The Medical Research Council

Submission from The Medical Research Council to the Nuffield Council on Bioethics consultation on Human bodies in medicine and research.

1. The Medical Research Council (MRC) is one of the main agencies through which the UK Government supports medical and clinical research. The MRC is dedicated to improving human health through the best scientific research. Funded by the Department for Business, Innovation and Skills (BIS), the MRC's work ranges from molecular level science to public health medicine and has led to pioneering discoveries in our understanding of the human body and the diseases which affect us all.
2. This evidence is submitted by the Medical Research Council (MRC) and represents the independent views of the research council. It does not include or necessarily reflect the views of the other UK research councils, Research Councils UK or the Department for Business, Innovation and Skills.

Introduction

3. The MRC welcomes this consultation which aims to address issues that arise in relation to some MRC-funded research such as the donation of gametes and embryos; volunteering for early stage clinical trials; the donation of samples such as blood or buccal swabs in large scale population studies. Access to human material and the recruitment of volunteers into early-phase trials and clinical studies are essential for the research that MRC funds and for delivery of progress in key strategic areas, such as regenerative medicine, the investigation of the link between genetics and disease, and increased translation of research findings into benefits for human health. We welcome the scrutiny by this Working Party of the difference between inducement, payment or reimbursement of expenses.
4. This consultation also relates to areas of regulation such as the Human Tissue Act where it has been argued that the legislative requirements exceed society's expectations in relation to small or 'waste' samples of tissue from the living..
5. The MRC's current policy in this area is set out in a publication in the MRC Ethics Series "Human tissue and biological samples for use in research: operational and ethical guidelines"[1]. This is now almost 10 years old, although short supplementary guidance on the implications of the Human Tissue Act was added in 2005. We plan to update this guidance soon, to ensure it reflects regulatory and other changes in recent years. The report of this Working Party will be taken into account in that update.
6. Issues relating to consent to donate tissues (but also data or time) are also of interest. The MRC supports the principle that consent can be broad and enduring to allow long-term storage of samples and use in future, ethically approved projects. This maximises potential benefit of donated samples but can

[1] see: www.mrc.ac.uk/Utilities/Documentrecord/index.htm?d=MRC002420

give rise to questions about what level of detail of information is required for consent and how to deal with unforeseen future research uses.

Question 1: Are there any additional types of human bodily material that could raise ethical concerns?

7. The list of material outlined in the consultation appears exhaustive except it does not specifically mention cells, other than stem cells. Some issues can arise relating to other cells and cell lines. The latter are specifically excluded from the Human Tissue Act 2004, but may become of increasing importance, for instance in regenerative medicine research aimed at growing replacement organs or tissue from cells, either in the laboratory or in situ. Also, some of the only case law on property rights and research material comes from the HeLa cell line case in the United States.
8. Material removed from the body during surgery or other procedures is of particular importance in medical research; for example, cancer research depends critically on the availability of tumour samples.

Question 2: Should any particular type(s) of human bodily material be singled out as 'special' in some way?

9. Gametes and embryos are treated differently in law. Many would support this as these are the cells and tissues with potential to become another life. In the UK this has led to the view that such material should be treated with particular respect, the status of which increases from gametes to embryos and with development of the embryo.
10. Particular care is required in obtaining properly informed consent from living donors of non-renewable material (such as whole organs) in view of the potential long-term health implications.

Question 3: Are there significant differences between providing human bodily material during life and after death?

11. Again, there will be different views on this. The series of inquiries of the 1990s showed the deep concern that can arise around use of post-mortem tissue, particularly from children, without the knowledge or consent of relatives. In Scotland the tissue legislation only relates to tissue and organs from the deceased. Some have argued that removal of tissue from the living is covered adequately under the common law of consent and that this could also address storage and use of that tissue without specific legislative control.
12. With donation after death, physical risk to the individual donor is not an issue, and the risks considered must be those to either their reputation (if privacy is breached) or to their relatives or friends. A particularly difficult issue arises when the deceased has agreed to donate material for research before they died but the relatives are not comfortable with that decision. Although the consent of the deceased takes precedence in law, many researchers many be uncomfortable complying with this in the face of opposition or distress from relatives.

Question 4: 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.

13. In relation to research, benefits are often altruistic - helping advance science towards treatments. Such treatments may be of potential direct benefit to the patient-participant but will more often be of indirect benefit to others. There may also be psychological benefits for either patients who are donors or for relatives of patients, in feeling that some good might come out of misfortune by directly facilitating research that could help improve treatments.
14. There may be financial reward in participating in some volunteer trials. However, this will be for time and costs of trial participation and not for donation of tissue. The MRC's guidance on Human Tissue and Biological Samples for use in Research - Operational and Ethical guidelines"[2], states (paragraph 2.5):
"The Council of Europe Convention on Human Rights and Biomedicine states that The human body and its parts shall not, as such, give rise to financial gain, and the MRC fully supports this principle: the sale of human biological samples for research is not ethically acceptable. Therefore, while reasonable expenses (e.g. travel expenses) may be reimbursed, research participants should never be offered any financial or material inducement to donate biological samples for research."
15. There are potential benefits and risks if information of diagnostic or predictive value derived from donated biological material is fed back to donors or their relatives. On one hand, this information might bring direct health benefits (for instance, by allowing early access to treatment or preventive measures). On the other hand such information may not be beneficial if the interpretation is unclear, there is no intervention available, if there are potential insurance or legal implications of the knowledge, or the potential for stigmatisation exists. Also, the relationship between the donor and researchers is not always direct and where feedback of information is via a health professional, the information could place those professionals in a difficult legal or ethical position.
16. Risks may relate to procedures undertaken to obtain blood or tissue; often this will be part of treatment but may involve additional surgical time or procedures. Risks may also relate to data storage and use, which needs to be done under appropriate IT security.

Question 5: 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?

17. It is important to remember that it is not only healthy volunteers that are involved in first in human trials. In some circumstances (for instance in trials of devices or new surgical interventions) patients may be involved, and the costs and risk/benefit considerations will often be quite different for this group.

[2] see: www.mrc.ac.uk/Utilities/Documentrecord/index.htm?d=MRC002420

18. The benefit for healthy volunteers is primarily an altruistic one of helping to develop a new treatment to benefit others, whereas patients may benefit directly if the intervention is effective. For healthy volunteers in commercially run trials there is usually some form of payment which, although intended as reimbursement for expenses may be considered by volunteers as a financial benefit or incentive. The MRC remains committed to the principle, as stated in our current guidance, that any payment should be to recompense for actual loss rather than representing financial gain to donors. It is reasonable to compensate for loss of earnings, but the amount available should be capped.
19. Risks depend on the intervention being used. There is an implicit assumption that first-into-human trials are inherently more risky than later phase trials, but we are unaware of any evidence that this is actually the case for short or long term adverse health events. The level of acceptable risk may depend on individual circumstances; for example, patients with serious conditions not responding to existing treatment options may quite reasonably be willing to accept a much greater level of risk than healthy volunteers.
20. The onus should be on researchers to ensure that potential volunteers have a sufficient understanding of the risks involved and are competent to consent. However, there should also be limits on the level of risk that can be undertaken even by those who fully understand and are committed to medical research.

Question 6: Are there any additional purposes for which human bodily material may be provided that raise ethical concerns for the person providing the material?

21. Tissues and cells for research may be used in projects involving embryos or animals which may raise ethical concerns for some participants.
22. The MRC supports the current position that embryos and gametes are treated with particular respect by the law.

Question 7: Would you be willing to provide bodily material for some purposes but not for others? How would you prioritise purposes?

Question 8: Would your willingness to participate in a first-in-human trial be affected by the purpose of the medicine being tested? How would you prioritise purposes?

23. Valuable tissue collections for research such as the UK Biobank and large cohort studies, which would be very difficult to renew or replicate need to have clear policies to prioritise requests for access, to ensure that maximum value is realised. Criteria should include quality, importance and potential impact of the research use proposed.
24. We do not wish to comment on prioritization of clinical use of donated tissue as this is outside the remit of the MRC.

Question 9: Are there any other values you think should be taken into consideration?

25. No, the list appears comprehensive. In relation to the values listed, it should be noted that dignity is a fundamental value under human rights law. Autonomy is normally considered a priority, but should not necessarily always take precedence. An example might be when an emerging new infection threatens to become a serious public health issue, in which case testing samples in an existing tissue bank without donor consent could be justified. Justice and solidarity are important values when considering research in resource poor settings and arrangements for access to new treatments after research is completed.

Question 11: Do you think that it is in any way better, morally speaking, to provide human bodily material or volunteer for a first-in-human trial for free, rather than for some form of compensation? Does the type or purpose of bodily material or medicine being tested make a difference?

Question 12: Can there be a moral duty to provide human bodily material, either during life or after death? If so, could you give examples of when such a duty might arise?

Question 13: Can there be a moral duty to participate in first-in-human trials? If so, could you give examples of when such a duty might arise?

26. At present the MRC considers altruistic participation and donation as preferable to doing so for financial gain. There could be argued to be some moral duty to assist research that will aid others and progress treatment development. In the UK everyone benefits from healthcare that is free-at-access via the NHS and some would argue that this places some responsibility on patients to support the research that treatments are based on (see John Harris). Certain individuals could be seen to have a moral duty to donate tissue for research. For example, it could be argued that there was an obligation on those who had received a novel experimental treatment to allow sampling to monitor the effect of the treatment or post-mortem analysis to be undertaken. However, this duty is not an overriding one and needs to be balanced against autonomy and individual views of risks and benefits.

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?

Question 16: Are there forms of incentive that are unethical in themselves, even if they are effective? Does it make any difference if the incentive is offered by family or friends, rather than on an 'official' basis?

Question 17: Is there any kind of incentive that would make you less likely to agree to provide material or participate in a trial? Why?*

Question 18: Is there a difference between indirect compensation (such as free treatment or funeral expenses) and direct financial compensation?

Question 19: Is there a difference between compensation for economic losses (such as travelling expenses and actual lost earnings) and compensation/payment for other factors such as time, discomfort or inconvenience?

27. It is important to positively recognise and support donation for, and participation in, research. Patients and healthy volunteers in publicly funded medical research usually do not expect financial rewards, although reimbursement of travel or other costs is usually offered. In this context any framework should avoid undue incentives to induce people to do things they are not comfortable with and would not consent to without. There is no evidence to suggest that the level of payment affects the availability of volunteers or donors for teaching or research in the UK.
28. The distinction between compensation and incentive is important. The principle of compensation in law is to put a person back to the position they would have been in had the event not happened. In this light, reimbursement of travel costs, loss of earnings or childcare costs can be seen as compensation whereas payment related to time or level of discomfort, and benefits such as free medical treatment or funeral expenses should be seen as incentives. Other potential incentives are less easily categorised: for instance, access to experimental treatment, when there is no proven treatment available, can be an incentive, as can the continued availability of treatment after completion of a trial (this was seen in the early AIDS treatment trials). As medical treatment is free in the UK there are few examples of access to free or reduced costs treatment. The MRC is aware of one example of this in a research study, where donors undergoing IVF treatment are offered reimbursement or part payment of treatment costs if they donate eggs for research (such an arrangement was already available for those donating eggs for treatment of others). The MRC is funding a parallel social science study of the participant's experience and views in this case in order to improve our understanding of the effect of such arrangements and inform our future position.
29. In principle, the MRC sees reimbursement of economic losses consequent on participation as acceptable and payment for time or discomfort less so. Payment that is related to the actual or perceived level of risk runs the clear risk of incentivising higher levels of risk taking, particularly amongst those on low incomes. However, the market for private sector trials and certain other research studies (such as psychological experiments) is perceived to operate differently at present, with the financial amounts available to volunteers clearly having the potential to act as incentives to those on lower incomes such as students.

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?

30. The availability of human bodily material will continue to be of critical importance for biomedical research. Indeed the pressures to reduce the use of animals in research, and the need for systems that closely replicate the clinical situation will drive the use of model systems using human material for in vitro testing. Advances in computational and systems biology and the increasing sophistication of computer models will mitigate this tendency to some extent. The current drive towards translational research, and the increasing pace of

development of biological therapies will mean a continuing demand for first-into-human trials. Research in regenerative medicine may in the longer term lead to successful development of artificial organs and thus a reduction in the requirement for organs for transplant, but this is still some way off.

Question 21: In your opinion are there any forms of encouragement or incentive to provide bodily material or participate in first-in-human research that could invalidate a person's consent?

31. Consent does depend on being able to make free decision. Undue influence could be exerted by potential financial gain but also by family pressure to help an ill relative. At present the former is not allowed but the latter could occur, especially in cases where power relationships are unequal.

Question 22: How can coercion within the family be distinguished from the voluntary acceptance of some form of duty to help another family member?

32. This is probably related to treatment more than research use, although family members may particularly want others to participate in research relevant to family members; this is often the case in genetics research on hereditary disorders. It is very difficult to distinguish what is and is not coercion, as this requires a clear understanding of family dynamics not usually available to an outsider.

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?

33. Yes, if tissue is stored for future research it will not necessarily be possible to outline all possible uses. This is seen for example in the UKBiobank consent process, which is seen as having moved towards a 'trust' model of consent, involving broad consent for certain categories of research use. It is important to ascertain if there are categories of future use which would be seen as unacceptable by the donor (for instance, relating to embryo creation, animal or commercial uses). However, it may be that in some cases researchers will choose not to store samples with such restrictions due to the difficulty of complying with them.
34. Older samples, such as those from birth cohorts, or pathology archives, may have been collected with very limited information and consent in keeping with standards of the times. However, donors did wish these to be used in research so it may be unethical to exclude them. Research Ethics Committees should continue to play a key role in determining appropriate uses of tissues with unclear consent and ensuring the interests of the donors are protected.

Question 24: Is there a difference between making a decision on behalf of yourself and making a decision on behalf of somebody else: for example for your child, or for an adult who lacks the capacity to make the decision for themselves?

35. There are difference, for example for an adult who lacks capacity it should be a 'substituted judgment' as to what that adult would have decided if they had

capacity. So the adult making the decisions may have different perspectives but should make the decision the incapacitated adult would be likely to have made. For children the decision should be in the best interests of the child. The MRC provides guidance for researchers addressing issues relating to these two groups of participants: Medical research involving adults who cannot consent[3] and Guidelines on Medical Research involving Children[4]. Adults not capable of consenting should not be completely excluded from early phase trials (an example might be treatment of head injury in unconscious patients).

Question 25: What part should family members play in deciding whether bodily material may be used after death (a) where the deceased person's wishes are known and (b) where they are unknown? Should family members have any right of veto?

36. Family members will usually be involved after death – although in law they have no right to veto a decision in practice researchers may be unwilling to go against a family's wishes. However, for example, if the deceased wished their brain to be donated for research it could be viewed as unethical to deny this wish. Ideally the deceased will have discussed their wishes with family members before death so that they understand and respect the expressed wishes.

Question 26: To whom, if anyone, should a dead body or its parts belong?

37. The MRC believes that it is for society, through the courts and government to decide this, and it is not appropriate for us to comment. The current position appears to work in practice, although the definition of added skill allowing rights to be asserted may be difficult to set down.

Question 27: Should the laws in the UK permit a person to sell their bodily material for all or any purposes?

Question 28: Should companies who benefit commercially from others' willingness to donate human bodily material or volunteer in a trial share the proceeds of those gains in any way? If so, how?

38. Although it is now generally accepted that there is no property in the human body, this does not really reflect contemporary reality. Advances in modern medicine mean that there is clearly a value to many parts of the human body, and it is an important question for society as to whether this should be recognised in legal as well as ethical terms. Selling bodily material as a straight financial transaction could give rise to concern about undue inducement or exploitation. However, if the level of compensation is below that would give rise to this concern then it is not necessarily inappropriate. There is clearly a grey area between payment, compensation and inducement, and the fact that money changes hands is not sufficient in and of itself to commodify human beings.
39. It could be perceived as unethical if private companies benefit from volunteers or donated tissue in developing drugs but then make large profits from sales. However, benefit sharing is a much bigger issue that should be dealt with

[3] see: www.mrc.ac.uk/Utilities/Documentrecord/index.htm?d=MRC004446

[4] see: www.mrc.ac.uk/Utilities/Documentrecord/index.htm?d=MRC002430

alongside debates in relation to intellectual property generally, not solely in relation to tissue donation. For instance this is a particularly important issue for research involving donors from resource-poor countries. There is normally significant interplay between the public and private sector in the development of new treatments, and the bringing to market of a new treatment usually represents the collective contribution of many different groups of study participants and tissue donors. It would be impractical to have separate positions for the public and private sector.

Question 29: What degree of control should a person providing bodily material (either during life or after death) have over its future use? If your answer would depend on the nature or purpose of the bodily material, please say so and explain why.

40. In relation to research, consent may be controlled and specific to a single project or could be broad with an explanation of potential uses. Both are seen as acceptable although the latter can facilitate greater benefit in relation to research gain from use donated tissue.

Submitted by:
Frances C Rawle PhD
Head of Corporate Governance and Policy
Medical Research Council
(16 July 2010)