Site visit inspection report on compliance with HTA minimum standards

Weatherall Institute of Molecular Medicine

HTA licensing number 12433

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**

2 November 2016

Summary of inspection findings

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

Although the HTA found that Weatherall Institute of Molecular Medicine (the establishment) had met the majority of the HTA standards, one minor shortfall was found in relation to risk assessments. The HTA has also given advice to the Designated Individual with respect to governance systems, procedural documentation, audit and traceability.

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

The HTA's regulatory requirements

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

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

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

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

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

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

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

Background to the establishment and description of inspection activities undertaken

The establishment collects, receives and stores various tissues for use in research. Tissue can be given by donors, following an informed consent process, at the establishment itself or be received from donors attending clinics/meetings elsewhere. These external clinics/meetings may be held by the establishment's researchers themselves or by other researchers from outside of the establishment and who are undertaking collaborative research with establishment staff. The establishment's researchers have both national and international collaborations and the establishment holds samples both acquired from within the UK and from overseas.

All research studies taking place at the establishment must have been given ethical approval by the establishment's research ethics committee prior to the commencement of sample collection.

Relevant material held at the establishment includes material held under the authority of the HTA research sector licence and material for which storage is lawfully exempted because it is for projects which have received approval from recognised research ethics committees. The DI encourages all holders of relevant material to follow the same governance systems, irrespective of whether the material is held under the authority of the HTA licence or not.

The establishment has a phlebotomy room, which is used for removing blood samples from staff for use in research being undertaken at the establishment. It was noted during the inspection that not all blood was being donated and used for the scheduled purpose of research 'in connection with the disorders or functioning of the human body'. Blood is also taken and used to support cell growth in cell culturing techniques or as a nutrient source for maintaining parasites. In these cases, although the cultured cells or parasites are being used for research, the blood obtained from donors is not, itself, the subject of the research.

The DI has developed a quality manual, including procedures developed by the DI, which researcher's working under the HTA research licence are instructed to follow. The quality manual includes a summary of the HT Act, its requirements and procedures to follow for: adverse event reporting; seeking consent; retention of tissue following the end of a study; monitoring of storage facilities and freezers; transport, and; disposal.

The quality manual also describes procedures for audits and annual declarations. The DI undertakes annual audits of research groups holding relevant material to assure herself that the researcher is complying with the requirements of the quality manual. These audits are undertaken at the same time as the annual health and safety audits conducted at the establishment. The DI reviews relevant records relating to the samples that are being held. The full details of areas covered by the audits, however, are not fully described on the audit finding record sheets (see Advice, item 5). In addition to these audits, all researchers are required to submit an annual declaration to the DI, detailing any human tissue that they are storing. If no tissue is being stored, the researcher must submit a 'nil' declaration.

All new research staff and students receive an induction by the DI, in addition to bespoke training given by external organisations regarding the HT Act, consent processes and general research governance.

Tissue is stored in various locations within the establishment, including four main freezer rooms containing both -80^{o}C and -20^{o}C freezers and a dedicated liquid nitrogen storage facility housing several liquid nitrogen storage tanks. Freezers and liquid nitrogen tanks holding relevant material are monitored using an electronic system which contacts establishment staff should temperatures deviate from the expected ranges.

The establishment has been licensed since August 2007 and this was the second routine site-visit inspection to assess whether it continues to meet the HTA's standards. The timetable for the site visit was developed taking into account the establishment's latest self-assessed compliance information, a review of the previous inspection findings and pre-inspection discussions with the DI. During the site visit, a visual inspection of the premises including all areas where human tissue was stored, a review of documentation, interviews with establishment staff and students undertaking research, as well as a number of audits, were undertaken.

A traceability audit was undertaken during the inspection. Details of four individual samples from four different studies were taken. The selection of both the studies and samples was random. All of the chosen samples were located in different liquid nitrogen storage tanks. Details of the sample's location were obtained from the researcher involved in each study and then the sample was sought. In all four cases, the sample tube was correctly labelled and located within the expected storage container, in the expected liquid nitrogen tank.

Where possible, records of consent were also sought for each of the four samples. In the first case, the sample had been provided by a collaborator who retained the original consent forms; however, on the paperwork that accompanied the sample, the person obtaining the sample had confirmed (by checking a box) that donor consent had been verified and records were contained within the donor's clinical records. In the second case the sample was imported from overseas. The consent requirements of the HT Act do not apply to imported

material; however, the researcher indicated that all study participants gave their consent to be part of the study in the country of origin. The third case involved a sample that was obtained, by one of the establishment's researchers, from another staff member working at the establishment. Following a review of the consent forms located in the establishment's phlebotomy room, the donor's consent form was found; however, only the use of the sample was detailed rather than the details of the study or study title for which it was to be used (see Advice item 7). The final sample had been sent to the establishment from another centre; however, for that particular study, copies of the consent forms are sent to the establishment for filing, and the signed form was reviewed.

In summary, all samples in the audit were found to be stored in the locations that had been recorded for them and where applicable, evidence that consent had been obtained for the storage and use of the sample was found.

Inspection findings

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

Compliance with HTA standards

Governance and Quality

Standard	Inspection findings	Level of shortfall
GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately.	The establishment has a range of risk assessments in place; however, they relate only to health and safety risks. Wider risks to donors and their material have not been documented. There was, however, evidence that some such risks had been considered, such as the risk of losing sample traceability, where procedures to mitigate against this risk had been implemented; for example, sample audits. See also Advice, item 8. *This shortfall relates to the findings during the inspection. Following the inspection and prior to the release of the final inspection report, the DI has submitted evidence to the HTA demonstrating that a new document has been put in place which identifies potential risks relating to the samples. This document instructs individual research groups to assess the identified risks and put in place appropriate mitigating measures against them. The HTA now considers this standard to be fully met.*	**Minor** ***Fully met***

Advice

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

No.	Standard	Advice
1.	C1	The DI is advised to ensure that all researchers maintain details, within their individual study folder which is issued by the DI, of the assurances that appropriate consent has been sought for the donation of any samples that they receive. Researchers currently maintain such records - for example, material transfer agreements or declarations by a collaborator - however, they are not always held in the study folder. In addition, the DI is advised to include a review of such records when undertaking her annual audit of research tissue being stored at the establishment.
2.	GQ1	The DI is advised to add greater detail to the establishment's quality manual detailing how all samples should be labelled and tracked. The DI is also planning on implementing the use of pre-labelled sample tubes by all researchers which is something that should be reflected in the quality manual upon commencing their use.
3.	GQ1	The quality manual gives examples when exceptions to the licensing requirements of the HT act may apply; for example, where ethical approval for a specific research study has been obtained. The DI is advised to amend these references to clarify that, for the exception to apply, the ethical approval must be from a recognised research ethics committee as defined in the HTA's code of practice on Research.
4.	GQ1	The DI has regular governance meetings with various staff at the establishment as part of the regular health and safety meetings. Although the DI reported that HTA issues are discussed at these meetings, the DI is advised to consider having a standing agenda item at these meetings so that any HTA-related matters can be discussed and minuted appropriately.
5.	GQ2	The DI undertakes annual health and safety audits of all areas within the establishment. As part of these audits, a review of any human tissue being stored by researchers is also undertaken. These reviews include reviews of the researchers' study files, freezers used to store samples and location records. Although a standard audit checklist form is used to prompt the auditor, and to record findings against the areas that have been reviewed, the section relating to human tissue has only one field (titled 'HTA'). Having only one field within the audit form means that it is not clear to an auditor which areas should be audited as part of a review of relevant material stored under the licence. The DI is advised to re-draft this audit form so that all areas which are reviewed during the audits of relevant material stored at the establishment are detailed within the audit form. This will help to clarify what should be reviewed during the audits and facilitate clear recording of any findings against each of these areas. In addition, the DI is advised to undertake a traceability audit where the actual location of a sample within the establishment's storage facility is cross-checked against the location records being held by the researcher for that sample. This will help to assure the DI that samples are being appropriately tracked and their details recorded.
6.	GQ6	During the inspection, it was learned that, on occasions, researchers may split an initial sample into multiple aliquots. In some research groups, these aliquot tubes were labelled with the same sample identifier as the original parent

		sample. The DI is advised to ensure that all individual sample tubes, including those containing an aliquot taken from another sample, are labelled with a unique identifier. The DI is introducing the use of pre-labelled sample tubes which will ensure that all samples and aliquots of samples are uniquely identified; however, in the interim, ensuring that all researchers add unique identifiers to their sample tubes will help to maintain full traceability of the relevant material being stored.
7.	GQ6	The DI sends reminders to research staff that anyone seeking consent and taking blood for use in research must complete a blood donation consent form with the sample donor. During the traceability audit that was undertaken during the inspection (described above), an example of a blood donation consent from was reviewed. Although the form detailed the procedure for which the blood was to be used, it did not reference the details of the relevant study. A review of other consent forms highlighted an inconsistent approach to how the study for which a sample is being obtained is referenced. The DI is advised to remind all researchers that, in addition to detailing the purpose for which the blood is being taken, a reference to the relevant study's details or title should also be recorded on the blood sample consent form. This information should facilitate the establishment in tracing the particular study in which the donated sample was used in. Additionally, the DI is advised to consider more frequent audits of these forms, reviewing all applicable fields on the form, to assure herself that researchers are complying with the establishment's procedures.
8.	GQ8	All establishments should identify the risks inherent in their key activities, and procedures should be developed in consideration of and to mitigate these potential risks where appropriate. DIs should also assess the risks associated with licensable activities. Documented risk assessments should include an evaluation of the level of the risk and, where appropriate, the mitigating actions identified and the level of residual risk. Risk assessments should include the risks relating to the premises, practices and procedures connected with licensed activities. The DI is advised to consider the risks posed to donors and their material, which could include but are not limited to the following: • receiving and/or storing specimens without appropriate consent; • storing or using human tissue after withdrawal of consent (if applicable); • storage failure or other damage affecting human tissue; • loss of human tissue; • sample mix-up or loss of traceability; • transport of specimens to and from the establishment; • security arrangements; • 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.

Concluding comments

Areas of good practice were also observed during the inspection. The DI demonstrated a commitment to improving governance systems and compliance with them. Examples of these improvements include:

- the recently-introduced individual study folders, in which researchers are expected to maintain key details relating to their study. This helps to assure the DI that the necessary information relating to the studies that are being undertaken at the establishment are being consistently maintained.
- a plan to facilitate accurate, consistent and indelible sample labelling, by introducing pre-labelled sample tubes. This will help in supporting the establishment's traceability systems and facilitate a consistent approach to sample tracking among the establishment's various researchers.

There are a number of areas of practice that require improvement, including one minor shortfall. The HTA has given advice to the Designated Individual with respect to consent documentation, governance systems, procedural documentation, audit and traceability.

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 / subject to compliance with the additional conditions applied to the licence.

Report sent to DI for factual accuracy: 29 November 2016

Report returned from DI: 7 December 2016

Final report issued: 4 January 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: 03 January 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.