

Human Tissue Authority written evidence to the Academy of Medical Sciences *Review of the regulation and governance of medical research*

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Key points

- *The HTA supports UK researchers at the forefront of medical science.*
- *Regulation is essential to ensure that both bench research and translational research is undertaken within a framework in which the public and professionals have confidence.*
- *Our work with other regulatory and governance bodies aims to streamline activities and reduce unnecessary barriers.*
- *The evidence in this submission demonstrates the effectiveness of the HTA's approach to regulation.*
- *Despite all the HTA has done to improve access to good-quality human material, there appear to be potential barriers at a local level.*
- *The HTA will continue to work with others to improve clarity and support research.*

The Human Tissue Authority

1. The Human Tissue Authority (HTA) was established by the Human Tissue Act 2004 (the Act) to regulate the removal, storage, use and disposal of human tissue. We support public confidence by ensuring that the wishes of the public are respected and that bodies and tissue are treated ethically and safely. As a regulatory body, our remit does not include the promotion of research.

The legislation under which the Human Tissue Authority regulates

2. The HTA regulates under two pieces of legislation: the Human Tissue Act 2004 (the Act) and the Human Tissue (Quality and Safety for Human Application) Regulations 2007 (the Q&S Regs). The Act covers England, Wales and Northern Ireland; there is separate legislation in Scotland – the Human Tissue (Scotland) Act 2006. The Q&S Regs cover the whole of the UK, including Scotland.
3. Under the Act, the HTA licenses the storage of tissues and cells used for research “in connection with disorders, or the functioning, of the human body”. The Act facilitates research by providing a number of consent and licensing exemptions. These exemptions are summarised in Appendices A and B of the HTA’s code of practice on Research, available at: www.hta.gov.uk/legislationpoliciesandcodesofpractice/codesofpractice/code9research.cfm.
4. Beyond the statutory requirements of the Act and the Q&S Regs, the HTA has worked hard to clarify the regulatory framework around the proper use of human material. Although the HTA regulates human material used for bench research under the Act, any material that may at some point be used as part of patient treatment is regulated under the Q&S Regs.
5. The Q&S Regs transposed the EU Tissue and Cells Directives into UK law. Under the Q&S Regs, the HTA licenses the procurement, testing, processing, storage, distribution and import / export of human tissues and cells for patient treatment.

The relative roles of other organisations relevant to medical research

6. Stem cell lines from any human source other than embryos, which have the potential to be used in patient treatment, fall within the regulatory remit of the HTA and the Medicines and Healthcare products Regulatory Authority (MHRA).
7. The MHRA regulates cell therapies deemed to be a “medicinal product” (MP) or an “investigational medicinal product” (IMP).
8. Where a stem cell treatment is defined as an MP or IMP (as opposed to a ‘graft or transplant’), the HTA only regulates in the early stages of its

development, including the donation, procurement and testing of the cells and tissues.

9. If a medical treatment containing human tissues or cells is not determined by the MHRA to be an MP or IMP, it will be regulated entirely by the HTA under the Q&S Regs.
10. The Human Fertilisation and Embryology Authority (HFEA) regulates the creation and use of embryos in the derivation of human embryonic stem (ES) cell lines. Its remit ceases at the point the embryo is dissociated, at which point the HTA's remit begins.
11. Subsequent manufacturing stages, clinical trials and marketing authorisations will be regulated under medicines legislation by the MHRA in the UK or the European Medicines Agency (EMA) in Europe.
12. The National Research Ethics Service (NRES) is a division of the National Patient Safety Agency and provides a system of ethical review that protects the safety, dignity and well being of research participants, whilst facilitating and promoting ethical research. It does this by:
 - providing ethical guidance and management support to Research Ethics Committees (RECs)
 - delivering a quality assurance framework for the Research Ethics Service
13. RECs review research projects requiring ethical review under the law or the policies of the UK Health Departments. This includes projects involving the collection, storage and use of human tissue. RECs also review voluntary applications for ethical review of research tissue banks. All research ethics committees within the Research Ethics Services of the UK are recognised as research ethics authorities for the purposes of the Act.

The challenges

14. The HTA has a broad regulatory remit, recognising five distinct sectors, namely: anatomy; post mortem; human application; public display and research. In practice, the activity of research can be associated with people within the regulatory framework for all our sectors e.g. there are anatomists, pathologists, etc who undertake research. The organisations we license in the research sector are also very heterogeneous. Unlike in our other sectors, there is no typical researcher and no typical research organisation.

15. We also know, from a mixture of sources, that there are local bottlenecks and potential barriers to researchers. It is reported that NHS Trusts are reluctant to support research and that R+D departments are risk-adverse, applying the regulatory framework in an overly stringent manner.
16. Medical science is fast-moving, with UK researchers at the forefront, and the HTA takes a dynamic approach to this area.
17. As mentioned at the start of this document, the HTA's remit and licensing requirements in relation to research activities falling under the Act do not extend to Scotland. We therefore encourage researchers in Scotland to refer to our codes of practice.

What the HTA has done to facilitate research

18. The HTA aims to set standards for the use of human tissue that are clear and in which the public and professionals can have confidence. We also support researchers in complying with our standards and work to reduce the burden on the research sector.
19. In 2009, the HTA launched a new research code of practice which provides guidance and expected standards for the research sector. Researchers were involved in the development of the code via consultation and workshops.
20. We encourage researchers to contact us if they have any questions or need advice and guidance. We have a well-resourced and well-utilised enquires system, and provide information for the research sector via our website and e-newsletter.
21. The HTA is committed to finding innovative ways to reduce unnecessary regulatory burdens; for example, in 2009 the HTA replaced fixed-term licences with a continuous licensing system, which was developed with input from the regulated sectors.
22. The HTA supports researchers by providing advice and guidance, and collaborating to ensure joined-up regulation and governance. Our work with other regulatory and governance bodies in the research sector aims to streamline activities and reduce unnecessary barriers. We also ensure that consistent messages are given to researchers and efforts are not duplicated.
23. We value collaboration and have responded to researchers' requests for consolidated guidance. The HTA has worked with the MRC to develop online

resources such as the Data and Tissues Toolkit and an e-learning module on human tissue research. As well as hosting our own events, we also participate in relevant research stakeholder events held by other organisations.

24. The HTA supports centralised tissue repositories and governance in order to give researchers wider access to high quality samples. Our advice and guidance gives researchers clear information about how best to consolidate stocks and the HTA encourages researchers to contact us if they have any questions.
25. We will continue to engage with the research community and listen to their views. If there are perceived difficulties with the regulation, we are keen to find out.
26. In 2007, the HTA established a Tissues and Cells Working Group (TCWG). The TCWG aims to clarify areas of regulatory responsibility, ensure consistency between regulatory bodies and; where relevant, to work with other regulators to agree joint statements. To further this aim, the HTA regularly invites other regulatory bodies to attend the TCWG to discuss regulatory matters of mutual interest.

Stem cell research

27. The HTA bridges the gap between bench research on stem cells and their use in clinical trials prior to their use in patient treatment. This ensures high standards of quality and safety at the early stages of the development of a stem cell line and acknowledges that there may be many years before derivative stem cell lines will be used for future patient treatment. This regulatory approach builds quality into each step of the development of a stem cell line to provide high standards of health protection.
28. Following concerns raised by stem cell scientists that the regulatory framework for organisations working with stem cells was complex and a potential deterrent to private investors in the UK, the HTA, worked with the Department of Health (DH) to develop a web-based regulatory tool for those conducting human stem cell research in the UK (<http://www.sc-toolkit.ac.uk/home.cfm>). The tool kit benefits both the private and public sector by bringing clarity regarding the regulatory requirements.
29. To ensure that any product or treatment developed from cell lines meets all the regulatory requirements, the HTA has advised scientists to consider all cell lines as potential starting materials for future treatments.

30. To support scientists the HTA has issued joint position statements with the HFEA and MHRA on the regulation of embryonic stem cell lines and Advanced Therapy Medicinal Products (ATMPs). The joint statements provide assurances that where there are several regulators that have remit that adjoin, the regulators are working together to provide consistent information and where possible, will work together to reduce the regulatory burden on the sector.
31. The HTA works collaboratively with stakeholders from across the stem cell sector and attends key stem cell network meetings – either on an ad hoc basis or as a formal observer. The HTA is a regular attendee at UK National Stem Cell Network, Gene Therapy Advisory Committee, Stem Cell Funders Forum and the Stem Cell Steering Committee. The HTA is also a member of the Stem Cell Communications Coalition and contributed to the development of the Medical Research Council's information pack about stem cell science in the UK.

HTA and NRES

32. The HTA has a Memorandum of Understanding (MOU) with NRES. This was put in place to offer clarification about consent and licensing requirements, and aims to avoid unnecessary duplication of work.
33. The HTA's work with NRES has made more tissue from tissue banks available to researchers without the need for additional ethics committee approval.

Tissue banks releasing tissue for research

34. Our work with NRES has also allowed the establishment of 120 research tissue banks that – as well as being licensed by the HTA – also have generic approval from a designated REC. This means that researchers receiving non-identifiable tissue who agree to the governance requirements of the bank, either: (1) do not need an HTA licence themselves or (2) do not need to gain additional project-specific REC approval.

Individual research projects

35. In the absence of the type of agreement described above, tissue – from the living or deceased – stored for future research would need an HTA licence unless it is stored for a REC-approved project. Consent is not needed if tissue for research is from the living, anonymised and has REC approval.

36. The HTA and NRES have provided and publicised a mechanism by which archives of diagnostic material can apply to become research tissue banks: www.hta.gov.uk/legislationpoliciesandcodesofpractice/positionstatementondiagnosticarchivesreleasingtissueforresearch.cfm

HTA and National Institute for Health Research

37. In order to tackle local barriers to medical research, DH's National Institute for Health Research (NIHR) has been working with a number of organisations and individuals to improve the efficacy of NHS R+D departments. The HTA has helped to develop a risk management toolkit, SOPs and competency / training frameworks by working with NIHR, DH and a consultancy company commissioned by NIHR (called "BearingPoint").

HTA and MHRA

38. The HTA is currently aware of a dozen establishments that fall within the regulatory remit of both the HTA and MHRA: this number is likely to increase as bio-industry grows. The HTA and MHRA have embarked upon a programme of joint inspections and a MOU is being drafted to underpin the collaborative work of both regulators.

39. The HTA has also issued joint position statements with the HFEA and MHRA to provide assurances to researchers that where there are several regulators that have remits that adjoin, the regulators are working together to provide consistent information and where possible, will work together to reduce the regulatory burden on the sector.

Evidence for HTA being an effective regulator

The Hampton Implementation Review has praised the HTA for the way in which we regulate

40. The HTA is a modern regulator and has implemented the Act and EU Directives in a collaborative, proportionate and well-considered way. Since we were set up, the HTA has built a firm regulatory foundation, which is based on the five key principles of Better Regulation – being transparent, accountable, proportionate, consistent and targeted.

41. The Better Regulation Executive (Department of Business, Innovation and Skills) conducted a Hampton Implementation Review (HIR) of the HTA, in December 2008. They endorsed the HTA's approach to regulation and found that the HTA is compliant with Hampton Principles. The review demonstrated that HTA is risk-based, proportionate and transparent. The Better Regulation Executive rated the HTA highly on provision of advice and guidance and minimisation of inspections and data collection burdens.

HTA's research evaluation project

42. At the end of 2008, the HTA commissioned Opinion Leader to conduct an independent evaluation of perceptions on how human tissue legislation and its required regulation by the HTA has affected researchers working with human tissue.

The results showed that there is a high awareness of the broad roles of the HTA, and most participants reported that the HTA performs well. Among other findings, most survey participants agreed that the human tissue legislation and HTA regulation has led to increased public confidence in what happens to their donated tissue and that we had improved standards for storage of tissue for research. However, participants found it difficult to distinguish between the range of research activities beyond the HTA's remit, which demonstrates the importance of organisations governing the research sector working closely together to streamline activities.

The House of Commons Science and Technology Committee report on Bioengineering

43. The HTA acknowledges the Government's aim to maintain the UK as a world leader in stem cell research and development, by ensuring the UK has a liberal but robust and carefully considered regulatory regime.

44. *The House of Commons Science and Technology Committee report on Bioengineering* (published 25 March 2010) praised the HTA's effective approach to regulation in the field of stem cell research, commending our commitment to inter-agency coordination, particularly in relation to the MHRA.

45. Stem cell researcher and Nobel prize winner Sir Martin Evans said to the committee: "I think the whole of our approach in Britain to regulation in this area has been exemplary and has led the world...It has been an example of how things should be done."

Concluding remarks

46. Regulation is essential to ensure that both bench research and translational research is undertaken within a framework in which the public and professionals have confidence. At the point at which bench research is ready for translation into patient treatment it is of fundamental importance to ensure the quality and safety of the treatment – this can only be ensured by applying a framework of proportionate but robust regulation at each step of the process.
47. The evidence in this submission demonstrates the effectiveness of the HTA's approach to regulation, and how we have worked with other regulatory and governance bodies to streamline activities and reduce unnecessary barriers.
48. Despite all the HTA has done to improve access to good-quality human material, there appears to be potential barriers at a local level. These appear to fall into two broad areas:
- A lack of support for research within the NHS and at Trust board level, despite the opportunities offered by patients and residual human material surplus to diagnostic requirements.
 - Excessive stringency about how the regulatory framework is applied.
49. The HTA will continue to work with others to improve clarity and support research. It is also important to state that there is now much guidance on the regulatory framework within the public arena, not just from HTA. The production of more guidance, however well intentioned, needs careful consideration. There is a risk of increasing the sum total of overlapping information and missing the key issue of ensuring the wealth of guidance is converted into action.