UNIVERSITY OF LIVERPOOL

Clinical Directorate Clinical Research Governance Team

Human Material Research Quality Manual

HTA004

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Approved on behalf of ratifying committee	**Date of Approval**
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Name of Committee	**Date**
Human Material Oversight Committee	27/06/2022

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1. Introduction

1.1 Background

The Human Tissue Act (HT Act) (2004)[1] applies to England, Wales and Northern Ireland. The HT Act (2004) established the Human Tissue Authority (HTA) to regulate all activities concerning the removal, storage, use and disposal of relevant human material. Relevant human material is defined as material, "other than gametes, which consists of or includes human cells" excluding embryos outside the human body, or hair and nails from the living, but including "surplus" tissue following clinical and diagnostic procedures[2].

Under the HT Act (2004), the HTA has the power to define expected standards (or Directions) to establishments and has produced Codes of Practice (COP)[3] that give guidance on the execution of procedures that lie within the remit of the HT Act (2004).

The HTA can also issue Directions to reflect changes in Policy and legislation or that are specific to a particular establishment. Directions 002/2009 were issued in September 2009 and updated in July 2014 to bring into force the HTA COPs and revoke 002/2006.

1.2 Licencing

The HTA regulates the removal, storage, and use of human bodies, body parts, organs and tissue for activities such as research, patient treatment, post-mortem examination, anatomical examination, and public display.

The HTA issues licences to establishments that carry out these activities in England, Wales and Northern Ireland, and inspect them to make sure regulatory requirements are met.

The University holds two Human Tissue Act licences, a Research Licence (HTA Research Licence) and a separate Licence for Anatomy. The Designated Individual (DI) for Research at University of Liverpool (University) and its associated sites is Dr Neil French. The Anatomy Licence has a separate DI, Professor Nathan Jeffery, and operates quality systems that are distinct from, but similar to, those outlined in this document for general research governance for human material.

The HTA research licence number for the University is 12020.

2. Governance structure

2.1 Responsibilities

A high-level human material governance organogram is summarised in figure 1. and highlights lines of responsibilities and communication.

[1] Human Tissue Act 2004
[2] HTA Relevant Material
[3] HTA codes of practice

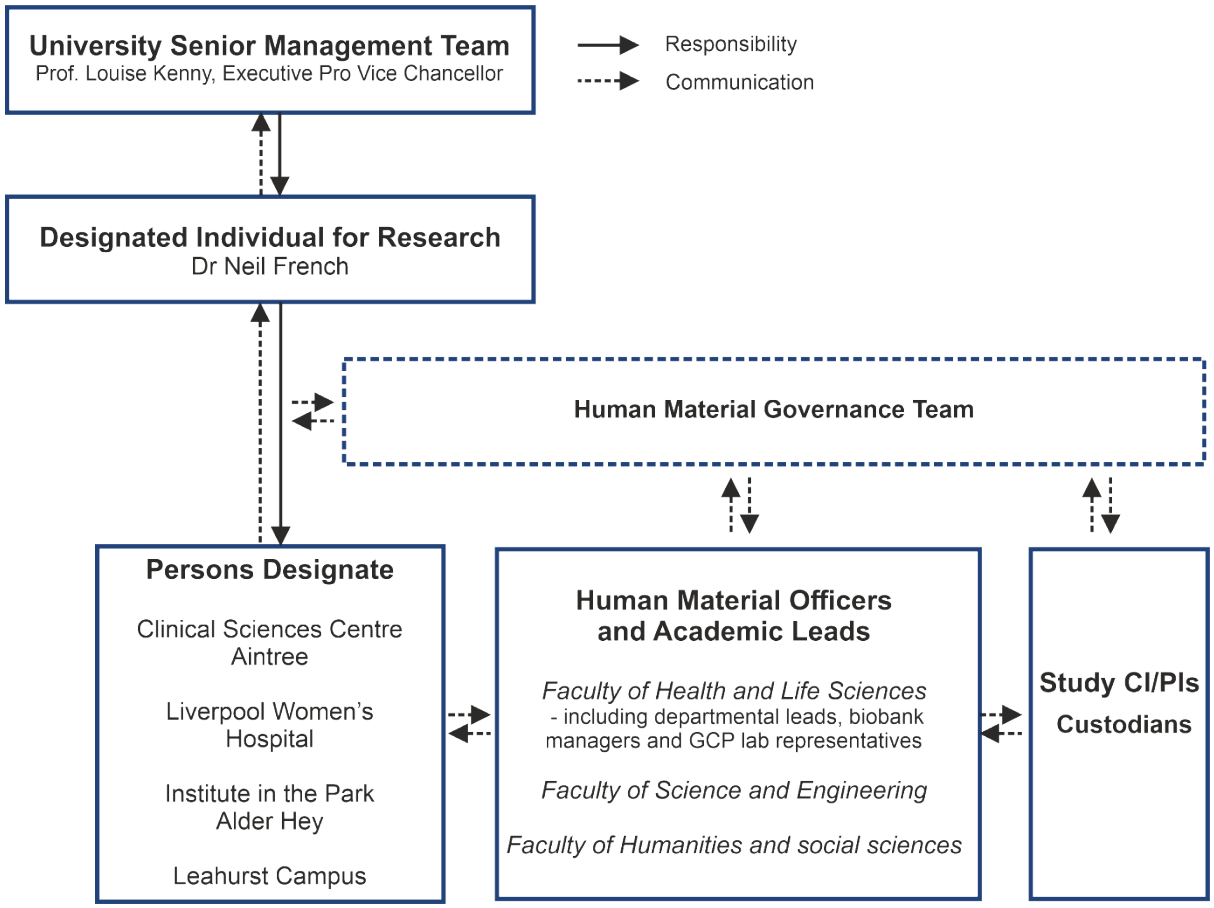

Figure 1. Human material organogram detailing communication and reporting lines.

The corporate licence holder is the University of Liverpool, whose representative is Professor Louise Kenny, Executive Pro-Vice-Chancellor.

The Designated Individual: Dr Neil Simon French

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The Designated Individual (DI) has specific responsibilities set out in the HT Act (2004) which are summarised as[4]:

- To supervise the licensed activity.
- To secure that the other persons to whom the licence applies are suitable persons to participate in the carrying out of the licensed activity.
- To secure that suitable practices are used by the persons under their supervision in the course of carrying out the licensed activity.
- To secure that the conditions of the licence are complied with.

Human Material Governance Team (HMGT)

The HMGT are responsible for maintaining central oversight of human tissue research activities on behalf of the DI. The HMGT are within the Clinical Research Governance Team, part of the Clinical Directorate within the Faculty of Health and Life Sciences. The HMGT also work closely with the University Research Tissue Banks and the GCP laboratory facilities at the University (See section 10.1).

The HMGT under the direction of the DI are responsible for the following activities:

- Providing training and support to users
- Maintain central human material records
- Document management of central human material governance documentation including this QMS and all related documentation.
- Managing a comprehensive program of audit.

Persons Designate (PD) work under the supervision of the DI to fulfill the same role as the DI in defined areas, for example, satellite sites. Satellite sites are geographically distinct areas of research activity operating to the same protocols and under the same governance system as the principal site. The DI at the University has delegated responsibility to the following Persons Designate:

- Dr B. Michaels, Clinical Sciences Centre, University Hospital Aintree.
- Professor D. Hapangama, Liverpool Women's Hospital.
- Dr L. Oni, Institute in the Park at Alder Hey.
- Professor N. Williams, Leahurst Campus.

The licence applies to anyone acting under the direction of the DI or PD. This includes Human Material Officers (HMOs), Chief/Principal Investigators (C/PI), and custodians of samples, who should all be fully conversant with the legislation and COPs. Researchers who use the samples (even if they have not been directly involved in the collection of the samples) must be aware that the samples:

- Must be obtained under ethical approval.
- Must be obtained following informed, relevant consent.

- Be processed and stored according to Standard Operating Procedures (SOPs).
- Must be associated with a log of their fate (i.e. tracked to disposal).

The DI has delegated the responsibility of Custodian to the respective managers of Research Tissue Banks that are held under the University Research Licence.

The University has a network of HMOs and Human Material Academic Leads placed in each operational area of the Faculty of Health and Life Sciences and at the Faculty level in the two other Faculties at the University.

The main roles of HMOs and human material academic leads are to advise and support researchers in recording the information required for project development and research monitoring and to assist in audit and monitoring of storage of relevant material in their areas.

2.2 Relevant Premises

The licence covers the whole of the main University campus, located in the city centre and its named satellite sites:

The Clinical Sciences Centre at Aintree University Hospital

The University Departments based at the Liverpool Women's Hospital

The University Departments based at the Institute In the Park at Alder Hey

The University Leahurst Campus

2.3 Oversight arrangements and reporting lines

Oversight arrangements are summarised in figure 2. The DI and the HMGT meet with the Human Material Oversight Committee (HMOC) every 4 months to discuss any matters arising, provide audit progress, corrective and preventative action updates and discuss regulatory updates and review relevant documentation relating to human material governance. The HMOC reports to the Research Integrity and Governance Committee (RIGC).

The DI, HMGT, PDs and HMOs meet a minimum of 3 times per year to review training, annual activity monitoring and adverse events.

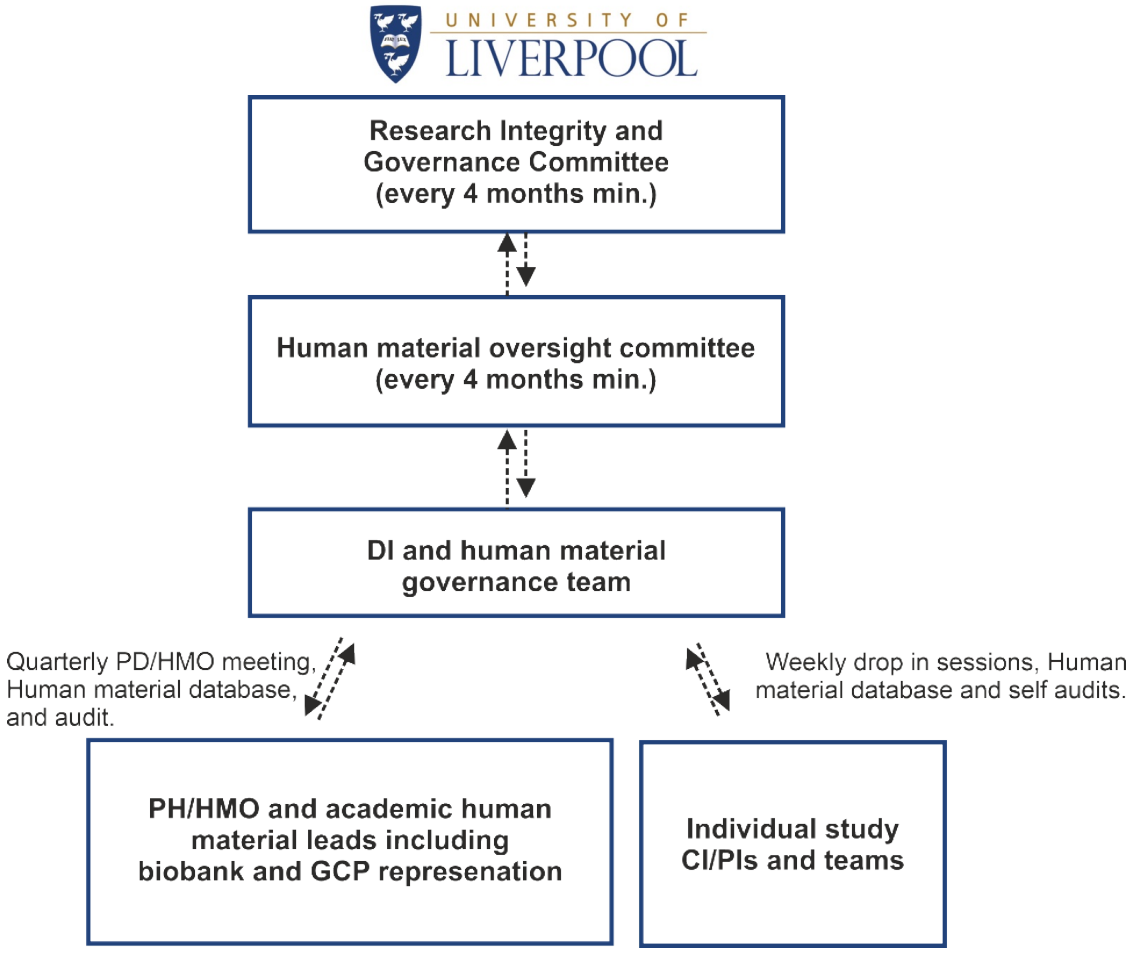

Figure 2. Oversight and feedback arrangements for human material governance.

3. Document management

All central human material governance documents are managed in a document management system. The documents fall into four levels each requiring different levels of approval.

3.1 Level 1. Core documents

Core level 1 documents require review and ratification by the HMOC Committee.

- University of Liverpool: Policy on the Use, Storage and Disposal of Human Material for Research Purposes - HTA001
- University of Liverpool: Human Material Code of Practice - HTA003
- University of Liverpool: Human Material Research Quality Manual – HTA004

3.2 Level 2. Supporting documentation

Level 2 supporting documentation is reviewed by the Senior Clinical Research Governance Manager and approved by the DI.

- University of Liverpool: Human Material Supplementary Document - HTA004s
- University of Liverpool: Summary Record of Documented Procedures Necessary to Ensure Compliance with the Human Tissue Act (2004) - HTA005
- University of Liverpool: HTA Licence Risk Assessment- HTA006
- University of Liverpool: Procedure for Internal Audit of Relevant Human Material - HTA007
- Research Tissue Bank Applications and Documented Procedures Necessary to Ensure Compliance with the Human Tissue Act (2004) - HTA008
- Human Material Supporting Document- Consenting for Research - SDS001
- Human Material Supporting Document- Movement of Human Material- SDS002
- Human Material Supporting Document- Use and Storage of Human material - SDS003
- University of Liverpool Human material users training slides

3.3 Level 3. SOPs and forms

Level 3 supporting documentation is reviewed by the HMGT and approved by the Senior Clinical Research Governance Manager.

- End of Study Human Material Holdings Declaration - FORMHTA001
- Human Material Disposal Form- FORMHTA002
- Registration of Human Material projects- FORMHTA003
- HTASOP001_Reporting of Adverse Events
- HTASOP002_Adverse Events report
- HTASOP003_Informed consent
- HTASOP004_Withdrawal of consent
- HTASOP005_Laboratory contingency plan
- HTASOP006_Data Contingency plan
- HTASOP007_Human material research record management
- HTASOP008_Equipment Use and Maintenance
- HTASOP009_Transporting samples
- HTASOP010_Human material Transfer Log
- HTASOP011_Sample Records labels and tracking

- HTASOP012_Sample tracking log
- HTASOP013_Sample use log
- HTASOP014_Induction and training
- HTASOP015_Training log
- HTASOP016_Production and control of SOPs
- HTASOP017_Security and storage
- HTASOP018_Human material disposal

3.4 Level 4. Local study/collection/lab documentation.

Level 4 documentation is reviewed and approved by the local teams and defined by the needs of the individual Group/Study/Project. HTA005 - The Summary Record of Documented Procedures Necessary to Ensure Compliance with the HT Act 2004 document should be used along with the level 3 templates to ensure there is an SOP in place to cover each of the procedures required.

4. Monitoring and audit

The HMGT are responsible for central monitoring of human material collections, annual reporting and audit practices.

4.1 Human Material database

The Human material database is a bespoke web-based database that acts a central record of all studies and collections involving human material. The database stores data on samples of human material stored and used in research from individual researchers and collates data on compliance with governance processes through a self-assessment questionnaire and regular audits.

Data from Sponsorship and University Ethics Committees identify new projects collecting, storing and using relevant material is collected by means of automated and manual e-mail notification when approval is granted by the respective teams. Studies can also be added to the database directly by individual PIs or the HMGT.

The information collected includes:

1. Data collected in relation to HTA licensing:
    - range of material collected
    - origin of material (living, dead)
    - conditions of storage
    - number of samples stored and distributed
    - adverse events

- documentation of disposal

2. Evidence or assurance that appropriate consent is obtained and that records are held securely.
3. Evidence of compliance with University policies and procedures relating to:
    - storage of tissues
    - risk management
    - regular governance meetings
    - complaints
    - training

4.2 Audit activities

Audits and inspections conducted by external bodies, such as the HTA, will be supported by HMGT and the PDs under the direction of the DI. All staff, students and visitors using human tissue samples for research purposes under the auspices of the University, whether on or off site, will be required to co-operate and make themselves available as required for audits.

All internal audits are conducted according to HTA007 Procedure for Internal audit of relevant material.

4.2.1 Research Tissue Banks

All RTBs undergo an annual audit by the HMGT.

4.2.2 Expired ethics studies

Studies retaining relevant material after the end of their ethical approval and therefore are stored on the Research licence are audited based on their risk profile.

4.2.3 Horizontal audits

The HMGT generate an annual schedule of horizontal audits across sub-sets of the human material holdings. The scope of the horizontal audits is determined by CAPA review, risk assessments and ad hoc process review.

4.2.4 Self-audit procedures

All PIs are advised and encouraged to conduct self-audit activities annually for studies that are under active ethics and those that are stored under licence.

4.2.5 Corrective and preventative actions and quarantine

Any shortfalls and non-compliance identified by the audits, whether internal or external, will result in a quality incident and the HMGT will be responsible for ensuring that any resultant investigations and actions are completed in a timely manner. The HMGT under the direction of the DI has the authority to

place samples under quarantine and to prevent their further use until the required actions are completed.

4.3 End of study procedures

All PIs who hold human material are responsible for notifying the HMGT when studies come to an end and complete an End of Study Human Material Holdings Declaration - FORMHTA001.

In addition, the human material database can produce a report detailing all studies that have reached the end of their ethical approval. The database can then be used to contact all PIs with recently expired ethics to remind them of their responsibility to complete FORMHTA001.

The Sponsorship team will also remind PIs to complete FORMHTA001 as part of their study closure procedures.

5. Training and support

It is important that all individuals utilising human material as part of their research projects have a good understanding of the HT Act (2004) and the HTA codes of Practice[2] relevant to their role.

5.1 Central user training

The HMGT conduct quarterly HTA training courses for Staff and Students utilising human material to ensure compliance. The full course content of which, is available on the University Human Material Governance web pages to view all year round.

New members of staff and postgraduate students who intend to collect, store, use and/or dispose of human material on University premises are required to read and sign the University's human material policy HTA001, the HM code of practice HTA003 and attend local training as soon as reasonably possible before undertaking such activities.

If attendance at the local training is not possible prior to onset of activities then completion of the MRC Research and human tissue legislation E-Learning package[5] entitled 'Research and human tissue legislation' must be completed.

In line with Good Clinical Practice (GCP) retraining requirements, human material training shall be repeated every 3 years. Copies of training certificates must be available for auditing purposes.

5.2 Specialty training

In addition to the standard training course for users, the HGMT run a series of bespoke training sessions focussing on particular aspects of human material governance for sub sets of staff and students. These include HTA awareness training for all laboratory technical staff, HTA considerations for facility managers and sessions for research nurses at the Satellite sites of the licence.

[5] MRC E-Learning module

5.3 Training material and Focus videos

In addition to the training slides, the HMGT generate a series of training materials and videos covering different areas of human material governance requirements which are made available on the Human material webpages.

5.4 Drop in sessions

In collaboration with the Clinical governance team, the HMGT run weekly drop in sessions for staff and students to offer guidance and advice on any aspects of human material or clinical governance.

6. Responsible research

The University recommends all staff who undertake research utilising human material strictly follow the guidance policies and procedures described within the University of Liverpool Research Integrity Policies and Guidelines[6] and the Human material research document suite relating to the storage, use and disposal of all human material for research.

6.1 Misconduct

Staff and students are reminded that failure to observe the HT Act (2004) or the University of Liverpool Policy on the use and storage of Human Material for Research Purposes[5] may represent misconduct and could result in disciplinary action being taken. Failure to comply with the HT Act can lead to criminal penalties and fines for the individuals concerned, the DI and the University.

All those to whom this HMR Quality Manual applies should report any known or suspected relevant misconduct. Members of staff and students are encouraged to raise concerns about suspected relevant misconduct either through their PD/HMO or in confidence under the Policy on Public Interest Disclosure[7]. The University has a responsibility to investigate allegations of misconduct. It also has a responsibility to protect staff and students from malicious, mischievous or frivolous allegations.

7. Abbreviations

CAPA/CAPAs	Corrective and Preventative Action/Actions
CI/PI	Chief/University Principal Investigator
COP	Code of Practice
DI	Designated Individual
GCP	Good Clinical Practice
HM Code	University of Liverpool Human Material Code of Practice
HMGT	Human material governance team

[6] UoL research integrity
[7] UoL Whistle blowing

HMO/HMOs	Human Material Officer/Officers
HRA	Human Research Authority
HT Act (2004)	Human Tissue Act (2004)
HTA	Human Tissue Authority
HTA Research Licence	Human Tissue Authority Research Licence
PD	Persons Designate
RTB	Research Tissue Bank
SOP	Standard Operating Procedure
University	University of Liverpool
UoL	University of Liverpool

8. Appendices

8.1 Organogram of the clinical directorate, HMGT highlighted in blue