Tissue Banking in a Regulated Environment – Does This Help the Patient?

Part 1 – Legislation, Regulation and Ethics in the UK

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Key Words

Biosamples · Patient views · Translational research

Abstract

The difficulties with ‘retained organs’ in the UK have resulted in a new legislation relating to human organs, tissues, and bodies – the Human Tissue Act 2004 and the Human Tissue Act Scotland 2006 are now in place. The new laws apply to a wide range of activities including transplantation, education, clinical audit, the practice of autopsies, anatomical examination and others, including the use of human tissues in research. Pathobiology research that uses human tissues is now undertaken in a regulated environment in the UK. The details of these regulations are described and the consequences discussed. In the second part of the paper the patient’s views and expectations in this new setting are forwarded.

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Introduction

The United Kingdom has experienced some well-publicised difficulties with ‘retained organs’ and tissues in recent years [1]. Most news worthy of these was the reten-

tion of human organs and tissues in the cities of Liverpool [2, 3] and Bristol [4, 5] following paediatric autopsies. Of course, the practices were not confined to these cities or to paediatric autopsies and were widespread throughout the United Kingdom. The practices that caused so much ‘scandal’ were considered acceptable by many pathologists and were probably only on the margins of normal practice in all but a few cases. In hospitals throughout the UK it was usual for pathologists to retain or archive tissues or organs during and after diagnostic procedures for potential future use in research. However, what proved to be problematical was not the actual retention or the intention to conduct research, but the fact that this was done without the consent or knowledge of patients or their relatives. The media made much out of this fact and labelled it as a covert activity, ‘stealing’, betrayal of trust and paternalistic behaviour by doctors. Pathologists in particular were demonised in the press and there were several high-profile pathologists who were pilloried and underwent disciplinary hearings for their actions.

The governments in the UK reacted to these events with incredible vigour – Ministers and Chief Medical Officers made public pronouncements [6], they launched plans to investigate and correct the situation, a ‘Retained Organs Commission’ [7] was launched in England in

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2001 and similar processes took place in Scotland, Wales and Northern Ireland. The end result was a wide-ranging review of the legislation and regulation relating to human organs, tissues and bodies – the Human Tissue Act 2004 [8] and the Human Tissue Act Scotland 2006 [9] are now in place. The new laws apply to a wide range of activities including transplantation, education, clinical audit, the practice of autopsies, anatomical examination and others, including the use of human tissues in research. Pathobiology research that uses human tissues is now undertaken in a regulated environment in the UK. The impact of this is still emerging, but the major effects are becoming visible and are shaping the way that human research tissue banking is conducted.

Consent, Regulation, Penalties and Best Practice Are the Central Elements

Many of those offended by tissue and organ retention made it clear during consultations that they did not fundamentally object to the use of organs or tissues in research and would have been happy to allow the retention of tissues from themselves or their deceased relatives if only they had been asked beforehand [10]. As a consequence, the new legislation in the UK makes *consent* (or ‘*authorisation*’) a central element prior to the retention of human materials.

The Human Tissue Act 2004 [8] legislated for the creation of a regulatory body, the *Human Tissue Authority* (<http://www.hta.gov.uk/>), which would oversee the implementation of the legislation, issue licences for certain activities and publish *guidance on best practices*. Lastly, the legislation created new *criminal offences* relating to human organs and tissues, with penalties such as imprisonment for storing human tissues without consent and for working without a licence.

These collective measures were intended to redress the balance from a doctor- or researcher-centric culture to one in which the rights and autonomy of the patients were central.

Scope of the Human Tissue Act 2004 [8]

This Act extends to *England, Wales and Northern Ireland* – only a small part of its scope applies in Scotland, most notably the measures relating to DNA.

It is the legislative framework for regulating the *storage* and *use* of human organs and tissues (referred to as

‘*relevant materials*’) that have been derived from a living person or a deceased person. In addition, it also regulates the *removal* of relevant materials from the body of a deceased person. The regulated uses of such material are referred to as ‘*scheduled purposes*’ – which are a listing of specific health-related uses that includes research.

Relevant material is defined as material that has come from a human body and consists of, or includes, human cells. Cell lines, hair and nail from living people are specifically excluded. However, *any* material that is cellular or supracellular is included where the intention is specifically to study the DNA of a person.

Scope of the Human Tissue Act Scotland 2006 [9]

The Act applying to Scotland was developed with the same intentions as the Human Tissue Act 2004, but does so through a more restricted scope and a less complicated pragmatic piece of legislation.

The key differences are: (1) the positive act of giving by donors is referred to as *authorisation* rather than consent (but should be considered as equivalents); (2) the Act only regulates samples derived from *deceased* donors, and (3) there is no regulatory body with statutory powers equivalent to the Human Tissue Authority in relation to research and tissue banking.

Consent and Authorisation

It is a central premise to the Acts that individuals who wish to donate pieces of their bodies for research or any other scheduled purpose should be allowed to do so as a *positive* act of consent or authorisation – presumption of consent or ‘absence of objection’ is not considered appropriate. However, the Acts are permissive of broad-ranging consent for research and allow for such consent to be long-lasting.

Generally speaking, all of the scheduled purposes require consent where the retrieval of samples is from a deceased donor, whereas only some require consent if the donor is living (for example, use of human tissue samples in teaching or laboratory quality control does not require consent if the donor is living at the time of sample retrieval). Research is a purpose that always requires donation with consent in England, Wales and Northern Ireland, but NOT in Scotland if the donor is living.

There is one significant exception to this rule – if the intention is to conduct DNA analysis, consent is always

required in all parts of the UK as it is a criminal offence to analyse DNA for research purposes without consent.

The Human Tissue Act 2004 does allow samples held before the 1st September 2006 to be used without consent – a set of samples deemed to be ‘*existing holdings*’. Similarly, consent is not a legal requirement (although perhaps still a matter of best practice) if the sample is donated outside of the UK. Also, the 2004 Act does permit research to be conducted using samples collected after the 1st September 2006 in the absence of consent if (1) the samples are anonymous in the eyes of the user (preserved linkage to identity is permissible) and (2) the research project is approved by a recognised research ethics committee. This apparent ‘loophole’ in the law was to allow important research that could be conducted using human samples, but was not foreseen at the time of removal of the samples and thus no consent was sought, to be legal as long as it was also considered ethical. The hurdle in this circumstance is, thus, the ethical approval which may not be possible without attempting to gain consent retrospectively in some instances. This is, therefore, more a permissive legal measure than a real opportunity to escape the need to seek consent.

Both Acts respect the primacy of the consent given by the donor, but in the event that the donor has not given consent, or is not capable of doing so, it defines the order of people in qualifying relationships who may legitimately give consent in lieu of the donor.

Codes of Practice

The Human Tissue Act 2004 requires the Human Tissue Authority to issue guidance to the sectors it regulates. One means of doing so is through the Codes of Practice that it issues. A number of codes have now been published and serve as reference points for those involved in, for example, research and tissue banking, to ensure that they conduct their work not only in ways that are legal, but also in ways that are considered as most appropriate. The codes that are most applicable to human pathobiology research and tissue banking are the codes on *Consent* [11] and on *Removal, Storage and Disposal of Human Organs and Tissues* [12].

Compliance with these codes of practice is not a legal requirement. However, in practice, these codes carry the weight of enforceable regulation as compliance is taken into consideration for decisions on licensing (see below).

Import and Export

The Human Tissue Authority intends to issue a code of practice on ‘import and export’ of human bodies, organs and tissues for scheduled purposes. Of course, many human samples travel in and out of the UK each year for use in research. The practical implications of complying with this code are not clear yet as the code is not published in its final form. At the time of writing, the code is available in draft form for consultation. The perceived problems that this code may introduce relate to bureaucratic burden, incompatibilities in consent and ethics between the UK and other countries and the barriers that these might introduce to hinder international cooperation and multi-centre research.

Trading in Human Samples

The new UK Acts [8, 9] specifically define offences relating to the trafficking of human organs and tissues for transplantation but do not extend those offences to other purposes such as research. In practice, this means that under these Acts it is legal to trade in human samples. However, there is a well-recognised principle that it is not permissible to trade for profit from the sale of materials derived from the human body. The principles that guide this in the UK are contained within the published Guiding Principles [13] of the UK Confederation of Cancer Biobanks – no doubt these principles are similar in intention to those considered appropriate in many other countries.

Licensing

The Human Tissue Act 2004 [8], but not the 2006 Act in Scotland [9], requires the Human Tissue Authority to regulate and licence establishments conducting scheduled purposes [14]. In practice this means that pathology departments need a licence to conduct autopsies and removal of samples from deceased persons, but the surgical pathology activities and diagnostic archives within such a department do not need a licence as long as the primary purpose is diagnosis. However, if the hospital (or any other establishment – university, research institution, commercial company, charity or not-for-profit organisation) holds a collection of human samples specifically for future use in research, then it requires a licence as a research tissue bank.

Exceptions to the need to obtain a licence exist – (1) if the material is more than 100 years old; (2) if the material is being stored for use in a specific research ethics-approved research project (*'qualifying research'*) and only that project, or (3) if the material is being stored temporarily (generally less than 1 week) awaiting transport to a licensed site.

Licences apply to physical premises in a single location or campus that are managerially aligned and controlled. In practice, this means that two research tissue banks in a single university that maintain independence from each other require to be licensed separately. However, if they can be managerially linked and share a governance framework, they can be covered by a single licence. If they exist in separate geographical sites, they can be linked via a main and a satellite licensing provision.

A facility gains a licence by making an application on-line – a *compliance report*. This application is made as a self-declaration – the topics covered focusing on arrangements for consent, premises and equipment, quality systems and management and arrangements for disposal of samples. Other factors such as personnel and overall governance are also important. To date, the Human Tissue Authority has indicated that all applications are assessed on paper (or screen) and that licences may be granted on this basis. In addition, however, the Authority may undertake inspections on an exceptional basis to validate the content of compliance reports. Licences come with costs – currently £5,200 for a main site licence lasting 1 year.

Ethics Approval

The last piece of the regulatory environment is the research ethics committee. Many such committees exist throughout the UK – some of which were originally established as local committees and some of which have had a multi-centre remit. These are parts of the National Research Ethics Service (NRES), which is part of the National Patient Safety Agency of the National Health Service.

NRES has recently launched a new voluntary method for research tissue banks to apply for approval by a research ethics committee. This has been introduced because many research tissue banks were seeking approval, but the existing mechanisms were created to accommodate project applications and did not cater well for tissue banks. This new innovation recognises that tissue banks exist to cater for future undefined research, that most of the ethical issues relate to the interaction with donors in

and around consent and the act of donation and the scope of the research supported by the bank. Thereafter, the issues related to the projects using the bank are mostly those of practicality rather than ethics-based issues. On that basis it is possible for tissue banks that apply by this mechanism to be granted approval to operate the bank, to obtain samples according to the methods described in the approved protocol and to issue samples to researchers. The researchers themselves would not need to apply for approval of the project as long as it was within the scope of the approval to the tissue bank.

The application process is an on-line application [15] that is searching about: the arrangements for recruiting and consenting donors; the arrangements for information management and privacy protection; the intentions to ensure that the samples are used, and the mechanisms for release of samples. Such applications are reviewed by a restricted set of research ethics committees that have been specially trained in the ethical issues related to research tissue banking.

This mechanism of application and assessment is open to any research tissue bank (public or private) in the UK. However, it is a voluntary scheme. Should the bank not seek such approval, researchers planning to conduct research using samples would need to seek project-specific approvals. Similarly, if an approved bank does not feel able to approve a request for access to samples for a project because it is a project out of scope of the approval given to the bank, or because the project raises new ethical issues, it may refer the researcher to seek a project-specific ethics approval prior to release of samples.

Overall Impact?

These regulatory measures have been met with very mixed reactions within the research community. For some researchers, the new legislation and regulation publicly defines the standards that they would expect themselves to work to – in other words, they see the new environment as little different from the way they already work. For others, they see the new environment as a burden of bureaucracy that they are ill equipped and poorly resourced to handle – they see the new environment as a costly burden. Unfortunately, there remain a few in the research community who still see the new environment as an insulting imposition that is unwelcome and will hinder their scientific freedom.

Where is the balanced view? It is probably that the regulation is a good thing, albeit that it does introduce cer-

tain administrative burdens that were not present previously. The new regulatory environment has begun to remove some of the uncertainties about what was permissible and what was not that prevailed over the period from around 2000 until 2006. It defines the proper steps of accountability, governance and good practice. As familiarity with the new regulatory environment is growing in the human pathobiology research community, confidence will also increase and, in a relatively short time, easy compliance will be the norm.

Has this environment placed obstructions in the way of researchers? Probably not – the pre-regulatory hiatus

did more to hinder research than the current regulation does. If this new approach also works to restore the confidence and willingness of patients to be subjects of research, then human biosample-based research will hopefully blossom.

The danger that remains is that other countries or jurisdictions will adopt similar approaches, but with local differences sufficient to make reciprocal recognition and cross-border compliance impossible. Pathobiology research will then return to small-scale institution-based studies that lack the power and the opportunities offered by trans-national collaborations.

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