Site visit inspection report on compliance with HTA minimum standards

Leicester Royal Infirmary

HTA licensing number 12384

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**

6 - 8 September 2016

Summary of inspection findings

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

Although the HTA found that Leicester Royal Infirmary (the establishment) had met the majority of the HTA standards, one minor shortfall was found with regard to the Premises, Facilities and Equipment (PFE) standards. It was in relation to weaknesses in storage temperature monitoring. Advice has been given relating to the Consent, Governance and Quality Systems and PFE standards, as well as to licence management.

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 (DI), Licence Holder (LH), premises and practices are suitable.

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

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

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

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

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

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

Background to the establishment and description of inspection activities undertaken

This report refers to the activities carried out by Leicester Royal Infirmary (the establishment). The establishment's licensing arrangements cover Leicester Royal Infirmary itself - the hub site - and two satellite sites (Glenfield General Hospital, satellite 1; the University of Leicester, satellite 2). The establishment was issued an HTA licence in November 2006 and was last inspected by the HTA in May 2011. The current inspection was a routine site visit to assess whether the establishment is continuing to meet the HTA's standards.

The establishment is licensed under the Human Tissue Act 2004 (HT Act) for the storage of relevant material for use for a scheduled purpose. In this case, relevant material from living and, occasionally, deceased donors is being stored for the scheduled purposes of: obtaining scientific or medical information about a living or deceased person which may be relevant to any other person (including a future person); research in connection with disorders, or the functioning, of the human body; education or training relating to human health; and quality assurance.

The DI supervising activities taking place under the licence is a Professor of Allergy and Respiratory Medicine, the (Corporate) LH (CLH) is the University of Leicester and the CLH Contact (CLHC) is the University Registrar. There are four Persons Designated (PDs) working under the licence: one at the hub, two at satellite 1 and one at satellite 2.

The establishment's licensed tissue collections are held by the College of Medicine, Biological Sciences and Psychology. This comprises eight University Departments, two National Institute for Health Research Biomedical Research Units (NIHR BRUs), two charity-

funded research centres and one unit funded by the Medical Research Council (MRC). Licensed tissue collections include: three Research Tissue Banks (RTBs); sample sets previously stored under NHS Research Ethics Committee (REC) project-specific approval (or those previously stored as part of UK Ethics Committee Authority, UKECA-approved clinical trials) where the approval has now expired; sample sets stored under the University of Leicester Ethics Committee approval; and imported samples. Sample sets stored under current REC or UKECA approval do not fall under the HTA licence.

Sample sources

Samples originate from adults, children and foetuses and include both tissue and bodily fluids. Tissue samples include formalin-fixed, paraffin wax-embedded material (blocks and sections on glass slides), isolated cellular preparations (e.g. peripheral blood mononuclear cells), fresh frozen tissue and frozen tissue sections on glass slides. Bodily fluids include urine, saliva and whole blood. In total, there are approximately 123,000 samples stored under the licence.

Samples are obtained from surgical operations within the adjacent University Hospitals of Leicester NHS Trust (the Trust), from the Trust diagnostic pathology archives and from healthy volunteers (students and staff) within the University of Leicester. Samples are also received from collaborators both within and outside the UK.

Consent is sought by University or Trust staff, who have received either Good Clinical Practice (GCP) training or consent training provided by the Trust Department of Research and Innovation. There are no agreements between the establishment and the Trust for tissue collection (*see Advice item 2*). The establishment uses project-specific or RTB consent forms and participant information sheets.

When tissue is provided by outside organisations, there are no agreements for tissue collection at present (*see Advice item 7*).

The hub site

The hub licence covers the University's Robert Kilpatrick Clinical Sciences Building based within the Leicester Royal Infirmary site of the Trust. Licensed tissue collections are those of the Departments of Cancer Studies, Cardiovascular Sciences, Genetics, Health Sciences, Molecular and Cell Biology, and Neuroscience Psychology and Behaviour. The Cancer Research UK Cancer Centre is also based here.

There are two RTBs (one containing solid tumours and one containing haematological malignancies) and 30 licensed sample sets. There are approximately 104,000 samples stored under the licence at this site.

Storage at the hub site. Samples are stored at room temperature, in -20°C and -80°C freezers, and in liquid nitrogen storage vessels (cryovessels). All freezers, apart from ten -80°C freezers in one area of the building (*see Shortfall under PFE3*), are linked to a continuous temperature monitoring unit which feeds into a wireless callout system. Temperature excursions outside the set ranges trigger both audible alarms and the callout system and the system is tested regularly. Labels on the freezers indicate steps to be taken if the audible alarms sound but these are out of date (*see Advice item 4*).

There are two liquid nitrogen storage areas. In neither area are the cryovessels linked to the continuous temperature monitoring system (*see Shortfall under PFE3*).

Satellite 1

This satellite licence covers the NIHR BRU Building, which houses the NIHR Leicester Respiratory and Cardiovascular BRUs, as well as covering 'embedded space' within the Trust. Tissue collections at satellite 1 are those of the Departments of Cardiovascular

Sciences and Infection, Immunity and Inflammation. As well as the two NIHR BRUs, the British Heart Foundation Cardiovascular Research Centre is also based here.

There are 11 licensed sample sets, including two imported sample sets. There are approximately 19,000 samples stored under the licence at this site.

Storage at satellite 1. Samples are stored at room temperature and in -20°C and -80°C freezers. All freezers are linked to the continuous temperature monitoring system. As with the hub site, labels on the freezers are out of date (*see Advice item 4*).

Satellite 2

This satellite licence covers the Hodgkin Building on the University campus, which houses the MRC Toxicology Unit.

There are four licensed sample sets. There are approximately 200 samples stored under the licence at this site.

Storage at satellite 2. Samples are stored at room temperature and in -80°C freezers. All freezers are linked to the continuous temperature monitoring system. As with the hub site, labels on the freezers are out of date (*see Advice item 4*).

Governance and record management

The establishment is working towards a model whereby all tissue collections are managed by individual PDs. Each collection will contain several sample sets and will cover the work of different principal investigators and research groups. Researchers will maintain paper and electronic records for their specific sample sets and PDs will have an overall record of sample sets within their collection (*see Advice item 1*).

The inspection process

The timetable for the site visit inspection was developed after consideration of the establishment's previous inspection report, compliance update information and communications with the DI. The inspection included a visual inspection of the laboratories and storage areas, discussions and interviews with key staff, and a review of documentation. Interviews were held with the DI, three PDs, the HTA Governance Officer, the Chair of the HTA Committee, the haematological malignancy RTB custodian and the Cardiovascular Sciences Departmental Manager. Audits of traceability were also carried out:

Audits at the hub. Six audits were carried out. 11 representative samples were randomly selected from the -80°C freezers, cryovessels or from room temperature storage, and labelling details were compared to paper and electronic records. The corresponding consent forms and consent training records of those who had sought consent were also examined. No discrepancies were noted.

Audits at satellite 1. Four audits were carried out. Seven representative samples were randomly selected from the -20°C and -80°C freezers or from room temperature storage. One discrepancy in one sample set was noted (in the NIHR Leicester Respiratory BRU). The number of slides cut from each of the two blocks was not recorded (*see Advice item 8*).

Audits at satellite 2. Three audits were carried out. Five representative samples were randomly selected from the -80°C freezers or from room temperature storage. No discrepancies were noted.

Inspection findings

The HTA found the DI and the CLH 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
PFE3 There are appropriate facilities for the storage of bodies, body parts, tissues, cells, consumables and records.	During the inspection it was noted that the continuous temperature monitoring system does not cover two liquid nitrogen storage areas and one freezer area at the hub. Although temperatures of the freezers and cryovessels in these areas are monitored, there is no temperature monitoring at weekends or during vacation periods. The freezers and cryovessels in these areas have audible alarms but the set ranges for the alarm system are not documented and the audible alarm system is not routinely tested. There is no documented procedure indicating steps to be taken if the audible alarm sounds. The establishment has not risk assessed the current arrangements for monitoring and recording temperatures and the effects that storage temperature deviations would have on the quality of samples stored.	**Minor**

Advice

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

No.	Standard	Advice
1.	N/A	The DI is advised to consider identifying further PDs at the hub site and to notify the HTA of such appointments. Appointing PDs will help to ensure that all tissue collections remain within the establishment's overall governance arrangements.
2.	C1	The DI is advised to consider putting in place an agreement between the Trust and the establishment to cover the seeking of consent by clinical staff. This will provide assurance that all samples for research have been obtained with appropriate and valid consent.
3.	GQ1	The Governance Officer has created a generic template for standard operating procedures (SOPs). The DI is advised to ensure that this template is used by PDs, principal investigators and researchers so that there is consistency in practices.
4.	GQ2	Several documents have passed their review date. These include: Trust policies (Data Protection, Freedom of Information, Whistleblowing); Departmental Induction Packs and Safety Manuals; freezer labels. The DI is advised to ensure that all SOPs, forms, labels and notices are included in the establishment's document control system.

5.	GQ2	The Governance Officer has carried out a high-level audit and gap analysis against HTA standards at each site. The Governance Officer has also created a generic audit template. The DI is advised to ensure that this template is used by PDs, principal investigators and researchers so that all samples and activities associated with each tissue collection are comprehensively covered. Types of internal audit carried out could include horizontal audits, to ensure that SOPs accurately reflect current practices, and vertical traceability audits, from records of consent and receipt to storage, use, distribution or disposal.
6.	GQ4	The Governance Officer has developed a master register of all licensed sample sets. The DI is advised to consider incorporating sample sets currently under REC and UKECA approval into the register, so that expiry dates of ethically-approved projects can be monitored.
7.	GQ5	Other licensed establishments have set up a register of 'approved suppliers'. Each potential supplier is sent a 'due diligence form', asking for details of governance structure, ethical approval, ethical warranties, informed consent forms, consent warranties and regulatory compliance (where appropriate). A Material Transfer Agreement (MTA) is then drawn up with each organisation using these criteria as the supplier's responsibilities. The DI is advised to consider adopting a similar approach.
8.	GQ6	Although only one discrepancy was found in 13 audits, the DI is advised to ensure that the number of slides cut from each block is recorded in all cases and that this is documented.
9.	GQ7	Staff are familiar with the process for reporting adverse advents but there is no SOP for identifying, recording and following up adverse events associated with sample receipt, storage, use, distribution or disposal. Although there is currently no requirement for establishments in the research sector to report adverse incidents to the HTA, if a DI has concerns about an adverse event, they are encouraged to contact the HTA for further advice. Relevant examples of adverse events include: • specimen loss • loss of specimen integrity (e.g. broken packaging) • missing or incorrect documentation • security breach • abnormalities in storage temperature readings • inappropriate disposal.
10.	GQ8	The Governance Officer has carried out a high-level risk assessment using a suite of risk assessments at each site. The Governance Officer has also created a generic template for risk assessments. The DI is advised to ensure that this template is used by PDs principal investigators and researchers so that all tissue collections have been suitably risk assessed.
11.	PFE2	The DI is advised to consider recording the cleaning and decontamination of all freezers and cryovessels and to document this procedure.

12.	PFE3	The DI is advised to consider labelling cabinets, freezers and cryovessels which contain human tissue to prevent sample mix-ups and to ensure staff are aware of the need to manage these samples in line with the regulatory requirements.
13.	PFE3	The DI is advised to ensure that there are documented contingency plans in the event of individual freezer or cryovessel breakdown, and that there is plan for premises failure.

Concluding comments

During the inspection, areas of good practice were noted:

- There is a HTA Committee, consisting of the University Director of Operations, both University of Leicester DIs and all PDs and other senior staff, which meets every three months.
- There is a systematic approach to staff competence training. The Governance Officer has set up a matrix to track staff training and to record familiarity and understanding of SOPs and risk assessments.
- The MRC 'Research and Human Tissue Legislation e-learning Module' is included in the training programme for all staff.
- The Governance Officer has made good progress in generating a comprehensive system of governance at all the sites. Template SOPs, audits and risk assessments are being used by each PD to document tissue collections, local practices and procedures, audits and training records. These are then held by each PD in 'master files' and are available to the DI, if required.

There are a number of areas of practice that require improvement, including one minor shortfall. The HTA has given advice to the DI with respect to the Consent, Governance and Quality Systems and Premises, Facilities and Equipment standards, as well as to licence management.

The HTA requires that the DI addresses 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 shortfalls identified during the inspection.

Report sent to DI for factual accuracy: 04 October 2016

Report returned from DI: 16 October 2016

Final report issued: 10 November 2016

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: 23 November 2017

Appendix 1: HTA standards

The HTA standards applicable to this establishment are shown below. 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 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.