Marlene Rose

Question 2

Is any particular type of tissue special? Yes it is. It would be sensible to distinguish between tissues which have been removed in the course of another procedure and material taken specifically for a research project. As this document says, materials taken in the course of another procedure are often treated as waste, but are invaluable for research. In the hospital where I work, we call these specimens 'tissues necessarily removed for treatment or diagnosis and surplus to diagnosis'. They can be anything from whole organs (in the case of organ transplantation, where the diseased organ is removed) to blood (taken for diagnosis) biopsies, placentas, or DNA (e.g. used for tissue–typing). Samples surplus to diagnosis are a huge potential resource for research workers. All diagnostic labs store their samples, as matter of routine, for many years after they were taken. HTA regulations stipulate that the overriding principle governing storage of human tissue for research is consent. Unfortunately the HTA does not distinguish between tissues necessarily removed and those removed solely for research. This has proved to be a costly mistake. Using samples necessarily removed and surplus to diagnosis for research poses no physical risk for the patient. Provided they are used in an anonymised form, there is no breach of privacy to the patient. The HTA demands that we require consent to store this material for research, then ethical permission to use it. In order to obtain consent, one has to devise a method of 'catching patients' well before the procedure and ask them to sign a form giving 'generic consent' for excess tissue to be used for 'research' – without specifying the nature of the research. Although this sounds as if it would be easy to do, it is very difficult and is currently taxing the R and D departments of hospital throughout the UK. I cannot calculate the huge number of man-hours that have been spent in my hospital trying to devise a system that both allows the patients to express their choice and is easily accessible to the individual researcher. If such a system exits, before using the samples, the researcher has to check that the patients have consented. If one has a collection of many hundreds of (say) biopsy samples, it is not feasible to go through the patients' notes to find the small number who have refused consent. The system has to be on a database, but this has also been very hard to implement. There is also the legal/ethical issue of whether asking someone to tick a box on the 'Procedure Consent Form' that they agree to excess samples being used for current or future research constitutes 'informed consent'. Really one needs a member of hospital staff, with an understanding or research, to sit-down with the patient and explain what this means. This could be done but has revenue costs for the hospital. On the ethical side, one might question why should someone refuse permission for excess samples to be used for research, in an anonymised form? As I understand the legal

situation, tissues do not 'belong' to the individual once they have left the body. For reasons of 'maximising health and welfare', reciprocity and solidarity, I think use of tissues 'necessarily removed and surplus to diagnosis' should be stored for research as a matter of course without need for consent. The alternative, allowing some choice would be an opt-out system. On the other hand, permission to be used for research projects should only be given after scrutiny by Peer Review and Ethics committee to ensure these valuable specimens are only used for worthwhile projects.

Question 4

See above, as well. There are different risks attached to donating different bodily materials. For example donation of blood or sperm are virtually risk free and can be done on many occasions, whereas donations of whole organs (e.g. kidneys, single lungs, liver lobes) incur considerable short-term and long-term risks. I do not think it is ethical to pay for any bodily material, because it will inevitably results in poor people selling their bodily material, and worse if substantial payments are concerned (e.g. for organ donation) it would results in coercion within families.

Question 5

Participation in first-in-human trials. This question really had me stumped, because I have become used to the idea that volunteers are paid to participate in clinical trials. In general, it seems likely that these pose few risks, although that is not to say they are without discomfort. In years gone-by, people interested in the results for professional reasons would probably volunteer without payment (scientists have been known to inject themselves with proteins to monitor immune responses! Medical students used to volunteer for first-in-human trials or as controls for research projects). I think everyone would expect payment now; it is a change of culture, plus the fact that (profitable) pharmaceutical companies are directly involved in the first-in–human trials and are perceived as financially benefiting from the products. However, from a strictly ethical stand-point if it is unethical to be paid to be a blood, sperm or kidney donor, it is also unethical to be paid to partake in first-in-human clinical trials. The fact is that no-one should be expected to sell any part of their body no matter what the purpose; it is demeaning and people only do it because they need the money. It is not a career option and is unlikely to provide self-esteem. Taken to its logical conclusion, one could imagine an under-class of people who take part in the clinical trials (and sell their blood, sperm and organs) and the rest of society who benefits from the sale of bodily parts. On the other hand, being paid for first-in-human clinical trials seems is less damaging to the donor that donating kidneys and has less impact on the quality of donation than blood or sperm for example. It is therefore the most acceptable of the policies involving 'payment for bodily parts'. It seems reasonable that levels of payment are related to risk.

Question 9

Question 3 Ethical values The concepts of Autonomy and Self-determination have become the most important principles that govern whether people donate bodily materials for research – and even whether they donate organs for life-saving transplant operations. There is no doubt in my mind that the altruistic concepts of 'maximising health and welfare', Reciprocity and Solidarity are sadly missing from discussions in this area. It is summed up quite well in the recent discovery that mistakes had been made in transplanting the wrong organs or tissues from 20 people on the Organ Donation Registry. It is not that they had not agreed to organ donation, but that organs or tissue they excluded were transplanted. Clearly this is a clerical error which should not have occurred. However, as a commentator in one of the newspapers said, the mistakes in this case are easily dwarfed by the number of occasions when no organ is donated from people who agreed, because relatives are not asked. Such cases have been audited, but they rarely come to the public attention. I cannot think of an ethical reason why one would not agree to donating an organ after death. At the recent meeting of the British Transplantation Society, there was a debate between representatives of the four main religions in this country and, as I understood at the time, no-one quoted religious reasons for not being an organ donor. However, it is clear that there is mistrust between various communities and lack of trust in the professionals who make decisions about organ donation. One could argue a moral duty to provide bodily materials either during life (as materials necessarily removed) or after death in the form of organ donation. It is self-evident, but people need to understand that if one lives in a society under the assumption that one will receive a life-saving heart or kidney when necessary – then someone has to agree to donate their organs. We are all in this together. Many other actions are mandated in society for the 'good of everyone' such as paying taxes, not drinking and driving. Vaccination programmes are an interesting analogy, they are not mandated, and some people object on the autonomy principle; of course it is safe for a small number of people not to be vaccinated, they won't get the disease because everyone else has been vaccinated! I think donation of bodily materials could be considered in the context of the 'good of everyone'. I cannot think of an ethical reason why someone would not allow tissues taken surplus to diagnosis to be used anonymously in an ethically approved research project. I am sure that if the lay public understood the time it takes hospital staff to determine who has not approved, and the number of research projects which simply do not start because of regulatory issues, 99% would be horrified. I am not sure that most people understand how much medical progress depends on using excess human tissues. The moral duty to allow ones' organs to be used after death could be extended to participation in first-in-human clinical trials, although this appears to be a very different situation. The principal is the same, if the public wish to see progress in understanding and treating disease, human material needs to be used and new therapies have to go through clinical trials. Maybe the moral obligation to Jury service is a useful analogy; every individual, at some time in their lives should be 'called' to take part in a first-in –

human clinical trial.

Question 14

Responding to demand There are increasing medical demands for extending life and increasing the quality of life. I do not know how this can be prioritised. Should spending on in-vitro-fertilisation be equated with organ donation which saves lives? Organ donation is a dramatic and highly efficient method of transforming both quality of life (eg kidney donation compared to life on dialysis) and saving lives (eg heart transplantation). In view of the success of organ transplantation in the last 20 years, it is ethical that all efforts are made to reverse the current disastrous decline in organ donation which is allowing patients to die unnecessarily on the waiting lists. It is, in my opinion unethical to pay for organs, apart from necessarily incurred expenses. Any policy which directly reimburses donors for their organs will result in poor people selling their organs to the rich. This can is exemplified by the current practice of 'Transplant Tourism' where wealthy patients from rich countries travel to poor countries to buy kidneys from poor people. The other real worry is that will be coercion of 'weak' family members to donate their kidneys that will go undetected despite laws and regulations that prohibit coercion for organ donation. There have to be more imaginative and effective way of engaging with the public about the necessity for organ donation and the benefits it brings to the whole community. For many years the system has been based on altruism, on the understanding that it is ethical to give people a choice; but the current system is not supplying enough donors. It would be ethical to introduce an opt-out system or mandated choice. In this way people are still given a choice but the odds are more in favour of producing more donors. In Jan 2010 Israel started a new system whereby patient is give priority for an organ if they have signed a donor-card. It will be interesting to see if this system results in more donors.

Question 30

I would like to comment of the special difficulty of obtaining tissues from cadaver donors (for transplantation) for research. Using tissues for research from cadaver transplant donors has been made virtually impossible because of a Ruling from the HTA that tissues cannot be taken from cadavers, for research, even with consent from relatives, unless the hospital site where the cadaver originates is licensed for Post-Mortems with the HTA. At the time of writing, very few hospitals are licensed for PMs by the HTA. The problems I have had over the last 2 years also highlight the lack of understanding between researchers, ethical committees and the HTA and a complete lack of uniformity of understanding the difference between 'Service Development' and 'Research' between researchers and experts on Tissue Governance (ie people on the Tissue Governance committees of hospitals). I wished to collect a small amount of extra blood from our brain-dead deceased donors to improve the cross-match procedure at the time of transplantation. Initially, when I applied for ethical permission, I was intending to obtain informed consent from the relatives of the deceased donors. The ethical committee to which

I applied approved the application but advised me not to ask for informed consent from the relatives because this would be too upsetting for them. I hence obtained ethical permission to take extra blood from the donors without informed consent. I then learnt from colleagues, and confirmed by the HTA, that blood could not be taken from cadaver donors for research if the site was not licensed with the HTA, but I could take blood for the 'purpose of transplantation'. The HTA advised me I must not have ethical permission for the project, because that would mean it is research. I therefore submitted a substantial amendment to my ethical application (which was asking permission for other procedures as well), removing all references to this method from the application. I was intending to call this 'Service Development', since if the method proved to be useful it would be immediately incorporated into the service my lab performs for transplant patients. There are a number of documents on the IRAS site explaining how to differentiate between Service Development and Research, but none of the criteria turn-out to be relevant to my project. It transpires this is a very grey area which requires subjective interpretation. Although many professionals who I talked to about this were satisfied that this project was 'Service Development', there were also those who thought it was research. Some colleagues were of the opinion that relatives should give informed consent, although this was prohibited by the first ethical committee. Some colleagues thought that if the project was to be called Service Development, we should be giving real-time reporting of the results, which would be possible, but would make jeopardise scientific interpretation of the results. It is interesting to note that in US, where the study is being performed, they do it under a straight forward research banner (informed consent not required). Studies in Europe which have used living donors, have done so with informed consent from the donors. These factors made me feel that calling it Service Development may not be correct. I therefore withdrew my centre from this study. Researchers require clear guidelines and regulations in order to do their work. This is an example of opaque and contradictory messages from those that authorise research projects.