Nuffield Council on Bioethics: Give and take? Human bodies in medicine and research

Response by the Wellcome Trust

July 2010

Introduction

1. The Wellcome Trust is a global charity dedicated to achieving extraordinary improvements in human and animal health. We support the brightest minds in biomedical research and the medical humanities. Our breadth of support includes public engagement, education and the application of research to improve health. We are independent of both political and commercial interests.
2. The ethical, legal and social issues surrounding the donation and use of human bodily material for research and treatment remain complex, not least because of continuing scientific developments in the field and the need to maintain public confidence. The Trust therefore welcomes the Nuffield Council on Bioethics inquiry into these issues, and is pleased to be able to respond to this consultation.
3. Given the Trust's remit, our comments focus primarily on the research perspective, and issues relating to public engagement. We also include details of relevant research that the Trust has funded, including recent biomedical ethics programmes. Further details about the Trust's biomedical ethics funding programmes are included at Annex A.
4. The main messages of our response are as follows:
    - the importance of a balanced and proportionate regulatory framework for research using human tissue, which ensures cutting edge research can continue while protecting patients and maintaining public confidence;
    - there are particular sensitivities surrounding egg donation for research;
    - the need to move towards a system of broad, generic consent for future research uses wherever possible;
    - the importance and need for public dialogue and engagement activities to raise awareness of the issues; and
    - the need for further research on the complex ethical issues surrounding the use of human bodily materials in medicine and research.
5. We draw your attention to one particular piece of research that the Trust has recently funded which may provide some useful perspectives to inform your discussions. In 2008, the Trust funded a five year Biomedical Ethics Strategic Award (£802K) 'The human body: its scope, limits and future'. In this multidisciplinary programme, Professor John Harris at the Institute for Science Ethics and Innovation, University of Manchester, in collaboration with Professor Sarah Cunningham-Burley, Professor of Medical and Family Sociology at the University of Edinburgh,

will investigate five strands of innovative research including the issues surrounding the donation and uses of human organs and tissues in research and medicine[1].

Nature of human bodily material and first-in-human trials

Q1: Are there any additional types of human bodily material that could raise ethical concerns?

6. We note that your list of types of bodily material does not include waste material and material that is normally acellular (including faeces, urine and other waste products). We support this exclusion, and suggest it would be appropriate to specifically rule these types of material out. There remains a lack of clarity in the Human Tissue Act as to whether material that is primarily acellular, but which occasionally contains a small amount of cellular material (e.g. urine may contain cells if it is contaminated with blood), is captured or not. Treating this type of material in the same way as tissue such as brains or other whole organs is difficult to defend ethically and in public policy terms, and raises significant practical difficulties.

Q3: Are there significant differences between providing human bodily material during life and after death?

Q4: What do you consider the costs, risks or benefits (to the individual concerned, their relatives or others close to them) of providing bodily material? Please distinguish between different kinds of bodily material if appropriate.

7. Apart from the differing risks and potential benefits for the donor, the main difference between providing human bodily material for research purposes during life and death mainly revolve around the ability to give consent, particularly for future research that could not be predicted at the time of donation. In particular, the long-term storage of tissue in tissue banks for undefined research use may have potential benefits for family members of both living and deceased donors and for society in general. Therefore it is appropriate in such circumstances that consent endures beyond the lifespan of an individual and that proxy consent can be obtained after death.
8. The current regulatory framework does allow the use of waste products from surgery for research provided that the material is anonymous. Focus groups with the public suggest that the consent process is seen as less significant around the use of waste tissue, although materials such as the products of a termination of pregnancy were seen differently[2].
9. ***Egg donation for research purposes:*** It is particularly challenging to strike an appropriate balance between realising the potential benefits for society of embryonic stem cell research – which requires human eggs for research – while adequately safeguarding those individuals who choose to donate eggs for research.
10. In relation to altruistic donation, the Trust supports the principle that altruistic egg donation for research should be permissible in certain circumstances with the caveat that it is strictly regulated. Key areas to consider include:
    - Information provided must include the short terms risks associated with the procedure and the fact there may potentially be long term risks that are as yet unknown;
    - Potential donors need to be aware of the research uses to which their eggs might be put and that, in most cases, research is still at a fundamental level and many years from any therapeutic use; and

[1] www.isei.manchester.ac.uk/research/wellcomestrategicprogramme/
[2] Attitudes to research governance p.7 (2006) http://www.wellcome.ac.uk/About-us/Publications/Reports/Public-engagement/WTX038446.htm

- Whilst the potential risks remain unknown, we feel it is appropriate to limit the number of times a woman can undergo the procedure to donate eggs.

11. In relation to egg sharing, we recognise that the incentives for donating eggs – either for treatment of others, or for research – are often large, as the donor may be offered access to reduced rates for fertility treatment, which is otherwise expensive. This must be balanced against the potential risk to the donor. The Trust will consider applications for funding on egg sharing on a case-by-case basis subject to approval from appropriate bodies and the Trust is satisfied with the scientific merits and ethical aspects of individual applications.

12. The debate on egg donation has tended to be dominated by the opinions and perspectives of academics, professionals and special interest groups. The Trust funded a biomedical ethics research project, "A comparative study of embryo donors' and non-donors' views on embryo experimentation for preimplantation genetic diagnosis and stem cell therapies' to provide much needed empirical research on the donor perspective. Led by Professor Erica Haimes, Professor of Sociology at Newcastle University and Director of Research, PEALS Research Institute, the findings from this study[3] were valuable in identifying the actual (rather than hypothetical) issues of concern to potential donors, which may help inform any appropriate boundaries and appropriate procedures for informed consent.

Participation in first-in-human trials

Q5: What do you consider the costs, risks or benefits (to the individual concerned, their relatives, or others close to them) of participating in a first-in-human clinical trial?

13. The consultation sets out to explore whether meaningful parallels can be drawn between those who provide bodily material for medical treatment and research, and those who provide their bodies, on a temporary basis, for first-in-human trials. It is important to note that the cost-benefit assessment for participation in first-in-human trials may differ significantly between a healthy volunteer and someone with a terminal or serious medical condition.

14. A more meaningful parallel for the donation of bodily material for medical research, which might be worth the Working Party considering further, is the use of patient information from medical records for research. The information contained in patient records can be extremely valuable for epidemiological and public health research, and the scale of the NHS records make patient records in the UK a particularly valuable resource. However, there remains a lack of clarity about the regulatory framework surrounding the use of personal information in research.

15. Some research can be conducted with anonymous information, from which it is not possible to identify an individual. In other cases, researchers need access to information from which it may be possible directly, or indirectly, to identify a patient by any means. All patient information is both sensitive and private, and different levels of anonymity offer different risks and benefits. Researchers are usually not interested in the identity of an individual person but may want to have data at an individual person level. The general public and patients must have confidence that the security and confidentiality of personal information is protected, and that appropriate procedures are in place to safeguard data. As a cancer patient recently commented, giving her anonymous data for research is "the most painless way she can help others get better".

[3] Haimes, Erica , Porz, Rouven , Scully, Jackie and Rehmann-Sutter, Christoph '"So, what is an embryo?" A comparative study of the views of those asked to donate embryos for hESC research in the UK and Switzerland', 2008 New Genetics and Society, 27:2, 113 – 126

Purposes of providing bodily material/volunteering in a trial

Q6: Are there any additional purposes for which human bodily material may be provided that raise ethical concerns for the person providing the material?

16. An additional purpose, not currently considered in the consultation, is the use of human bodily material for display purposes in museums and art galleries, such as the Wellcome Collection. Whilst not directly research, such displays, when handled sensitively, are an invaluable means for engaging the public and raising awareness about science and medical research. For example, the 'Skin' exhibition currently at the Wellcome Collection includes a feature called 'Skin Lab' which explores through five contemporary artists recent cutting-edge research and technological developments, from plastic surgery to regenerative medicine in relation to skin from the mid-20th century onwards[4]. We note that the Human Tissue Act has separate Codes of Practice for the display of human tissue.

17. We also note that human bodies may be used for education and training purposes.

Q7: Would you be willing to provide bodily material for some purposes but not for others? How would you prioritise purposes?

18. It is important that policy-makers and regulators have access to up-to-date information about public attitudes and opinions. In 2009, the Wellcome Trust Monitor survey[5] sought the views of a random sample of 1179 adults on various aspects of biomedical research. The findings relating to attitudes towards participation in medical research may be of particular interest to the Nuffield Council's inquiry. The main messages were as follows:

    - Willingness to take part in medical research varied according to the type of project: 70% would be very or fairly willing to give a blood or tissue sample; 74% to allow access to their medical records; while only 30% would be willing to test a new drug or treatment.
    - Willingness to take part was related to age, health and past participation in medical research. For example, the 65+ age group was twice as likely to say they would be very unwilling to give blood or tissue samples compared to all other age groups.
    - Three-quarters (75%) said they would have concerns about testing a new drug or treatment for medical research. Amongst this group, the most common concern was the possible risk to one's health (93%). Those with a disability or health condition (14%) were much more likely to say they were very willing to test a new drug or treatment than those with no disability (2%).
    - Just under a quarter of adult respondents or a family member (23%) had taken part in medical research; the most common activities were providing a blood or tissue sample and testing a new drug or treatment. Participation was higher among the 65+ age group, and those with a disability or long term illness.

19. The factors contributing to concerns about participating in clinical trials would be worth exploring further, for example whether this is a result of media coverage of the Northwick Park Trials in 2006, or whether there is low awareness of the need for healthy people to take part in early stage trials. The data in the Wellcome Trust Monitor survey demonstrate the need for effective communication with potential participants about the costs, benefits and risks of taking part in medical research.

[4] http://www.wellcomecollection.org/whats-on/exhibitions/skin/skin-lab.aspx
[5] The Wellcome Trust Monitor (2009): A survey of adults' and young people's awareness, interests, knowledge and attitudes to biomedical research. http://www.wellcome.ac.uk/About-us/Publications/Reports/Public-engagement/WTX058859.htm

20. A more detailed study, commissioned by the Trust in 2006 to examine issues of biomedical research governance, drew similar conclusions[6]. A series of focus groups suggested there was strong support for the value and importance of participating in biomedical research. Altruistic motivations were identified as the primary reason why people would take part in research. The most commonly expressed concerns were: negative press coverage; risk and safety; lack of information and transparency; and ethical, religious or cultural reasons for not participating.

Increasing supply

Introduction of an 'opt-out' system for organ donation:

21. In considering a 'soft' opt out system for organ donation (i.e. where it is presumed that people are willing to donate their organs after death unless they opt out) we recognise that this system will not necessarily achieve the desired outcome of increased organ donations. Furthermore, we recognise that such a model needs to be coupled with improved infrastructure and effectiveness of current organ donation services. It will also be crucial to foster an environment where both NHS staff and the general public fully understand the concept of presumed consent, and trust the safeguards and regulatory framework within which it will operate.

22. The House of Lords European Union Committee inquiry into 'Increasing the Supply of Donor Organs within the European Union' recognised the benefits of exploring the option of an opt out system, tempering this by noting that it could not be introduced immediately. Significant evidence of support for an opt out system was presented to the Committee, and we reiterate the view of Sir Liam Donaldson that public acceptability will require "educating and informing the public and making absolutely sure that every opportunity was taken to make people aware of their right to opt out".[7]

23. However, we draw attention to the potential impact that the introduction of an 'opt-out' model of consent for organ donation may have on consent models in other areas of medical treatment and research, including effect on public confidence. We urge the Nuffield Council's Working Party to take these issues into consideration when developing its recommendations.

24. Recognising the importance of public engagement on this issue, Wellcome Collection, the Trust's public engagement space at 183 Euston Road, held a public debate on the subject of organ donation in March 2008[8].

Question 15: Should different forms of incentive, compensation or recognition be used to encourage people to provide different forms of bodily material or to participate in a first-in-human trial?

25. The Trust has funded a five year Biomedical Ethics Strategic Award (£855K) to explore the question 'when is it right to use financial incentives to improve health?' Professor Theresa Marteau at Kings College London and colleagues is leading a multidisciplinary programme that combines philosophy, psychology and economics to analyse the relationship between financial incentives, coercion, equity, autonomy and behaviour in order to evaluate the acceptability and effectiveness of financial incentives to improve population health[9]. Findings from this programme due to end 2013, will be valuable in informing the regulatory framework and informed consent procedures in this area.

[6] Attitudes to research governance p.7 (2006) http://www.wellcome.ac.uk/About-us/Publications/Reports/Public-engagement/WTX038446.htm
[7] See paragraph 291 of the House of Lords Committee Report
[8] http://www.wellcomecollection.org/exhibitionsandevents/pastexhibitionsandevents/inorout/index.htm
[9] www.kcl.ac.uk/schools/biohealth/research/csincentiveshealth/introduction.html

Alternatives to increasing supply

Question 20: Are you aware of any developments (scientific or policy) which may replace or significantly reduce the current demand for any particular form of bodily material or for first-in-human volunteers? How effective do you think they will be?

26. New developments in regenerative medicine offer opportunities to reduce the use of bodily material from human donors. The Trust's Technology Transfer department has funded a range of different regenerative medicine projects, for example:

    - development of a bio-resorbable, load bearing, tissue regenerative meniscal cartilage implant;
    - the development of a highly porous scaffold for orthopaedic applications;
    - the development of 'living bandages' using stem cells for the treatment of burns and chronic wounds.

27. We would be pleased to provide further information about the Trust's funding in this area if it would be useful. We particularly draw your attention to a recent award we have funded which aims to address the shortage of blood for clinical transfusion:

    - In 2009, the Trust awarded a £3 million Strategic translational award to Professor Marc Turner, Director of the Scottish National Blood Transfusion Service (SNBTS). Professor Turner is leading a collaboration between NHS Blood and Transplant, SNBTS, the Irish Blood Transfusion Service (IBTS), the Universities of Glasgow and Edinburgh, and Roslin Cells to look at the potential of using stem cells to generate red blood cells for use in transfusions. Building on existing technology, the research team will turn stem cells into type O negative red blood cells, which in theory can be used for almost any patient in need of blood and ensure that the resulting cells are safe to use in patients. The project will use human embryonic stem cells, which will come from embryos between three and five days old that would otherwise be discarded as part of routine IVF (in vitro fertilisation) treatments. The research will be conducted in accordance with Human Fertilisation and Embryology Authority (HFEA) procedures. If successful, this project could in the long-term lead to a new and sustainable source of blood for use in transfusions and fulfil the unmet demand for blood within the UK and around the world.

The role of consent

Consent for future unknown ('secondary') uses of bodily material

Question 23: Are there circumstances in which it is ethically acceptable to use human bodily material for additional purposes for which explicit consent was not given?

28. When collecting tissue samples for research purposes, the Trust strongly supports a consent process that is generic and enduring. Future scientific developments and research needs cannot always be predicted, but it is often impracticable and not necessarily possible to seek consent for any additional use of tissue in subsequent research. Obtaining generic consent therefore helps to maximise the potential value of the donated tissue. We therefore endorse the guidance given in the HTA Codes of Practice relating to consent and research.

29. Focus groups with the public also suggest that the notion of one-off consent is seen to be the most practical.[10] There was recognition of the wide variety of opinions, and a suggestion that a one-off consent process that allowed people to choose between different levels of consent would provide an acceptable solution. These could range from the most permissive blanket

[10] Public Attitudes to research governance Chap 6 p.54-55 (2006) http://www.wellcome.ac.uk/About-us/Publications/Reports/Public-engagement/WTX038446.htm

permission for any collected tissue to be used for research for any medical purpose, to other options that specified time limits or the nature of the research, who it was that would be conducting the research (NHS vs. private company), and/or how any re-consent process would be effected.

30. However, in some situations it may not be possible to seek generic consent. In such cases, the Wellcome Trust considers that it is acceptable to use samples/medical data for secondary purposes without returning to the participant for specific consent, if the proposed research:

    - complies with relevant national laws
    - complies with any binding codes of practice or ethical guidance (such as professional guidelines or licensing regulations)
    - is not inconsistent with the original consent as approved by an ethics committee
    - uses samples or data which have been anonymised (either fully or, at a minimum key coded so that researchers are not able to identify the participants)
    - meets policy requirements regarding secondary use as required by the principal investigator's employing institution.

31. The framework established for UK Biobank provides a useful example of a successful large scale model to enable bodily material to be used for additional research purposes. The scale and duration of the study (30-40 years) required a mechanism that used broad consent, as it was recognised that it was not always possible to envisage future research uses of donated material. However, to provide reassurance to participants, an Ethics and Governance Framework was developed and an Ethics and Governance Council established to provide advice to UK Biobank and advise on the interests of both participants and the general public. Participants are informed that only research uses that have been approved by both UK Biobank and a relevant ethics committee will be allowed, and that data and samples will be anonymised before being provided to research users. It is envisaged that further consent will be sought for any proposed activities that do not fall within the existing consent.

Any other issues?

32. The Terms of Reference note the international context of research, but the primary focus of this consultation is within the United Kingdom. It is important to consider the different regulatory requirements for use of tissue, particularly since research often includes international collaborations where samples may be collected in one country but analysed in another. The consent provisions of the Human Tissue Act do not apply to imported tissue, although the HTA recommends that there should be mechanisms in place to provide assurance that the tissue has been obtained with valid consent. The practical implications of achieving this may merit further consideration.

33. In relation to current regulatory framework surrounding the use of human tissue, the research community raised significant concerns at the time that the Human Tissue Bill was first introduced as there were concerns that the proposals would introduce unnecessary bureaucracy. We note that the situation has moved on significantly since that time. Most importantly, a number of secondary Codes of Practice have been developed through an iterative process of consultation with the research community and in general, researchers find the Codes useful and easy to follow. A study of a range of health professionals, funded by the Wellcome Trust following the introduction of the Human Tissue Act 2004 and the Human Tissue (Scotland) Act 2006, found that although there were still residual concerns regarding

consent, on the whole, the changes in the law were seen as helpful in providing clarity and reassurance to professionals, patients and relatives.[11]

34. However, there are two areas where greater clarity in the definitions in the Codes and amendments to the legislation itself would be helpful: the need for broad consent for research purposes, and the definition of 'relevant materials' (including very small sample sizes). Storage provisions could also be usefully reformed to allow for storage of appropriately consented samples beyond a single approved project. Currently researchers cannot store samples which have appropriate consent in unlicensed storage facilities in the absence of REC approval for a specific project. The cost of storage in a licensed facility makes keeping samples already used in one project prohibitive, even though they might be of value for future research.

35. The amendments to the Human Fertilisation and Embryology Act in 2008, relating to the use of embryos and embryonic stem cells, should facilitate research within a robust framework, although we note that the provisions regarding the ability to undertake research to create human admixed embryos are yet to be tested.

[11] Campbell AV, McLean SAM, Gutridge K, Harper H. 'Human tissue legislation:listening to the professionals' *J Med Ethics 2008: 34: 104-1-08*

ANNEX A: Wellcome Trust biomedical ethics funding programme

The Trust recognises the importance of debate and research exploring the complex range of ethical, social, cultural and philosophical issues associated with many aspects of science and medicine (such as the donation of human material) and supports a range of activities in this area, through our Public Engagement funding programme http://www.wellcome.ac.uk/Funding/Public-engagement/index.htm, the Wellcome Collection http://www.wellcomecollection.org/, and our Biomedical Ethics funding programme http://www.wellcome.ac.uk/Funding/Biomedical-ethics/index.htm.

Through our Biomedical Ethics funding programme, we support research that explores ethical and moral dilemmas arising in the conduct of biomedical research and the development and delivery of healthcare in the UK and low and middle income countries around the world. We fund large collaborative multidisciplinary research and capacity-building programmes, provide support for the brightest postdoctoral scholars in biomedical ethics through our Research Fellowship scheme, and fund health professionals and scientists interested in carrying out research to explore the dilemmas they face in the course of their work through our Research Fellowship and Research Leave Award schemes for Health Professionals and Scientists.

Through our International Ethics programme http://www.wellcome.ac.uk/Funding/Biomedical-ethics/International-ethics-grant-schemes/index.htm, we provide a range of support to strengthen the capacities of researchers based in low and middle income countries to carry out research to explore the ethical, legal and socio-cultural aspects of biomedical research and the development and delivery of healthcare in low and middle income country settings.'