Site visit inspection report on compliance with HTA minimum standards

North West Embryonic Stem Cell Centre
HTA licensing number 22627

Licensed for the

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

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

8 October 2013

Summary of inspection findings

This was the second inspection of the North West Embryonic Stem Cell Centre (NWESCC, the establishment) since it was licensed by the HTA in September 2011.The HTA undertook this inspection as a pilot joint inspection with the HFEA. The HTA regulates the processing, storage and distribution of stem cell lines for human application. The HFEA licenses clinics which provide fertility services and regulates the processing involved in the creation of an embryo, the use of embryos for research and the derivation of stem cell lines. The HFEA's remit does not extend to the regulation of the stem cell lines.

This inspection report covers the assessment of the HTA licensing standards; a separate report which covers the assessment of HFEA licensing standards will be issued by the HFEA.

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

Although the HTA found that the NWESCC had met the majority of the HTA standards, two shortfalls were found; one major shortfall relating to storage of cell lines on unlicensed premises and a minor shortfall relating to environmental monitoring. Following the inspection, the establishment implemented corrective actions which addressed the minor shortfall relating to environmental monitoring. The establishment has made significant improvements to record keeping since the previous inspection. Particular examples of strengths and good practice are included in the concluding comments section of the report.

The HTA would like to thank staff at the NWESCC for their participation in the HTA-HFEA pilot joint inspection and for providing feedback to help in the development of the joint inspection process.

The HTA's regulatory requirements

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

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

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

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

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

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

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

Licensable activities carried out by the establishment

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

'TPA' = Third party agreement; the establishment is licensed for this activity but another establishment (unlicensed) carries out the activity on their behalf.

Tissue type	Procurement	Processing	Testing	Storage	Distribution	Import	Export
Embryonic stem cells		**E**		**E**	**E**		

Background to the establishment and description of inspection activities undertaken

The North West Embryonic Stem Cell Centre (NWESCC) consists of two sites - Department of Reproductive Medicine, Old St Mary's Hospital, and the Core Technology Facility at the University of Manchester. The Core Technology Facility undertakes the derivation and culture of human embryonic stem cell (hESC) lines and is licensed by the HTA. Old St Mary's Hospital, which is one of the hospitals under the Central Manchester NHS Foundation Trust, is licensed for fertility treatment by the Human Fertilisation and Embryology Authority (HFEA). The NWESCC also holds a Research licence (R0171/2/a) from the HFEA jointly at both sites which covers research on embryos up to the point of disruption of the embryos. The University of Manchester is the corporate licence holder under the HTA licence and the Associate Vice President for Compliance, Risk and Research Integrity acts as the corporate licence holder contact.

The NWESCC deposits cell lines in the UK Stem Cell Bank, which assesses the conditions used to derive, culture and store hESC lines in order to determine if they meet the criteria for banking cell lines for clinical use. Once banked, the cell lines will be provided to users as starting materials only, and careful evaluation must be undertaken by the user in order to determine their suitablility for the intended use. The inspection team was informed that the UK Stem Cell Bank takes responsibility for transporting of cell lines to the UK Stem Cell Bank.

The consent process, donor testing, embryology and the transport of the embryos to the Core Technology Facility to generate hESC lines are carried out under the supervision of the Person Resposible to the HFEA for the research licences in embryo research and embryonic stem cells. The 'Egg and Embryo acquisition checklist' which accompanies the embryos, contains details such as the unique embryo ID and donor test results for - Hep B (including Hep B anti core), Hep C and HIV I/II. Embryos are cultured for a maximum of 14 days and the inner cell mass is used to derive hESC lines.

Processing steps such as embryo culture, dissociation, culturing of stem cells, addition of cryopreservative and all steps involved in preparation of the master cell banks and working cell banks are performed in the Class II microbiological safety cabinets located in a dedicated clean room. Cells from a well established and characterised GMP human dermal fibroblast feeder cell line are mitotically inactivated and used to support the growth of the embryonic stem cell cultures.

The NWESCC has a service agreement with another establishment which provides a Quality Manager and arranges for regular qualification of the cleanroom, training of staff who undertake sessional monitoring, and the supply of plates and other services for monitoring fungal and bacterial contamination. Staff at the NWESCC are provided with Environmental Monitoring Excursion Reports in the event that alert or action levels for viable and non-viable particulates are reached.

Following the previous inspection in March 2012, the HTA was informed that NWESCC implemented a procedure to monitor non-viable particulates during critical processing. However during this inspection it was noted that monitoring of non-viable particulates takes place in the clean room where the Class II cabinets are located (Grade B zone), but not in the Class II cabinets (Grade A zone) where critical processing takes place.

Human embryonic stem cell lines are placed in cryovials and stored in the vapour phase of liquid nitrogen. The liquid nitrogen tank is located in a secure area. The temperature inside the liquid nitrogen tank is continuously monitored and the temperature alarm is linked to the switchboard.

The NWESCC also stores some hESC lines in the storage area at the Old St Mary's hospital site. These premises are not licensed by the HTA and the establishment is required to ensure

that these premises are licensed as a matter of urgency. These hESC lines are contained in cryovials and stored under liquid nitrogen in the liquid phase. The liquid nitrogen levels in the tanks are monitored and the tanks are linked to an alarm system with an automatic call out procedure. Storage of ovarian tissue under the HFEA licence also takes place at the Old St Mary's Hospital site.

Since the previous HTA inspection in March 2012, the NWESCC implemented several improvements including documenting donor testing undertaken by the Old St Mary's Hospital for all embryos received at the Core Technology Facility and recording of consummables, feeder cells and any excursion from the accepted limits for environmental monitoring in the 'NWESCC Stem cell line derivation and maintenance record'.

This inspection included interviews with the two co-directors of the NWESCC (one co - director is the DI under the HTA licence and the other is the Person Responsible under the HFEA licence), two research technicians and the quality manager employed by the establishment which provides services to the NWESCC.

A document review was carried out. Documents reviewed included standard operating procedures, cleaning records, reports provided by the company which monitors the clean room, monthly reports on personnel monitoring, environmental monitoring covering settle plates, contact plates as well as reports on non-viable particulates in the Grade B zone and maintenance records.

A number of audit trails were carried out. Records of receipt of embryos, donor virology testing and testing for syphilis undertaken by Old St Mary's Hospital and records relating to the derivation and culture of three hESC lines through several passages. The records covered microbial monitoring and consumables used during processing, cryopreservation and storage. No discrepancies were noted.

Inspection findings

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

Compliance with HTA standards

Premises, Facilities and Equipment

Standard	Inspection findings	Level of shortfall
PFE1 The premises are fit for purpose. .		
	Some hESC lines are stored on unlicensed premises at the Old St Mary's Hospital. These cell lines do not meet the licensing requirements of the Human Tissue (Quality and Safety for Human Application) Regulations 2007. The Old St Mary's Hospital site falls under the governance arrangements of the NWESCC, but is some distance away from the Core Technology Facility which is the named premises on the HTA licence held by the NWESCC.	**Major**

Standard	Inspection findings	Level of shortfall
PFE2 Environmental controls are in place to avoid potential contamination.		
b) Where processing of tissues and / or cells involves exposure to the environment, it occurs in an appropriate, monitored environment as required by Directions 003/2010.	Non-viable particulate monitoring is not carried out during critical processing in the Class II cabinets when embryos/stem cells are exposed to the environment during stem cell derivation, culturing and cryopreservation. The current European Guide to Good Manufacturing Practice (GMP), Annex 1 of Directive 2003/94/EC, clearly indicates that non-viable particle monitoring must be undertaken for the full duration of critical processing. This has been graded a minor shortfall and not a major shortfall after taking the following into consideration - (i) The establishment monitors non-viable particulates in the clean room where the Class II cabinets are located during processing. (ii) The establishment monitors viable particulates (*ie* microbial monitoring) during processing by placing settle plates and contact plates in the Class II cabinets and in the clean room where the Class II cabinets are located. (iii) The establishment undertakes personnel monitoring at the end of each processing session, which includes finger dabs and chest and arm monitoring of viable particulates. (iv) The hESC lines processed by the NWESCC under the above conditions are not directly distributed for human application, but will undergo additional processing steps before they are used for patient treatment. *Following the inspection the establishment addressed this shortfall by updating the SOP "How to perform sessional environmental monitoring samples within the cleanroom facility" and implementing a system of particle monitoring within the Grade A zone during critical processing.*	**Minor**

Advice

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

No.	Standard	Advice
1.	GQ1	The DI is advised to consider updating the service agreement between the NWESCC and the establishment which provides the Quality Manager and arranges for regular qualification of the cleanroom, training of staff who undertake sessional monitoring, and the supply of plates and other services for monitoring fungal and bacterial contamination.The service agreement issued in April 2012 does not detail all the services which are provided to the stem cell derivation laboratory at the NWESCC.
2.	GQ7	The DI is reminded to amend the timeline for reporting of SAEARs to the HTA to within 24 hours of discovery and to confirm that the Person Designated on the licence have registered with the HTA Portal. This will enable the PDs to report to the HTA in the event that the DI is away on leave. *Following the inspection the DI informed the HTA that the SOP has been updated to require reporting of SEAERs within 24 hours.*
3.	PFE 3a	Cell lines stored at St Mary's Hospital are contained within cryovials which are in turn immersed in liquid nitrogen. Cryovials have not been validated for use in liquid nitrogen. The DI is advised to risk assess the use of cryovials to store cell lines in liquid nitrogen and to take adequate precautions to reduce the risk that liquid nitrogen enters the cryovials during storage. The DI is advised to consider overwrapping individual cryovials using impermeable sheathing or placing cryovials in a sealed secondary container before they are stored in the liquid nitrogen storage tanks.

Concluding comments

There was evidence of good communication between staff based at the Core Technology Facility and staff at Old St Mary's Hospital. Staff attend regular Stem Cell Laboratory meetings. They also attend joint meetings- Culture and Derivation meetings - with staff based at the Old St Mary's Hospital. The HTA Governance group at the University of Manchester holds quarterly meetings which the DI attends.

The establishment undertakes detailed vertical and horizontal audits as appropriate, which cover records, documented procedures, monitoring of storage conditions, equipment maintenance, traceability and training.The establishment has implemented an effective system to record consumables, feeder cell batches and checks on environmental monitoring during derivation and culturing of hESC lines. The establishment also undertakes a range of risk assessments which cover risks to the quality of cells including cross contamination, loss of traceability, equipment failure and security breaches.

There are a number of areas of practice that require improvement. One major shortfall relates to the storage of hESC lines in unlicensed premises at the Old St Mary's Hospital site. The HTA has given advice to the Designated Individual with respect to updating the current agreement with the establishment which provides quality management and environmental monitoring services to the NWESCC and risk assessing the storage of hESC lines in liquid nitrogen.

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: 5 November 2013

Report returned from DI: 11 November 2013

Final report issued: 3 December 2013

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.

Date: 2 July 2015.

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

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

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

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

1. **Critical shortfall:**

   A shortfall which poses a significant direct risk of causing harm to a recipient patient or to a living donor,

   Or

   A number of 'major' shortfalls, none of which is critical on its own, but viewed cumulatively represent a systemic failure and therefore are considered 'critical'.

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

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

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

   (3) A notice of suspension of licensable activities

   (4) Additional conditions being proposed

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

2. **Major shortfall:**

   A non-critical shortfall.

   A shortfall in the carrying out of licensable activities which poses an indirect risk to the safety of a donor or a recipient

   or

   A shortfall in the establishment's quality and safety procedures which poses an indirect risk to the safety of a donor or a recipient;

   or

   A shortfall which indicates a major deviation from the **Human Tissue (Quality and Safety for Human Application) Regulations 2007** or the **HTA Directions**;

   or

   A shortfall which indicates a failure to carry out satisfactory procedures for the release of tissues and cells or a failure on the part of the designated individual to fulfil his or her legal duties;

or

A combination of several 'minor' shortfalls, none of which is major on its own, but which, viewed cumulatively, could constitute a major shortfall by adversely affecting the quality and safety of the tissues and cells.

In response to a major shortfall, an establishment is expected to implement corrective and preventative actions within 1-2 months of the issue of the final inspection report. Major shortfalls pose a higher level of risk and therefore a shorter deadline is given, compared to minor shortfalls, to ensure the level of risk is reduced in an appropriate timeframe.

3. **Minor shortfall:**

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

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

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

Follow up actions

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

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

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

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