Site visit inspection report on compliance with HTA minimum standards

NIHR-National Biosample Centre

HTA licensing number 12624

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**

22 October 2015 and 9 November 2015

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.

NIHR-National Biosample Centre (the establishment) was found to have met all HTA standards. Advice has been given relating to the Governance and Quality Systems (GQS) and Disposal (D) standards, as well as to licence 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 (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 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 activities carried out by the National Institute of Health Research (NIHR) - National Biosample Centre (the establishment). The establishment's licensing arrangements cover the hub site (based at Java Park, Milton Keynes) and the satellite site (based at Osney Mead, Oxford). The hub and satellite have separate nominated Persons Designated (PDs) who report to the DI.

NIHR - National Biosample Centre was opened in January 2015 with the aim of providing high throughput biosample processing, storage and retrieval services for research groups throughout the UK. It has the capacity to store up to 20 million samples and was funded with a grant from the Department of Health (DH) to the University of Oxford. 10 staff are currently employed.

The establishment is licensed by the HTA under the Human Tissue Act 2004 for the storage of relevant material for use for scheduled purposes. The scheduled purposes applicable to this licence are: 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 ('research'); and, quality assurance. This was the first site visit inspection of the establishment since it was issued a HTA licence in November 2014. It was a routine inspection, to assess whether the establishment is continuing to meet the HTA's standards.

The hub site

The hub site is a 55,000 square foot light industrial unit that houses the plant, offices, sample processing and sample storage areas. Entry and exit points are monitored by CCTV and there is electronic access control. There are out-of-hours intruder alarm systems. Lone working and out-of-hours unaccompanied access occasionally occur and there are procedures to cover these activities.

The establishment currently stores approximately 500,000 samples, all at the hub site. Stored relevant material includes blood, buffy coat layer, saliva and urine samples, all from living donors.

Processing. The sample processing area contains three high-throughput fully automated robotic liquid handling modules for sample aliquoting and blood counting. A second laboratory is configured for high-throughput nucleic acid extraction and contains three automated DNA and two automated RNA extraction modules. There is a separate area for nucleic acid amplification containing 10 machines.

Storage. The establishment stores customers' samples using its own storage facilities and also provides space to accommodate the customer's own storage equipment.

The establishment has six fully automated -80°C robotic storage archive modules and two -20°C modules. There are also has two vapour phase liquid nitrogen storage vessels. All freezers and liquid nitrogen tanks are linked to a data-logged, continuous temperature monitoring facility which feeds into a wireless callout system. Temperature excursions outside the set ranges trigger both audible alarms and the wireless callout system. Power failure to the storage facilities also triggers the alarms and the call-out system. The system is tested regularly.

The liquid nitrogen storage area contains fixed oxygen depletion monitors and staff carry portable monitors. The monitors are linked to an alarm system. There is an automatic cryofilling system for the tanks. Failure of the cryofilling system triggers the audible alarms and the wireless callout system.

There are emergency back-up freezers and liquid nitrogen storage vessels as well as offsite facilities in the event of complete facility failure.

The storage area for customer freezers currently houses twenty -80°C freezers. These are also linked to the wireless callout system.

Sample management. The establishment sets up a service contract with each new customer. The contract ('statement of work') provides assurance that informed donor consent has been given for each sample and that ethical approval has been obtained. The establishment currently has contracts with UK Universities, NHS Trusts, Research Institutes, charities and DH.

Individual samples are received into the establishment in validated transport containers and are logged into the establishment's electronic database. Samples are given unique identifiers by the establishment. There is an integrity check of each sample and a check of the temperature of the shipment packaging. Non-conformances are dealt with by a specific procedure.

Samples received in customer freezers remain untouched and are not logged into the electronic system unless specifically agreed.

Samples are sent out from the establishment to customers in dry shippers and there is a procedure for confirmation of order and receipt.

Electronic management. Individual samples are logged into the database with key data and information on their location in the storage facility. The database is updated as samples are

used, depleted or destroyed. The database is backed up regularly on the main servers. In some cases customers also have limited access to their own samples from their desk via a web-based sample management tool. This enables users to view and manage their collections and to request withdrawal, shipping or specific assays (e.g. DNA extraction).

The satellite site

The satellite site is a 14,500 square foot light industrial unit with similar security arrangements to those of the hub site. It has the capacity to store 140 vapour phase liquid nitrogen storage vessels. Arrangements for temperature monitoring, oxygen depletion and cryofilling are the same as those of the hub site. The satellite also has documented contingency arrangements for complete storage failure.

The inspection process

The timetable for the site visit inspection was developed after consideration of the establishment's licence application, compliance update information and discussions with the DI. The site visit inspection included a visual inspection of the storage areas and storage facilities for tissue and records.

Meetings were held with staff working under the licence. They were: the DI (Chief Executive Officer); the PDs ((i) Hub - Biorepository Site Director; (ii) Satellite - Laboratory Director); the Database Manager; two Quality Managers; and a Project Manager.

A documentation review and two vertical audits were carried out; details of these are provided below. For both audits the establishment was blinded in order to fully test the system.

In the first audit, the patient identifiers of five consented samples, along with scanned consent forms, were provided by the Principal Investigator (PI) of one of the studies. These were traced on the establishment's database to the location in the relevant liquid nitrogen storage vessel.

In the second audit, five samples were chosen at random from a second study and were traced from their location in the liquid nitrogen storage vessel to the database and to the consent documentation held by the PI.

There were no discrepancies in either audit.

Inspection findings

The HTA found the DI and the (Corporate) LH (CLH) to be suitable in accordance with the requirements of the legislation.

Compliance with HTA standards

All applicable HTA standards have been assessed as fully met.

Advice

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

No.	Standard	Advice
1.	N/A	The current CLH Contact (CLHC) is also the DI. A new CLHC needs to be appointed who would be senior enough to be able to substitute the DI, if necessary.
2.	GQ2	The DI is advised to modify the existing audit schedule to include vertical audits of tissue traceability.
3.	GQ3	The DI may wish to consider including the Medical Research Council

		'Research and Human Tissue Legislation e-learning Module', which was developed with input from the HTA, as part of the staff training programme.
4.	GQ4	It was noted that the refrigerator temperature recording form contains the freezer temperature limits. This should be modified.
5.	D2	The DI should ensure that the reason for disposal of each tissue sample is recorded and that the necessity for recording the reason is included in the relevant standard operating procedure.

Concluding comments

During the inspection several areas of strength and good practice were noted:

- The DI is well supported in his role by the PDs and together they have good oversight of licensable activities.
- There is a detailed suite of risk assessments covering all activites relating to the receipt, storage, use, transfer and disposal of human tissue.
- The premises and storage facilities are well-maintained and there are comprehensive temperature monitoring and alarm call-out procedures for storage units at the establishment.

The HTA has given advice to the DI with respect to the Governance and Quality Systems and Disposal standards, as well as to licence management.

The HTA has assessed the establishment as suitable to be licensed for the activities specified.

Report sent to DI for factual accuracy: 7 December 2015

Report returned from DI: 8 December 2015

Final report issued: 22 December 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 marked as '**N/A'**.

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 N/A
• Standard operating procedures (SOPs) detail the consent process **N/A** • Evidence of suitable training of staff involved in seeking consent **N/A** • Records demonstrate up-to-date staff training **N/A** • Competency is assessed and maintained **N/A**

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.