# Enacting regulation: tissue in practice

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**Abstract**

This paper steps to the side of the usual discussions of the status of tissue in ethics and law to consider instead the enactment of regulation in the daily practice of researchers. This is a separate and often overlooked area between regulation as drafted by legislators and policy makers, and as experienced by those who work within that regulatory frame. The paper considers the governance and procedures put in place and the expertise made available in one research centre.

Focus on the bridging, facilitation activity of a particular research tissue bank affords an on-the-ground account of how ethical and legal requirements related to the use of human tissue in research in the United Kingdom work out in the everyday practice of collecting, storing and providing tissue for research.

**Keywords** consent; Human Tissue Act; human tissue research; research governance in practice; tissue banking

The status and use of human tissue in research is complex, at times contested, and an area of ongoing ethical and legal discussion. Companion articles in this issue's symposium address some of the areas of current debate. The use of human tissue in research has been the source of scandal[1–3] and litigation[4–6] as well as the foundation of innovation and medical advance.[7,8] Human tissue and its use is a matter of interest not only to pathologists and scientists, but to lawyers, philosophers, policy makers, clinicians and the public — whether patients or currently healthy individuals. Not least because of the multiple interests of these various parties and the special status of human biological material, its use in research is closely regulated.

What does this mean for those intending to undertake research? Some have commented on — and objected to — the legislative burdens they experience, while others are bemused, confused or deterred from entering research by what they see to be a hazy labyrinth of red tape.[6,9] There is also concern that regulation has reduced collection of and access to samples, thus threatening to impede medical advance.[10]

This paper steps to the side of the usual discussion of the status of tissue in ethics and law to consider instead the enactment of regulation in the daily practice of researchers. This is a separate and often overlooked area between regulation as drafted by legislators and policy makers, and as experienced by those who work within that regulatory frame. The paper considers the governance and procedures put in place and the expertise made available in one research centre, in order for researchers to proceed with their specialized work without first needing an advanced degree in law or ethics.

The paper focuses on the bridging, facilitation activity of a research tissue bank at the University of Oxford by providing an on-the-ground account of how ethical and legal requirements related to the use of human tissue in research in the United Kingdom work out in day to day practice of collecting, storing and providing tissue for research. After a description of the regulatory and research contexts within which the tissue bank and its research facilitation service operate, a series of scenarios illustrate issues that arise with tissue in practice: in the governance of its collection, storage and provision to researchers.

## Regulatory context

Within the England, Wales and Northern Ireland, the requirements for research involving human biological material are primarily based on two pieces of legislation: the Human Tissue Act 2004 (HTA 2004) with its accompanying Codes of Practice,[11] and the Medicines for Human Use (Clinical Trials) Regulations (2004).[12] In addition, if researchers intend to use identifying patient data, this information is subject to the common law duty of confidentiality and the requirements of the Data Protection Act (1998).[13] In circumstances where individuals lack capacity to consent, the provisions of the Mental Capacity Act (2005) may also be relevant.[14]

The Human Tissue Act 2004 (HT Act) consolidated previous legislation and created the Human Tissue Authority (HTA) to "regulate the removal, storage, use and disposal of human bodies, organs and tissue."[11] The HTA describes itself as "a watchdog that supports public confidence by licensing organisations that store and use human tissue for purposes such as research, patient treatment, post-mortem examination, teaching, and public exhibitions".[15] The HTA conducts regular inspections to assess whether licenced establishments follow required procedures and maintain good standards and appropriate records.

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While the HTA concerns itself with procurement and storage of human tissue, its remit does not include the ethical approval of the research undertaken with that tissue. This comes under the purview of the National Research Ethics Service (NRES) and its Research Ethics Committees. These committees, in turn, tend to the provisions of Clinical Trials Regulations. The EU Clinical Trials Directive[16] was transposed into UK law in May 2004 in the form of the Clinical Trials Regulations.[12] The Regulations were intended to apply only to clinical trials and not medical research more broadly, but it is UK Department of Health policy that the operating procedures required by the Directive and the Regulations "should also apply in general to the review by RECs (Research Ethics Committees) in the UK of all other research involving human participants within the NHS".[17]

With one body taking responsibility for storage and another for research use of human biological material, it is necessary for the HTA and NRES to work in close alignment. They issued a Joint Statement in 2009, outlining their working arrangements.[18] These include agreement that while human biological material is being used in a research project for which ethics approval has been given, it does not require registration under an HTA licence. Such an arrangement allows researchers who collect samples from participants as part of their ethically approved research to proceed without reference to the HTA. At such time as ethical approval for a research project expires, materials still held for which there is consent for storage and further use must be transferred to a licenced facility. They can be accessed again subject to ethics approval.

Renewed access to previously collected samples need not entail return to a REC for every research project proposed. The HTA and NRES also arranged for Research Ethics Committees to be able to give generic ethical approval for a research tissue bank. A research tissue bank is defined as "A collection of human tissue or other biological material, which is stored for potential research use beyond the life of a specific project with ethical approval or for which ethical approval is pending."[19] A tissue bank storing human tissue for use in as yet unspecified research must obtain a licence from the HTA. It may then apply to an REC for generic ethical approval for its arrangements for collection, storage and release of tissue, in keeping with the programme of research it is designed to support. Research tissue bank approval can thus extend to specific projects requiring non-identifiable tissue from the bank.[18,20] In this way, the REC devolves governance for its collections to the research tissue bank itself. The bank submits annual reports to the REC, renews its ethical approval every five years, and is subject to the licencing requirements of the HTA. The result is that researchers can access tissue from a central place with the brunt of regulatory administration being handled by the bank. Researchers will need to satisfy the access requirements of the tissue bank, but these are less involved and can be facilitated in a shorter time frame than is possible with REC review.

## Consent

A central tenet of both the Human Tissue Act and research ethics is consent. The importance of obtaining and recording consent from individuals for the use of their biological material underpins Human Tissue Legislation. Consent is a similarly fundamental concern running through the ethics of research involving human participants. The Nuremberg code, developed following the post WW2 Nuremberg trials, articulated clearly the principle of voluntary, informed consent for research.[21] This has been developed further in the various versions of the World Medical Association's Declaration of Helsinki.[22] Informed consent as described in the Declaration of Helsinki in turn forms the basis for the consent requirements in the EU Clinical Trials Directive. Consequently, it is an area of Research Ethics Committee review in the UK context.

In addition to biological material being collected specifically for research purposes, including biobanking, tissue may be available as a clinical by-product. Consent for research, including biobanking, is sought before any intervention. Tissue obtained in the course of diagnosis, such as a blood or urine sample or a tissue biopsy, or as a result of treatment, such as when an organ or tumour is removed, can also be used in research under certain conditions. Trusts have policies in place to obtain consent for investigation or treatment, and their consent provisions may include an option for patients to give permission for the use of removed material in research. This material will be stored in a diagnostic archive; the samples form part of a patient's medical record. In some instances, and when a patient has consented, additional surplus material may be stored in a research tissue bank.

Consent can be broad in both time and scope: it does not need to be project-specific. Where individuals are consenting to use of tissue in further research without knowing the nature of that research, they are instead consenting to governance. Information provided to support their decision explains how and by whom decisions will be made about the use of their tissue.

Since the consent requirements of the HT Act are not retrospective, it is not necessary to obtain or confirm consent for use of material that was already stored — whether in a research or archival setting — when the HT Act came into force on 1 Sept 2006. These are considered 'existing holdings.'

Tissue for which consent has not been sought for research use (other than existing holdings) can only be released if it 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;
- there are research ethics approval provisions in place, such that material is either:
  - released by a research tissue bank with generic ethical approval from a REC for research within the terms of its approval *or*
  - to be used for a specific research project approved by a REC.[18,23]

These regulatory requirements, even with their arrangements to align responsibility and governance, are still some distance from the work done by pathologists and researchers with tissue itself. Between the regulation and the research there is need for a facilitating gateway where requirements are enacted in order to facilitate proper lawful and ethical use of human tissue for research. What follows is a description of one such gateway, and instances in which it enables sound research practice.

## Oxford Radcliffe Biobank

The Oxford Radcliffe Biobank (ORB) is a research facility of the Oxford University Hospitals NHS Trust (OUH) and the University