Inspection report on compliance with HTA licensing standards
Inspection date: **20 November (remote) and 21 November (site visit) 2023**

Weatherall Institute of Molecular Medicine

HTA licensing number 12433

Licensed under the Human Tissue Act 2004

Licensed activities

Area	Storage of relevant material which has come from a human body for use for a scheduled purpose	Removal from the body of a deceased person (otherwise than in the course of an anatomical examination or post-mortem examination) of relevant material of which the body consists or which it contains, for use for a scheduled purpose other than transplantation
Weatherall Institute of Molecular Medicine	Licensed	Not licensed

Summary of inspection findings

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

Although the HTA found that the Weatherall Institute of Molecular Medicine ('the establishment') had met the majority of the HTA's standards, six minor shortfalls were found against standards for Governance and quality systems and Traceability.

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.

Compliance with HTA standards

Minor Shortfalls

Standard	Inspection findings	Level of shortfall
GQ1 All aspects of the establishments work are governed by documented policies and procedures as part of the overall governance process		
a) Ratified, documented and up-to-date policies and procedures are in place, covering all licensable activities.	The establishment did not have documented policies and/or ratified standard operating procedures (SOP) in place covering all licensable activities, including: • the purchasing of relevant material • the quarantining and adoption of samples under the licence when a study with recognised research ethics committee approval ends • the use of tissue tracking databases • work instructions within research study groups	**Minor**
c) There are change control mechanisms for the implementation of new operational procedures.	The establishment had a change control SOP but it did not detail how change requests were to be raised, the risks of any planned changes, any validation required and how implemented changes will be reviewed.	**Minor**

GQ2 There is a documented system of audit		
b) Audit findings include who is responsible for follow-up actions and the timeframes for completing these.	Local audits undertaken by Tissue Responsible Officers (TRO) in each research group did not record or fully document findings.	**Minor**

GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills		
a) Qualifications of staff and all training are recorded, records showing attendance at training.	The establishment did not have records to evidence that SOPs had been read and acknowledged by staff as part of their training.	**Minor**

GQ4 There is a systematic and planned approach to the management of records		
b) There are provisions for back-up / recovery in the event of loss of records.	There were no provisions in place for the back-up and recovery of paper consent records within the phlebotomy room in the event of their loss.	**Minor**

T1 A coding and records system facilitates the traceability of bodies and human tissue, ensuring a robust audit trail		
a) There is an identification system which assigns a unique code to each donation and to each of the products associated with it.	An identification system for donated material was in use within the Nerlov research group but - due to a mislabelling error - a number of relevant material sample vials were incorrectly identified, resulting in a loss of traceability.	**Minor**

The HTA requires the DI to submit a completed corrective and preventative action (CAPA) plan setting out how the shortfalls will be addressed, 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.

Advice

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

Number	Standard	Advice
1.	GQ1(a)	The DI is in discussion with the University of Oxford's Human Tissue Governance team to implement a centralised electronic quality management system capable of managing, recording and documenting training records, audits, CAPAs, adverse events, risk assessments and the control of documents. The DI is advised to identify and implement a suitable quality management system, as soon as practicable, to strengthen governance across all research groups.
2.	GQ1(a)	Appendix 1 of SOP HTA016 Import/Export and Transfer of Relevant Material is a form to be used, once formally ratified, to notify the DI and PD of relevant material that is to be received at the establishment and to confirm relevant documentation relating to the samples is in place. The DI is advised to amend this document to additionally confirm consent is in place for the samples to be used in research.
3.	GQ1(a)	The DI is advised to consider amending SOP HTA003 Disposal of Human Tissue to identify a full list of reasons for relevant material disposal e.g. withdrawal of consent, sample used in experiment and end of study etc., and clarify the context for each reason. This should help to ensure all research groups are recording disposal reasons correctly and consistently.
4.	GQ1(a)	Each research group has a 'white folder' containing SOPs and training records but this folder had not been maintained with the most up-to-date SOPs by one research group. The DI is advised to ensure research groups

		have access and are working to current SOPs to improve governance and ensure consistent practices at the establishment.
5.	GQ2(a)	The approach to documenting audits varies significantly between research groups. The DI should consider reviewing the current approach to documenting audits and developing guidance for staff on the expected level of detail. This should help to ensure that audit forms are completed consistently and sufficiency of detail is provided.
6.	GQ2(a)	An audit on the completeness of consent forms, undertaken in 2021, identified issues which included consent forms not being signed and/or dated, and boxes being ticked rather than initialled as expected. There were no concerns identified around the validity of consent. At the time of the inspection, the corrective actions following this audit had still not been completed due to limited staff resourcing resulting in the quarantine of samples. The DI is advised to complete these corrective actions as soon as possible so the samples can be released from quarantine.
7.	GQ2(b)	The audit report template has columns to record if a research group is compliant, non-compliant or partly compliant with an HTA standard. Currently, if a standard is not applicable to a research group it is marked as non-compliant. The DI is advised to amend the audit report template to include a 'not applicable' column to better reflect the practices undertaken within each research group and to prevent a misleading assumption that a non-compliance exists when it does not.
8.	GQ2(b)	The CAPA plan template is included at the end of the audit report. To strengthen the quality of auditable information, the DI is advised to add additional columns to separate and identify the date by which the CAPA is due to be completed, the actual closure date and the documentary evidence reviewed to confirm that the remedial action has been concluded.
9.	GQ2(b)	CAPA entities are identified by sequential numbering. The DI is advised to include the HTA standard to which the CAPA relates to improve the tracking and management of auditable information.

10.	GQ2(b)	CAPAs fall into three classifications – critical, major and minor. The DI is advised to implement defined timeframes for audit follow-up actions to be resolved based on the classification of the non-compliance, to help ensure an equitable and consistent approach across research groups.
11.	GQ3(a)	Some TROs and researchers could not identify which relevant material was stored under the governance of the HTA licence or qualifying Research Ethics Committee (REC) approval and expressed minimal understanding of HTA's regulatory requirements. To improve and maintain knowledge, the DI is advised to provide or encourage additional or regular refresher training on the regulatory framework that is relevant to staff who may work with human tissue.
12.	GQ3(a)	Research groups held up to date training records for staff but the due date of refresher training was not recorded. The DI is advised to identify the date staff refresher training is due within records to improve the ease in which employees can be identified and ensure training is arranged and completed in line with the establishment's policies and procedures.
13.	GQ4(a)	There is currently no centralised oversight of relevant material being purchased by research groups within the establishment. Appendix 1 of SOP HTA016 Import/Export and Transfer of Relevant Material will rectify this governance 'gap' once the document has been ratified. The DI is advised to ratify and implement this form within the establishment's quality management governance documents as soon as possible to ensure a robust audit trail.
14.	GQ4(a)	The DI is advised to include a check box or other documented check step on the University's REC approval application form to confirm the person applying to work with relevant material has completed up to date consent and relevant material training. This will help to provide additional assurance that expected training requirements have been met.
15.	GQ5(b)	The Adverse Event Incident Reporting Form in Appendix 1 of SOP HTA011 provides for the recording of pertinent information on discovery of an adverse event and initial corrective actions taken. The DI is advised to

		amend and expand the reporting form to record information in relation to any investigation undertaken and the resulting corrective and preventative actions to ensure the process is fully documented and managed through to closure.
16.	GQ5(b)	The DI is advised to amend SOP HTA011 Recording Human Tissue Act Related Adverse Events to include the management of CAPAs arising from reported adverse events to ensure the process is fully documented and managed through to closure.
17.	GQ6(a)	One research group had undertaken their own risk assessment for the receipt of samples received under a material transfer agreement (MTA). However, the risk assessment was completed after the samples had been received and had no review date. The DI is advised to ensure that, where individual research groups are undertaking additional risk assessments associated with their licensed activities, these are: • completed before the activities commence • reviewed on a regular basis • available for internal audit to ensure all risks are identified and mitigated.
18.	GQ6(a)	The establishment had an overarching risk assessment but risks which may be associated with research tissue banks (RTB) were not documented. To provide assurance that all relevant risks have been identified and managed, the DI is advised to undertake an assessment of risks associated with the RTBs, identifying any control measures to mitigate potential risks.
19.	T2(b)	Some research groups did not have columns within their tissue tracking databases to record the date, reason and method of disposal. In these cases, no disposal of samples had taken place. To ensure compliance with this standard, the DI is advised to ensure each research group and their tissue tracking databases are set up to be able to record disposal correctly when it does take place.

20.	PFE1(b)	Relevant material stored in critical storage locations (ultra low freezers) may be accessed by all staff, visitors and contractors. Access is required at all times by certain staff to respond to freezer breakdowns and to implement the transfer of relevant material to back-up freezers. The DI is advised to undertake and document a risk assessment of the security of critical storage locations and accessibility to relevant material to provide assurance that suitable security arrangements are in place and confidentiality is maintained.
21.	PFE1(c)	There are documented cleaning and decontamination procedures but written evidence to confirm these have been completed within the research groups was absent in some instances. The DI is advised to ensure cleaning and decontamination of relevant material storage areas is documented to evidence compliance with governance procedures.
22.	PFE2(c)	Appendix 5 of SOP HTA004 Management of Freezers is a form to record the results of alarm challenges within relevant material critical storage areas. The DI is advised to expand this form to include a column to confirm if alarm responders are alerted when there is a temperature excursion providing further assurance alarms can be acted upon.

Background

The Weatherall Institute of Molecular Medicine undertakes research in molecular and cell biology, with the aim of improving human health. There are two research tissue banks operating at the establishment. The Weatherall Institute of Molecular medicine has been licensed by the HTA since August 2007. This was the third inspection of the establishment; the most recent previous inspection took place in November 2016.

Since the previous inspection, there has been a change in the Designated Individual and Persons Designated and significant changes to standard operating procedures within the quality management system.

Description of inspection activities undertaken

The HTA's regulatory requirements are set out in Appendix 1. The inspection team covered the following areas during the inspection:

Standards assessed against during inspection

46 out of 47 HTA licensing standards were covered during the assessment (standards published 3 April 2017). One standard was not applicable as the establishment does not store bodies or body parts [standard PFE2(b)]. All other standards were assessed.

Review of governance documentation

The inspection included a review of documentation relevant to the establishment's licensable activities. This included policies and procedural documents, audits, adverse event reporting, training requirements, temperature monitoring of the relevant material storage areas, equipment servicing records, contingency plans and a review of the HTA tissue tracking databases used to record and track relevant material.

Visual inspection

The visit included a visual inspection of the areas where the establishment undertakes licensable activity. This included critical storage areas.

Audit of records

DS Neonate Project

An audit of two samples, from traceability records and the corresponding consent form to storage locations, and an audit of one sample, from storage location to traceability records and the corresponding consent records, were undertaken. There were no discrepancies identified.

HaemBio BioBank

An audit of two samples, from traceability records and the corresponding consent form to storage locations, was undertaken. There were no discrepancies identified.

Nerlov Research Group

An audit of one sample, from traceability records and the corresponding material transfer agreement to storage location, was undertaken. The sample was labelled incorrectly and upon further review it was identified that this error affected several vials *(Minor shortfall, T1(a)).*

Chakraverty Research Group

An audit of one sample, from traceability records and the corresponding consent form to storage location, and an audit of one sample, from storage location to traceability records and the corresponding consent records, were undertaken. There were no discrepancies identified.

Ahmed Research Group

An audit of three samples, from traceability records and the corresponding consent form to storage locations, and an audit of one sample, from storage location to traceability records and the corresponding consent records, was undertaken. There were no discrepancies identified.

Demyelinating Diseases Research Tissue Bank

An audit of three samples, from traceability records and the corresponding consent forms to storage locations, was undertaken. There were no discrepancies identified.

OGG

An audit of two samples, from traceability records and the corresponding material transfer ageeement to storage locations, was undertaken. There were no discrepancies identified.

Tao Research Group

An audit of one sample, from traceability records and the corresponding consent form to storage location, and an audit of one sample, from storage location to traceability record,s was undertaken. There were no discrepancies identified.

Meetings with establishment staff

The assessment included meetings and discussions with the DI, PD, TROs, Human Tissue Governance Officer and a Research Nurse.

Report sent to DI for factual accuracy: 12 December 2023

Report returned from DI: 8 January 2024

Final report issued: 12 January 2024

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 2024

Appendix 1: The HTA's regulatory requirements

Prior to the grant of a licence, the HTA must assure itself that the DI is a suitable person to supervise the activity authorised by the licence and that the premises are suitable for the activity.

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.

Its programme of inspections to assess compliance with HTA licensing standards is one of the assurance mechanisms used by the HTA.

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. They are grouped under four headings:

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

This is an exception-based report: only those standards that have been assessed as not met are included. Where the HTA determines that there has been a shortfall against a standard, 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 provided.

HTA inspection reports are published on the HTA's website.

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 Human Tissue Act 2004 (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 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:

   - A notice of proposal being issued to revoke the licence
   - 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.
   - A notice of suspension of licensable activities
   - Additional conditions being proposed
   - 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 Codes of Practice, 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 review or at the time of the next 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 the final inspection report. Establishments 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 inspection
- a request for information that shows completion of actions
- monitoring of the action plan completion
- follow up at next routine inspection.

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