HUMAN TISSUE IN RESEARCH:

MANUAL FOR BU RESEARCHERS AND STUDENTS

Version 0.1, August 2019

Author: Dr Juan Campos-Perez

Clinical Research Coordinator

Bournemouth University Clinical Research Unit

CONTENT

1. INTRODUCTION

In the recent past, the general public's confidence in the medical profession has been damaged by several serious incidents and the media fuelled storms that followed. Notably amongst these are the murders committed by the general practitioner Harold Shipman, the enquiry into cervical screening at Kent and Canterbury, the activities of the gynaecologist Rodney Ledward, the Bristol heart enquiry and the enquiry into the retention of paediatric organs at the Royal Liverpool Children's Hospital NHS Trust (the "Alder Hey enquiry"). Of these, the Alder Hey enquiry is notable in that it will continue to have serious ramifications for the practice of research, anatomy and pathology [(1)].

The Alder Hey scandal arose in the autumn of 1999 when it became public knowledge that the discovery of more than 2000 pots containing organs and tissues removed from the bodies of 850, predominantly young children and infants, had been routinely retained after post-mortem for subsequent diagnostic, teaching, audit and research purposes. In the aftermath of the revelations, parents expressed two main concerns: first, they believed they had not given their "informed consent" for organs and tissues to be retained and secondly, a significant number of parents felt they had buried or cremated an "empty shell" instead of a whole body. In July 2002, responding to the frequent calls for legislative change, the Department of Health issued the consultation document "Human Bodies, Human Choices", which fed into and informed the introduction of the Human Tissue Act 2004 in which consent is posited as key [(2)].

2. THE HUMAN TISSUE ACT 2004

The Human Tissue Act (HT Act) defines a legal framework for regulating the storage and use of human tissue from the living and activities related to the removal, storage, and use of human tissue from the deceased. Under the HT Act, tissue is considered "relevant material" while the activities related to it are considered "scheduled purposes". It was fully implemented on 1st September 2006 in England, Wales and Northern Ireland; with Section 45 being implemented UK wide (including Scotland). With consent as its fundamental underlying principle, the HT Act aims to ensure that all human tissue is now managed in an ethical and sensitive manner, by providing a consistent legislative framework for matters relating to body donation and the removal, storage and use of human organs and tissues [(3)].

The HT Act also sets out the remit of the Human Tissue Authority (HTA), which is the body created for the purpose of regulating (through licensing) the activities defined under the HT Act. The HTA has produced a range of guidance documents called the Codes of Practice and Standards (CoP). The HTA CoP provides guidance on activities within the scope of the HTA's remit. With regards to the research sector, the HTA CoP defines the actions which ensure that potential tissue donors are given the information they need to make the best decisions requiring their consent. It is also mandatory for regulated organisations to manage human material in accordance with expressed wishes, removing, storing, using and disposing of material properly and respectfully.

2.1 How is human tissue regulated in Scotland?

Only one section of the HT Act applies in Scotland: Section 45, which regulates DNA analysis. Scotland has its own legislation covering human tissue: the Human Tissue (Scotland) Act 2006. A summary of the legislation applicable to Scotland can be found elsewhere [(4)].

3. THE HUMAN TISSUE AUTHORITY

The HTA is a regulator set up in 2005. The HTA was created by Parliament as a non-departmental public body of the Department of Health, and is overseen by an authority of lay and professional members appointed by the UK government. The HTA is governed by four guiding principles and seven Codes of Practice [(5)]. The guiding principles are summarised in Table 1 below.

The HTA regulates organisations that remove, store, and use human tissue for research, medical treatment, post-mortem examination, education and training, and display in public. It also gives approval for organ or bone marrow donations from living people.

The interests of the public and regulated bodies are central to the HTA's work. The rationale is that if patients and families know the use of human tissue and organs is regulated, they will have more confidence in knowing that their wishes will be respected, that organs and tissue used in treatment will be safe and of high quality and that tissue used for research or other purposes will be put to the best possible use. By fostering an environment of trust, it is believed that more people will be willing to donate their tissue for scientific and medical research, their organs for transplants, and their bodies for medical education and training.

Table 1: Summary of the HTA's guiding principles:

CONSENT	• Human tissue or bodies should be used in accordance with the expressed wishes of donors or their relatives • Donors and their relatives should be given the information they need to be able to make the right decision • Those seeking consent should do so sensitively
DIGNITY	• The dignity of the donor should be respected at all times • There should be mechanisms in place to protect tissues, organs and bodies from harm • The privacy of the individual should be maintained • The disposal of human tissue should be managed sensitively • Disposal of human tissue from the deceased should, where possible, be in line with their wishes and those of their relatives • Where human tissue is imported, it should be sourced from a country that has an appropriate ethical and legal framework
QUALITY	• Practitioners should be competent and have undertaken appropriate training and other relevant professional guidance • Practitioners' work should be subjected to a system of governance that ensures the appropriate and safe storage of human tissue and which safeguards the dignity of the living or deceased • Premises, facilities and equipment should be clean, secure and subject to regular maintenance • Proper and accurate records and information should be maintained to ensure full traceability of human tissue and bodies

	• Patient data should be held securely and confidentially
HONESTY AND OPENESS	• Communication with a donor, or person from whom consent is being sought, should be open, honest, clear and objective • Serious incidents involving human bodies and tissues should be subject to rigorous investigations • Establishments should adopt a policy of transparency when dealing with serious incidents • Discussions about medical investigation or treatment are kept entirely separate from discussions related to consent for tissue or organ donation • Establishments should be open and transparent in relation to arrangement for charging and reimbursement

3.1 Regulating research

The term "research" is often used to mean a wide range of activities which might be laboratory or treatment based. The type of research regulated by the HTA is perhaps best thought of as "laboratory bench" research. It is accepted that research using human tissue is crucial in order to advance our understanding of health and disease, but additionally that human tissue must be removed and stored in an appropriate and well managed way.

The HTA's licensing role in research is limited to licensing premises – such as tissue and brain banks – for storing tissue from the living and the deceased. They also license establishments – including post mortem establishments – where tissue is removed from the deceased for research.

Although the Act requires that removal of tissue from the deceased for research is licensed, its storage can be exempt from licensing. A significant amount of tissue stored for research is automatically exempted from licensing and consent requirements, because it comes from living people and there is project-specific approval from a recognised Research Ethics Committee (REC).

The activities licensed by the HTA under the HT Act are:

- Carrying out an anatomical examination
- Making a post-mortem examination
- Removal of "relevant material" from a deceased person
- Storage of "relevant material" for a number of "scheduled purposes"
- Storage of anatomical specimens and
- Public display of a body or relevant material from a deceased person

3.2 Satellite licensing

Satellite establishments are small premises that are under the same governance process as a larger establishment (the hub) and are supervised by the same DI as the hub. The DI at the hub must have systems in place to ensure that the governance framework is properly implemented and maintained.

3.3 What are "scheduled purposes"?

The HT Act 2004 defines the following activities requiring consent, as "scheduled activities":

- Anatomical examination
- Determining the cause of death
- Establishing after a person's death the efficacy of any drug or other treatment administered to him or her
- Obtaining scientific or medical information about a living or deceased person which may be relevant to any other person (including a future person)
- Public display
- Research in connection with disorders, or the functioning of the human body
- Transplantation

And, also requiring consent, the following activities related to deceased persons:

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

3.4 **What is "relevant material"?**

"Relevant material" is defined by the HT Act as material, other than gametes, which consists of or includes, human cells. The fundamental principle underpinning the Act is that if a sample is known to contain even a single cell that has been created inside the human body (i.e. bodily material) then the sample should be considered as relevant material.

However, the following materials are not considered relevant material:

- Embryos outside the human body (this is covered by the Human Fertilisation and Embryology Act 2008)
- Hair and nails from the body of a living person
- Cells produced outside the human body (such as cell lines)

For a comprehensive list of relevant materials, please see Appendix 1.

Material such as bodies, organs and tissues, which consist largely or entirely of cells, are easily identifiable as relevant material. However, there are instances when the distinction is less clear such as:

- Processed material which has been rendered acellular following a process (such as plasma or serum) is no longer considered relevant material.
- Plastinated tissue and body parts (where the cellular structure is retained by the plastination process) are considered relevant material
- Cell deposits or tissue sections on microscope slides are considered relevant material. This is because they are likely to contain whole cells or are representative of whole cells.
- Bodily waste products such as excretions and secretions are regarded by the HTA as relevant material as they may contain whole cells.

If in any doubt, please contact (TBC)

3.5 What about DNA?

DNA is not considered relevant material hence the storing of DNA without a license is not considered an offence under the HT Act.

However, under Section 45 of the HT Act, it is an offence to hold bodily material with intent to analyse its DNA without qualifying consent from the donor. The term "qualifying consent" is only used within Section 45 of the HT Act and is the same as any other consent for research, the only difference being who can provide it. The requirements differ depending on whether the person is deceased or living, an adult or a child [(6)].

Schedule 4 of the HT Act describes the interpretation of "qualified consent", and is explained in more detail in SOP (TBC).

3.6 What are the consequences of non-compliance?

Should an establishment be found to be non-compliant, this would have significant reputational and practical implications for the institution. Depending on the situation and on a case by case basis, the HTA may refer the matter to the police if any offences are suspected of being, or have been committed, under the applicable legislation.

Under the HT Act, the following are regarded as offences:

- The removal, storage or use of human tissue for scheduled purposes without appropriate consent
- Storage or use of human tissue donated for a scheduled purpose but used for another purpose
- Trafficking of human tissue for transplantation purposes
- Carrying out licensable activities without holding a license from the HTA
- Having human tissue including hair, nails, and gametes with the intention of analysing its DNA without the consent of the donor or those close to them if they have died (except for medical diagnosis and treatment and criminal investigations).

A person also commits an offence if he/she falsely represents to a person whom they know or believe is going to conduct a licensable activity where:

- There is appropriate consent to conduct the activity, or
- The activity is not a licensable activity, and
- He/she knows that this is false or does not believe it to be true

A person guilty of committing an offence shall be liable, on summary conviction to a fine not exceeding the statutory maximum. Following conviction on indictment, the person shall be liable to imprisonment for a term not exceeding 3 years, or to a fine, or both.

Individuals who fail to comply with the HT Act as described above are committing an offence unless he/she reasonably believes:

- That the activity they have conducted is not a licensable activity, or
- That the activity was conducted with appropriate consent, or

- The individual acts under the authority of a license

If following an inspection, a licensed establishment was found to be in breach of the HT Act regulations, the HTA may take action against the establishment and/or the Designated Individual (DI), for example by:

- Proposing additional conditions to the HTA license
- Issuing special directions that impose requirements on a licensed establishment with immediate effect
- Suspending or revoking a license

4. ROLES AND RESPONSIBILITIES UNDER THE HT LICENSE

The HTA prescribes that every establishment holding an HTL must clearly designate staff for the following roles:

License holder (LH)

Designated Individual (DI)

Persons Designated (PD)

License holder: the license holder is usually a corporate body (such as a University or an NHS Trust) with an individual's details provided as a contact person and to act as representative for the corporate body.

- The main role of the LH is to appoint a DI. However the potential DI must agree to take the role prior to applying for an HTL.
- The LH role does not impose any legal responsibility as this this is transferred to the DI.
- The LH has a right to variance. This enables them to substitute another person as the DI and allows the establishment to cover circumstances where the DI is unable or incapable of overseeing the licensable activities. Consequently, the HTA requires individual LH to be more senior than the DI.

Designated Individual: The DI is the person with ultimate legal responsibility for the establishment's compliance with the HT Act. This individual is appointed by the LH and must be suitable qualified to impose their authority. According to the HTA it is a requirement that the DI must have:

- A diploma, certificate or other evidence of formal qualification in the fields of medical or biological sciences; or
- Be otherwise considered by the HTA to be suitably qualified on the basis of academic qualifications and practical experience; and
- Have at least two years' practical experience which is directly relevant to the activity to be authorised by the license

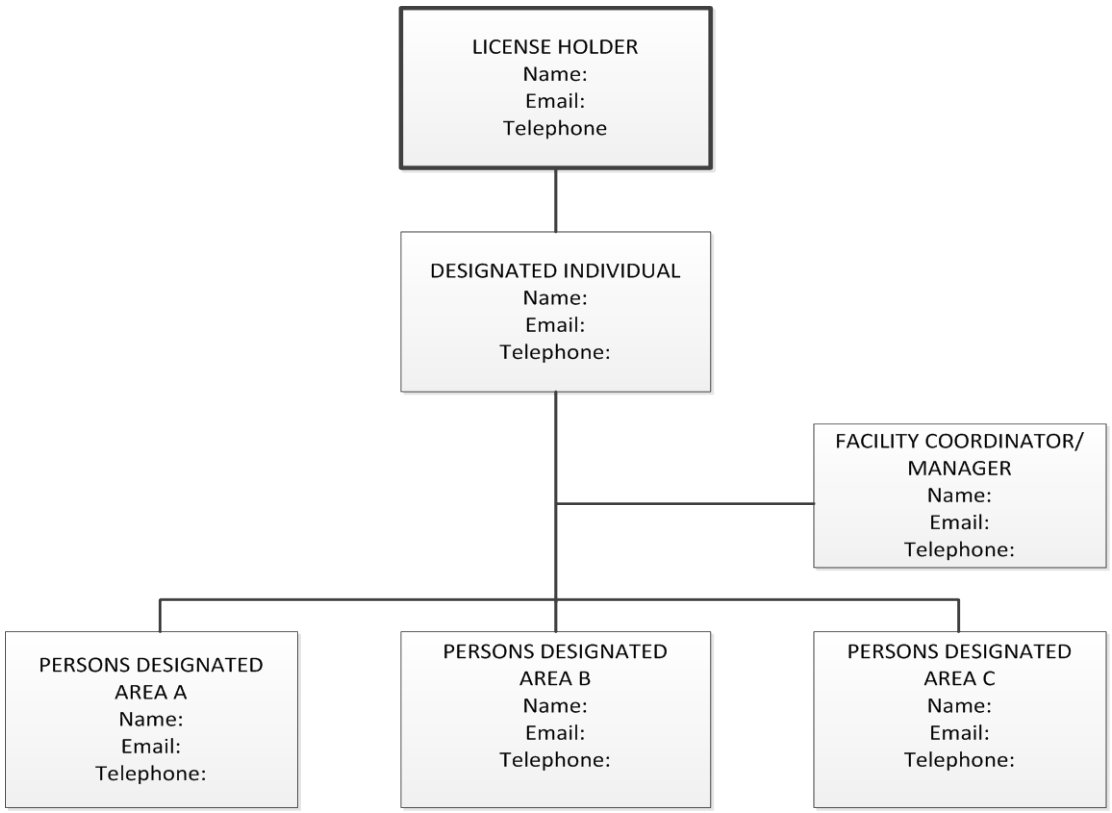
According to the HT Act, the designated individual is the person under whose supervision the licensed activity is authorised and their duties are:

- That every person working under an establishment's license is suitable to conduct the licensed activity
- That suitable practices are used in the course of carrying on that activity, and
- That the conditions of the license are complied with

Persons Designated: The PD(s) are designated by the DI. The HTA sees the role of the PD as supplementary to that of the DI in the governance framework, although the DI remains responsible for supervising the activities to be authorised by the license. The PD could act at a local level to support the DI. This could be, for example, to advise other persons to whom the license applies about the procedures and systems agreed by the DI that ensure compliance with the HT Act. The PD role does not impose any legal responsibility, but all PDs must formally accept the role. Figure 1 below shows how these roles and responsibilities are assigned within BU's human tissue facility.

Facility Manager/Coordinator: TBC

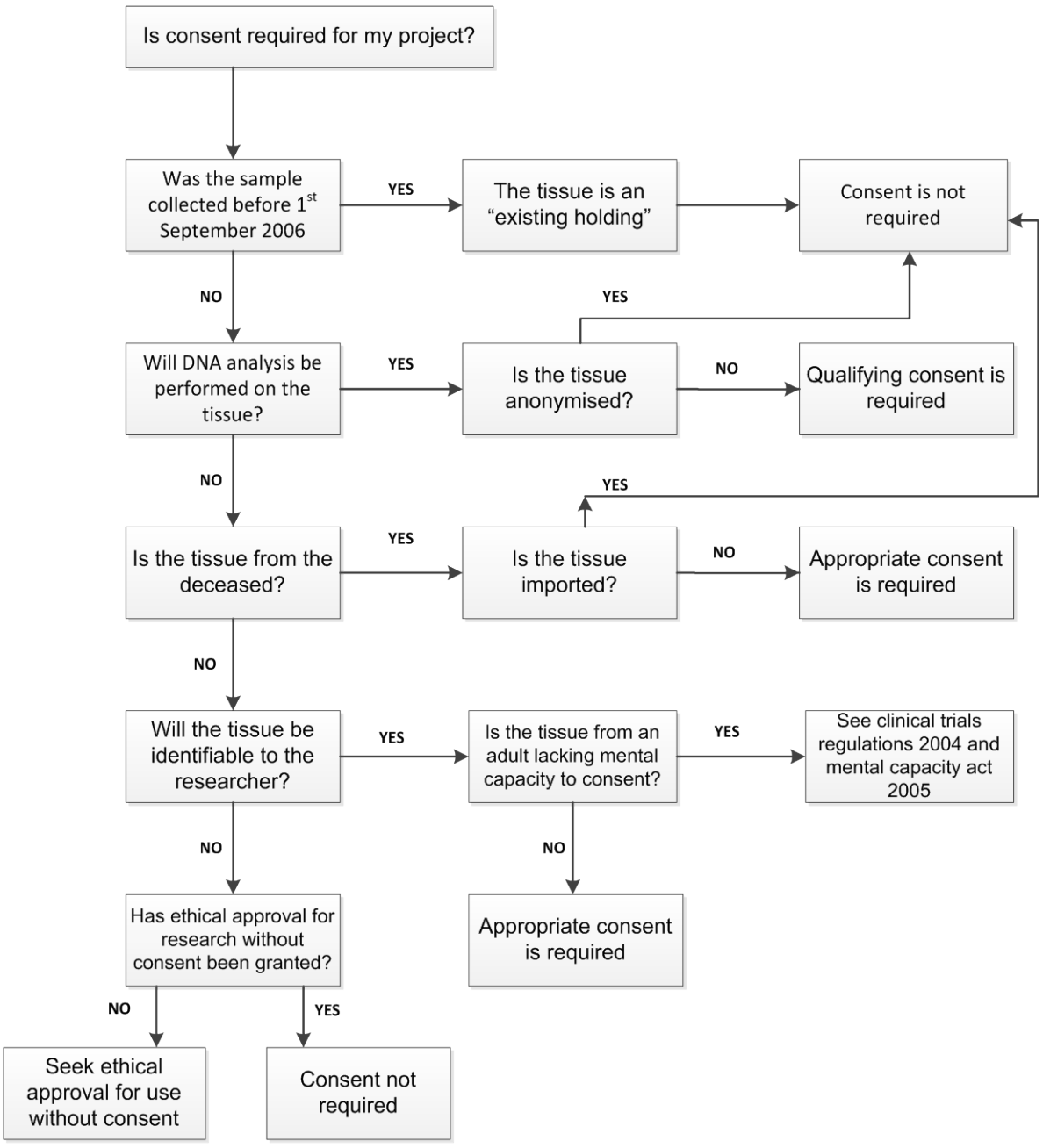
Figure 1. Structure of responsibility within BU's human tissue facility



5. CONSENT

The HT Act describes specific circumstances under which appropriate consent is required for removing, storing and using relevant human material for scheduled purposes. If appropriate and valid consent has been provided, then this is sufficient for an activity covered by the HT Act to proceed. Figure 2 below summarises these circumstances.

Fig 2. Decision tree for consent requirements



The HT Act and common law establish the principle that the decision to consent rests first and foremost with the person whose body, organs, tissues or cells are being used. When that person has died, their nominated representatives or relative should be sensitively supported to respect that person's consent to ensure the best chance of their wishes being fulfilled.

5.1 Valid consent

For consent to be valid it must satisfy the following requirements:

It must be given voluntarily by an appropriately informed person who has the capacity to understand the activity and the risks involved.

Consent may be specific or broader in scope (sometimes referred to as generic consent). Specific consent is given in relation to a defined project, whilst generic consent may be given for an as yet unknown research project.

If a donor expresses objections to specific types of research, these must be respected. A donation may not proceed if a donor places conditions on their consent which cannot be met or guaranteed.

To ensure that consent is properly informed, non-commercial organisations must ensure that materials provided to individuals to aid their decision making are accurate.

Consent should be recorded wherever possible. However, a signature on a form will not, in itself, make consent valid. Valid consent presupposes that individuals, including their families where appropriate, have had the opportunity to discuss the issue fully, ask questions and make an informed choice.

5.2 Broad and enduring consent

The MRC, HTA, HRA and several funding bodies recommend that broad and enduring consent (also known as generic consent) should be sought whenever possible. This allows for efficient use of samples, fosters trust with donors and avoids the need to either obtain further consent at a later date or use the samples without consent.

When seeking generic consent, participants should be informed that samples may be used in future research, the nature of which may be unknown. A disease area may be specified or for medical research more generally. If relevant, it should be made clear that possible future uses of the sample could include areas seen as "sensitive", where it may reveal clinically relevant findings, or there is the potential to identify participants. Participants should be notified that any future research will conform to all relevant legal, governance and ethical requirements.

5.3 Withdrawal of consent

Consent may be withdrawn at any time, whether it is generic or specific. Withdrawal should be discussed at the outset when consent is being sought. Withdrawal of consent cannot be acted upon where tissue has already been used. Remaining samples should be destroyed,

except when consent has been given for more than one scheduled purpose and consent has been withdrawn for a specific purpose.

5.4 **Is consent always required?**

There are times when it is not practicable to obtain consent and it is considered ethical to use samples for research without consent. The importance of many existing collections of human biological material (including pathology archives) is acknowledged even when in such cases retrospective consent is not practical, desirable or even ethical (see figure 1).

Situations where consent is not required:

- Tissue from the living may be stored and used for research provided that 1) the research has ethical approval (from an NHS REC) and 2) the tissue is anonymised
- **Existing holdings -** The consent requirements of the HT Act are not retrospective. This means that it is not necessary to obtain consent for material that was already held for use for a scheduled purpose when the HT Act came into force on 1st September 2006. However, ethical approval may still be required for research involving existing holdings.

RELEVANT DOCUMENTS:

SOP XXXX

SOP XXXX

SOP XXXX

6. ETHICAL APPROVAL

The process to follow, with regards obtaining ethical approval for a given project, will depend on whether the tissue is collected from NHS patients or members of the public ("healthy volunteers"). Ethical approval may also be required to use existing tissue samples already held in storage facilities.

Ethical approval for obtaining tissue from NHS patients – In order to collect new tissue samples from NHS patients, researchers must obtain the approval of the Health Research Authority (HRA). HRA approval now includes the ethical review of the project by an independent NHS REC and also includes additional review of governance and legal compliance. For more information on the HRA please visit:

https://www.hra.nhs.uk/

Applications for HRA review must be done via the IRAS system, which can be accessed here:

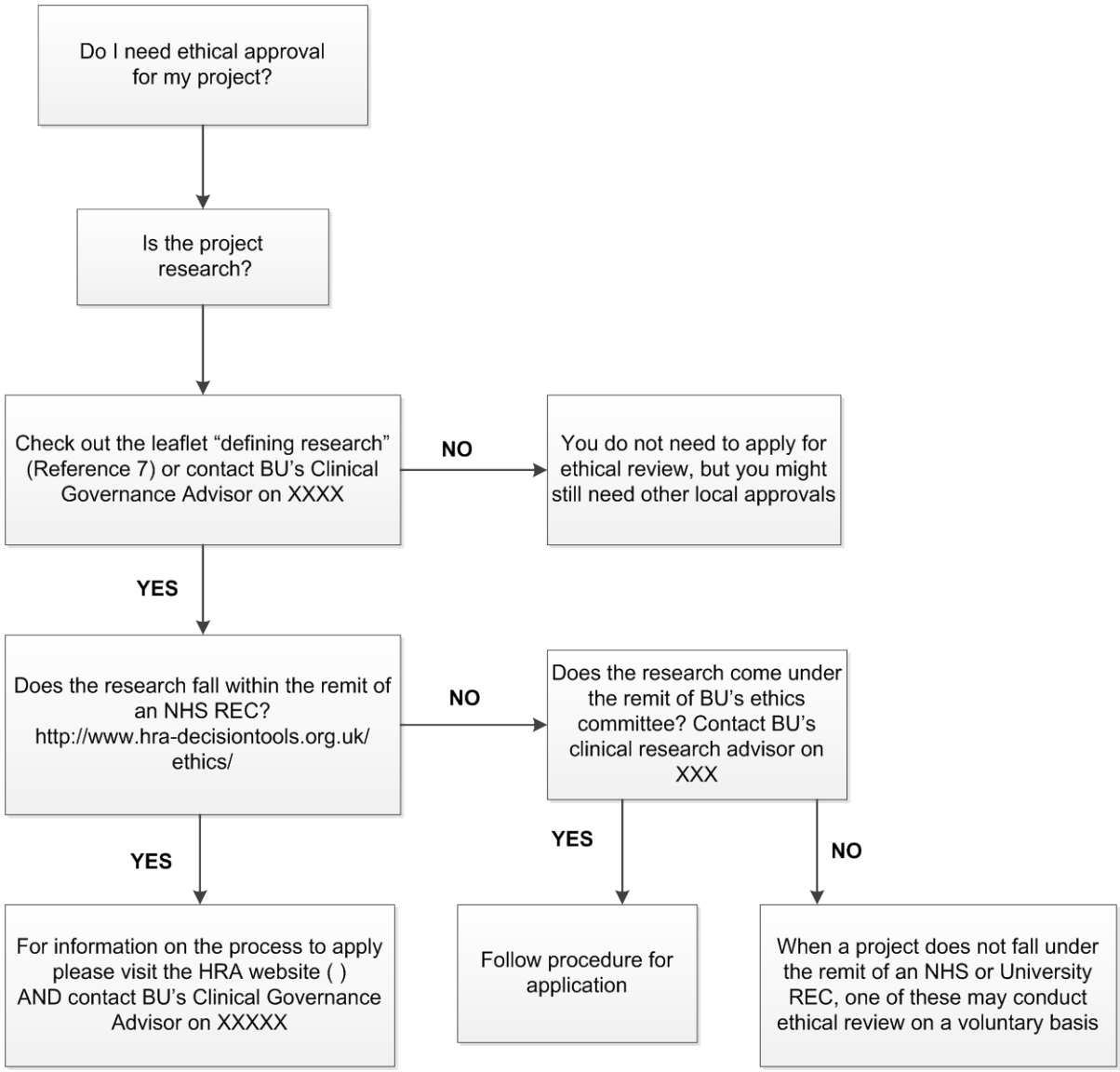
https://www.myresearchproject.org.uk/

Researchers applying to collect material for future, yet unspecified use ("research tissue bank") will receive a list of terms and conditions that must be abided by. One of the conditions of approval is that the Chief Investigator registers the tissue bank on the UKCRC national directory of tissue banks:

https://www.biobankinguk.org/

Ethical approval for using pre-existing tissues – Some research tissue banks already have ethical approval in place for research to be conducted on the samples. This approval is obtained from an NHS REC and may cover any research project involving tissue for which generic consent has been granted.

Figure 3 below offers guidance regarding ethical approval for research



RELEVANT DOCUMENTS:

SOP XXXX

SOPXXXX

SOP XXXX

7. QUALITY SYSTEMS

Bio-specimen collection is fundamental to both diagnostics and clinical studies, often performed in the context of clinical research and clinical trials. Results of analysis of biological samples can be influenced by conditions that samples have been exposed to during sampling, processing, transport and storage prior to usage. Human tissue facilities therefore need to ensure that samples are interchangeable, without institute-dependent intrinsic bias, offering industry/academic researchers an assurance of the accuracy, reproducibility and compatibility of research results [(8)].

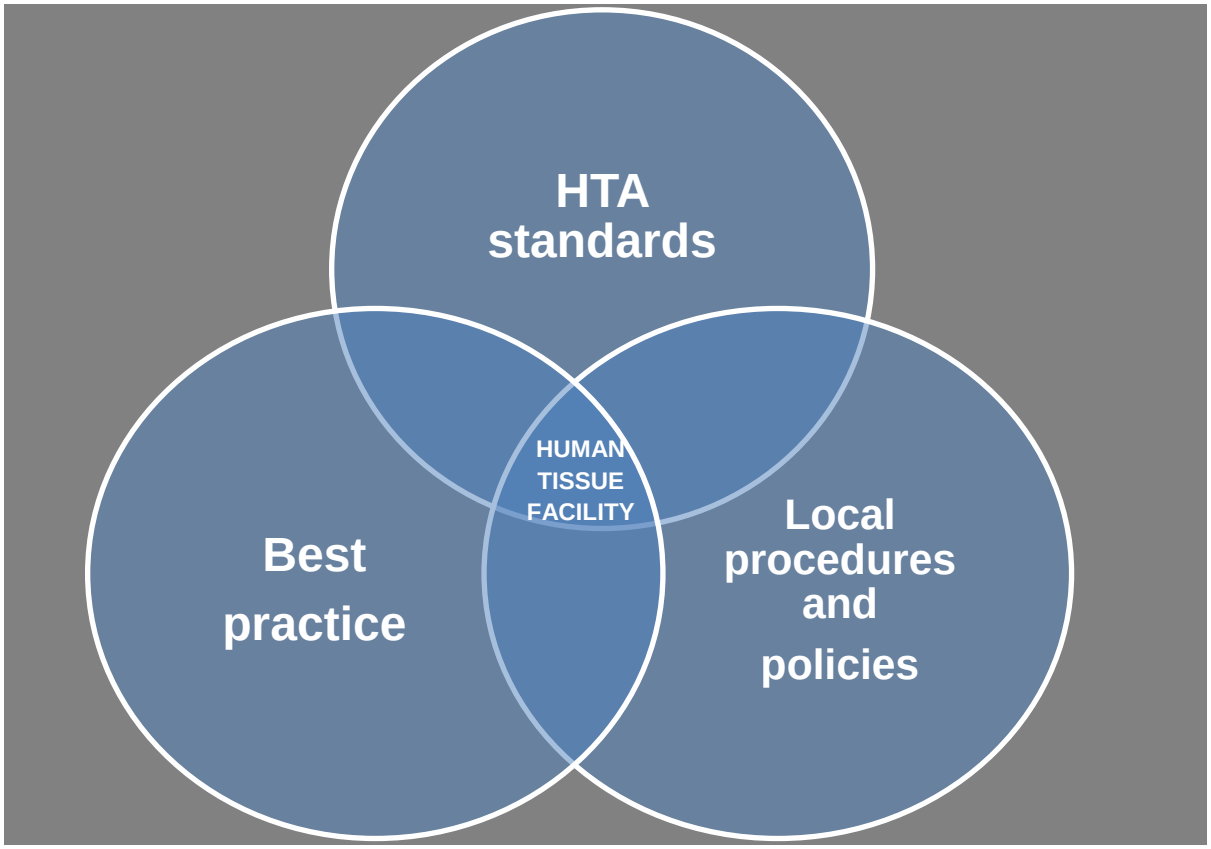
Poor quality control systems on the other hand can lead to the waste of valuable samples e.g. storage at an incorrect temperature or the use of misidentified cell lines can lead to inaccurate research results or the inability to reproduce research results.

In addition to the above, a good governance framework should define the organisational structure of the facility, for day to day management and oversight of its strategic policy. The facility should also have a structure of committees and appropriately qualified personnel in relevant roles to oversee its governance. The size, type, and number of committees and their composition will vary depending on the size and purpose of the facility.

7.1 **What quality systems and policies underpin BU's human tissue facility?**

As described in section 3, the HTA sets the standards to which all human tissue storage units must adhere to. However, the HTA does not favour any particular method used in order to achieve the required standard, since such methods will be influenced by the local environment such as resources, purpose of the facility and local policies. Further guidance is available as "best practice" documents developed by experts in the field and published by national and international organisations (Figure 4).

Quality systems use a combination of procedures (SOPs), processes and records systems to ensure that researchers know how the samples have been handled and how this will affect the samples' quality. It is therefore important that investigators adhere to these procedures and maintain all records up to date in order to demonstrate that samples are "fit for purpose" for their own uses and, where applicable, provide assurances to collaborators.



The documents, information and guidance available within BU which support the quality assurance of the tissue samples stored within the facility are available here:

(TBC) (link to the human tissue facility's governance webpage)

And relevant BU policies can be found here:

https://www.bournemouth.ac.uk/research/research-environment

7.2 Responsibilities of all those working under the HT license

In addition to the formal roles set out by the HT Act and described in section 4, it is the responsibility of all staff working under BU's HTA license:

- To know their responsibilities under the Act
- To treat donated material with dignity and respect
- To protect the privacy and wishes of donors and maintain data confidentiality
- To attend training sessions or follow self-guided training as required
- To read SOPs, guidance and other materials available and ensure those working under them (such as students, technicians, etc) are also trained and competent in their role
- To keep up to date with changes in the legislation and/or human tissue facility rules by reading the email newsletter circulated at regular intervals

- In accordance with the terms and conditions of BU's HTA license, the DI must be aware of ALL material stored at the University. This includes cases where the material is covered by a specific NHS REC approval where the HTA license is not required

If you are unsure as to what your responsibilities are under the HT Act or how to comply with the above rules, please contact (TBC).

7.3 Sample tracking

Across any given organisation, different teams tend to use their own particular methods and systems to keep records and store data. These systems range from paper records, Microsoft Word documents, Microsoft Excel and Access databases, to advanced bespoke solutions. Most of these systems are not suitable and fail to meet the standards required to fulfil the University's obligations, the main issue being the lack of an audit trail.

Under the HTA standards on traceability (see Appendix 2) it is a requirement to ensure that:

- There is a system which assigns a unique code to each sample and each of the products associated to it
- A register of donated material, and the associated products where relevant, is maintained
- An audit trail is maintained which includes details of: when and where the tissue was acquired and received, the consent obtained, all sample storage locations, the uses to which any material was put, when and where the material was transferred, and to whom
- A system is in place to ensure that traceability of relevant material is maintained during transport, including:
  - Records of transportation and delivery are kept
  - Records of any agreements with courier or transport companies are kept
  - Records of any agreements with recipients of relevant material are kept

In order to avoid any significant regulatory and reputational risk as a result of non-compliance, the University provides researchers with a unified approach by investing in the (TBC) system. This system provides a simple solution to the auditing and tracking issues by providing tissue samples with a unique sample number, quick and easy regulatory reporting, audit trail and full traceability to donor consent documents.

RELEVANT DOCUMENTS:
SOP XXXX
SOP XXXX

7.4 Training

It is the responsibility of all staff and users of the facility to ensure they are appropriately trained for the activities they conduct. Appropriate training should be identified during the induction process and regularly updated every (TBC) years or as identified during annual performance reviews.

For a list of local training sessions and dates please visit:

(TBC) (courses and dates on governance website)

Training is free to all BU staff and students. If you do not have a BU email address but are involved in a project sponsored by BU or actively involved in the collection of samples to be transferred to BU's human tissue facility, you are eligible to access the training for free.

RELEVANT DOCUMENTS:

SOP XXXX: Human tissue training

7.5 Oversight

Oversight for strategic decisions and risk management regarding BU's human tissue facility is covered by the following groups:

Committee 1: TBC

Remit:

Committee 2: TBC

Remit:

Committee 3: TBC

Remit:

7.6 Best practice

In addition to the HTA standards and local policies, guidance has been developed by several national and international organisations in an attempt to reach a consensus regarding how human tissue facilities should be run. These guidance documents are known as "best practice" documents. The term "best practice" is used in cases where a level of operation is indicated that is above the basic recommended practice or more specifically designates the most effective practice. Whilst it is acknowledged that best practice may not be achieved currently by all organisations, organisations are expected to work towards achieving best practice.

One of such organisations is the International Society for Biological and Environmental Repositories (ISBER) whose document "Best practices for repositories: collection storage,

retrieval and distribution of biological materials for research" is a comprehensive tool to guide researchers in a wide range of activities covering infrastructure, equipment, security and training [9]. Another comprehensive guidance document for the management of human tissue facilities but with a focus on cancer research is provided by Mendy et al: "Common minimum technical standards and protocols for biobanks dedicated to cancer research" [10]. With regards to the UK, the National Cancer Research Institute, in collaboration with the Confederation of Cancer Biobanks has developed a set of guidelines entitled "Biobank quality standard: collecting, storing and providing human biological material and data for research" [11]. All three documents are recommended as further reading for those interested in learning about the management of human tissue storage facilities in more detail.

7.7 Data protection

The protection of individual privacy is enshrined in legal instruments and is a benchmark of civil society. Although privacy is not an absolute right, interference must be justified in the public interest and/or according to law. Within research, the expectations and norms associated with different kinds of research can lead to variation in the practices that apply. Some privacy risks that have been identified include disease status, future likelihood of a disease or condition, or an individual's ancestry or relatedness. Hence, protections must be established to prevent discrimination against research participants and ensure that their medical and personal information is not disclosed to third parties such as their family and community members, their employers, or insurance companies, against their wishes. This is particularly important when DNA analysis is involved since it may have implications not only for the participant but for their family members for generations to come [12].

The protection of identifiable data is not included in the HT Act, but is governed by the General Data Protection Regulation (GDPR) which came into effect in May 2018. In practice, data collected during clinical research activities will likely be either:

Identifiable data: Data which is clearly related to an individual such as name, address, email, date of birth, etc.

Coded/link-anonymised data: Data which cannot directly identify an individual but can be re-connected to a donor, if required, by means of a code.

Anonymised data – data which cannot be linked back to the donor, as all links have been removed.

- If you wish to collect identifiable data, provide participants with detailed information about how their data will be managed (WHO will have access to the data, WHAT data will be stored, WHY it is needed, WHERE the data will be stored)
- Respect participants' consent options during access, use and transfer of data
- Whenever possible, use a method to protect privacy such as de-identification, coding, or link-anonymisation, and consider how this affects re-contact and return of results
- Develop a policy or procedure that describes the process of re-identifying participants
- Coded data and codes should be stored separately
- Develop robust data management systems and audit trails
- Manage, limit and trace rights of access to such data management systems
- Limit physical access to data storage areas (e.g. store paper documents in rooms with limited access) and implement electronic security procedures (password protected computers) where possible

For further information regarding BU's data protection policy, please visit:

https://www.bournemouth.ac.uk/about/governance/access-information/data-protection-privacy

8. COULD ANY INTELLECTUAL PROPERTY (IP) ARISE FROM A HUMAN TISSUE BIOREPOSITORY?

Repositories of human tissue (such as biobanks) are a relatively new research resource and their main purpose is to allow ground-breaking research for the benefit of patients. Any consideration of IP rights in the context of biomedicine arouses a wide range of views. While some people claim that IP rights cause blocks to innovation and prevent academic and scientific research, others think IP incentivises innovation and leads to the development of new treatments.

It is worth noting at this point that information by itself cannot be owned. As a result, an individual genetic profile in a biobank is not the subject of IP rights. However, elements of the infrastructure involved in running a biobank, or innovations produced as a result of research conducted using biobank resources can sometimes lead to IP rights, which are summarised as below [13]:

- A biobank may be the subject of copyright protection as a database (under UK law, a database is protected as a literary work). However, the database will only be protected if it is the author's own intellectual creation, by reason of the selection or arrangements of the contents of the database.
- Another type of IP right that may arise in a biobank is the database right. This right arises if there has been a substantial investment of financial, human or technical resources. The creation of a biobank would quite clearly satisfy these requirements.
- IP might also arise in other areas which aid the biobank's functionality: software, manuals or SOPs could all potentially be the subject of copyright and thus protected from unauthorised copying and also be licensed commercially, or placed in the public domain.
- When research gives rise to innovation, then the invention could potentially be patentable. In Europe, patents are only available for inventions and not for discoveries. As such, patents are available for inventions in the form of products such as chemicals or useful objects, and also processes or methods. The invention must be novel and it must be useful in some way.
- The human body at any stage of development, and the simple discovery of one of its elements, including a total or partial sequence of a gene, is not a patentable invention. However when an element is isolated from a human body or otherwise produced by means of a technical process, it may be a patentable invention. By way of an example, a genetic diagnostic test which is the technical embodiment of the discovery of a relationship between a gene and a disease is patentable, while the mere relationship between the gene and the disease is not.

To summarise, it is important to note that although researchers may not originally own a tissue sample itself, they can come to "own" the product of work or skill applied to the sample. This may involve IP rights generated from a sample. Patenting of inventions based on, or using, biological material of human origin is covered by the EU directive on the Legal Protection of Biotechnological Inventions [(14)].

If you believe your research has given rise to IP rights, or for more details on this subject, please contact (TBC) for further information.

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APPENDIX 1. Full list of relevant material as per the HTA

MATERIAL	RELEVANT MATERIAL FOR THE PURPOSES OF THE HUMAN TISSUE ACT 2004?
Antibodies	No
Bile	Yes
Blood	Yes
Bone marrow	Yes
Bones/skeletons	Yes
Brain	Yes
Breast milk	Yes
Breath condensates and exhaled gases	No
Buffy coat (interface layer between plasma and blood cells when blood is separated)	Yes
Cell lines	No
Cells that have divided in culture	No
Cerebrospinal fluid	Yes
Cystic fluid	Yes
DNA	No
Eggs (ova)*	No
Embryonic stem cells (cells derived from an embryo)	No
Embryos (outside the body)*	No
Extracted material from cells (nucleic acids, organelles, proteins, etc)	No
Faeces	Yes
Foetal 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 (cells derived from the body)	Yes
Non-foetal products of conception (amniotic fluid, umbilical cord, placenta and membranes)	Yes
Organs	Yes
Pericardial fluid	Yes
Plasma (complete absence of blood cells)	No
Platelets	Yes
Pleural fluid	Yes
Primary cell cultures	Yes
Pus	Yes
RNA	No
Saliva	Yes

Serum	No
Skin	Yes
Sperm cells (spermatozoa)*	No
Sputum (or phlegm)	Yes
Stomach contents	Yes
Sweat	No
Teeth	Yes
Tumour tissue samples	Yes
Umbilical cord blood stem cells	Yes
Urine	Yes

Notes

*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).

Appendix 2. Summary of HTA standards

CONSENT STANDARDS	
C1. Consent is obtained in accordance with the requirements of the Human Tissue Act 2004 and as set out in the HTA's code of practice.	Consent procedures are documented and these, along with any associated documents, comply with the HT Act and the HTA's Codes of Practice
	Consent forms are available to those using or releasing relevant material for a scheduled purpose (*Guidance: Legal requirements, such as the Data Protection regulations and the common law duty of confidentiality, need to be considered in such circumstances*)
	Where applicable, there are agreements with other parties to ensure that consent is obtained in accordance with the requirements of the HT Act and the HTA's Codes of Practice.
	Written information is provided to those from whom consent is sought, which reflects the requirements of the HT Act and the HTA's Codes of Practice
	Language translations are available when appropriate
	Information is available in formats appropriate to the situation *General guidance:* *Consent is the fundamental principle of the Human Tissue Act (2004) and the HTA Codes of Practice A (Guiding principles and fundamental principles of consent) and E (Research) are the primary sources of guidance for compliance with this standard. For health related research in general i.e. not limited to that involving human tissue, the Health Research Authority (HRA) provides resources such as template consent forms and participant information sheets.*
C2. Staff involved in seeking consent receive training and support in the essential requirements of taking consent	There is suitable training and support of staff involved in seeking consent, which addresses the requirements of the HT Act and the HTA's Codes of Practice.
	Records demonstrate up-to-date staff training.
	Competency is assessed and maintained. *General guidance* *It is important that consent training is not considered a one-off event and that proficiency in seeking consent is upheld. There is no set requirement for the frequency of consent training.* *Individuals taking consent are expected to maintain awareness of current standards through reference to published guidance and relevant policies. Training may need to be updated when legislation has changed, new policies or practices have been implemented, different research activities are to be undertaken or a significant period of time has elapsed since research activities have been conducted.*

GOVERNANCE AND QUALITY SYSTEMS STANDARDS	
GQ1. All aspects of the establishments work are governed by documented policies and procedures as part of the overall governance process	Ratified, documented and up-to-date policies and procedures are in place, covering all licensable activities *Guidance* *At a minimum, it is expected that most establishments will have standard operating procedures (SOPs) covering the following activities: **consent; collection; receipt; labelling; specimen preparation / preservation; storage; relevant transport arrangements; cleaning and decontamination; disposal.*** *More complex establishments, especially those releasing material, may need to cover more areas in their suite of documents.* *A standard operating procedure (SOP) should be a clear and accurate representation of an existing procedure or process, preferably set out in the format of a stepwise guide. SOPs should be understandable to enable new staff to follow a procedure from beginning to end. They should be detailed enough to ensure uniformity between staff in the performance of a specific function and should be followed to the letter by all staff who have been appropriately trained.* *People undertaking the processes should be involved in developing the SOPs to ensure that the written procedures reflect actual practices. Regular review of SOPs will help to prevent incremental departure from written processes with the passing of time and allow establishments to identify improvements. Establishments should introduce a system to record that staff have read and understood SOPs.* *If human tissue is to be transferred between establishments, consideration must be given to minimise the likelihood of theft, damage or loss during transport.* *Some form of formal transfer arrangement, for example, as part of a Material Transfer Agreement (MTA), should define how the human tissue is preserved, any potential contamination risks associated with it; and who is responsible for disposal, if applicable. We do not specify or endorse any particular format for MTAs; a number of template agreements are publically available and can be adapted to suit individual circumstances. Transportation procedures should also give sufficient detail to ensure the integrity of the tissue.*
	There is a document control system. *Guidance* *- Governance documents should include:* *- Revision history and version number; Effective from' date; Review date (at least every three years); Pagination; Author and reviewer names*
	There are change control mechanisms for the implementation of new operational procedures. *Guidance* *Change control mechanisms should take into account the risks of any planned changes, any validation required, any training required and how implemented changes will be reviewed.*

	Matters relating to HTA-licensed activities are discussed at regular governance meetings, involving establishment staff. *Guidance* *All staff working under the HTA licence should be aware of the governance arrangements in place, and they should be represented at governance meetings.* *Overall governance processes should be supported by regular meetings with staff at the establishment who are engaged in licensed activities. Formal meetings should be minuted and the actions should be noted and followed up.* *Documented minutes of meetings should be distributed to all relevant staff to help to ensure that they are aware of all important information relating to licensed activities at the establishment. National and local information relevant to activities should also be disseminated.*
	There is a system for managing complaints. *General guidance* *A formal quality management framework helps to establish minimum expectations for governance and quality systems, and facilitates continuous improvement. The work of the staff at the establishment must be subject to a system of governance. This means that there should be clear reporting lines and accountability (particularly with regard to individual staff and the DI), documented roles and responsibilities. Establishments are encouraged to have an over-arching quality document which provides an overview of the establishment's main purpose, organisation and structure and approach to governance and quality. This document should be accessible to all staff involved in licensed activities.* *The HTA recommends that establishments adopt a harmonised approach to sample management as there are risks of varying practices where samples being stored for REC-approved projects are managed differently to samples subject to HTA's licensing standards.*
GQ2. There is a documented system of audit	There is a documented schedule of audits covering licensable activities
	Audit findings include who is responsible for follow-up actions and the timeframes for completing these *General guidance* *Audits will demonstrate compliance with our standards and demonstrate whether establishments are meeting the requirements of their own systems.* *A documented schedule of audits should be in place at each establishment.* *Vertical audits of records and specimens will allow the establishment to assure itself that specimens and records are fully traceable from consent to disposal.* *Records, including records of consent, should be audited regularly to ensure completeness, accuracy and legibility.* *Audits should ideally include horizontal audits by staff involved in the processes, to ensure that SOPs accurately reflect actual practices and to identify areas for improvement. All audit findings and related corrective and preventative actions should be recorded to allow the establishment to demonstrate compliance with HTA standards and follow-up outstanding actions.* *Audit processes can benefit from being undertaken by a person who is not normally involved in the activity at the establishment: a 'fresh eyes' view. Internal auditors should not be involved in auditing their own work.* *Some establishments may be able to make use of existing in-house expertise or services.*

GQ 3. Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills	Qualifications of staff and all training are recorded, records showing attendance at training.
	There are documented induction training programmes for new staff.
	Training provisions include those for visiting staff.
	Staff have appraisals and personal development plans. *General guidance* *Training and induction packages help to ensure that staff are fully trained on all policies and procedures relevant to their work. Establishments should ensure that training and development plans are in place and that these are reviewed periodically.* *Staff should be encouraged to attend professional meetings and training events to ensure that they keep abreast of good practices in their areas of expertise.*
GQ4. There is a systematic and planned approach to the management of records	There are suitable systems for the creation, review, amendment, retention and destruction of records. *Guidance* *Documented records are used by establishments to evidence traceability and ensure a robust audit trail. In this context, traceability refers to the completeness of auditable information about every step in the pathway for the use of relevant material, from consent through to disposal, or the material has been used up entirely. Documented procedures for the creation, review, amendment, retention and destruction of records are required to help to ensure that records are maintained appropriately. SOPs should detail the frequency of document review required to ensure that documents are regularly reviewed and updated as necessary.*
	There are provisions for back-up / recovery in the event of loss of records. *Guidance* *Records may be in various formats, including paper based, electronic, or stored on recordable media. A centralised system for the storage of records can help to ensure that records are regularly backed-up.*
	Systems ensure data protection, confidentiality and public disclosure (whistleblowing). *Guidance* *Consideration must be given to other relevant legislation, including compliance with the Data Protection regulations where tissue has been taken from the living, and compliance with professional guidelines where applicable*

GQ5. There are	

systems to ensure that all adverse events are investigated promptly	Staff are instructed in how to use incident reporting systems
	Effective corrective and preventive actions are taken where necessary and improvements in practice are made. *General guidance* *All establishments licensed by the HTA are required to have an internal system for reporting adverse events and, where necessary, instigating an investigation or root cause analysis.* *Clearly assigning responsibilities for incident management is important. As the DI is responsible for licensed activities at the establishment, there should be a process in place to allow them to be made aware of adverse events so that proper investigation and reporting can take place. There should be an adverse incident SOP detailing how adverse incidents are logged, reported, addressed and monitored.* *Although there is currently no requirement for establishments in the research sector to report adverse incidents to the HTA, if a DI has concerns about an adverse event, they are encouraged to contact us for further advice.* *Relevant examples of adverse events include: specimen loss; missing or incorrect documentation; security breach; abnormalities in storage temperature readings; Inappropriate disposal*
GQ6. Risk assessments of the establishment's practices and processes are completed regularly, recorded and monitored	There are documented risk assessments for all practices and processes requiring compliance with the HT Act and the HTA's Codes of Practice. *Guidance* *All establishments should identify the risks inherent in the key activities, and procedures should be developed in consideration of and to mitigate these potential risks where appropriate. Establishments may tend to focus risk assessments on health and safety issues which, in themselves, are not sufficient to meet our standards. DIs should also assess the risks associated with licensed 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 remaining.* *Risk assessments should include the risks relating to the premises, practices and procedures connected with licensed activities, including: receiving and/or storing specimens without appropriate consent; documentation; storing or using human tissue after consent withdrawal; storage failure or other damage affecting human tissue quality for useful research; 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 are reviewed regularly. *Guidance* *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.*
	Staff can access risk assessments and are made aware of risks during training. *Guidance* *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.*

TRACEABILITY	
T1. A coding and records system facilitates the traceability of bodies and human tissue, 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.
	A register of donated material, and the associated products where relevant, is maintained.
	An audit trail is maintained, which includes details of: when and where the bodies or tissue were acquired and received; the consent obtained; all sample storage locations; the uses to which any material was put; when and where the material was transferred, and to whom.
	A system is in place to ensure that traceability of relevant material is maintained during transport.
	Records of transportation and delivery are kept.
	Records of any agreements with courier or transport companies are kept.
	Records of any agreements with recipients of relevant material are kept. *General guidance* *Where relevant, through their coding and records systems, HTA-licensed establishments should be able to demonstrate their awareness and ability to track ethical approval expiry dates and any relevant conditional agreements, such as consent opt-outs.*
T2. Bodies and human tissue are disposed of in an appropriate manner	Disposal is carried out in accordance with the HTA's Codes of Practice.
	The date, reason for disposal and the method used are documented. *General guidance* *Establishments should carefully document disposal. Supporting procedures should detail the requirements for recording the details of disposal, including the date, reason and method. Records of disposal should be kept in order to provide a complete audit trail from donation through to disposal.*

PREMISES, FACILITIES AND EQUIPMENT STANDARDS	
PFE1. The premises are secure and fit for purpose	An assessment of the premises has been carried out to ensure that they are appropriate for the purpose. *Guidance* *The establishment must be clean, well maintained and subject to a programme of planned preventative maintenance. Suitable environmental controls should be in place to avoid potential contamination.* *Establishments should periodically review risk assessments of premises, facilities and equipment. This should ideally include an audit of the premises and equipment in order to identify areas requiring rolling maintenance, refurbishment or upgrade. This will help to ensure that remedial actions are implemented in a timely manner so that the premises, facilities and equipment remain fit for purpose.*
	Arrangements are in place to ensure that the premises are secure and confidentiality is maintained *Guidance* *Security measures include the use of locks, alarm systems and protections against unauthorised access.* *Establishments are expected to have policies in place to review and maintain the safety of staff, visitors and other relevant people e.g. students or donors.*
	There are documented cleaning and decontamination procedures *Guidance* *Documented cleaning and decontamination procedures should be supported by schedules.*
PFE2. There are appropriate facilities for the storage of bodies and human tissue	There is sufficient storage capacity.
	Where relevant, storage arrangements ensure the dignity of the deceased.
	Storage conditions are monitored, recorded and acted on when required. *Guidance* *Documented temperature monitoring allows establishments to easily visualise and identify when temperatures are out-of-range. It can also demonstrate temperature trends, to identify when storage conditions may be deteriorating and to alert staff to developing equipment failure. Temperature alarms should be regularly tested and manually challenged periodically to ensure that they are operating as expected.* *Signs should be added to freezers to define alarm set points for the temperature ranges so that staff are visually reminded of minimum and maximum temperatures.* *Where storage is critical, an appropriate remote temperature monitoring alarm and callout system may be required.* *Checks and filling of liquid nitrogen dewars should be documented. Where material can be stored at ambient/room temperature, this does not mean that storage conditions do not need to be monitored.*
	There are documented contingency plans in place in case of failure in storage area. *Guidance* *The establishment must have contingency arrangements in place should there be an emergency situation that renders the premises unusable for the storage of human*

	tissue; this may need to be through a formalised arrangement with another HTA-licensed establishment for transfer of material. *General guidance* *Areas used for storage of human tissue for use in research must provide an environment that is safe for those working under the licence and preserves the integrity of the tissue.* *Refrigerators, freezers and other vessels which contain human tissue should be appropriately labelled so that staff are aware of the necessity to maintain the quality, safety and security of such material and prevent mix-ups with other tissues.* *Human tissue must be stored in such a way that it minimises the risk of contamination to those working under the licence. If necessary, the DI should work with health and safety personnel to implement environmental controls and appropriate equipment to reduce the risk of contamination.*
PFE3. Equipment is appropriate for use, maintained, validated and where appropriate monitored	Equipment is subject to recommended calibration, validation, maintenance, monitoring, and records are kept. *Guidance* *Equipment must be regularly maintained to ensure that it is suitable for use.* *Equipment should be made of material that is easy to clean, impervious, nonrusting, non-decaying and non-staining.*
	Users have access to instructions for equipment and are aware of how to report an equipment problem. *Guidance There should be a system for renewing items that are no longer suitable through wear and tear.*
	Staff are provided with suitable personal protective equipment. *Guidance Staff must have access to the protective clothing, materials and equipment they need.*