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HUMAN TISSUE IN CLINICAL RESEARCH MANAGEMENT PROCEDURE

Introduction and Aim

This document has been developed to support Cardiff and Vale University Health Board (UHB) Research Governance Policy UHB 099. Cardiff and Vale UHB has a Duty of Care to any patient who has donated tissue, blood or other human material for research purposes to ensure that the tissue is treated with respect and is handled in accordance with the appropriate national legislation and good practice. This procedure has been produced to provide instruction to any individual(s) who has responsibility for human tissue, which has been donated for research purposes, and to any researcher who wishes to gain access to such samples.

Relevant material from a human body according to the Human Tissue Act 2004 is defined as: material which consists of, or includes, human cells. It does not include gametes, embryos outside the human body, or hair and nails from the body of a living person. For the purposes of this procedure relevant material will be referred to as ‘’human tissue‟.

Objectives

The purpose of this document is to detail the UHB management procedure for Human Tissue in Clinical Research in line with the requirements of the Human Tissue Authority (HTA).

The objective of this procedure is to ensure the UHB compliance with the Human Tissue Act 2004 and ethical considerations in relation to research using human tissue. This procedure are an integral part of the UHB’s research governance arrangements.

This is not a guide covering all aspects of the Human Tissue Act as it relates to research. Researchers working on human tissue are expected to follow best practice on handling, transport and storage and consent as described by the Human Tissue Authority. Detailed guidelines on the regulatory requirements and codes of practice are available from the Human Tissue Authority website at:

https://www.hta.gov.uk/hta-codes-practice-and-standards-0

Scope

This procedure applies to all of our staff in all locations including those with honorary contracts.

Equality and Health Impact Assessment	An Equality and Health Impact Assessment (EHIA) has been completed and this found there to be no impact
Documents to read alongside this Procedure	Research Governance Policy UHB 099
Approved by	Research Governance Group

Accountable Executive or Clinical Board Director	Medical Director
Author(s)	Governance Officer HTA - Research

Disclaimer

If the review date of this document has passed please ensure that the version you are using is the most up to date either by contacting the document author or the Governance Directorate.

Summary of reviews/amendments

Version Number	Date of Review Approved	Date Published	Summary of Amendments
1	17.07.19	30/08/2019	New document to support Research Governance Policy *UHB 099*. On publication the following documents to be withdrawn: • Human Tissue Management Policy UHB097 • Procedure For Governance & Compliance Audit of Human Tissue For Research Purposes UHB 134 • Procedure For Training In Use of Human Tissue Obtained For Research Purposes UHB 137

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Background

Historically, Cardiff University has been the holder of the Human Tissue Authority (HTA) Licence for all research undertaken on the Heath Park site and Cardiff and Vale University Health Board (the UHB) had jointly administered and regulated the activities arising from the Licence. Cardiff University had the responsibility to pay for the licence. The University applied to the UHB for a recharge of 50% of the licence fee for the Heath Park site.

The licence was inspected in December 2015 and in March 2016 the UHB was advised by the Designated Individual at Cardiff University that the UHB had been removed from the licence with effect from 8th February 2016 but any tissue needing storage could be held under the licence at a cost and a Service Level Agreement (SLA) would be established.

This procedure has been revised to reflect the current status in relation to tissue held by the UHB and outlines responsibilities and actions to be undertaken. This procedure is underpinned by the Research Governance Policy UHB 099.

Human Tissue Act 2004

The Human Tissue Act 2004 covers England, Wales and Northern Ireland. The Act established the Human Tissue Authority (HTA) to regulate activities concerning the removal, storage, use and disposal of human tissue for research, medical treatment, post-mortem examination, education and training, and displays in public, along with giving approval for organ and bone marrow donations from living people. The HTA issues licenses for the storage and use of human tissue, carries out inspections on licensed premises and promotes good practice on all aspects of the handling, use, storage and disposal of human tissue. The Human Tissue Act 2004 made it an offence to store human tissue without a licence and/or recognised Research Ethics Committee approval.

'Relevant Material' under the Act, is any material, other than gametes, removed from the body that consists of or includes human cells. In the Human Tissue Act references to relevant material from a human body do ***not*** include:

- embryos outside the human body,
- hair and nail from the body of a living person,
- cell lines or any other human material created outside the human body,
- serum, plasma, DNA and RNA.

A list of relevant material can be found in Appendix 1 and Appendix 2 has information on DNA Theft.

Storage of Relevant Material by the UHB

A licence is required to store relevant human material, unless you have ethical approval from an NHS Research Ethics Committee (REC) for a specific research project. A licence is required where tissue is being stored for distribution to other researchers and where tissue samples are imported from outside England, Wales and Northern Ireland.

The UHB does not currently hold a HTA Licence. Therefore, no researcher can store relevant material unless one of the following exemptions apply:

- A research project using relevant material that has been approved by a recognised research ethics committee (e.g. NRES) and the researcher cannot identify the individual from whom the material has come. The relevant material may be stored without a licence for the duration of the project and at the end of the project, the relevant material must either be destroyed or stored on licensed premises. A university ethics committee is not considered to be a recognised research ethics committee for this purpose
- A research project using tissue provided by a REC-approved bank which has generic ethical approval. The recipients do not need to store relevant material under an HTA licence during the period of the research project. On completion of the project, the researcher must return tissue to the bank or to an alternative HTA-licensed establishment, apply for project-specific approval by a REC or destroy it.
- Where relevant material is being held with the intention of processing to render the material acellular (e.g. extracted DNA or protein lysates) prior to research. Tissue may be stored without a licence providing that the processing takes a matter of hours or days and certainly no longer than a week. Directorates that supply tissue to research tissue banks will need to be assured that this is satisfied.

Acquisition and Importation of New Relevant Material at the UHB

New human tissue samples may be acquired as part of an NHS REC- approved project or from a REC-approved Research Tissue Bank. If a Chief Investigator or a Principal Investigator (PI) is a collaborator on a project using human tissue being led by another institution and for which the UHB is not a sponsor, it is essential that they are aware of the content of any ethics application submitted to an external REC. They have a number of responsibilities:

- ensuring that ethical approval remains in place for the duration of the project
- ensuring that Material Transfer Agreements (MTA) are in place for any incoming/ outgoing tissue transfers
- maintaining relevant and good quality records
- drafting and updating risk assessments
- adverse event reporting
- implementing recommendations made following an internal audit or HTA inspections
- advising the R&D Office when ethical approval of the study ends and confirming that samples have been destroyed or transferred to an organisation that holds a HTA licence.

Research Governance Section of the Research and Development Office

The Research and Development (R&D) Office of the UHB has a Research Governance team that serves the UHB research community. The team aims to advise on the UK Policy Framework for Health and Social Care Research and the conduct of clinical research, as well as provide an effective research governance environment for researchers. In relation to the Human Tissue Act, the Governance Officer Human Tissue Act – Research, a post holder within the team, supports them.

A research project will require confirmation of capacity and capability from the UHB R&D department if the research involves the use of any UHB resource, its patients, staff, their data, tissue or organs. All projects are reviewed by the R&D department prior to confirming capacity and capability. If a project involves the use of tissue samples the review process required will expect to see documented evidence of:

- What tissue samples are required and the quantity.
- What process is to be employed to gain access to such samples.
- Details of consent.
- What the tissue disposal process will be.
- Inclusion of a MTA if samples are to be transferred to an organisation outside of the UHB as appropriate.

The UHB maintains a database of all research projects utilising UHB resources and the Governance Officer Human Tissue Act – Research will produce a report to identify all projects due to complete in the following 3 months. CIs and/or PIs will be contacted and asked to confirm that all tissue will be destroyed, once the study has ended. If they intend to retain tissue at the end of the study there are 3 options

1. Negotiate transfer to premises that hold a HTA licence.
2. Negotiate transfer to a Research Tissue Bank that has a HTA licence.
3. Apply for NHS Ethical approval.

Tissue Banks and Biobanks

Some research requires the transfer of tissue samples, blood samples, or samples of other bodily material obtained from UHB patients to a tissue bank or bio-bank facility. The UHB has a duty of care to protect its patients by providing a robust system governing how such research tissue is managed. The following process has been established not to hinder research, but to implement a process to provide clarity. It describes the procedure to be followed when transferring a tissue sample(s) from a UHB patient, to a Tissue Bank. The following system is therefore in operation:

- Individual tissue banks are required to be in licensed premises under the Human Tissue Act (2004) and optionally approved as a Research Tissue Bank (RTB) by an NRES committee.
- Samples to be collected for Cardiff University Tissue Bank (CUB) must be processed in accordance with the management approval confirmed by the UHB via the UHB Hospital Services Management Board.
  - An MTA is in place between the UHB and CUB to acknowledge and oversee the transfer of tissue from the UHB (via the patient) to the RTB and that they accept the conditions of transfer.
  - Directorates that supply tissue to RTBs will need to be assured that the processing takes a matter of hours or days and certainly no longer than a week, as the UHB does not have a HTA licence.
  - Subsequent research projects that are eligible for portfolio adoption will require confirmation of capacity and capability by R&D.
  - Tissue surplus to requirements will be disposed of according to procedures that meet requirements of the Human Tissue Act (2004).

- Individual tissue banks that receive UHB samples, require confirmation of capability and to ensure that the UHB meets its duty of care to its patients by ensuring that the following conditions are met:
  - An MTA is in place with the directorate to acknowledge and oversee the transfer of tissue from the UHB (via the patient) to the RTB and that they accept the conditions of transfer.
  - Directorates that supply tissue to RTBs will need to be assured that the processing takes a matter of hours or days and certainly no longer than a week, as the UHB does not have a HTA licence.
  - Storage and use of tissue is according to the codes of practice specified by the HTA and compliant with the Human Tissue Act (2004).
  - Subsequent research projects will require confirmation of capability from R&D if the project involves:
    - contact with, or identification of the tissue donor,
    - uses further UHB resources such as UHB patients, staff, their tissue, organs or data.
  - Tissue surplus to requirements will be disposed of according to procedures that meet requirements of the Human Tissues Act (2004).

Disposal

Human tissue must be disposed of with respect. Appropriate methods of destruction, storage and arrangements with people involved must be planned and arranged in advance. Risk Assessments of the disposal of human tissue must be made and regularly reviewed.

Acknowledgement:
This document was based on HTA Policies produced by University of Wolverhampton and Nottingham NHS Trust and we are very grateful to use their work as a basis for our document.

APPENDIX 1

Supplementary list of materials

This list is intended to provide supplementary guidance to the HTA's broader policy framework on 'relevant material'.

The list is not intended as exhaustive or exclusive, but is intended to provide guidance to stakeholders in respect of a number of materials that guidance on the status of, as relevant material or otherwise, has previously been sought. The HTA will review and update the list periodically.

The list currently refers solely to which human body parts, tissues and cells are defined as 'relevant materials' for the purposes of the Human Tissue Act 2004, in line with the statutory definition above. The HTA intends to expand the list in the future to also provide guidance to the human application sector on which 'tissues and cells' are regulated under the Human Tissue (Quality and Safety for Human Application) Regulations 2007.

Where a material is not included within the following list stakeholders should refer to the policy framework to formulate their own assessment of the material's status in line with the guidance provided in the framework.

Materials classified in the following list as relevant material are done so subject to the following general caveat that they are relevant material except where:

- They have divided or been created outside the human body
- They have been treated, processed or lysed through a process intended to render them acellular. This would include the freezing or thawing of cells only where that process is intended to render the material acellular.

Material	Relevant materials for the purposes of the Human Tissue Act 2004?
Antibodies	No
Artificially created stem cells*	No
Bile	Yes
Blood	Yes
Bone Marrow	Yes
Bones/Skeletons	Yes
Brain	Yes
Breast Milk***	Yes
Breath Condensates and exhaled gases	No
Buffy coat layer (interface layer between plasma and blood cells when blood is separated)	Yes

Material	Relevant materials for the purposes of the Human Tissue Act 2004?
Cell lines**	No
Cells that have divided in culture	No
CSF (Cerebrospinal fluid)	Yes
Cystic fluid	Yes
DNA	No
Eggs*	No
Embryonic stem cells (cells derived from an embryo)**	No
Embryos (outside the body)*	No
Extracted material from cells, e.g. nucleic acids, cytoplasmic fraction, cell lysates, organelles, proteins, carbohydrates and lipids.	No
Faeces	Yes
Fetal tissue	Yes
Fluid from Cystic lesions	Yes
Gametes*	No
Hair (from deceased person)	Yes
Hair (from living person)	No
Joint Aspirates	Yes
Lysed Cells	No
Mucus	Yes
Nail (from deceased person)	Yes
Nail (from living person)	No
Nasal and Bronchial Lavage	Yes
Non blood derived stem cells (i.e. derived from the body)	Yes
Non fetal products of conception (i.e. the amniotic fluid, umbilical cord, placenta and membranes)	Yes
Organs	Yes
Pericardial fluid	Yes
Plasma (Please note: Depending on how plasma is prepared and processed, it may contain small numbers of platelets and other blood cells. If any of these cells are present then the plasma must be regarded as relevant material).	No

Material	Relevant materials for the purposes of the Human Tissue Act 2004?
Platelets	Yes
Pleural fluid	Yes
Primary cell cultures (whole explant/biopsy present)	Yes
Pus	Yes
RNA	No
Saliva	Yes
Serum	No
Skin	Yes
Sperm*	No
Sputum (or Phlegm)	Yes
Stomach contents	Yes
Teeth	Yes
Tumour tissue samples	Yes
Umbilical cord blood stem cells	Yes
Urine	Yes

* While outside the definition of relevant material for the purposes of the HT Act, these materials fall under the remit of the Human Fertilisation and Embryology Act 1990, and are regulated by the Human Fertilisation and Embryology Authority (HFEA).

** Cell lines and embryonic stem cell lines fall within the regulatory remit of the HTA by virtue of the Human Tissue (Quality and Safety for Human Application) Regulations 2007, which regulates the processing, storage and distribution of stem cell lines for human application. Both the HFEA and the Medicines and Healthcare products Regulatory Agency (MHRA) also have a regulatory remit in respect of cell lines and embryonic stem cells lines. A joint position statement issued by the HTA, HFEA and MHRA provides guidance on the relevant regulatory remits.

*** Breast milk does not constitute tissue or cells for human application under the (Quality and Safety for Human Application) Regulations 2007, but is classified as relevant material for the purposes of the Human Tissue Act 2004 where stored or used for a scheduled purposes.

Appendix 2

DNA Theft

DNA (as opposed to the bodily material from which it originates) is not considered to be relevant material under the Human Tissue Act and can be stored without the need for an HTA Licence. However, the Human Tissue Act does make it an offence to analyse DNA without consent.

It is possible to use the results of DNA analysis without consent, providing the bodily material from which the DNA is extracted:

- is from a living person;

and

- the researcher is not in possession, and not likely to come into possession of information that identifies the person from whom it has come;

and

- the material is used for a specific research project with recognised ethical approval.

Although no offence will be committed in this situation, the HTA recommends that, where practical, consent is obtained.

An offence will be committed where somebody has bodily material intending to analyse its DNA and use the results for research without consent for non-excepted purposes (see HTA Code of Practice 1: Consent).