appropriately. Procedures should include the requirement that the method and date of disposal are logged for each tissue sample that is disposed of.
10.	PFE3	The DI is advised to consider testing freezer alarms to ensure that the alarm system is functioning correctly. Regular testing of the alarm system helps to minimise the risk of a freezer failure going unnoticed.
11.	N/A	The DI and Chief Investigator are reminded that whilst project-specific REC approval may exempt the storage of relevant material from the licensing requirements of the HT Act, it does not provide an exemption from the consent requirements of the HT Act. The DI should also consider drafting guidance for all relevant staff to be able to access.
12.	N/A	The establishment intends to set up a research tissue bank. This research tissue bank will be subject to HTA-licensing requirements. The DI is advised to address the areas identified during this inspection as requiring improvement before the tissue bank becomes active. Following that, the DI is advised to seek guidance from the HTA about future licensing arrangements.
13.	N/A	Although samples can be exempted from the licensing requirements of the HT Act by virtue of being under a project-specific REC approval, the establishment should ensure that all samples are catalogued and fully traceable.

Concluding comments

Although the establishment has several areas for improvement, the research staff particularly demonstrated a commitment to improve and strengthen the governance surrounding storage of tissue for research.

Furthermore, some areas of good practice were identified during the inspection. Staff working in the Apheresis Unit have a good working relationship and there is good communication between staff. The apheresis unit has moved to a new, purpose-designed facility since the last HTA inspection. This new facility includes a dedicated private room for patients whilst they are undergoing apheresis. There is a robust competency training provided to nurses involved in apheresis and the establishment has put in place systems to ensure that staff rotate practices to ensure that they maintain competency in these procedures.

There are a number of areas of practice that require improvement, including four major shortfalls and four minor shortfalls against the HT Act standards and five minor shortfalls against the Human Application standards.

The HTA has given advice to the Designated Individual with respect to termination of activities, storage of raw data, storage of critical reagents, dealing with emergencies and maintenance of critical equipment (Human Application standards). The HTA has also provided advice with respect to, consent training, testing of freezer alarms, incident reporting, risk assessments and disposal procedures (HT Act standards).

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: 23 May 2017

Report returned from DI: 6 June 2017 (with comments)

Final report issued: 30 June 2017

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: 22 February 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
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 003/2010 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.
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.
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 003/2010.
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 003/2010, is collected and maintained.
g) There is a system to ensure records are secure and that donor confidentiality is maintained in accordance with Directions 003/2010.
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 003/2010 are kept for 30 years after the use, expiry or disposal of tissues and / or cells.
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 003/2010.
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 003/2010.
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.
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.
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.
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.
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 003/2010.
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
• Consent forms comply with the HTA's Code of Practice • Consent forms are in records and are made accessible to those using or releasing relevant material for a scheduled purpose • If the establishment obtains consent, a process is in place for acquiring consent in accordance with the requirements of the HT Act 2004 and the HTA's Codes of Practice • Where applicable, there are agreements with third parties to ensure that consent is obtained in accordance with the requirements of the HT Act 2004 and the HTA's Codes of Practice • Consent procedures have been ethically approved
C2 Information about the consent process is provided and in a variety of formats
• Standard operating procedures (SOPs) detail the procedure for providing information on consent • Agreements with third parties contain appropriate information • Independent interpreters are available when appropriate • Information is available in suitable formats, appropriate to the situation • Consent procedures have been ethically approved

C3 Staff involved in seeking consent receive training and support in the implications and essential requirements of taking consent
• Standard operating procedures (SOPs) detail the consent process • Evidence of suitable training of staff involved in seeking consent • Records demonstrate up-to-date staff training • Competency is assessed and maintained

Governance and quality system standards
GQ1 All aspects of the establishments work are supported by ratified documented policies and procedures as part of the overall governance process
• Policies and procedures are in place, covering all activities related to the storage of relevant material for research in connection with disorders, or the functioning, of the human body • Appropriate risk management systems are in place • Regular governance meetings are held; for example, health and safety and risk management committees, agendas and minutes • Complaints system
GQ2 There is a documented system of quality management and audit
• A document control system, covering all documented policies and standard operating procedures (SOPs). • Schedule of audits • Change control mechanisms for the implementation of new operational procedures
GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills
• Qualifications of staff and training are recorded, records showing attendance at training • Orientation and induction programmes • Documented training programme, (e.g. health and safety, fire, risk management, infection control), including developmental training • Training and reference manuals • Staff appraisal / review records and personal development plans are in place
GQ4 There is a systematic and planned approach to the management of records
• Documented procedures for the creation, amendment, retention and destruction of records • Regular audit of record content to check for completeness, legibility and accuracy • Back-up / recovery facility in the event of loss of records • Systems ensure data protection, confidentiality and public disclosure (whistle-blowing)

GQ5 There are documented procedures for distribution of body parts, tissues or cells
• A process is in place to review the release of relevant material to other organisations • An agreement is in place between the establishment and the organisation to whom relevant material is supplied regarding the tracking and use of material and eventual disposal or return
GQ6 A coding and records system facilitates traceability of bodies, body parts, tissues and cells, ensuring a robust audit trail
• There is an identification system which assigns a unique code to each donation and to each of the products associated with it • An audit trail is maintained, which includes details of when and where the relevant material was acquired, the consent obtained, the uses to which the material was put, when the material was transferred and to whom
GQ7 There are systems to ensure that all adverse events are investigated promptly
• Corrective and preventive actions are taken where necessary and improvements in practice are made • System to receive and distribute national and local information (e.g. HTA communications)
GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately
• Documented risk assessments for all practices and processes • Risk assessments are reviewed when appropriate • Staff can access risk assessments and are made aware of local hazards at training

Premises, facilities and equipment standards
PFE1 The premises are fit for purpose
• A risk assessment has been carried out of the premises to ensure that they are appropriate for the purpose • Policies in place to review and maintain the safety of staff, authorised visitors and students • The premises have sufficient space for procedures to be carried out safely and efficiently • Policies are in place to ensure that the premises are secure and confidentiality is maintained
PFE 2 Environmental controls are in place to avoid potential contamination
• Documented cleaning and decontamination procedures • Staff are provided with appropriate protective equipment and facilities that minimise risks from contamination

- Appropriate health and safety controls are in place

PFE3 There are appropriate facilities for the storage of bodies, body parts, tissues and cells, consumables and records.

- Relevant material, consumables and records are stored in suitable secure environments and precautions are taken to minimise risk of damage, theft or contamination
- Contingency plans are in place in case of failure in storage area
- Critical storage conditions are monitored and recorded
- System to deal with emergencies on 24 hour basis
- Records indicating where the material is stored in the premises

PFE 4 Systems are in place to protect the quality and integrity of bodies, body parts, tissues and cells during transport and delivery to a destination

- Documented policies and procedures for the appropriate transport of relevant material, including a risk assessment of transportation
- A system is in place to ensure that traceability of relevant material is maintained during transport
- Records of transportation and delivery
- Records are kept of any agreements with recipients of relevant material
- Records are kept of any agreements with courier or transport companies

PFE5 Equipment is appropriate for use, maintained, quality assured, validated and where appropriate monitored

- Records of calibration, validation and maintenance, including any agreements with maintenance companies
- Users have access to instructions for equipment and receive training in use and maintenance where appropriate
- Staff aware of how to report an equipment problem
- Contingency plan for equipment failure

Disposal Standards

D1 There is a clear and sensitive policy for disposing of human organs and tissue

- Documented disposal policy
- Policy is made available to the public
- Compliance with health and safety recommendations

D2 The reason for disposal and the methods used are carefully documented
• Standard operating procedures (SOPs) for tracking the disposal of relevant material detail the method and reason for disposal • Where applicable, disposal arrangements reflect specified wishes

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.

Classification of the level of shortfall (Research)

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.

4. **Critical shortfall:**

A shortfall which poses a significant risk to human safety and/or dignity or is a breach of the Human Tissue Act 2004 (HT Act) or associated Directions

or

A combination of several major shortfalls, none of which is critical on its own, but which together could constitute a critical shortfall and should be explained and reported as such.

A critical shortfall may result in one or more of the following:

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

(7) 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.

(8) A notice of suspension of licensable activities

(9) Additional conditions being proposed

(10) Directions being issued requiring specific action to be taken straightaway

5. **Major shortfall:**

   A non-critical shortfall that:

   - poses a risk to human safety and/or dignity, or
   - indicates a failure to carry out satisfactory procedures, or
   - indicates a breach of the relevant CoPs, the HT Act and other relevant professional and statutory guidelines, or
   - has the potential to become a critical shortfall unless addressed

   or

   A combination of several minor shortfalls, none of which is major on its own, but which, together, could constitute a major shortfall and should be explained and reported as such.

   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.

6. **Minor shortfall:**

   A shortfall which cannot be classified as either critical or major, but which indicates a departure from expected standards.

   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 or site visit.

   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.