Site visit inspection report on compliance with HTA minimum standards

UCLH

HTA licensing number 22650

Licensed for the

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

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

15 December 2016

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 UCLH (the establishment) had met the majority of the HTA standards, two shortfalls were found in relation to governance and quality systems. The shortfalls relate to an absence in contingency plans to ensure that traceability records are transferred to licensed premises in the event of closure, and to the storage of blood samples prior to testing and how this relates to the validation of the testing kits.

Particular examples of 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 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
Cells for DLI			**E/TPA**				
PBSC			**E/TPA**				
Cord blood			**E/TPA**				

Background to the establishment and description of inspection activities undertaken

This report refers to the activities carried out by UCLH (the establishment). UCLH is licensed for testing under the Human Tissue (Quality and Safety for Human Application) Regulations 2007. It is also licensed for the storage of relevant material which has come from a human body for use for a scheduled purpose under the Human Tissue Act 2004, although the establishment is currently not undertaking this activity. This was a routine site visit to assess whether the establishment is continuing to meet the required HTA standards. This was the second site visit inspection of the establishment since it was issued a HTA licence in September 2014.

The licensed activity takes place at UCLH's Department of Virology, which sits within the Pathology Division under the UCLH Medical Board. The establishment has a third party agreement with an organisation that is a partnership between UCLH NHS Trust, a second NHS trust and a private testing laboratory. Through the organisation, testing and diagnostic

services is performed at UCLH's Department of Virology and at a second nearby site where the private laboratory is based. The organisation is responsible for management and maintenance of facilities and equipment at both premises, under the terms of the agreement. The DI is a virology consultant at UCLH and holds an honorary contract with the organisation.

At the second site, UCLH has a reception for the submission of samples and requests for screening tests. Samples arrive here either by a pneumatic system from the nearby hospital or by courier from other clinics. The samples arrive labelled with the patient's name, patient number and date of birth together with a request form listing out the tests required. Depending on the requested tests, samples are placed into colour-coded baskets and delegated to relevant sections of the laboratory. Laboratory staff place identifying barcode stickers onto the tubes and on the request form. These stickers generate a unique barcode ID for the sample that is time-traced from arrival right up to testing of the sample. The supervisor in charge of each section performs verification checks to ensure the samples are labelled with the same unique barcode ID to that of the request form to ensure traceability and that the correct assays are performed. Sample details are then added onto an electronic database together with the scanned copy of the original request form.

Mandatory serology tests for all samples are conducted at the second site with the exception of certain non-automated serology tests (such as VZV and EBV) and manual enzyme immunoassays (such as Hepatitis D and E) which are performed at the serology lab in UCLH. In the event that one of these tests is requested in addition to the mandatory serology tests then the blood sample is tested initially at the second site and then transferred to the UCLH serology lab. However, if multiple blood samples are available then testing at both locations occurs simultaneously. If any of the samples are positive for the mandatory serology tests then the samples are sent to the molecular testing lab at UCLH for confirmatory testing by nucleic acid amplification technique (NAT) using commercial kits for HIV, HBV and HCV. Each test kit is validated by biomedical staff scientists before being released for general use in the laboratory. Nucleic acid extraction and PCR amplification are carried out in separate areas of the laboratory.

The establishment uses computerised systems to manage the release of results for review. At the private lab, results are transferred onto a 'middleware' database system, which sits between the test analysers and the lab information management system (LIMS) where it is reviewed by senior laboratory staff. In the case of manual screening the conversion of raw data to diagnostic values are verified by senior staff prior to being recorded onto the Trust's LIMS system. The results from analysers at the UCLH laboratories are transferred automatically onto LIMS where non-conforming results are reviewed by senior staff before release. In the case of an anomalous result, the DI, or another clinical lead, are notified for review and comment.

All original blood samples are transferred to the UCLH laboratories and stored at 4°C for one week in case retesting is required. Only a small proportion of samples, in the form of plasma, serum or DNA, are kept for longer storage at -20°C in case further retests are needed. Prior to disposal, samples are checked to ensure that there are no further tests outstanding.

The establishment takes part in External Quality Assessment schemes that include mandatory biological tests required for human application donor screening.

The timetable for the site visit included interviews with the DI, Molecular Operational Manager, Serology Section Lead and members of the Quality Management Group. A visual inspection was conducted of the UCLH Department of Virology comprising of the serology and molecular laboratories and of the nearby second premise comprising of the sample receipt area and the testing laboratory.

A traceability audit was conducted to ensure that the raw data is traceable to an individual patient. Ten sample aliquots for two patients were checked from the electronic management

system against blood sample tubes stored at 4°C for retesting or interim storage. No discrepancies were found.

Inspection findings

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

Compliance with HTA standards

Governance and Quality

Standard	Inspection findings	Level of shortfall
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's practices do not ensure that samples held for serological testing are stored in conditions that are aligned with the validation for the test kits. For example, samples awaiting allocation to the UCLH molecular laboratory may be kept at room temperature for up to 48 hours after receipt, when NAT kits for HIV are only validated for samples stored at 2-8°C after an initial 24 hours at room temperature. Furthermore, the establishment's practices do not reflect relevant authorised standard operating procedures (SOPs) which instruct storage of samples at 2-8°C upon receipt (SOPs VIR-LP-HBVSerol for HBV testing and VIR-LP-HEVSerol for Hep E testing).	**Minor**
GQ4 There is a systematic and planned approach to the management of records.		
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.	There is no procedure or written agreement with another HTA-licensed establishment to transfer traceability records and raw data in the event of termination of licensable activities.	**Minor**

Advice

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

No.	Standard	Advice
1.	GQ1b	The DI should review SOPs relating to receipt and storage of samples and ensure that staff are trained to carry out procedures in accordance with authorised protocols.
2.	GQ7a	The DI is advised to appoint Persons Designated at each site who are able to report serious adverse events and reactions (SAEARs) in the DI's absence and to notify the HTA of the appointments. The amended chain of personnel responsible for reporting SAEARs should be included in the staff training programme.
3.	GQ7a	The DI is advised to ensure that the service level agreement with another HTA-licensed establishment for provision of testing services is amended to include the stipulation for reporting serious adverse events and reactions to the HTA within 24 hours from the point of discovery 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.
4.	PFE5c	During the inspection at the UCLH serology laboratory, it was noted that one of the analysers was displaying an 'amber' alert. The HTA is satisfied following discussions with the laboratory staff that this was due to the routine use of uncapped tubes, as the analyser has been programmed only for use with capped tubes. However, the DI is advised to risk assess the routine use of the analyser in the 'amber' mode as should a problem arise that would warrant another 'amber' alert, staff may not be notified appropriately.

Concluding comments

The HTA saw examples of good practice during the course of the inspection. Staff at the establishment are knowledgeable and have a vast experience in screening procedures. The establishment has implemented practices to validate any new kits employed to assure themselves of the quality of services provided. The establishment has formed a cohesive quality management team with third parties and have together developed strong governance systems, which serve to safeguard the quality of testing services in the future.

Two areas of practice were identified during the inspection that require improvement, each resulting in minor shortfalls. These relate to the absence of contingency plans to ensure the maintenance of traceability records in the event of closure and to the storage of blood samples prior to testing. The HTA has given advice to the Designated Individual in relation to reviewing procedures, SAEARs reporting and equipment monitoring with the view to help the establishment further develop their working practices and governance systems.

The HTA requires that the Designated Individual address the shortfall 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 shortfall identified during the inspection.

Report sent to DI for factual accuracy: 11 January 2017

Report returned from DI: 30 January 2017

Final report issued: 01 February 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: 04 August 2017

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.
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.
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.
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.
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.
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.
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.
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.

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.
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.
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.

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.