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Human Samples in Research

Storage of Human Tissue

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1. Purpose

The purpose of this Standard Operating Procedure (SOP) is to ensure that staff and students involved in research covered by the Human Tissue Act 2004 (HT Act) understand the procedures, requirements and legislation for the storage of human tissue for this purpose. All research involving human tissue that is defined as 'relevant material' by the HT Act must be conducted in accordance with relevant legislation, Human Tissue Authority (HTA) Codes of Practice, core joint Swansea University/ABM University Health Board (ABM UHB) HTA SOPs, policies and quality manual. This SOP applies to all Swansea University and ABM UHB students and employees who are responsible for collecting, storing, using and disposing of human tissue for research.

2. Background

This SOP forms part of a joint Swansea University / ABM UHB Quality Management System (QMS) for the governance of the collection, storage, use and disposal of human samples for research. Successful implementation of the QMS will ensure that all research involving relevant material is carried out in compliance with the licensing requirements of the HT Act and to the licensing standards set out by the HTA. The HTA defines relevant material as any material containing even a single cell that could be subjected to research. Information on which tissues and samples are considered to be relevant material for the purposes of the HT Act and HT licensing is available at:

https://www.hta.gov.uk/policies/relevant-material-under-human-tissue-act-2004

A supplementary list which provides additional guidance to the HTA's policy on 'relevant material' is available at:

http://www.hta.gov.uk/_db/_documents/Supplementary_list_of_materials_200811252407.pdf

This SOP has been produced in accordance with the HT Act 2004 which came in to force on 1 September 2006, and should be read in conjunction with the HTA Code of Practice E: Research.

3. Roles and Responsibilities

It is the responsibility of the Designated Individual (DI) to ensure that appropriate procedures and practices are in place for the storage of relevant material, that those involved are appropriately informed and trained and that the conditions of a HTA licence are complied with.

It is the responsibility of the Principal Investigator (PI), as custodian of the samples, to understand and follow the organisational procedures and practices for the storage of relevant material, attend training and comply with the conditions of the HTA licence, under the supervision of the DI.

The Human Tissue Act Governance Officer is responsible for ensuring that this SOP remains fit for purpose.

4. Procedure / Principles

4.1 General Principles of Storage of Relevant Material for Research

The HT Act does not define the term storage in relation to relevant material for research. Neither does it give any minimum or maximum term for storage of human tissue for research. Therefore, the HTA considers 'storage' to be when tissue is kept for any period of time for the purpose of research. The HTA expects relevant material for research to be held under the governance of ethical approval from a recognised committee or a HTA licence. Where the ethical approval is not by a recognised ethics committee, relevant material should be held under the governance of both. The term 'recognised ethics committee' means a HRA Research Ethics Committee (REC) established under and operating to the standards set out in the Department of Health document titled *Governance arrangements for research ethics committees* or an ethics committee recognised by United Kingdom Ethics Committee Authority (UKECA), to review clinical trials of investigational medicinal products under the Medicines for Human Use (Clinical Trials) Regulations 2004. University ethics committees are not considered to be recognised committees.

The HTA advises that researchers gain ethical approval before embarking on any research. HTA licences should not be viewed as alternatives to ethical approval by a recognised REC. An application for ethical approval is considered to be pending from the point it has been submitted until the decision of the committee has been communicated to the applicant.

4.2 Existing Holdings

The consent requirements of the HT Act are not retrospective. This means that legally it is not necessary to obtain consent under the HT Act to store or use an 'existing holding' for a scheduled purpose. An existing holding is material from the living or deceased that was already held at the time the HT Act came into force on 1st September 2006. If the wishes of the deceased person are known, they must be respected.

4.3 Storage of Relevant Material from the Living

Material from the living is defined as tissue that was collected when the donor was alive, whether or not they have died since. Consent is required to store tissue from the living for the scheduled purpose of research into disorders, or the functioning, of the human body. The HT Act makes it lawful to store relevant material taken from a living person provided that consent from an 'appropriate person' is obtained. Refer to the Swansea University/ABM UHB SOP on consent (*HTA-02-SOP-Consent*) for details of appropriate and valid consent.

Where it is not possible to obtain consent, it is lawful to store relevant material from the living for research if the study is approved by a recognised ethics committee and the material is anonymised. The researcher should not seek to identify a link between anonymised samples and patient information.

Material can be collected from the living and stored without consent for:

- Clinical audit
- Education or training relating to human health
- Performance assessment
- Public health monitoring
- Quality assurance

4.4 Storage of Relevant Material from the Deceased

It is an offence under the HT Act to store relevant material from the deceased for the purpose of research without consent.

4.5 Storage of Specific Relevant Material

4.5.1 DNA

Whilst DNA falls outside of the definition of relevant material therefore can be stored without a HTA licence, the HT Act also defines the term 'bodily material' as tissue from which DNA originates. Bodily material falls under the remit of the HT Act. It is an offence to be in the possession of any bodily material (including hair, nails and gametes) with the intention of analysing DNA for the purpose of research without consent. The HTA recognises holding DNA in such a manner as an offence of 'non-consensual DNA analysis' and makes a distinction in this context between relevant material and bodily material.

However, the results of DNA analysis may be used for research without consent provided:

- The bodily material from which DNA is extracted is from the living

  and

- The researcher is not in possession of and does not seek to come into possession of the information that identifies the donor

  and

- The material is used for a specific research project with recognised REC approval.

For example: a researcher is using the results of DNA analysis extracted from tissue biopsies from living people as part of a research project that has been approved by a REC. The researcher will not come into possession of any patient identifiable information. No offence will be committed if consent is not obtained.

4.5.2 Cell Cultures

Cell cultures are classed as relevant material if they contain cells that were created inside the human body, e.g. if the culture contains original cells from a biopsy or blood sample. The HTA considers cells which have divided once outside the body to be non-relevant material. Individual researchers will need to make a judgment as to when cells in culture no longer contain original cells.

4.5.3 Processed Material

When the result of application of a specific process is generally consistent in that the processed material either retains cellular material or is rendered acellular (as a result of the process), then the presumption should be that all examples should be regarded as such. For example:

- Plastinated body parts are considered to be relevant material since the plastination process is designed to preserve cellular structure.

- Plasma and serum are not relevant materials, provided the processing is sufficient to remove cellular material. The process applied should be documented to evidence that it is sufficient to render the material acellular.

4.5.4 Bodily Waste

Bodily waste is considered to be relevant material reflecting the view that it may contain a single cell that could be subjected to research. Bodily waste includes secretions and fluids such as urine, saliva, sweat, stool, pus and lavages.

4.5.5 Cells and Tissues on Slides

Cells or tissues on slides which are intended to be representative of whole cells are considered to be relevant material. Staining of cells does not render them exempt from the definition.

4.6 Old Tissue

A licence is not required to store human tissue for research if it is from a person who died over 100 years ago.

4.7 Storage Incidental to Transport

Under the HT Act, where human tissue is in storage pending transfer elsewhere, providing it is held for a matter of hours or days and certainly no longer than a week, the HTA takes the view that the storage is incidental to transportation and a HTA licence is not required. For example, a number of sites collecting material for transfer to HTA licensed establishment do not need to store the material under a HTA licence. This exception extends to material collected for research that is not covered by REC approval.

4.8 Storage Incidental to Rendering Acellular

Where human tissue is being held whilst it is processed with the intention to extract DNA or RNA, or other subcellular components that are not relevant material (i.e. rendering the tissue acellular), the HTA views this as analogous to the incidental to transportation exception. A licence is not therefore required, providing the processing takes a matter of hours or days and certainly no longer than a week. Examples might include the centrifugation of clotted samples to collect and store serum. This exception extends to material collected for research that is not covered by HRA REC approval.

4.9 Storage of Material Created Outside of the Body

For the purposes of research that does not involve any application of tissues or cells into humans (i.e. transplantation), material that is created outside the body does not fall under the remit of the HTA.

4.10 Storage Prior to Analysis

Where relevant material is being held for a short period prior to conducting analysis and subsequent disposal, this is considered as storage for a scheduled purpose (i.e. research). Such storage requires that the material be held under a HTA licence or recognised REC approval for the specific project.

The HTA advises that researchers gain ethical approval before embarking on any research. A HTA licence should not be viewed as an alternative to ethical approval by a recognised REC.

4.11 Unlinked Samples

Although samples are generally unlinked, the linking of samples can be made through a third party where necessary. In addition, the HT Act does not prohibit the persons holding the samples from carrying out the research. When research involves clinicians who may have access to databases making identification possible, the sample will still be regarded as non-identifiable provided the researcher does not attempt to link the tissue with the patient. Research in this context is permissible without consent if approved by a recognised REC. Obtaining consent is ordinarily considered best practice, negating the need for complex systems for keeping samples unlinked.

4.12 Storage Following Expiry of Ethical Approval

Tissue stored for a specific research project which has been approved by a recognised REC does not need to be stored under a HTA licence. However, once the approval expires, or no further approval is pending, legally the tissue must be stored under an HTA licence or disposed of in line with *HTA-04-SOP-Disposal*. Where it is to be used for further research that does not have REC approval, the research must be in accordance with the initial consent obtained or, if appropriate, further consent should be obtained.

4.13 Storage in Research Tissue Banks

Some specific RECs have been authorised to give generic ethical approval for research tissue banks which will then be required to work under REC SOPs. This means that a specified programme of research is permitted without the need for further individual project specific REC approval. The relevant material in these research tissue banks must be stored on HTA-licensed premises.

The recipients of tissue supplied by HTA licensed, REC approved banks do not need to store the material under a HTA licence during the period of the research project, subject to the condition that the research falls within the broad programme of work approved by REC. If the research is not carried out in accordance with these requirements, specific project approval by a recognised REC will be required or,

alternatively, the samples will need to be stored at the recipient premises under a HTA licence.

If tissue is stored in a HTA-licensed research tissue bank that does not have broader ethics approval, each researcher acquiring human tissue from the bank must store the tissue under a HTA licence, or apply for specific project approval by a HRA REC. The tissue bank should have appropriate processes in place to review and approve applications for access to the tissue.

On completion of research using tissue from a REC-approved research tissue bank, the individual researcher must transfer any residual tissue back to the bank or to an alternative HTA-licensed establishment, store the tissue under a HTA licence within their own organisation, apply for specific project approval by a REC or dispose of the human tissue.

4.14 HTA Storage Compliance Requirements

Human tissue should be stored in line with good practice within facilities that are appropriate for the storage of bodies, body parts, tissues and cells. The HTA also requires that there be suitable storage for records and consumables.

4.14.1 Storage Facilities

Storage areas refer to the rooms and buildings, freezers, fridges and containers in which tissue is being held. The following information on each storage unit containing human tissue should be logged:

- Storage unit number/identifier
- Location (building/room number/bay/side room)
- Manufacturer
- Model number
- Serial number
- Asset number (NHS or University)
- Description (e.g. -80℃ freezer)
- Human tissue (yes/no)
- Person responsible

Storage areas for human tissue should be:

- Secure and lockable.

- Traceable - records should detail the location of tissues specifically the building, room, individual storage unit, shelf, container (e.g. box, plate, bag) and position within container.

- Risk assessed, including the risks to staff, students and to the integrity of the tissues being stored.

- Maintained, including routine and ad-hoc cleaning and maintenance of the storage area and units.

- Subject to contingency arrangements in the event of storage area failure (refer to *HTA-09-SOP-Risk Management* and *HTA-10-SOP-Equipment Maintenance*).

4.15 Storage and Labelling Guidelines

- Human tissue must be stored using recognised methods and guidance and labelled accordingly (see Appendix A - example storage label). All human samples must be uniquely identifiable to ensure traceability. Where samples are further divided for storage, each individual sample should be labelled with a new unique identifier in order that all parts of a primary sample may be traceable.

- The label must describe the tissue sample type and be safely secured to the sample container. Each label should be legible and suitable for the storage conditions to which it will be exposed.

- Labels should not contain patient identifying information.

- Storage records should be maintained and conform to *HTA-07-SOP-Management of Records*.

- Human tissue held under licence must be stored in a locked area. Ideally, the storage container should also be lockable. A copy of the HTA Licence should be displayed in any area storing human tissue.

- If a storage unit is used to store both human tissue and other material, the human tissue should be stored separately and be clearly labelled as such. Ideally relevant material should not be stored with other material, reagents or consumables.

- Calibration and maintenance of storage units must be in line with manufacturer's guidance, MHRA guidance and *HTA-10-SOP-Equipment Maintenance*. Records of calibration, monitoring of storage conditions and maintenance should be kept in accordance with *HTA-07-SOP-Management of Records*.

- Records of cleaning, including any cleaning schedules, should be kept for each storage unit containing relevant material (refer to *HTA-10-SOP-Equipment Maintenance*).

- Storage units (i.e. freezers, fridges) should be validated as fit for purpose (Refer to *HTA-10-SOP-Equipment Maintenance*).

- A risk assessment relating to the storage of human tissue should be made in accordance with *HTA-09-SOP-Risk Management*, and should cover, as a minimum, what actions should be taken in the event of failure of storage provision, consideration of what emergency/contingency procedures should be in place and details of possible alternative storage. A separate risk assessment of the storage of consumables should be completed if applicable. Risk assessment guidance is available in *HTA-09-SOP-Risk Management*.

- Any adverse event or 'near-miss' involving the storage of human tissue should be reported in accordance with *HTA-11-SOP-Adverse Event Reporting*.

- Where required, local or project SOPs should be developed and followed.

4.16 Appropriate Storage Period

The HTA does not define a time limit for the storage of tissues and organs for research, therefore tissue kept for any period is considered to be 'stored' (subject to exceptions detailed in 4.6-4.9). The HTA expects relevant material to be held under the governance of recognised REC approval or a HTA licence. Where storage is not governed by recognised REC approval it should be governed by both.

Tissue collections being held under a HTA licence must be reviewed annually and details reported to the DI for submission to the HTA Annual Survey of Holdings.

4.17 Storage Unit Labelling

All storage units used for human material must be labelled clearly in accordance with the following instructions. All labels should be laminated card and placed on the front of the unit.

a. All storage units will have an identifier, for example:

ILS1 Floor 2
Freezer 12

b. Storage units that contain human samples that are not held under a HTA Licence and are in use for a REC-approved research project or are being held prior to transport or processing to render acellular (no longer than one week) should be labelled as below:

Contains Human Samples TO BE KEPT LOCKED

c. Where human samples are being held for a specific REC-approved study (not held under a HTA licence) the contact details of the lead investigator/person responsible shall be displayed on the front of the unit to enable action to be taken in the event of malfunction.

Contact in the event of malfunction Contact name: Contact number:

Where robust, validated software-based temperature monitoring systems are in use, this sign may be omitted. Such systems must be subject to ongoing performance assessment.

d. Storage units that contain no human samples (relevant or non-relevant) must display the following laminated sign:

NO HUMAN SAMPLES ARE STORED IN THIS UNIT

e. Contingency freezers for use in the event of malfunction should have the following laminated sign affixed to the front:

> Contingency Freezer
>
> Not for general use
>
> In the event of malfunction, please contact:
>
> Contact name:
> Contact number:

f. Where samples are held under a HTA licence, units will be locked and access to samples will only be possible following discussion with the DI. Storage notices detailing the licence information will be included in this SOP once a licence has been granted.

g. The HTA requires that steps are taken to minimise contamination of human samples and to protect the handler from infection. Therefore the sign below should be affixed to the front of each storage unit where the wearing of gloves is required. Where human tissue is stored in ultra-low temperature units, protective padded gloves must be worn when accessing the tissue. Where possible human and animal samples should be stored in separate units to avoid cross-contamination of tissue.

h. Where human samples pose a risk of infection to handlers, the sign below should be affixed to the front of the storage unit

4.18 Security and Keys

All storage units that contain human samples should be lockable and located in access controlled rooms which are accessible only by authorized University / ABM UHB personnel. All storage units containing human tissue held under a HTA licence must be locked. Storage units that do not contain human tissue do not need to be locked. Contingency freezers should not be locked when in standby; however, once samples held under the licence have been transferred to them due to unit malfunction or an adverse event, they should be locked.

5. References

HTA Code of Practice A: Guiding Principles and the Fundamental Principle of Consent
https://www.hta.gov.uk/sites/default/files/files/HTA%20Code%20A.pdf

HTA Code of Practice E: Research; Code of Practice and Standards
https://www.hta.gov.uk/sites/default/files/Code%20E.pdf

6. Risk Assessment

A risk assessment for this HTA governance SOP is not required.

7. Definitions

Chief Investigator – The individual who takes overall responsibility for the design, conduct and reporting of a study if it is at one site; or if the study involves researchers at more than one site, the Chief Investigator takes responsibility for the design, management and reporting of the study, co-ordinating the investigators who take the lead at each site.

Consent – Process by which an individual confirms his/her willingness to participate in a particular procedure. The individual must have been informed of all aspects of the procedure/request that are relevant to the decision to participate. The individual must be competent to take the particular decision, be acting voluntarily and not be acting under duress.

Designated Individual – The person who is authorised and who supervises activities under a licence issued by the Human Tissue Authority.

Human Tissue – Any and all constituent parts of the human body formed by cells.

Human Tissue Act 2004 - Legislation that regulates the removal, storage and use of human tissue, defined as material that has come from a human body and consists of, or includes, human cells. The HT Act covers England, Wales and Northern Ireland. Consent is the fundamental principle of the legislation and underpins the lawful removal, storage and use of body parts, organs and tissue. Different consent requirements apply when dealing with tissue from the deceased and the living. The Human Tissue Act lists the purposes for which consent are required (Scheduled Purposes).

Human Tissue Authority – The independent regulator established by the HT Act to protect public confidence by ensuring human tissue is used safely and ethically, and with proper consent. The HTA licenses and inspects organisations that collect, store and use human tissue for the Scheduled Purposes, for which appropriate consent is required (unless exemptions apply).

HTA Codes of Practice - Provide guidance and lay down expected standards for each of the sectors regulated by the HTA (e.g. research) and under the HT Act. They are designed to support professionals by giving advice and guidance based on real-life experience.

HTA Standards - Core standards in four key areas that must be met for an organisation to obtain an HTA licence, relating to the provisions in the HT Act and the regulatory requirements: Consent; Governance and Quality Systems; Premises, Facilities and Equipment; Disposal.

Research Ethics Service – A core function of the Health Research Authority (HRA). It provides an efficient and robust ethics review service to protect the rights, safety, dignity and well-being of research participants.
Person Designate – Individual appointed by the DI to assist in supervising the licensable activities carried out within their organisation.

Principal Investigator – A Principal Investigator is the primary individual responsible for the preparation, conduct, and administration of a research grant, cooperative agreement, training or public service project, contract, or other sponsored project in compliance with applicable laws and regulations and institutional policy governing the conduct of sponsored research.

Relevant Material – Any material, other than gametes, removed from the body which consists of or includes human cells. In the HT 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,

See the Human Tissue Authority website1 for the HTA Supplementary List of Materials.

Research - A study which addresses clearly defined questions, aims and objectives in order to discover and interpret new information or reach new understanding of the structure, function and disorders of the human body. Research attempts to derive new knowledge and includes studies that aim to generate hypotheses, as well as studies that aim to test them or develop practical applications of new knowledge.

Risk Assessment - a careful examination of what could cause harm to people or resources. Workers and others have a right to be protected from harm caused by a failure to take reasonable control measures.

Scheduled Purposes - The activities relating to the removal, storage and use of human organs and other tissue that require consent, listed in Schedule 1 of the HT Act, e.g. research in connection with disorders or the functioning of the human body.

Standard Operating Procedure (SOP) – Detailed, written instructions to achieve uniformity of the performance of a specific function which an integral part of a quality management system. In the context of research using human samples, SOPs document all the processes that affect the quality and safety of those samples (e.g. acquisition, storage, transfer and disposal).

Storage – Maintaining the tissue under appropriate controlled conditions.

8. Appendix A – Example Sample Storage Label

Study:

Sample ID:

Sample Type:

Date Collected: