

Submission by the Human Tissues Working Party to the Review of the regulation and governance of medical research: Academy of Medical Sciences (1st June 2010)

Please note: This submission is on behalf of the Human Tissues Working Party (www.safermedicines.org/humantissues/) and as such, deals only with the regulation & governance of medical research as it pertains to human tissue acquisition and research.

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What are the principles that should underpin the regulation and governance of medical research?

Respect for the rights and dignity of individuals, and every effort to comply with their wishes, are paramount.

Notwithstanding that proviso, regulation could also be viewed as a means of promoting quality control, standardization and hence transferability of data & specimens between labs. This would facilitate cooperation between tissue banks,

and make it easier for researchers to collate the large numbers of samples often required for high quality, statistically valid research.

What are the most significant regulatory and governance impediments to medical research in the UK? In each case, is the impediment caused by: the underpinning regulation (or absence of regulation); its implementation at national or local level; the guidance and support provided for researchers (or lack of it)?

(a) Restriction on the availability of human tissues for research purposes

The focus on guaranteeing the rights of a small minority who may not wish to donate means that the system adopted throughout the UK for donation of post mortem and surplus surgical human tissue is currently one of opt-in. The widespread desire amongst members of the public to contribute to medical research in this way therefore frequently goes unfulfilled because many potential donors are not made aware of the possibilities of donation. The situation is often exacerbated by what is widely viewed as a complex and time-consuming bureaucratic process, time constraints amongst staff, a lack of appreciation amongst hospital staff of the importance of high quality tissues, or a lack of resourcing-cohesion in the processes required for tissue to reach the researcher promptly once a donation has been made.

(b) Ethical review process

In addition, many Research Tissue Banks require that the submission to the ethical committee includes a detailed scientific proposal in order to provide applicants with access to human tissues. The scientific proposal needs to prove to the committee that the use to which the tissue will be put is "worthy". Very often this appears to require that the research using the tissues must be novel and lead to new findings. However,

- novelty can be difficult to prove where researchers are investigating whether phenomena observed in cell lines or animal tissues apply to intact human tissues,
- tissues may be required for routine screening of potential drug candidates, and
- where commercial companies are involved, research teams are generally unable to divulge full details of novel research to scientific committees who monitor access to tissues.

The result in some cases is that researchers will avoid the regulatory complexities associated with use of human tissues and instead find alternatives (e.g. cell lines, animal models) that may be less relevant to human biology.

Finally, this review process can be very slow, which for commercial researchers represents a serious impediment to research.

(c) Consent: a need for further guidance

There appears to be a lack of clarity amongst researchers about what exactly constitutes sufficiently informed, yet usefully generic consent. Although a recognised Research Ethics Committee may approve a consent form that seeks consent for use of samples for other, broader, research purposes, discussions at a recent NRES workshop strongly suggested that further guidance on best practice in obtaining optimally generic consent for research may be helpful.

Another approach to the issue of consent would be to ask participants if they wished to opt-out of certain types of research for which their tissues could potentially be used, e.g. for admixed embryo research (please see comments on the model followed by the US-based International Institute for the Advancement of Medicine).

(d) Feedback to donors/patients

Another area where further guidance could be useful is whether, how, and over what timescale, potentially clinically relevant information should be fed back to donors of tissues for research. As was discussed at the recent NRES Workshop, informing donors that they will not benefit directly from research and that results will not be fed back absolves and protects researchers from any legal obligations, but still leaves an ethical minefield associated with doing this. However, there may be a clear ethical case for feeding back results which could directly impact donor health, e.g. identifying, in a donated tissue sample, expression of a gene variant known to place the donor at high risk for a certain type of cancer. This feedback could be done through the appropriate medical professional caring for the patient. This is a complex area, particularly when one considers that there may be degrees of evidence or uncertainty over the risk posed by carrying certain gene variants or other findings. Further guidance would therefore be welcomed.

Which parts of the regulatory and governance framework are working well and why?

Respect for patients' rights and wishes must always be paramount, and current regulatory requirements are very good at ensuring that anyone who may not wish to donate their tissues does not do so. No patient should ever feel in any way coerced or be in any way disadvantaged by their decision to donate tissue or not, and the current regulatory framework achieves this. On the other hand, with provision of appropriate information to potential donors, such protection could equally well be achieved through an opt-out system while at the same time increasing the extent of tissue donation.

What can we learn from the regulatory and governance framework in the different nations of the UK and from outside the UK?

(a) Government initiatives:

Initiatives such as the Scottish government's organ donation promotion programme for secondary schools (<http://news.bbc.co.uk/1/hi/scotland/8467844.stm>) are doing tremendous work in raising the profile of human tissue donation in Scotland. This initiative should be extended throughout the UK and should also aim to increase public awareness of the importance of donating human tissues for research as well as for transplant.

Such a programme could also be extended to develop better public understanding of the value of surplus surgical tissues for research (and acceptance of a reduction in the burden of meeting regulatory requirements on the part of scientists). Evidence suggests that the vast majority of patients agree to their surplus tissues being used in research. Moreover, they are equally happy for their tissues to be used by academic, biotech or pharmaceutical laboratories, as they understand that many players are required to bring new treatments to patients.

(b) Patient power

The importance of the patients themselves in this process should also not be forgotten. The Wales Cancer Bank is an excellent example of patient empowerment through information about research and their vital role in it, resulting in the patients actively campaigning for the establishment of a repository to facilitate and help direct research using their samples. Patient representatives continue to be involved in the running of the bank, for example in the drafting of patient information etc (www.walescancerbank.com/organisation.html). This model should be examined closely by anyone wishing to set up a tissue bank.

(c) Greater use of exclusion, rather than inclusion, criteria

It may also be helpful to examine the operation of the International Institute for the Advancement of Medicine (IIAM), which is responsible for the nationwide collection & distribution of non-transplantable organs (& whole bodies) in the US (www.iiam.org). The IIAM operates across many states with different regulations, some of which give donors' families the opportunity to withhold their relatives' tissues from certain applications. Rather than specifying which areas of research a person's tissues may be used in, it may be simpler and more helpful to give participants the option of opting out of certain areas, such as reproductive research, the creation of mixed-species embryos etc.

What changes to the regulatory and governance framework would provide the greatest improvement to the progress of medical research, without putting patients at unnecessary risk?

(a) Make standard the taking of consent for research use of surplus tissue

It needs to become standard practice for patients' widespread desire to contribute to medical research in this way to be facilitated. This may be hastened

by the introduction of guidance or regulations mandating this as part of the service provided by hospitals. Consenting for surplus tissues to be used and stored for research could be incorporated into the process when the patient is first seen, or admitted to hospital, as is now the case at the NHS Greater Glasgow and Clyde Bio-repository (<http://www.gla.ac.uk/departments/glasgowbiomedicine/complementaryfacilities/>).

(b) Introduction of presumed consent:

An alternative, and perhaps more long-term, goal might be for both hospital staff and the public to become so well-informed about the value of de-identified surplus tissue for ethically-approved medical research that presumed consent could be introduced, as was considered recently for organ donation. In the case of surplus surgical tissue, presumed consent (with opt-out) could greatly increase the amount of tissue available for medical researchers in academia, biotech and the pharmaceutical industry. This would require changes to the regulatory requirements to reflect the lower risk posed by this sort of donation, and would need to be accompanied by a widespread education campaign explaining the benefits of human tissue-based research. In the case of post mortem tissues, the use of organs or tissues for transplant or treatment must of course take first priority. However, non-transplantable organs are a tremendous source of extremely high quality tissues, which are invaluable to researchers, yet these too are not routinely consented for research. This is a wasted opportunity.

(c) Improved funding

Both surgeons and pathologists, who are responsible for classifying and handling specimens, as well as providing the clinical data which must accompany samples in order to make the best possible use of the tissue, operate under a great deal of time pressure. Furthermore, many pathology departments suffer from a lack of funding. Their collective efforts need to be recognised, and the time and materials involved in participating in, or gathering samples for, research must be better recognised, resourced and compensated. Minimum funding levels for pathology service provision could be established, to ensure that ring-fenced funding is channeled into pathology research and biobanking services.

(d) Greater clarity on sources of guidance

There is some confusion surrounding the different roles of the various regulatory and approval bodies. The existence of resources such as the Medical Research Council tool kits (<http://www.mrc.ac.uk/Ourresearch/Ethicsresearchguidance/RegulatorySupportCentre/Toolkits/index.htm>) need to be promoted as a single source of guidance which can be broadly applied. Ignorance and over-interpretation of the guidelines by researchers or ethics bodies can hamstring fruitful research and the international collaboration which is the lifeblood of research.

(e) Changes in the stance of regulatory documentation

Research should be regulated with the presumption of good intent. At present, however, the language used in connection with the regulation of research may give the impression that researchers cannot be trusted, rather than endorsing the view that researchers' principal desire is to help patients. The over-use of terms such as 'putting patients at risk', 'protection', 'safeguards' etc., can give the impression that patients need to be protected from scientists wishing to somehow misuse their tissues perhaps for personal or corporate gain. The public perception of medical research is also not enhanced by the use of such defensive language and overly paternalistic regulation which seems to imply that researchers' aims may be improper or not commensurate with the interests of patients, and that patients are not able to decide what constitutes appropriate uses of their tissues.

(f) Improved public education

Surplus tissue donation needs to be promoted as an altruistic opportunity for the public to contribute to the good of society, possibly eventually bringing benefits for themselves or their loved ones, as research using human tissues leads to better diagnostic tests, improved understanding of disease and ultimately, new therapies. This public education could be brought about by developing information leaflets and posters in GP surgeries and key patient contact areas in the hospital environment (waiting rooms, for example).

Is there a need for a more risk-based approach to medical regulation and how might this be developed and adopted?

The risk to the patient of participation in research using surplus surgical tissues, which would otherwise be incinerated, is small, and hence perhaps lighter touch regulation would be appropriate. Where the potential donor is deceased or unable to give consent due to age or infirmity, further precautions are naturally necessary. Consent should also specifically be sought where extra tissue is proposed to be removed for research, rather than what would normally be removed purely for treatment or diagnosis.