Nuffield Council on Bioethics
Forward Look Seminar
8th May 2008

Note of meeting

Present:

Guests
Professor Richard Ashcroft
Dr Mark Bale
Professor Michael Banner
Dr Susan Bewley
Professor Peter Braude
Dr Helen Busby
Professor Tony Cass
John Crowley
Dr Hugh Davies
Dr Christiane Druml
Professor Philip Dyer
Dr Jenny Gunning
Professor Göran Herméren
Professor Emily Jackson
Pablo Simón Lorda
Professor Jean McHale
Professor Brigitte Nerlich
Dr Janet Radcliffe Richards
Professor John Ryan
Dr Ruth Warwick

Members of Council
Professor Albert Weale (Chair)
Professor Roger Brownsword
Professor Sian Harding
Professor Ray Hill
Professor Søren Holm
Dr Rhona Knight
Professor Alison Murdoch
Professor Hugh Perry
Professor Peter Smith

Secretariat
Hugh Whittall
Harald Schmidt
Katharine Wright
Catherine Joynson
Julia Trusler
Kate Harvey

TOPIC 1: NANOTECHNOLOGY

The science of nanotechnology

1 Nanotechnology was a term that included a broad range of enabling technologies spanning molecular biology, quantum physics, materials science and molecular chemistry. The rate of increase in R&D investment has been very rapid in this area. Applications of nanotechnology included carbon nanotubes, nanoelectronics, environmental remediation, drug delivery technologies and nano-implants. The focus today would be on nanotechnologies in the area of biology and medicine, such as nano therapeutics, molecular imaging and synthetic devices.

2 Current developments included advances in DNA translocation, where nanotechnologies might soon allow processes at the DNA level to be seen much more clearly than is currently possibly. Possible future applications included antibacterial treatments and targeting cancer drugs. Self-assembling DNA nanostructures were also being developed, which might be used for drug delivery in future. Gold nanoshells vary in colour depending on the thickness of the shell. Research was being carried out on attaching infrared gold nanoshells to cancer tumours, which could then be targeted with a laser.

Ethical issues

3 UNESCO had published a report on 'The Ethics and Politics of Nanotechnology' in 2006, which identified a number of issues. It highlighted that an overall question to consider was whether there were some nanotechnologies that were not permissible in principle, and whether there were some that were permissible if certain conditions were met.

4 It was not clear how unified the field of nanotechnology was and whether nanotechnologies raised specific ethical issues. The two most developed areas of research, materials science and medicine, were not well connected at all. This may mean that 'nanotechnologies' should not be the focus of concern as such, and that fixating on this one area might take the focus away from more urgent ethical issues in biology and medicine.

5 It could be argued, however, that there are a number of distinctive features of nanotechnology which raise unique ethical issues, including:

- The invisibility and size of nanoparticles, which raise concerns about informed consent and safety, for example related to the inhalation of nanoparticles, the transgression of biological barriers, and environmental affects.
- The fast pace of research, which may mean that regulation begins to lag behind.

6 Other possible risks of nanotechnology, which are not necessarily unique, included:

- Safety issues related to toxicity, low or non-existent biodegradability, and the unknown life-cycle of the materials. Risk assessment technology would need to keep up with the development of nanotechnology.

- The global impact and the 'nano divide', i.e. the possibility that nanotechnologies may only benefit richer countries.
- Issues around invasions of privacy, for example because nanotechnology has the capability of improving surveillance devices.

7 The 'unseen' and 'unknown' nature of nanotechnology meant that it had the potential to raise public concerns. It could be argued that if nanotechnology is publically finanaced then there should be a large-scale debate on the ethical issues. Some public dialogue activities had already taken place in the UK, such as the 'Nanodialgues' initiative which had been funded by a consortium of public and private bodies.

Regulation

8 Most of the existing applications of nanotechnology were covered by existing legislation, but there was a need to look ahead. The question about whether nanotechnology raised unique issues was also relevant to regulation. However, even if nanotechnology was not totally 'new' there might still be regulatory challenges. These included:

- Uncertainty about where nanotechnology research was heading, which could make it a difficult area to regulate.
- Definitional problems – what exactly was nanotechnology?
- Risk and safety issues.
- The broad range of laws and regulations that was applicable to nanotechnology and nanomedicine in the UK and EU which may cause definitional problems. Would a drug delivery mechanism at the nano scale be classed as a drug or a device?

9 There was a range of legal principles that were relevant to nanotechnology, such as consent, protection of personal privacy and human rights. There were also concerns about negligence liability, diagnostic tests available on the internet and patenting issues.

10 The European Union had already done much work in developing policy around nanotechnology and had published, for example 'Nanosciences and Nanotechnologies: An Action Plan for Europe 2005-9', and a code of conduct for responsible nanoscience and nanotechnologies research (2008). There had also been a number of initiatives at the national level to meet the regulatory and ethical challenges of nanotechnology, for example the Royal Society/Royal Academy of Engineering report (2004), a programme of government-funded public dialogue activities, and a Council for Science and Technology review of government progress on its policy commitments (2007).

11 The Royal Society recommended that the government should establish a group to look at new and emerging nanotechnologies and identify areas where potential health, safety, environmental, social, ethical and regulatory issues may arise and advise on how these might be addressed. However, it may be too early to decide whether the UK needs an advisory or regulatory body specifically for nanotechnology. The answer would depend on how the technology developed in future.

An international perspective

12 There were 580 products that use nanotechnology on the international market. There were 356 products in the health and fitness category and 66 in the food and beverage category. One of the largest subcategories was cosmetics with 89 products.

13 The Austrian National Biothics Commission published an opinion on nanotechnology in June 2007. The conclusions were similar to those of the UNESCO report 'The Ethics and Politics of Nanotechnology', published in 2006. Broadly these were that nanotechnology raised no fundamental new ethical issues and therefore there was no need to develop a specific legal framework for this area of research. The Commission recognised that there is a knowledge gap with regard to the dangers of nanotechnology, but weighing up the benefits and risks for the medical, food and technology sectors would be required by existing licensing procedures. A proactive dialogue with the public on nanotechnology was recommended.

SESSION 2: VOLUNTEERING, DONATION AND PAYMENT IN CLINICAL PRACTICE AND RESEARCH

Donation, volunteering and payment in clinical trials

14 No consensus existed on whether and how much participants in clinical trials should be paid. There was also little guidance on this area, for example guidelines from the Royal College of Physicians advised that no payment should be given for incompetent adults but there was no mention about payments for competent adults. Where participants were to receive money for their involvement in research, there were several possible approaches, each of which had pros and cons:

- Wage payment – paying according to the amount of time involved, and at an unskilled labour rate

This is an egalitarian approach, but likely to exacerbate inequity by appealing primarily to unemployed and low wage earners

- Market model – paying however much the market demands, based on principles of supply and demand
  Again this is likely to exacerbate inequity by appealing primarily to unemployed and low wage earners, and also could be criticised on the basis that researchers were seeking to pay as little as they could get away with.
- Expenses only
  This may attract few people, although it ensured that there was no reason to conceal information regarding eligibility for the research.
- Reimbursement of expenses and salary lost
  Any financial sacrifice by the participant should have been minimal, and the burden would theoretically have been spread equally across the population, but there may have been difficulty recruiting participants given the lack of benefit to them.

15 One issue discussed was whether payment should be considered to undermine voluntariness. Money could influence or persuade people to do things they otherwise would not, but was this a problem? Money was used in this way in many contexts, including potentially risky ones, and questions remained over whether there something different or particularly problematic about payments in clinical research that they required particular attention. Reasons for thinking that this was problematic included the nature and degree of the risks involved, and concerns over the potential for payments to promote inequity in the burden of research, through disproportionately attracting those who were poor or vulnerable.

Donation, volunteering and payment involving gametes and embryos

16 Regarding sperm donation, there was no shortage of donors for research purposes without payment, but there was a shortage in relation to donation for treatment. The number of donors had reduced since the law changed to remove their anonymity. This was problematic in terms of demand exceeding supply and also the concerns about couples going elsewhere to obtain sperm, for example using internet sources. Limited payment rates for donors' expenses, which were determined by the Human Fertilisation and Embryology Authority (HFEA), could leave donors out of pocket.

17 Regarding egg donation for research, there was an international agreement that donors should not be paid for donating. There were, however, so-called 'egg-sharing' systems for research in the UK, whereby individuals could receive half-price IVF treatment if half of the eggs

collected during the treatment were donated for research. This created a system in which some donors could receive substantial non-financial benefits, but others could not receive similar financial benefits for donating. A lack of NHS funding of IVF meant that many people would fund this themselves, and a 50 per cent reduction may have been very appealing to those who may be desperate for treatment but lacking resources.

18 While there was some shortfall in the number of eggs donated for research, there was a greater shortfall of eggs for treatment, and the number of donations was declining. The number of donors had been influenced by the removal of anonymity of donors, and there were concerns over the possibility that donors were going elsewhere in the world where they could receive higher payments for eggs than the expenses rates allowed by the HFEA.

19 Regarding embryos, it was explained that it was extremely rare for unwanted IVF embryos to be donated for treatment, but these were often donated for research. It was suggested that offering money generally would not alter people's decisions about donating embryos where they had a moral view on this.

Donation, volunteering and payment for transplantation

20 Different situations existed in relation to living and deceased donors. Regarding the latter, the number of transplants being performed was remaining fairly stable, while the number of patients awaiting transplants was increasing. It was noted that on average 1500 people in the UK die each day, of whom on average of three donate their organs for transplantation. If ten per day were to donate their organs, this would meet the current demand. The wishes of a deceased person were supposed to be paramount in relation to whether their organs could be used in transplant, but it was suggested that relatives often express objections and their wishes would then have been followed. Conditional donation was not allowed, and neither was payment or coercion to donate organs.

21 Regarding live donor organ transplant, largely for kidney and liver, these generally took place where the donor and recipient were related, although in six cases in the UK unrelated altruistic donation had occurred. Payment of donor expenses was allowed, including compensation for leave from work, but no other payments were permitted. Payments for organs were condemned at an international level, although they do occur in some countries. Particular concerns regarding payment include the risk to the

recipient from receiving an organ from a poorly screened donor, and concerns over inequalities resulting from those who were poorest in society donating their organs.

Ethical and legal issues in relation to volunteering, donation and payment

22 It was suggested that ethical issues in these areas varied according to a number of factors, including who the giver was, who the recipient was, the relationship between them, and the type of thing being given. Particular significance was suggested for different body parts according to how they relate to identity, and as such egg and sperm would be particularly sensitive, while hair and internal organs would be less so.

23 It was noted that there was no overarching legal approach governing all of the areas under consideration. This had allowed for the variability to arise over how donation and volunteering were regulated, whether payments were allowed and how the amounts would be calculated. It was noted that in some cases the current system was based on practical (and potentially consequentialist) considerations, i.e. payments were allowed for research participant because there wouldn't otherwise have been enough participants volunteering. However, this had not always been the case, for example, it would be cheaper for the NHS to pay for people to donate kidneys than to pay for kidney dialysis, but concerns over paying these donors override these practical considerations.

SESSION 3: THE ESTABLISHMENT AND USE OF CORD BLOOD AND OTHER CELL BANKS

Cord blood banking – the bank's perspective

24 Umbilical cord blood was rich in haemopoietic stem cells (HSCs), which could be used for bone marrow transplantation. It also contained very small numbers of mesenchymal stem cells (MSCs), which could be used for regenerative medicine. Around 10,000 cord blood transplants have been carried out, mostly to treat leukaemia but also for a variety of genetic disorders. Worldwide there were around 300,000 unrelated cord blood samples stored within the public sector, and 600,000 samples stored by relatives commercially. In contrast, there were 11 million registered bone marrow donors worldwide. Whilst cord blood is rich in haemopoietic stem cells, with 100 millilitres of cord blood being equivalent to 1.5 litres of bone marrow for transplantation doses, cord blood is only availble in small volumes. Cord blood could be stored for decades.

25 The UK public Cord Blood Bank currently accepts donations from a small number of hospitals close to the bank which had been selected because they cared for high numbers of people from ethnic minorities. The likelihood of finding a good match was much lower for people from these groups so the NHS scheme was skewed towards these populations. The NHS also ran a 'directed banking' programme for families considered at high risk because they already have a family member with a condition which can be treated by bone marrow transplantation. There was an international collaboration to match cord blood and bone marrow donations with patients. Bone marrow transplants had been decreasing since 2000 with peripheral blood transplants and cord blood transplants have been steadily increasing. However, only 1.5 per cent of banked donations from the NHS cord blood bank have been released for use at the current time.

26 Commercial banks allowed individuals to pay to store cord blood in case the donor needed stem cell treatment in future. The Virgin Health Bank had a policy of providing 80 per cent of the cord blood it received for public use, and keeping 20 per cent for use by the donor. Some commercial banks stored cord blood purely for use by the donor. There was some concern that commercial banking companies used claims in their marketing materials which are not currently available, and that potentially this could have a deleterious effect on access to allogeneic cord blood from public banks.

27 Pre-implantation genetic diagnosis or tissue typing had been used in the past to create 'saviour siblings', whose cord blood or bone marrow could be used to treat to a sibling. This raised questions about the commodification of the person and the legitimate rights of families.

Cord blood banking – the obstetrician's perspective

28 Parents were able to read about commercial blood banks on the Internet and obstetricians were increasingly being asked questions about the benefits. The obstetrician's priority, however, was the safe delivery of the baby and the health of the mother.

29 Umbilical cords were currently routinely clamped. The earlier the cord was clamped the higher the volume of blood collected for banking. However, at birth, without clamping, newborns went through placental transfusion, gaining 30-40 per cent blood volume, and there was increasing evidence that placental transfusion benefits both full-term and premature infants. The evidence showed that placental transfusion decreased the risk of intraventricular hemorrhage, necrotizing enterocolitis,

anaemia and postnatal hypovolaemia (although it may increase the risk of jaundice). Immediate clamping of the umbilical cord caused a 30-50 per cent reduction in a newborn animals' blood volume. There had been little research on the time when a baby had two circulation systems, which only lasted for around 20 minutes.

30 Most healthcare professionals had no view on cord clamping and carried out the procedure as a matter of normal practice. However, for some, clamping was an intervention that required justification. The Royal College of Obstetricians and Gynaecologists had advised that there was "insufficient evidence to recommend directed commercial cord blood collection and stem-cell storage in low-risk families".

31 There were a number of ethical concerns raised by cord blood banking, including:

- whether human tissue should be used as an investment opportunity;
- safety concerns for the baby;
- misleading claims about the benefits leading to exploitation of parents;
- the ownership of the cord blood; and
- whether commercial banks undermine social solidarity.

Cord blood stem cell banking: parents and moral reasoning

32 It was important to consider the parents' perspective in any discussion of cord blood banking. Research, funded by the Wellcome Trust, was being carried out on the perspectives of parents involved in private and public cord blood banking. It was often assumed that parents that were involved with public banking schemes were altruistic, and that the cord blood would be used for allogeneic transplantation (i.e. for a sister, brother or parent) and to treat cancer. Conversely, parents who paid for private cord banking were assumed to be doing it for selfish reasons, that the cord blood would be used for autologous therapies (i.e. for the donor themselves) and would be used for regenerative medicine. However, the motivations and profiles of parents were often more complex. The research had found that those paying for private banking sometimes did so because they needed a 'directed donation' that the NHS would not fund. For example, the NHS may not pay for banking the cord blood of a baby born while a sibling was in remission for leukaemia, but the parents might wish to pay for cord banking in case the cancer returns in their other child. Other reasons included if the parents were concerned about mixed ethnicity and access to matched tissues, or if there was a family history of a particular disease and the parents saw themselves as pioneers. Commercial banking was not without its problems though, for example it would only benefit those that could afford to pay. Parents may

also be confused as to why they could not donate cord blood to a public bank by choice (because the NHS could not afford to administer banking at more than a few specific hospitals).

Legal and regulatory issues

33 The EU Tissues and Cells Directive 2004 came into force in April 2006. It was a Parent Directive that created a common framework across the EU to ensure high standards in the procurement, testing, processing, storage and import and export of human cells and tissues. There were two Technical Directives (2006/17/EC and 2006/86/EC) which specified the standards for carrying out the activities covered by the Parent Directive. The focus was on quality assurance and safety rather than ethical issues, which were generally dealt with at the national level.

34 The Human Tissue Act 2004 arose from concerns raised by events at Bristol Royal Infirmary and Alder Hey Childrens' Hospital. It focused strongly on consent and established the Human Tissue Authority as a licensing body. The Act applied to material other than gametes which consists of or includes human cells. It did not apply to embryos outside the human body or hair and nails from the body of a living person

35 There were around 150 establishments in the non-reproductive sector that were licensed for the storage of human cells and tissues. Of these, three store human umbilical cord blood stem cells. A further four companies had a third party agreement for the storage of cord blood cells. The remaining two private UK cord blood banks stored cells outside the UK, in Belgium and the USA. From 5th July 2008, new rules for cord blood collection will mean that any cord banking facility would need a licence.

36 The UK Stem Cell Bank was established in 2003 to store ethically sourced, quality controlled human stem cell lines (adult, fetal and embryonic) on a single site. The Human Fertilisation and Embryology Authority (HFEA) required all UK-derived human embryonic stem cells to be deposited at the UK Stem Cell Bank. Applications for research and use were approved by the UK Steering Committee of the Bank. The HFEA's regulatory responsibility was for human embryo research, and therefore stem cells taken from an embryo were no longer subject to regulation by the HFEA.

37 Tissue or cord blood banking was now heavily regulated and it may be that previous concerns about private cord blood banks were no longer

relevant. Issues still remained about the ownership of cord blood, but from a legal standpoint these would only be addressed through case law.