Site visit inspection report on compliance with HTA minimum standards

Royal Devon and Exeter Hospital

HTA licensing number 12276

Licensed under the Human Tissue Act 2004 for the

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

8 & 9 February 2017

Summary of inspection findings

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

Although the HTA found that the Royal Devon and Exeter Hospital (the establishment) had met the majority of the HTA standards, two shortfalls were found in relation to governance meetings and adverse event management.

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

The HTA's regulatory requirements

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

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

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

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

Background to the establishment and description of inspection activities undertaken

This report refers to the research-related activities carried out by Royal Devon and Exeter Hospital (the establishment) under this HTA licence. The licence covers two premises: Royal Devon and Exeter Hospital at the Wonford Site (the hub, for the purposes of HTA licensing) and Royal Devon and Exeter Hospital at the Heavitree Hospital site (the satellite). The establishment has been licensed since 2007 and the last inspection was in 2012. This report describes the second routine site visit inspection of this establishment. Since the last inspection the establishment has greatly increased the number of sample collections stored under the licence.

The DI is the Operations and Finance Manager. The Corporate Licence Holder is Royal Devon and Exeter Hospital and the Corporate Licence Holder contact (CLHc) is the Research and Development Division Manager. The DI relies on Persons Designated (PDs) to manage all freezers. The PDs are split into junior and senior roles. A total of seven senior PDs manage freezers under the governance of the licence and nine junior PDs manage freezers which contain samples not under the governance of the licence, for example samples used in projects approved by an NHS research ethics committee (REC). The DI maintains oversight of all samples held in the establishment through the two levels of PD.

The establishment is on Royal Devon and Exeter Hospital NHS Foundation Trust premises and there is a formal partnership in place between the NHS and the University of Exeter.

University staff working at the establishment have honorary contracts with the NHS. The primary freezer store is in the Research Innovation Learning and Development (RILD) building, with an additional external store on the grounds. Research undertaken at the establishment facilitates biomarker discovery and clinical trials.

The DI has oversight of all relevant material stored at the establishment. To avoid storage of samples outside of the governance of this licence and in other areas of the hospital, the CLHc sends an annual email to all staff reminding them that storage of all relevant material must be covered under the arrangements for the HTA licence and governance of the DI.

Samples

Samples in the establishment have several origins: they may relate to projects which have ethical approval from a recognised REC; they may be held in a REC-approved Research Tissue Bank (RTB); or they may relate to projects which have University research ethics approval; or may have been imported.

Tissues are procured in the hospital from adults, children and cord blood. In addition, there is some tissue stored which was removed from the deceased before the implementation of the Human Tissue Act 2004. Tissue samples include fresh frozen tissue, bodily waste products (e.g. faeces), formalin-fixed paraffin wax-embedded material (blocks and sections on glass slides). Bodily fluids include urine, saliva and whole blood. There is a collection of samples which pre-date the HT Act which are catalogued and currently used in a research project which has approval from a recognised REC.

For samples stored under the HTA licence, consent for the storage and use of tissue for research is sought by hospital or University staff who have received Good Clinical Practice (GCP) training or local consent training (see Advice, item 3). Consent forms and participant information sheets for these sample collections have been approved by recognised RECs. The consent forms detail the study for which the samples are being collected and may include an enduring consent statement which allows samples to be transferred to the relevant RTB once the study has completed. Samples are only transferred to a RTB if consent has been given for this.

RTBs

There are five REC-approved RTBs at the establishment:

- Royal Devon and Exeter Tissue Bank;
- Peninsula Research Bank;
- Peninsula Twins Research Bank
- Genetic Beta Cell Bank; and
- Exeter Archival Diabetes Biobank.

These RTBs have generic ethical approval for collection, storage and release of tissue. Each RTB works directly under the establishment's HTA licence. The largest RTB is the Peninsula Research Bank. This RTB contains approximately 100,000 samples, from the living. Each registered RTB has the authority to release samples to researchers under the conditions of the REC approval.

Each RTB is managed on a day-to-day basis by a PD, who reports to the DI. The PD is responsible for ensuring sample traceability is maintained, freezers are appropriately monitored, and performing biannual audits.

A Steering Committee governs the RTBs. The committee reviews all applications for request for material and data. The committee members include the DI, clinicians, statisticians and lay

people. Samples from the RTBs may be released to Royal Devon and Exeter, UK and oversees researchers.

Sample management

Studies involving human tissue are catalogued on a database, which provides the ethical approval reference, the status of the study, if there is tissue remaining following the study, and whether there is consent to move the samples to an RTB once the research project has concluded. There are around 120 current research studies; approximately 10 studies due to close and 40 studies closed at the establishment. The database provides the relevant information to allow the DI to maintain oversight of samples due to enter an RTB, and hence be stored under the HTA licence (see Advice, item 9). A colour-coded map on the door of each freezer indicates whether the samples fall under the licence or not.

The establishment's PDs are responsible for sample management under the licence. An in-house tracking system has recently been installed and all new samples which may be stored under the HTA licence must be recorded on this system. A unique barcode and number is assigned to each sample, and all associated documentation and information is recorded on the database.

Samples which do not fall under the licence are managed by individual researchers. They are not required to be recorded on the in-house tracking system, however there is an expectation that a robust tracking system will be in place. All samples not under the licence are audited by researchers, however the audit results are not communicated with the DI.

The RTBs are located in three buildings, including one building at the satellite. The primary freezer store is located at the hub site and is monitored using the remote call out system which alerts the relevant PD. While alarm temperatures are monitored, the establishment does not formally test that the alarms function as expected and are responded to by staff (see Advice, item 11). Freezers are serviced twice each year and temperature probes are calibrated once each year. Staff at the establishment clean the freezers and maintain the filters regularly throughout the year.

An external freezer store at the hub site and the satellite are monitored using a second remote call out system. The system alerts switchboard in the event of a temperature deviation and the relevant PD will be contacted. These freezers are located in remote areas of the establishment and are not regularly accessed by staff (see Advice, item 12).

While the DI has good communication with the majority of PDs, there are no formal governance meetings with all PDs overseeing for human tissue collections (see Shortfall under GQ1).

Imported samples

There are three collections of imported material which include brain, pancreas and whole blood. These collections were inspected and audited during the site visit. Imported samples are stored under the licence, and there are material transfer agreements in place, and confirmation of appropriate consent for all samples.

Inspection process

The site visit inspection included a visual inspection of the storage areas and storage facilities, documentation review, and interviews with staff working under the licence. The Diabetes Tissue Bank Manager, Clinical Research Facility Technicians, Research Technicians, Nurse Managers and the Designated Individual were interviewed. A total of 24 audits were carried out during the site visit. Two anomalies were found during the audits: one blood sample was not recorded on the register as being present in the freezer; and one

sample traceability form had not been updated to reflect that one sample had been returned to the establishment (see Advice, item 6).

Inspection findings

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

However, the DI has breached one of the conditions of their licence. A copy of the licence certificate is not currently on display at the establishment. Standard condition eight of Annex B of the HTA licence mandates the following:

"A copy of the Certificate of Licence (first page of the licence) describing the activity authorised by the licence must be displayed at the premises to which the licence relates in a position or positions in which it can be read easily by persons who are involved in the carrying out of the licensed activity or providing relevant material for use for the purpose of activities governed by the Act, or who may wish to do so."

This breach must be rectified with immediate effect and notified to the HTA.

Compliance with HTA standards

Governance and Quality

Standard	Inspection findings	Level of shortfall
GQ1 All aspects of the establishment's work are supported by ratified documented policies and procedures as part of the overall governance process.	While the DI meets with the majority of the PDs regularly on an informal basis, there are no formal meetings where issues, including incidents, audits and CAPAs, relating to the HTA licence can be discussed.	**Minor**
GQ7 There are systems to ensure that all adverse events are investigated promptly.	The establishment has a number of ways that incidents could be reported, however the procedure for reporting incidents relating to activities under the HTA licence has not been formalised. There is no standard operating procedure (SOP) detailing what an incident relating to relevant material would be, or the appropriate manner to escalate.	**Minor**

Advice

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

No.	Standard	Advice
1.	C1	The consent form used for seeking consent for the TWINS study contains an additional yes/no field which is not linked with a question. The DI is advised to review this form to remove this box to ensure that the form is clear.

2.	C2	The consent SOP does not include information about ensuring that consent is obtained in accordance with the requirements of HT Act, does not detail the methods through which a participant can withdraw their consent, and it is not clear that a translator should sign the consent form when their services have been used. This SOP should be reviewed and updated to ensure those seeking consent have sufficient information. The DI is advised to include information in the consent SOP that details a central address and telephone number of the relevant party to contact should the participant wish to withdraw their consent.
3.	C3	The DI is advised to review the consent training provided to ensure that those seeking consent are aware of the requirements of the HT Act. The Clinical Nurse Orientation Research Pack includes information on GCP, however it does not refer to the HTA. Providing a specific training package on the requirements of the HT Act would raise awareness of the requirements when seeking consent, and ensure that appropriate and fully informed consent is sought.
4.	GQ1	While SOPs are adequately detailed, they should be reviewed in line with the new codes and standards, and particular attention should be paid to typographical errors, inaccuracies and clarity. For example, the term 'relevant material' is frequently used to differentiate between samples under the licence and those exempt from the licensing requirements of the HT Act by virtue of project-specific REC approval from a recognised REC. The DI should review these documents to ensure that staff working under the licence are clear about the definition of relevant material and the licensing requirements under the HT Act.
5.	GQ1	The HTA logo currently appears on the form used to indicate whether relevant material is stored in the freezers. The HTA does not permit the use of its logo in documents they have not been involved in creating. The DI is asked to remove the HTA logo from all documentation with immediate effect. The HTA's logo and branding policy can be found on the HTA website: www.hta.gov.uk/policies/hta-logo-and-branding-policy
6.	GQ2	While there are documented policies and procedures in place, the system to ensure version control should be strengthened. For example, the document used to record samples in the freezers is not dated or version controlled. In addition, during an audit it was noted that an old form was being used to log the storage location of a sample and this resulted in the sample not being located initially.
7.	GQ2	Although regular audits are carried out, the corrective and preventative actions are not captured in a dedicated section of the form which includes information on deadlines and completions, or circulated amongst PDs. The DI should create a separate form which includes deadlines and closure statements and use it to share learning amongst PDs.
8.	GQ3	New staff working in the RILD building must complete an induction provided by the Facilities Manager. Those accessing freezers have an HTA induction. The DI is advised that the induction for all staff should include information about the HT Act to raise awareness of the requirements of the HT Act and regulatory framework.
9.	GQ6	The establishment implemented a system of recording all projects using relevant material in November 2016. The DI is advised to ensure this record is

		up to date and that the expiry date of each project-specific REC approval is recorded. This will ensure that the DI has oversight of all samples that will need to be stored under the licence once project-specific REC approval expires.
10.	GQ8	While risk assessments are in place, the DI should expand the risks assessed to include the following: • receiving and/or storing specimens without appropriate consent documentation; • storing or using human tissue after consent withdrawal; and • incorrect disposal. Risk assessments should be reviewed periodically (typically, every 1-3 years) and the actions to mitigate risks updated as necessary. Risk assessments should also be reviewed following an incident. By documenting risk assessments, staff are made aware of identified risks, which helps to prevent risks materialising and informs the development of procedures and relevant documentation.
11.	PFE3	All freezers are linked to call out systems which alert relevant staff to any deviations in temperatures beyond the set limits. The alarm systems are maintained and calibrated on a yearly basis, however no formal testing of the alarm systems is undertaken. In addition, temperature records are not reviewed for trends. The DI should implement a formalised system where alarms are tested to ensure the procedure works. Reviewing temperature records on a regular basis may anticipate a freezer failure.
12.	PFE3	One freezer store at the hub and the satellite site are located in areas not regularly accessed by staff. To ensure alarms are responded to out of hours, should the remote call out systems fail, the DI is advised to formalise an agreement with nearby departments who may hear an alarm sounding. In addition, the relevant contact details should be added to the doors of both buildings so that staff working in these areas are aware of who to contact in the event of an alarm sounding.
13.	PFE3	The establishment also stores a range of biological material. To avoid the risk of sample confusion, and to ensure that human tissue samples are handled in line with the regulatory requirements under the HT Act, the DI should assure herself that all freezers and containers holding human tissue are labelled appropriately.
14.	D2	When material is disposed of, the reason for disposal is recorded on the disposal log. This is not reflected in the SOP, and as such, should be updated.

Concluding comments

During the inspection a number of areas of good practice were noted, including good working relationships between the DI and the PDs, and the considered nature of the consenting process for providing samples to the RTBs, including the time for participants to read the patient information sheets prior to formal consent discussions. In addition, a robust sample tracking system, which has been designed in-house, allows for easy location of all samples, and associated documentation, including the consent documents.

There are a number of areas of practice that require improvement, including two minor shortfalls. The HTA has given advice to the Designated Individual with respect to improving

documentation for consent, document version control, updating SOPs and risk assessments, as well as licence management.

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: 28 February 2017

Report returned from DI: 08 March 2017

Final report issued: 20 March 2017

Completion of corrective and preventative actions (CAPA) plan

Based on information provided, the HTA is satisfied that the establishment has completed the agreed actions in the CAPA plan and in doing so has taken sufficient action to correct all shortfalls addressed in the Inspection Report.

Date: 22 May 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.

Consent standards
C1 Consent is obtained in accordance with the requirements of the Human Tissue Act 2004 (HT Act) and as set out in the code of practice
• Consent forms comply with the HTA's Code of Practice • Consent forms are in records and are made accessible to those using or releasing relevant material for a scheduled purpose • If the establishment obtains consent, a process is in place for acquiring consent in accordance with the requirements of the HT Act 2004 and the HTA's Codes of Practice • Where applicable, there are agreements with third parties to ensure that consent is obtained in accordance with the requirements of the HT Act 2004 and the HTA's Codes of Practice • Consent procedures have been ethically approved
C2 Information about the consent process is provided and in a variety of formats
• Standard operating procedures (SOPs) detail the procedure for providing information on consent • Agreements with third parties contain appropriate information • Independent interpreters are available when appropriate • Information is available in suitable formats, appropriate to the situation • Consent procedures have been ethically approved
C3 Staff involved in seeking consent receive training and support in the implications and essential requirements of taking consent
• Standard operating procedures (SOPs) detail the consent process • Evidence of suitable training of staff involved in seeking consent • Records demonstrate up-to-date staff training • Competency is assessed and maintained

Governance and quality system standards
GQ1 All aspects of the establishments work are supported by ratified documented policies and procedures as part of the overall governance process
• Policies and procedures are in place, covering all activities related to the storage of relevant material for research in connection with disorders, or the functioning, of the human body • Appropriate risk management systems are in place

- Regular governance meetings are held; for example, health and safety and risk management committees, agendas and minutes
- Complaints system

GQ2 There is a documented system of quality management and audit

- A document control system, covering all documented policies and standard operating procedures (SOPs).
- Schedule of audits
- Change control mechanisms for the implementation of new operational procedures

GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills

- Qualifications of staff and training are recorded, records showing attendance at training
- Orientation and induction programmes
- Documented training programme, (e.g. health and safety, fire, risk management, infection control), including developmental training
- Training and reference manuals
- Staff appraisal / review records and personal development plans are in place

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

- Documented procedures for the creation, amendment, retention and destruction of records
- Regular audit of record content to check for completeness, legibility and accuracy
- Back-up / recovery facility in the event of loss of records
- Systems ensure data protection, confidentiality and public disclosure (whistle-blowing)

GQ5 There are documented procedures for distribution of body parts, tissues or cells

- A process is in place to review the release of relevant material to other organisations
- An agreement is in place between the establishment and the organisation to whom relevant material is supplied regarding the tracking and use of material and eventual disposal or return

GQ6 A coding and records system facilitates traceability of bodies, body parts, tissues and cells, ensuring a robust audit trail

- There is an identification system which assigns a unique code to each donation and to each of the products associated with it
- An audit trail is maintained, which includes details of when and where the relevant material was acquired, the consent obtained, the uses to which the material was put, when the material was transferred and to whom

GQ7 There are systems to ensure that all adverse events are investigated promptly
• Corrective and preventive actions are taken where necessary and improvements in practice are made • System to receive and distribute national and local information (e.g. HTA communications)
GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately
• Documented risk assessments for all practices and processes • Risk assessments are reviewed when appropriate • Staff can access risk assessments and are made aware of local hazards at training

Premises, facilities and equipment standards
PFE1 The premises are fit for purpose
• A risk assessment has been carried out of the premises to ensure that they are appropriate for the purpose • Policies in place to review and maintain the safety of staff, authorised visitors and students • The premises have sufficient space for procedures to be carried out safely and efficiently • Policies are in place to ensure that the premises are secure and confidentiality is maintained
PFE 2 Environmental controls are in place to avoid potential contamination
• Documented cleaning and decontamination procedures • Staff are provided with appropriate protective equipment and facilities that minimise risks from contamination • Appropriate health and safety controls are in place
PFE3 There are appropriate facilities for the storage of bodies, body parts, tissues and cells, consumables and records.
• Relevant material, consumables and records are stored in suitable secure environments and precautions are taken to minimise risk of damage, theft or contamination • Contingency plans are in place in case of failure in storage area • Critical storage conditions are monitored and recorded • System to deal with emergencies on 24 hour basis • Records indicating where the material is stored in the premises

PFE 4 Systems are in place to protect the quality and integrity of bodies, body parts, tissues and cells during transport and delivery to a destination
• Documented policies and procedures for the appropriate transport of relevant material, including a risk assessment of transportation • A system is in place to ensure that traceability of relevant material is maintained during transport • Records of transportation and delivery • Records are kept of any agreements with recipients of relevant material • Records are kept of any agreements with courier or transport companies
PFE5 Equipment is appropriate for use, maintained, quality assured, validated and where appropriate monitored
• Records of calibration, validation and maintenance, including any agreements with maintenance companies • Users have access to instructions for equipment and receive training in use and maintenance where appropriate • Staff aware of how to report an equipment problem • Contingency plan for equipment failure

Disposal Standards
D1 There is a clear and sensitive policy for disposing of human organs and tissue
• Documented disposal policy • Policy is made available to the public • Compliance with health and safety recommendations
D2 The reason for disposal and the methods used are carefully documented
• Standard operating procedures (SOPs) for tracking the disposal of relevant material detail the method and reason for disposal • Where applicable, disposal arrangements reflect specified wishes

Appendix 2: Classification of the level of shortfall

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

   or

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

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

   (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 that:

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

   or

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

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

3. **Minor shortfall:**

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

This category of shortfall requires the development of a corrective action plan, the results of which will usually be assessed by the HTA either by desk based or site visit.

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

Follow up actions

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

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

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

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