Site visit inspection report on compliance with HTA minimum standards

London Neurodegenerative Diseases Brain Bank

HTA licensing number 12293

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**

12 May 2016

Summary of inspection findings

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

Although the London Neurodegenerative Diseases Brain Bank was found to have met most of the HTA standards, three minor shortfalls were identified in respect of the GQ1 (documentation), GQ6 (traceability) and GQ8 (risk assessments).

The establishment was provided with advice and guidance about areas that could be improved further. 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 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 describes the second site visit inspection of the London Neurodegenerative Diseases Brain Bank (''the Brain Bank'') located at the Institute of Psychiatry, Psychology and Neuroscience, King's College London. The brain bank has been licensed by the HTA since 2007 and stores whole brain, spinal cord and cerebrospinal fluid; it also has approval to operate as research tissue bank (RTB) from a NHS research ethics committee (REC). Also under this licence, a second RTB - the 'National institute for Health Research (NIHR) Biomedical Research Centre (BRC) BioResource for Mental and Neurological Health'' (''the BioResource'') - operates under a separate NHS REC approval and stores a range of relevant material, including urine, faeces, blood and saliva.

At the time of the inspection, the Brain Bank had initiated transferring all specimens across to a different building located within the Institute of Psychiatry, Psychology and Neuroscience, King's College London. The visual inspection included a review of the tissue receipt and transport procedures, all tissue storage areas and traceability audits of the two tissue bank collections. The inspection also included, document review and interviews with key staff involved in licensable activities.

London Neurodegenerative Diseases Brain Bank

The brain bank persons designated (PDs) are responsible for seeking consent for brain donation in the bank. All prospective donors are assigned a unique number at the time of giving their consent and a register of consent is maintained on the database. When a donor dies, the brain bank will be notified. The brain bank PD receives requests from researchers to access the tissue and such requests are reviewed by the 'Tissue Request Committee'. Once approval is given, a material transfer agreement (MTA) is set up by the contracts team at the University before any tissue is transferred.

The establishment has agreements in place with mortuaries in the local area and the donor will be transferred from the place of death to the mortuary by funeral directors. Once the brain is removed, a specialist medical courier will transport the material from the mortuary to the establishment in a transport box containing cool packs. The brain bank PD will receive the material and assign a unique reference number, known as the 'autopsy number', to the brain and spinal cord. This unique number will link to the donor, wet tissue and blocks and slides. A neuropathologist will separate the whole brain into its two hemispheres (left and right); one of which will be formalin fixed and the other frozen. Tissue blocks are created from the formalin fixed hemisphere and are used to confirm a diagnosis. Once a diagnosis is confirmed the fixed tissue will be stored in the brain bank. Researchers are provided with small amounts of tissue for research purposes. In terms of the frozen hemisphere, approximately 50 or more samples can be made.

There are sixteen -80^{0}C freezers storing frozen brain samples in a dedicated purpose-built area which is access controlled. The critical storage conditions are continuously monitored using an electronic software system. An audible alarm will sound if the freezer temperatures go outside of set parameters and staff members will be notified through an automated dial-out system. Security staff will patrol the area out of hours and this provides an additional measure to prevent a freezer failure going unnoticed. However, the freezers are not subject to routine testing (see Advice item 7) to ensure that the alarm system is functioning correctly. Furthermore the brain bank has two empty freezers for contingency purposes.

A forward traceability audit was carried out. Two specimens in freezer storage were identified and traced back to the brain bank database, consent forms and paperwork. For one of the specimens, the wet brain tissue had been disposed of and evidence of this was seen in the disposal logs. Furthermore, the audit trail for this specimen also focussed on the release of two tissue slides to researchers as well as the tissue blocks in storage. No discrepancies were identified. For the other specimen, there was a discrepancy between the number of blocks in storage and the number of blocks documented in the brain bank database and corresponding paperwork (minor shortfall, GQ6). The traceability audit for this specimen included the wet tissue. No other discrepancies were identified.

A reverse traceability audit was carried out. A donor was identified using the brain bank database and the consent form and corresponding paperwork were reviewed. The frozen samples of the brain were in the correct location and evidence that the wet tissue had been transferred to the local hospital for diagnosis was also seen. No discrepancies were identified.

NIHR BRC BioResource for Mental and Neurological Health

The BioResource is a distinct collection of tissue and bodily fluid samples for research into mental and neurological health. Samples are obtained from living donors, both adults and children. The donors are recruited from outpatient clinics and wards at hospitals specialising in the disease area and will give consent to donate tissue samples or bodily fluids. Age-appropriate information sheets and consent forms are used as children may also be approached to donate tissue samples. In the event that a donor decides to withdraw consent, there are mechanisms in place to remove and dispose of stored tissue samples.

There are two PDs for the BioResource, one with the responsibility for overseeing a team of staff involved in recruitment and consent, the other with the responsibility of overseeing management of tissue within the BioResource. The BioResource is managed by a 'senior advisory board', which reviews all requests for material and for associated data from the BioResource. Applications to the BioResource have come from researchers both within the University and outside. There are template access request forms to the BioResource, along with project initiation forms, which provide a summary of the project to ensure that it is within the remit of the BioResource.

The BioResource contains tissue and fluid specimens from approximately 18,000 donors. Collections include samples from people with schizophrenia, bi-polar affective disorder, depressive disorder, attention deficit hyperactivity disorder, epilepsy, Alzheimer's disease, motor neurone disease and Parkinson's disease. Samples include whole blood, urine, cerebrospinal fluid (CSF), peripheral blood mononuclear cells (PBMCs), saliva, and faeces. Electronic management of the BioResource is currently undertaken using two separate systems and the establishment is moving to an improved quality system. The BioResource also has laboratory facilities and provides a DNA/RNA extraction service and cytokine analysis to other users within KCL.

There are fifteen -80^{0}C freezers storing samples for the BioResource. The critical storage conditions are also monitored using an electronic software system. An audible alarm will sound if the freezer temperatures go outside of set parameters and staff members will be notified through an automated dial-out system. However, like the Brain Bank, the freezers are not subject to routine testing to ensure that the alarm system is functioning correctly. In addition, there are separately eleven -80^{0}C freezers storing samples for projects with active NHS REC approval (see Advice item 3).

Traceability audits were carried out using six tissue samples, including urine, CSF, whole blood and PBMCs, chosen at random. Samples were identified from their storage location and traced to the relevant documentation and electronic databases. All samples were fully traceable; however, two samples were not in their correct locations (see Advice item 3). No other discrepancies were identified.

Inspection findings

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

Compliance with HTA standards

Governance and Quality

Standard	Inspection findings	Level of shortfall
GQ1 All aspects of the establishments work are supported by ratified documented policies and procedures as part of the overall governance process	Although the Brain Bank has in place a wide range of comprehensive standard operating procedures (SOPs) covering all activities taking place in the bank, the procedures in relation to the BioResource do not contain sufficient detail and were out of date. Furthermore, the BioResource does not have a quality manual in place and there were no SOPs describing the consent seeking process and sample delivery. Please also refer to Advice item 1.	**Minor**
GQ6 A coding and records system facilitates traceability of bodies, body parts, tissues and cells, ensuring a robust audit trail.	During the traceability audit in the Brain Bank, the database and corresponding paper records indicated that 13 blocks had been created from the wet tissue. However, there were 14 blocks in storage. The Brain Bank PD confirmed that the tissue from one original block had been replaced and two new tissue blocks had been created. This had not been documented.	**Minor**
GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately	Although health and safety risks to staff had been addressed, there was no evidence of risk assessments associated with licensable activities, such as, consent, storage of tissue, transport and disposal for the Brain Bank and the BioResource. Please also refer to Advice item 6.	**Minor**

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

No.	Standard	Advice
1.	GQ1	There are two pieces of advice in this section: 1. The DI should consider reviewing the documented procedures of the Brain Bank in order to replicate this level of detail in the BioResource's procedures. 2. Furthermore, although the Brain Bank and BioResource have regular team meetings, the HTA Committee - which the DI and all PDs are required to attend- only meets on an annual basis. The DI is advised to consider making these more regular to enable matters, such as standardisation of documents, changes to SOPs, audits and their findings, competency and regulatory training, management of incidents, risk assessments, the setting up of agreements, to be discussed and to promote shared learning between the tissue banks.
2.	GQ2	Currently, two audits are carried out by the DI on an annual basis which includes an assessment of compliance with procedures and interviews with staff involved in licensable activities. The DI is advised to audit the entire process; from consent, transport, storage, use and disposal. The DI is advised to ensure that information collected during the audit is carefully documented to demonstrate compliance with HTA standards, local documented procedures and traceability.
3.	GQ4	There are three pieces of advice in this section: 1. During the traceability audits in the BioResource, it was noticed that two of the six samples were in a different location to that stated on the database. The DI is advised to incorporate a regular check of record completeness for both tissue banks to ensure that the systems are populated and updated accurately. This is particularly important as the Brain Bank will be setting up a new barcode tracking system to enable better traceability within the Brain Bank. 2. The DI is advised to ensure that they have access to records of all research studies under project specific ethical approval as well as respective ethical approval expiry dates. The DI is advised to liaise with the R&D Office to obtain this information. 3. The DI is advised to maintain a register of all tissue collections and to develop a register of the NHS REC-approved projects, including dates of expiry, so that suitable arrangements can be made to store the relevant material under the HTA licence once the NHS REC approval has expired.
4.	GQ6	The frozen brain samples are stored within small bags and then placed into one large bag. The autopsy number and surname of the deceased is written on the outer bag as well as on the smaller bags containing the brain tissue. During the traceability audit for one donor, it was difficult to decipher the autopsy number as the ink had faded over time. Although the smaller bags were legible and the Brain Bank will be moving towards a bar coding system in

		the near future, the DI is advised to review the current labelling system as it may pose a risk to loss of traceability.
5.	GQ7	Section 3.6 of the 'Adverse Events/Incident Reporting Relating to Human Tissue' procedure refers to the Serious Adverse Event and Reaction Reporting (SAEARs) requirements under Human Tissue (Quality and Safety for Human Application) Regulations 2007. The DI is advised to remove this reference from the document as it is not relevant to establishments licensed only under the HT Act. The DI is also advised to set out the types of incidents that would need to be reported and investigated. Incidents may include, but are not limited to: • receiving and/or storing specimens without appropriate consent documentation; • storing or using human tissue after consent withdrawal; • storage failure or other damage affecting human tissue quality for useful research; • loss of human tissue; • sample mix-up or loss of traceability; • transport of specimens to and from the establishment; • security arrangements; • incorrect disposal.
6.	GQ8	To address the minor shortfall against GQ8, the DI may wish to undertake risk assessments against the type of incidents laid out in advice item 5. Furthermore, the DI should also consider reviewing the current approach to storing the tissue blocks in the Brain Bank. During the traceability audit, one box containing tissue blocks appeared to be over filled posing a risk of loss of tissue. Moving forward, the DI should review the storage system for the tissue blocks.
7.	PFE3	The freezer alarms are not subject to routine testing. The DI is advised to incorporate a manual challenge of the alarm system to ensure that it is functioning correctly.
8.	N/A	The Principal Investigator (PI) for the BioResource is not a Person Designated (PD) on the licence. The DI is advised to add the PI as a PD.

Concluding comments

The establishment has worked to achieve a level of compliance with the HTA's licensing standards. A number of areas of good practice were seen during the inspection:

- All staff involved in seeking consent receive training in the HTA requirements of consent, which also includes a test and is provided by the University;
- There is a comprehensive emergency action protocol to deal with freezer malfunction;
- All freezers and ambient storage areas are subject to temperature monitoring using the electronic software system;
- A specialised courier is involved in transporting brains to the Brain Bank and specialist couriers to transport samples to and from the BioResource.

- The brain bank asks for feedback from users to make improvements in the service.
- At a high level, there is a HTA Management Committee, consisting of all the University's DIs and the Corporate Licence Holder contact, which meets every six months.

There are some areas of practice that require improvement, including minor shortfalls against, GQ1, GQ6 and GQ8. The HTA has given advice to the Designated Individual on a range of issues to make further improvements.

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:

Report sent to DI for factual accuracy: 10 June 2016

Report returned from DI: 24 June 2016 (with comments)

Final report issued: 30 June 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: 15 May 2018

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.