Site visit inspection report on performance against HTA quality standards
Nottingham University Hospitals NHS Trust
HTA licensing number 11035

Licensed for the

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

1 and 2 March 2011

Executive Summary

A site visit inspection of the Nottingham University Hospitals NHS Trust ("the establishment") was carried out by the HTA on 1 and 2 March 2011.

The HTA found the Designated Individual and the Licence Holder to be suitable. Overall, the premises and the practices were found to be suitable in accordance with the requirements of the legislation; the establishment was found to meet the majority of the HTA standards, though shortfalls in standards were identified across the four areas of consent; governance and quality; premises, facilities and equipment; and disposal. However, areas for improvement were identified; these are discussed under the relevant standards.

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

Background to the establishment and description of inspection activities undertaken

This report refers to the activities carried out under the authority of the licence held by Nottingham University Hospitals NHS Trust within the Clinical Tissue Laboratory (CTL) at Queen's Medical Centre (QMC), Nottingham and the Nottingham Bone Bank (main site at QMC and satellite site at Nottingham City Hospital, NCH).

The CTL was a new processing and storage facility at the time of the previous HTA site visit inspection in March 2009 and was set up to support clinical trials being carried out within the Trust and Nottingham University. At the time of this inspection no clinical trials involving the CTL were underway; however, the facility was being used for donor testing, processing and storage of amniotic membrane (procured in theatres) used in ocular surgery (end use in theatres), and for storage of one unit of ovarian tissue for potential future autologous transplant.

The Bone Bank undertakes procurement, donor testing, storage and distribution of femoral heads from living donors for autologous and allogeneic transplant. Femoral heads from living donors are procured on behalf of the Bone Bank by three local hospitals under third party agreements. Tendons and cortical struts are occasionally purchased from another licensed establishment and stored in the Bone Bank for end use. Storage of acellular products for end use is not currently regulated and therefore this storage was not included in this inspection.

This was the second routine inspection of this establishment. The CTL and the Bone Bank premises at QMC, NCH and one Relevant Third Party Premises were visually inspected. The remaining two Relevant Third Party Premises were not visually inspected.

Various audit trails for traceability from donor to recipient were carried out during the inspection. The ovarian tissue in storage was audited at the time of the previous inspection, and no anomalies were found. Further detail about the audit trail findings is given under standards GQ4 (b and c) and GQ6 (b).

- An audit was conducted of the amniotic membrane in storage at CTL against the storage and release records; no anomalies were found.
- In the Bone Bank at QMC three femoral heads were audited (two in quarantine and one which was issued for release) against Bone Bank and patient records. Although no anomalies were found in relation to traceability, there were minor issues with record keeping.
- An NHSBT-issued tendon in storage at the Bone Bank at QMC for end use was audited against the related records; no anomalies were found.
- The records for two femoral heads were audited at the NCH. The records for one procured head indicated that it had been sent to the QMC site but it had not been logged as received there. The records for one head released for end use did not contain the recipient's details; instead, the surgeon and nurse name were entered in

this space. Additionally, the date the head was received for surgery was not recorded.

- The records for two procured femoral heads in storage awaiting transfer to the QMC site were reviewed at a Relevant Third Party Premises. Neither of these had been entered into the register of procured material.
- Six sets of patient records were used to audit femoral heads which had been released for use. In one instance the incorrect donor code had been transcribed in the recipient's records while in another, the bone bank register recorded that bone had been released for autologous use when it had been used allogeneically.

Meeting the HTA's licensing standards

The HTA developed its licensing standards with input from its stakeholders, in order to ensure the safe and ethical use of human tissue. The HTA expects licensed establishments to meet these standards (see Appendix 2; standards which do not apply to this licence are highlighted).

This is an exception-based report: only those standards that have been assessed as not met are included. Where the HTA determines that a licensing standard is not met, the level of the shortfall will be classified as 'Critical', 'Major' or 'Minor' (see Appendix 3: Classification of the level of shortfall).

Unless otherwise advised, the establishment is required to inform the HTA within 14 days of the receipt of the final report of the corrective and preventative actions (CAPAs) that will be taken to ensure that the improvements are addressed. A template for this purpose will be provided as a separate Word document along with the final report.

HTA standards not met

Note that CTL refers to the Clinical Tissue Laboratory and BB refers to the Nottingham Bone Bank in comments made in relation to the standards.

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.		
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, the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (Q&S Regulations) and the HTA's Codes of Practice.	CTL: The CTL is a processing and storage facility but procurement is carried out under the licence if this facility will be used. Consent is taken by individuals (trained by the CTL) who carry out projects and consent forms are checked and held by the CTL. However, the quality manual section on consent does not reflect this arrangement for the consent process. BB: The only documented consent procedure (Consent Training, 37.0) does not fully meet the requirements of this standard. This has been addressed in part under standard C1 (c) and C2 (a); additionally, the document does not describe the consent process from start to finish.	**Minor** **Also see C1 (c) and C2 (a).**
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, the Q&S Regulations and the HTA's Codes of Practice.	BB: Acceptable practices are clearly embedded at the establishment but the documentation does not fully support this. There are third party agreements in place with procurement sites, however the agreements do not provide for the requirement of this standard. Third party procurers are provided with standard operating procedures (SOPs) by the Bone Bank, however the consent procedure does not fully meet the requirements of this standard as described in C1 (c) and C2 (b).	**Minor** **Also see C1 (c) and C2 (b).**
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.	BB: The only documented consent procedure (Consent Training, 37.0) does not describe how potential donors are identified (i.e. by whom or according to which criteria).	**Minor**

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.	BB: The leaflets used to discuss consent with donors clearly demonstrate that they are provided with appropriate information by the establishment, however SOP 37.0, Consent Training, does not include what information should be provided to donors.	**Minor**
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 003/2010 is included.	BB: See C2 (a) above.	**Minor**

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.		
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.	BB: SOPs in the Bone Bank do not have: • An author or authoriser identified • Effective from dates or review dates • Version control. Advice relating to this standard was provided following the previous HTA inspection: *A regular review date should be set for each procedure to ensure that it is up to date and is fit for purpose. The DI should also ensure that only current documents are in use.*	**Minor**

g) There are procedures to ensure that an authorised person verifies that tissues and / or cells received by the establishment meet required specifications.	CTL: There is no documented procedure to ensure that an authorised person verifies that tissues and / or cells received by the establishment meet required specifications. BB: There are two documented SOPs (34.0, Inspection of Materials and 46.0, Tissue received from other establishments). However, neither of these identifies an authorised person.	**Minor**
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.	BB: Although this practice is clearly embedded at the establishment and third party procurers, there are no documented SOPs relating to the need to quarantine until verification is complete.	**Minor** See also PFE2a below
i) There are procedures to ensure tissues and / or cells are not released from quarantine until verification has been completed and recorded.	This is addressed under standard GQ1 (h).	**See GQ1 (h).**
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.	CTL and BB: Advice relating to this standard was provided following the previous HTA inspection: *The DI is advised to ensure that there are procedures in place which ensure that in the event of termination of activities, stored tissues and/or cells are transferred to another licensed establishment or disposed.* This SOP is not in place at either the CTL or the Bone Bank.	**Minor**
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.	BB: Third party agreements are in place with third party procurers and companies which transport bone between sites. These agreements do not meet the requirements set out in Directions 003/2010.	**Minor**

r) Third party agreements specify the responsibilities of the third party and meet the requirements set out in Directions 003/2010.	BB: During this inspection it was identified that femoral heads were being stored for greater than 48 hours both following procurement (while awaiting transfer from the satellite and third party procurers to the Bone Bank) and when bone was delivered to the satellite and external sites for end use. In the absence of storage licences at the external sites, the DI was advised during the site visit to collected procured bone within 48 hours and to deliver bone immediately prior to end use. This means that this standard will now apply to the Bone Bank; at present there is no SOP for this.	**Minor**
GQ2 There is a documented system of quality management and audit.		
a) There is a quality management system which ensures continuous and systematic improvement.	This is addressed under standard GQ2 (b).	**See GQ2 (b).**
b) There is an internal audit system for all licensable activities.	CTL: Each processing procedure is audited via a checklist, however there is no audit schedule which includes process, traceability and record audits. BB: An audit schedule is in place but it does not sufficiently cover the activities carried out by the Bone Bank. • Third party procurers, the satellite site and theatres at the main site are not currently included in audits. • The audit reports reviewed during this inspection were not titled, issues were not clearly identified, and where recommendations were made there were no corrective and preventative actions identified. • The audit schedule reviewed during this inspection did not fully cover process, traceability and records audits.	**Major**

GQ4 There is a systematic and planned approach to the management 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.	CTL and BB: Advice relating to this standard was provided following the previous HTA inspection: *The DI is advised to ensure that 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.* This has been addressed under standard GQ2 (b).	**See GQ2 (b).**
c) Written records are legible and indelible. Records kept in other formats such as computerised records are stored on a validated system.	BB: During the visual inspection of the Bone Bank several of the yellow carbon-copy forms which accompany the stored bone contained illegible hand-written information.	**Minor**
k) There are documented agreements with end users to ensure they record and store the data required by Directions 003/2010.	CTL: There is an agreement in place with Ophthalmology which does not meet the requirements of Directions 003/2010. BB: The Bone Bank does not have end user agreements in place.	**CTL: Minor** **BB: Major**
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.	CTL and BB: The establishment does not record the acceptance or rejection of tissue and / or cells that it receives and in the case of rejection why this rejection occurred.	**CTL: Minor**
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.	This has been partly addressed under GQ1 (l). The SOP should also cover • storage and traceability of records (for 30 years following the use, expiry or disposal of the material) and raw data (for 10 years following the use, expiry or disposal of the material) • storage of tissue registers, donor records and information relating to SAEARs.	**Minor** **Also see GQ1 (l).**

GQ6 A coding and records system facilitates traceability of bodies, body parts, tissues and cells, ensuring a robust audit trail.		
b) An audit trail is maintained, which includes details of when the tissues and / or cells were acquired and from where, the uses to which the tissues and / or cells were put, when the tissues and / or cells were transferred elsewhere and to whom.	BB: Advice relating to this standard was provided following the previous HTA inspection: *The DI is advised to ensure that an audit trail is maintained for all samples. This should include 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.* An audit trail is maintained via patient records and the ledger. However, there are three forms used to track the movement of bone among the main, satellite and third party/external sites. The forms do not cover all movement of bone and the information recorded does not always allow clear traceability. This means that the documentation does not fully support the information contained in patient records. <u>Form 5.6</u> (Between the hub site and Nottingham City satellite and Relevant Third Party Premises): • There is a space for the graft number to be entered but the recipient information is being recorded here. • Receipt is not always confirmed. <u>Form 5.9</u> (Between the hub site to Nottingham City satellite and Relevant Third Party Premises): • Receipt is not always confirmed. <u>Form 7.5</u> (Relevant Third Party Premises to the hub site following procurement): • There is no title on this form. • There is no space to identify the graft number. • Receipt is not always confirmed.	**Major**

GQ7 There are systems to ensure that all adverse events are investigated promptly.		
a) There are procedures for the identification, reporting, investigation and recording of adverse events and reactions, including documentation of any corrective or preventative actions.	Advice relating to this standard was provided following the previous HTA inspection: *The DI should ensure SOPs for the reporting, investigation and recording of adverse events/reactions are put in place and risk assessed.* BB: An SOP for SAEARs (35.0) is in place and staff indicated that they would inform the Quality Manager in the event of an incident. However, it was not clear that all staff understood how to identify an incident (particularly an equipment failure) nor that they would be reported in a timely manner. SOP 35.0 does not provide information on how to identify an incident or SAEAR and does not clearly state the requirement to report SAEARs to the HTA with 24 hours. The SOP does not address how incidents and SAEARs should be managed and reported in the absence of the DI. The SOP does not cover how incidents and SAEARs will be managed, including the responsibilities of each party. There were records of a number of incidents in the Bone Bank ledger, leading to disposal of substantial proportions of procured tissues, but no incident reports were observed. This suggests the incidents were not investigated and that no corrective and preventative actions were identified or carried out.	**Major**
c) The responsibilities of personnel investigating adverse events and reactions are clearly defined.	This is addressed under GQ7 (a).	**See GQ7 (a).**
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.	CTL and BB: There is no SOP in place for this.	**Minor**
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.	This is addressed under standard GQ4 (k).	**See GQ4 (k).**

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.	This is addressed under standard GQ4 (k).	**See GQ4 (k).**
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.	CTL: Risk assessments refer to COSHH and Health and Safety risks, but not those which relate to the safety and quality of tissues and cells.	**Minor**
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.	Advice relating to this standard was provided following the previous HTA inspection: *The DI is advised to ensure that 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.* The processing of amniotic membrane has changed since the previous inspection. There is no SOP which covers this risk assessment.	**Minor**

Premises, Facilities and Equipment

Standard	Inspection findings	Level of shortfall
PFE1 The premises are fit for purpose.		
e) There are procedures to ensure that the premises are secure and confidentiality is maintained.	BB: Storage equipment inspected at Relevant Third Party Premises was located in an unsecured area and not locked.	**Minor**

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.	This is addressed under standard GQ1 (h).	**See GQ1 (h).**
b) Where processing of tissues and / or cells involves exposure to the environment, it occurs in an appropriate, monitored environment as required by Directions 003/2010.	CTL: Advice relating to this standard was provided following the previous HTA inspection: *The DI is advised to ensure that at rest' and 'in operation' particle and environmental monitoring ensures a Grade A environment every 6 months; that routine environmental monitoring takes place in between these periods, that appropriate alert and action limits are set for the results and that a trend analysis is performed on the data to ensure that the equipment is performing to the expected standard. SOPs should define the limits and actions to be taken if they are exceeded. See:* *http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-4/2008_11_25_gmp-an1.pdf* 'At rest' particle monitoring is carried out every month (under a contract with the QC department) to ensure that the clean rooms maintain a Grade A environment. However, in-operation particle monitoring is not being carried out or simulated according to a schedule in the Grade A zones or within the Clean Room. Additionally, the CTL quality manual does not identify the alert and action limits for these results.	**Major**
PFE3 There are appropriate facilities for the storage of bodies, body parts, tissues, cells, consumables and records.		
c) Tissues and / or cells are stored in controlled, monitored and recorded conditions that maintain tissue and / or cell integrity.	This is addressed under PFE1 (e).	**See PFE1 (e).**

PFE4 Systems are in place to protect the quality and integrity of bodies, body parts, tissues and cells during transport and delivery to a destination.		
c) There is a system to ensure that traceability of tissues and / or cells is maintained during transport.	This is addressed under standard GQ6 (b).	**See GQ6 (b).**
d) Records are kept of transportation and delivery.	CTL: The Ophthalmology release request and the CTL release paperwork are in order but there is no documentation of movement of amniotic membrane between theatres and the CTL for either procurement or end use. BB: This standard is addressed in part under standard GQ6 (b). Additionally: • The collection of bone (following procurement or for delivery for end use) or blood (for serology) by the transport company is not recorded. • The receipt of blood in the Microbiology lab is not recorded. • At the Relevant Third Party Premises, the records were unclear whether the bone was being signed in to the freezer following procurement or for end use.	**Minor** **Minor** **Also see GQ6 (b).**
g) Critical transport conditions required to maintain the properties of tissue and / or cells are defined and documented.	BB: SOP 45.0, Transportation of tissue, does not identify the transport box which must be used to move bone among the sites. The reader would not know where to find the box or what the identifying features are.	**Minor**

PFE5 Equipment is appropriate for use, maintained, quality assured, validated and where appropriate monitored.		
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.	BB: Although records indicate that there is routine service and maintenance of all freezers, the chart reading on the freezer at the inspected Relevant Third Party Premises was 10 degrees cooler than the digital display. There was no indication that this issue had been identified or acted upon by the establishment.	**Major**
i) Staff are aware of how to report an equipment problem.	This is addressed under standard GQ7 (a).	**See GQ7 (a).**

Advice

Below are matters which the HTA advises the DI to consider.

No.	Standard	Advice
1	All	The DI is advised to ensure that references within information, forms, SOPs and other documentation refer to: • The Human tissue (Quality and Safety for Human Application) Regulations 2007 (under which the establishment is licensed). • The HTA *Guide to quality and safety assurance for human tissue and cells for patient treatment*, which were brought into force via General Directions 003/2010 and repeal HTA Directions 001/2006, 002/2007 and 002/2004.
2	GQ4(i)	The DI indicated that the CTL records will be transferred to an off-site storage facility after 10 years. The DI is therefore advised that the records must be stored at an HTA-licensed establishment and the DI (for CTL) must have a system for accessing the records in the event that he is notified of a SAEAR.
3	N/A	The DI is advised to amend the agreements in place with individuals and areas outside of the CTL which carry out activities/where activities are carried out under the licence. At present the agreements are prepared in the same manner as the establishment's other (third party) agreements. Improvements could be made so that the responsibilities of each party are more clearly identified.

Concluding comments

Although areas for improvement were identified during the inspection, there were a number of examples of good practice at the establishment.

In the clinical tissue laboratory there is a floor map in the entrance which clearly indicates the graded zones of the clean room. Additionally, there is a lot of signage relating to personal protective equipment throughout the facility to ensure that staff are clear on what is required before they move between rooms.

The Bone Bank keeps a separate log for tissue that is purchased from NHSBT, which facilitates audits carried out under their end user agreement. The Quality Manager is commended for her success in fostering teamwork throughout the Bone Bank sites; it is clear that her leadership and support are very highly regarded. This is particularly impressive given that the sites are not physically linked and the number of staff involved.

Information about actions taken at the establishment in response to the shortfalls identified during the inspection was received from the DI after the draft inspection report was issued. The HTA considers the following standards to be met the time of issue of the final inspection report: C1 (a, b), C2 (a, b), GQ1 (g, h, l), GQ2 (b), GQ4 (b, c, l, m), GQ6 (b), PFE1 (e), PFE4 (d, g) and PFE5 (c). Details of the actions taken in relation to these standards will be provided in the Corrective and Preventative Action plan, which will be published when all actions in the plan have been completed.

Report sent to DI for factual accuracy: 28 March 2011
Report returned from DI: 12 April 2011
Final report issued: 15 April 2011

Appendices

Appendix 1: HTA inspection process

The Human Tissue Authority (HTA) regulates the removal, storage, and use of human bodies, body parts, organs and tissue for activities such as research, transplantation, and education and training. The legal requirements for establishments which carry out such activities are set out in the Human Tissue Act 2004 and The Human Tissue Act 2004 (Ethical Approval, Exceptions from Licensing and Supply of Information about Transplants) Regulations 2006.

The HTA is also the designated Competent Authority for the purposes of the European Union Tissue and Cells Directives (the Directives) so far as they relate to tissues and cells for use in human application (using tissues and cells for patient treatment). On 5 July 2007 the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (the Regulations) came into force. The Regulations formally transposed the Directives into UK law. Under the Regulations the HTA regulates and licences the procurement, testing, processing, storage, distribution, import or export of tissues or cells intended for human application. The HTA has produced detailed Directions to complement the implementation of the Directives.

As part of the regulatory framework, the HTA licenses establishments and undertakes inspections to assess compliance with expected standards.

Inspections

We use the term 'inspection' to describe when we:

- visit an establishment to meet with staff, view premises and facilities, and review policies and procedures (a site-visit inspection); or
- assess written information we have requested from an establishment (a desk-based assessment / inspection).

We carry out inspections to assess if the Designated Individual (DI) is suitable to supervise the activity covered by the licence, as it is their responsibility to ensure that:

- other staff working under the licence are suitable;
- suitable practices are used when carrying out the activity;
- the conditions of the licence are met;
- the conditions of third party agreements are met; and
- the information and confidentiality requirements set down in the Regulations are complied with.

We also need to be satisfied that the licence applicant or holder, the establishment's premises, and the practices relating to licensed activities, are suitable.

To help us reach our decisions, we have developed standards under four headings: Consent; Governance and Quality; Premises, Facilities and Equipment; and Disposal.

After every site visit inspection, we write a report documenting our findings. Where we find a particular standard is not fully met, we will describe the level of the shortfall as 'Critical', 'Major' or 'Minor'. In most cases, it will be the responsibility of the DI to seek the HTA's agreement on how they will address the identified shortfalls. More information about the classification of shortfalls can be found in Appendix 3.

The majority of our site-visit inspections are announced. If we have concerns about an establishment, we can also undertake an unannounced site visit inspection.

You can find reports for site visit inspections which took place after 1 November 2010 on our website.

Appendix 2: HTA Standards

Standards which are not applicable to this establishment have been highlighted.

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 003/2010 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 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.
f) There are procedures for tissue and / or cell procurement, which ensure the dignity of deceased donors.
g) There are procedures to ensure that an authorised person verifies that tissues and / or cells received by the establishment meet required specifications.
h) There are procedures for the management and quarantine of non-conforming consignments or those with incomplete test results, to ensure no risk of cross contamination.
i) There are procedures to ensure tissues and / or cells are not released from quarantine until verification has been completed and recorded.
j) There are procedures detailing the critical materials and reagents used and where applicable, materials and reagents meet the standards laid down by the European directives on medical devices and in vitro diagnostic medical devices.
k) There is a procedure for handling returned products.
l) There are procedures to ensure that in the event of termination of activities for whatever reason, stored tissues and / or cells are transferred to another licensed establishment or establishments.
m) The criteria for allocating tissues and / or cells to patients and health care institutions are documented and made available to these parties on request.
n) The establishment ensures imports from non EEA states meet the standards of quality and safety set out in Directions 003/2010.
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.
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 003/2010.
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.
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.
GQ7 There are systems to ensure that all adverse events, reactions and/or incidents are investigated promptly.
a) There are procedures for the identification, reporting, investigation and recording of adverse events and reactions, including documentation of any corrective or preventative actions.
b) There is a system to receive and distribute national and local information (e.g. HTA regulatory alerts) and notify the HTA and other establishments as necessary of serious adverse events or reactions.
c) The responsibilities of personnel investigating adverse events and reactions are clearly defined.
d) There are procedures to identify and decide the fate of tissues and / or cells affected by an adverse event, reaction or deviation from the required quality and safety standards.
e) In the event of a recall, there are personnel authorised within the establishment to assess the need for a recall and if appropriate initiate and coordinate a recall.
f) There is an effective, documented recall procedure which includes a description of responsibilities and actions to be taken in the event of a recall including notification of the HTA and pre-defined times in which actions must be taken.
g) Establishments distributing tissue and / or cells provide information to end users on how to report a serious adverse event or reaction and have agreements with them specifying that they will report these events or reactions.
h) Establishments distributing tissues and / or cells have systems to receive notifications of serious adverse events and reactions from end users and notify the HTA.
GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately.
a) There are documented risk assessments for all practices and processes.
b) Risk assessments are reviewed regularly, as a minimum annually or when any changes are made that may affect the quality and safety of tissues and cells.
c) Staff can access risk assessments and are made aware of local hazards at training.
d) A documented risk assessment is carried out to decide the fate of any tissue and / or cells stored prior to the introduction of a new donor selection criteria or a new processing step, which enhances the quality and safety of tissue and / or cells.

Premises, Facilities and Equipment

Standard
PFE1 The premises are fit for purpose.
a) A risk assessment has been carried out of the premises to ensure that they are fit for purpose.
b) There are procedures to review and maintain the safety of staff, visitors and patients.
c) The premises have sufficient space for procedures to be carried out safely and efficiently.

d) Where appropriate, there are procedures to ensure that the premises are of a standard that ensures the dignity of deceased persons.
e) There are procedures to ensure that the premises are secure and confidentiality is maintained.
f) There is access to a nominated, registered medical practitioner and / or a scientific advisor to provide advice and oversee the establishment's medical and scientific activities.
PFE2 Environmental controls are in place to avoid potential contamination.
a) Tissues and / or cells stored in quarantine are stored separately from tissue and / or cells that have been released from quarantine.
b) Where processing of tissues and / or cells involves exposure to the environment, it occurs in an appropriate, monitored environment as required by Directions 003/2010.
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 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.

Appendix 3: Classification of the level of shortfall

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, which individually do not pose a direct risk of harm to a recipient or living donor, 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 or 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/or cells.

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 at the time of the next inspection.

Follow up actions

A template corrective and preventative action plan is available as a separate Word document. 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.