

Report

Contract number 011993, Design Study

To: Symposium Participants
From: Simon Woods and Ken Taylor

Symposium of invited experts to seek to identify areas of consensus on standards of training, governance and decision-making.

1. Introduction.

A symposium of invited experts was organised and took place on 28th February and 1st March 2007 at the Centre for Life, Newcastle upon Tyne. Its purpose was to produce a framework of considerations for the governance of the *DGEMap* infrastructure. This aim was to be achieved by inviting speakers from backgrounds in science, sociology, law and philosophy to present some of their work that would be of relevance to the *DGEMap* project and future infrastructure.

2. Delegates.

22 delegates attended and their profiles are presented in Appendix 1.

In summary the delegates comprised:

- 2 Academic lawyers based in the UK.
- 5 Sociologists from the UK.
- 3 Philosophers all Scandinavian, though based in the UK.
- 5 Scientists not part of *DGEMap*, representing UK, France and Russia.
- 1 UK based research midwife.
- remainder *DGEMap* team.

In addition, one practicing solicitor accepted an invitation, though was unable to attend due to illness on the day.

It was perhaps unfortunate that the Croatian Brain Research Centre, Zagreb, was hosting a conference on the same days as the DS3 symposium, meaning that a significant group of scientists were not represented in Newcastle. However, the views of this organization will be sought during the interviews with senior scientists that will be undertaken as part of DS3. The delegates were all respected individuals, many with high international profiles.

3. Academic programme.

The academic programme was designed to provide a mixture of presentations and group discussion of issues raised by those presentations and a number of specific areas identified from the literature review for DS3 (the subject of a separate report, D3.1). The programme for the symposium is attached as Appendix 2.

In summary the event included:

- Session 1 and 2. Practice and Issues.
 - Science in the UK and France.
 - Collaboration between UK and Russia.
 - Seeking consent from women to donate tissue.
 - Some findings from the literature.
- Session 3. Sociological perspectives.
 - Foetal tissue in stem cell research.
 - Donation of human tissues and governance of UK Biobank.
- Session 4. Legal and ethical perspectives.
 - Moral status and non-viability.
 - Legal aspects of patents and life science.
 - Governance concepts and considerations.

4. Discussions.

The design of the programme was such that opportunity existed for discussions to extend into areas of interest raised by participants, rather than be confined to the subjects chosen *a priori*. This was indeed the case and although some of the subjects raised were not strictly a part of discussion on governance, they were areas of significant interest to the long term success of the *DGEMap* project. In summary the themes that arose over the two days are:

1. Regulation.
 - 1.1. Law.
 - 1.2. Guidelines.
2. Consent and collection of tissue.
 - 2.1. Information.
 - 2.2. Sharing tissue and data.
3. Storage of tissues.
 - 3.1. Anonymous vs anonymised.
4. Definition of terms.
5. Public engagement.
 - 5.1. Education vs consultation.
 - 5.2. Trust.
 - 5.3. Public Relations.
 - 5.4. Concern about anti-abortion groups.

The discussions on each of these areas will now be reported in more detail.

4.1 Regulation

Two aspects of regulation are apparent in the discussions, compliance with national legislation and compliance with voluntary guidelines.

4.1.1 Laws.

It was noted by a number of delegates that current law on research uses of human tissue is complex and contradictory in relation to the aborted human embryo or foetus. This human entity appears to fall between the laws relating to the IVF (pre-implantation) embryo and laws on human tissue for transplantation. The laws on abortion also have a significant impact on the availability of the tissue in the UK and elsewhere. For example, in France, there is a requirement that a woman should wait for one week between seeking a termination and that procedure being carried out. This period of reflection has a practical impact on researchers in that they cannot generally access embryos of less than around 5 weeks development (since it is possible that the woman would have been unaware she was pregnant for four weeks). Complexity in law was compounded by the differences on the use of terminology, as will be discussed in section 4.4.

Another aspect of the legislative environment that was raised was that of frequent change, especially in response to what was termed 'moral panic' or 'scandal', and this was discussed in the cases of France and the UK. In both countries, agencies have been set up by governments to regulate the acquisition and storage of human tissues in response to the public exposure of ethically contentious practices in retaining organs and tissues from autopsy. In the UK the 'scandals' of Alder Hay and Bristol have led to the Human Tissue Act (2004) which established the Human Tissue Authority (HTA). In France, a similar exposure of autopsy practices in Paris resulted in the establishment of the Agence de Biomédecine in 2005.

Further evidence of the frequent change in this area was discussed as the HTA will merge with the Human Fertilisation and Embryology Authority (HFEA) in 2008 to become the Reproductive and Tissues Authority (RATE). It was noted that the consequences of this could not yet be appreciated.

It was noted by those delegates with experience in EU level law that there is an acknowledgement that no consensus was possible on the use of human embryonic and foetal tissue in research. The plurality of views throughout Europe therefore, leads to legislation on these matters being devolved to member states.

Finally, it was noted that law tends to lag behind developments in science and that it was thus wise to consider voluntary codes of practice and professional guidelines as a basis for the governance of *DGEMap*.

4.1.2. Regulation - Guidelines.

Guidelines were described as being based on best practice and taking into account current thinking on the ethics of the research in question. The most frequently mentioned guidelines were those of Polkinghorne, in the UK, and in a wider context, those of the Network of European CNS Transplantation And Restoration (NECTAR).

Guidelines on the use of human foetal tissue in research exist in other countries, and they appear to be based on the Polkinghorne Guidelines.

Delegates of all nationalities, and with knowledge of multiple jurisdictions, confirmed that there is a general requirement throughout the EU member states for local ethical approval of research. It was, however, noted that in the UK, and elsewhere, there is no national level comparison made of local ethics committee recommendations and so no data on the consistency of decisions reached by such bodies. Data was presented by the delegates leading the “Forgotten Fetuses” Project (see Appendix 1) suggesting that there is variation in the decisions reached by ethics committees throughout the UK on some issues. Their research has shown that some foetal stem cell collection processes gained approval that would be considered unethical under the Polkinghorne guidelines.

4.2 Consent and collection of tissue.

As there is not yet a fixed vision of the final structure of *DGEMap*, discussions were encouraged to range across all topics of concern to research that uses human embryonic and foetal tissues. One such topic was the nature of consent given when donating tissue and the practice of obtaining this consent.

4.2.1 Information.

It was noted that current collection into the Human Developmental Biology Resource (HDBR) in the UK was done within the recommendations of the Polkinghorne guidelines. As such, the person seeking consent cannot discuss any specific research projects the tissue may be used in or whether it will be used at all. It was noted that this is in conflict with other governance frameworks within the National Health Service (NHS).

For example, the Research governance framework for health and social care states that “Informed consent is at the heart of ethical research”. However, since the Polkinghorne guidelines specifically exclude discussion of the type of research envisaged, then the consent obtained is best described as general rather than informed.

The inability to discuss the type of research proposed with women was described as a problem by the research midwife present.

Discussion touched on conditional consent, e.g. the ability to withdraw samples or not donate if cell lines are to be created from the tissue. However, it was noted that this, again, would be in conflict with the Polkinghorne guidelines, where donation was seen as in terms of ‘gift’.

4.2.2. Sharing tissue.

There was some discussion of sharing tissue between organisations and across national borders. The Russian delegate noted that she had experience of this but that she had not imported tissue into the UK since the HTA had been established. It was also noted that the recent EU directive on the storage, transport and use of human

tissues specifically excludes tissue that will be used only for research and so does not apply to the type of work envisaged by *DGEMap*.

One particular issue about sharing tissue across borders that raised some concern was the possibility that there would not be the same level of control on the provenance of tissue as presently exist, for example, in the UK and France. This is an issue to which particular attention should be paid in the research governance framework for *DGEMap*.

Another aspect of sharing tissue was raised by one delegate who suggested that centralised collections that could be distributed to researchers was 'more ethically acceptable' than *ad hoc* collections by individual laboratories. This was suggested on the basis that best use could be made of what is a scarce and ethically contentious tissue; individual labs may not be willing to share material with other researchers. However, this view was challenged from the basis that the guidelines drawn up by Polkinghorne saw a central collection and distribution body as being a way to engender confidence amongst the wider public that tissue was being ethically collected and used. Polkinghorne did not see a central collection as intrinsically more ethical than individual collections.

4.3. Storage of tissues.

One aspect of the storage of donated tissue that was agreed to be of great significance was the distinction between anonymous and anonymized collections. The HDBR maintains an anonymous collection, where there is no link between the donor and the tissue. Discussion of the merits of this system centred around the benefits of avoiding issues of confidentiality and data protection laws. This system was also described as ethical since it results in a situation that is identical for women who donate and those who do not. In circumstances where collections are not made, or are declined, no information is made available to the woman regarding any genetic or other anomalies in the aborted embryo. In cases where tissue is collected, no anomalies found by researchers can be communicated to the woman, since there is no link between the tissue and the donor. This parity thus should ensure that there is no inducement to donate.

The delegates from the Hopital Necker, Paris, indicated that the collection of normal developmental samples they have is link-anonymised. That is, a connection can be made, if necessary, between the tissue and the donor. In their case this allowed checks to be made of the woman's medical records when a member of was injured with a contaminated sharp.

Discussions of the collections of human developmental material indicated differences in approaches to tissue gathered from 'social' termination and material collected from spontaneous abortion or termination advised on medical grounds because of a condition carried by the embryo. In these cases there was a link maintained between the woman and the tissue, both in France and the UK. In the UK, the HDBR will communicate any karyotype information to the woman only if the results indicate that there are implications for future pregnancies. However, after this the link to the donor broken and the tissue is then held anonymously in the collection.

4.4. Definition of terms.

Early in the discussion sessions it became apparent that there is a concern about the variable use of terms such as ‘embryo’ and ‘foetus’. For embryologists these terms have precise meanings, however, it has become apparent that ‘embryo’ is now used widely to imply the pre-implantation (IVF) embryo and ‘foetus’ is used to describe the developing human *in utero*. This, perhaps less rigorous, use of ‘embryo’ and ‘foetus’ was noted by delegates not only in legislation but also on advertising material used by the HDBR in the UK. The definition of terms was thus observed to be context dependent and this was felt to be a serious issue when considering interactions between scientists and policy-makers or the wider public.

Another aspect of definition of terms was raised during discussions of the presentation on research in France. Under French law the foetus of 22 weeks development or more is considered to be a legal person. This has significant implications for scientists considering retention of tissue or organs post-autopsy, and even in the conduct of an autopsy. The potential implications of this for the sharing of tissue between France and other member states was unclear and warrants further investigation.

4.5. Public debate and engagement.

Delegates raised the subject of public engagement and debate on many occasions and some argued that this should be a subject to which the *DGEMap* infrastructure applies itself. Some delegates suggested that there should be a ‘mature debate’ on the use of human developmental tissue and at least one scientist was clear that such a debate was needed. This was envisaged to include the transfer of information to the ‘public’ in order to distance science from inappropriate use of foetal tissues such as presently happens, outside the EU, for cosmetics or bogus medical treatment.

Other delegates believed we should be wary of opening up a debate and putting scientists into positions where they have to discuss their work openly, as researchers sometimes keep their work private, not to hide it but rather in order to cope with what it is they do; given the particular nature of the tissue and the means by which it is obtained.

It was in this context that suggestions were made to define new terms for the developmental tissues under discussion, or to create new terminology to shelter behind until public debate makes such work more generally acceptable. This suggestion was opposed by some delegates who observed that scientists engaging in such a strategy may be open to accusations by the European parliament of obscuring the work being done, since parliamentarians would not have automatic access to Commission documents that defined any new terminology. It was noted, however, that there was no simple answer, not least since ‘the public’ is a contested concept.

5. Outcome.

The final plenary session of the symposium aimed to draw together the different strands of discussion and lead to a deeper understanding of the areas and issues that need to be considered when designing an ethics framework for the proposed *DGEMap* infrastructure. No firm answers were reached on questions such as whether or not tissue collections should be anonymous or anonymised, but a greater understanding of the benefits of each was reached.

It was clear that no specific governance document could be produced from such a meeting as this, but rather a series of general and specific questions were raised for consideration.

- What should a governance framework do?
- What must a governance framework do?
- What does a governance framework not need to do?

- Who decides on the quality of a research proposal?
- What appeals procedure can we have for those who are turned down?
- How can we ensure dissemination of negative findings?
- Should the framework be pragmatic or aspirational?

On a practical level, significant outcomes of the event were the establishment of a good relationship between *DGEMap* team members of DS3 and DS4 with the research group in Paris and the consolidation of the working relationship between DS3 and Professor Pfeffer and Dr Kent of the ESRC funded “Forgotten Foetuses” project.

The symposium closed with many expressions of thanks and subsequent communication with delegates indicates that the event was considered to be worthwhile and stimulating.



Appendix 1: Delegates

Professor Søren Holm is Professorial Fellow in Bioethics at Cardiff Law School and Professor of Medical Ethics (part-time) at the University of Oslo. He has written extensively on issues in stem cell research and his first international conference presentation in 1988 was on the topic "To whom do the aborted fetuses belong?"

Professor Naomi Pfeffer is Professor of Social and Historical Studies of Health at London Metropolitan University. Her research investigates controversial developments in medicine during the second half of the twentieth century, specifically reproductive technologies, human tissue collections and the development and conduct of medical research ethics.

Dr Julie Kent is Reader in Sociology of Health Technology at the University of the West of England, Bristol. She is researching social aspects of the development of regenerative medicine including tissue engineering and stem cell technologies.

Dr Irina Bystron is a Senior Research Scientist in Department of Morphology, Institute of Experimental Medicine, St Petersburg. Irina has a major research interest in human brain development and neurotransplantation. Her recent project on early development of the human forebrain in University of Oxford was started under the Royal Society grant and was selected to receive a Pilot and Exploratory award from the Kavli Institute for Neuroscience. Together with Professor Colin Blakemore, Irina is studying the earliest stages of formation of the cerebral cortex in human embryos, using immunocytochemical methods and techniques for tracing the outgrowth of axons to examine the proliferation of neural stem cells, the production, migration and differentiation of cortical neurons, as well the formation of connections into and out of the developing cortex.

Dr Heather Etchevers Staff researcher, Institut National pour la Santé et la Recherche Médicale INSERM U781, Hôpital Necker - Enfants Malades. Dr Etchevers is joint coordinator of the normal human embryo collection at Necker Children's hospital in Paris along with Dr. Tania Attié-Bitach. Her research group, affiliated with INSERM, is focussed on the transcriptome of human embryonic

primordia such as undifferentiated neural crest cells and certain derivatives. They are located in the human genetics department and generate and test hypotheses about candidate genes for human congenital diseases and malformations.

Dr Férechté Encha-Razavi is Associate Professor at Descartes University and Head of the Unit of Genetic of Embryo-Foetal Development, Necker-Enfants Malades Hospital, Paris. Férechté is president of the French Society of Foetopathology and is involved in the ethical and legal aspects of this research and is part of the working groups patronized by the ministry of health and the Assistance Publique-Hôpitaux de Paris.

Professor Matti Häyry studied philosophy and ethics at the University of Helsinki in Finland. Before joining Manchester University's School of Law in October 2004 he held Chairs in Philosophy at the University Kuopio and in Moral Philosophy at the University of Central Lancashire. He has been a Director of the International Association of Bioethics since 2001, and he was made a Member of the Finnish Academy of Science and Letters in 2005. Matti's current research interests include the ethics of human enhancements, and he has recently launched a new Doctoral Programme in Bioethics and Medical Jurisprudence in Manchester.

Dr Tuija Takala is Lecturer in Bioethics and Moral Philosophy at the University of Manchester and Adjunct Professor in Practical Philosophy, University of Helsinki, Finland. She is also a member of the Executive Board of the European Society for Philosophy of Medicine and Health Care, and is Chair of the Editorial Board of the Cambridge Quarterly of Healthcare Ethics. Tuija has published widely on the ethical issues related to genetic information and her current research interests lie in issues of identity.

Dr Mark Cutter is Senior Lecturer in Medical Law and Bioethics at the Lancashire Law School, University of Central Lancashire. A qualified Barrister, his research focuses broadly on the development of governance structures for new technology.

Dr Dianne Gerrelli is the manager of the Human Developmental Biology Resource (HDBR) London. The HDBR is a Wellcome Trust/MRC-funded resource run at the Institute of Human Genetics, University of Newcastle and at the Institute of Child Health, University College London whereby material from terminations of unwanted pregnancy is preserved for gene expression studies.

Ruth Graham is a Lecturer in Sociology at Newcastle University, specialising in medical sociology. Her current research interests focus on the area of reproductive health, particularly parent and professional perspectives on providing care at the thresholds of viability in antenatal and neonatal care.

Ms Allison Farnworth has a background in midwifery and has been working in clinical research for the past 7 years. Her research interests are based around reproductive health, specifically relating to midwifery care and pregnancy loss. She has been employed by the HDBR in Newcastle since 2004 as a research midwife and is responsible for co-ordinating the clinical activities relating to the resource; this includes obtaining consent for fetal tissue donation from women attending for termination of pregnancy or management of miscarriage.

Professor Aurora Plomer has research interests and publications on the interface between bioethics and human rights, with a focus on the European and international regulation of biomedical research and new biotechnologies through the new supra-national legal instruments in biomedicine. More recently she has been working on the interface between European and national ethical controls on research and the patent system in a European FP6 project which she coordinated. Aurora is currently exploring further some of the emerging legal, social and ethical issues on hESC patents in a project funded by the Wellcome Trust and in other collaborative projects with Canadian and US partners.

Ms Leanne Bell studied medicine for two years before becoming a lawyer. She studied medical law at Northumbria University before completing her legal training with Dickinson Dees law firm in Newcastle, specialising in intellectual property and commercial law. She now works for North east England Stem Cell Institute, dealing with the law, regulation and commercialisation of stem cell science.

Professor Erica Haines is Professor of Sociology in the School of Geography, Politics and Sociology, University of Newcastle and is also Executive Director and Director of Research in PEALS Research Institute. Her research interests include; interdisciplinary research on social, ethical and legal aspects of the life sciences with particular reference to reproductive and genetic technologies and the relationship between states, families and medicine with particular reference to assisted conception.

Dr Simon Woods is Senior Lecturer and Director of Learning at the Policy Ethics and Life sciences Research Institute (PEALS). Simon also works closely with the 'Life Knowledge Park' – the Genetic Knowledge Park in the North East. He has 10 years clinical experience as a cancer nurse and holds bachelor and doctoral degrees in philosophy. He has conducted empirical and conceptual research and has taught and published widely in the health care ethics field.

Dr Michael Barr is an RCUK Fellow at PEALS in the Life Sciences, Security, and Society. He has residue interests in informed consent and biobanking, psychiatric pharmacogenomics, and the history of bioethics. However, his current interest and the focus of his future work lies in the geopolitical and bioethical aspects of security, including: forensic databases, biometrics, and bioterrorism.

Professor Susan Lindsay has a major research interest in human development. Some of her projects are focussed on the early development of the human brain, including expression analyses of key developmental and disease-related genes and, in collaboration with colleagues in Edinburgh and Murcia, the development of a computer-based atlas of the developing human brain. Susan also examines the development of a specific system in the central nervous system over a more extensive period of development.

Dr Marie-Laure Muiras (MBA) is the *DGEMap* Project Manager. After gaining her PhD from the University Pierre et Marie Curie in Paris, Marie-Laure developed her career in the molecular biology of ageing at the Foundation Jean Dausset-CEPH and in the R&D department of the cosmetics company, L'Oreal. She moved to the German Cancer Research Centre in Heidelberg before joining Newcastle University in the Institute of Ageing and Health in 2001. While completing an Executive MBA at Durham Business School, Marie-Laure left the bench and is now interested in the development and management of international R&D programmes.

Dr Ken Taylor is a research associate in Peals and works on the *DGEMap* project. He began his career in plant pathology before moving to the Scottish Crop Research Institute, Dundee, where he worked on the malting quality of barley and then set up the DNA sequencing and DNA and peptide synthesis services for the institute. After completing a management degree at Dundee University, Ken moved to Newcastle to undertake a PhD in the Politics Department in which he explored the contrasting responses of the UK government and the British public to developments in GM crops and human genetics.

Dr Demetrius Vouyiouklis is a senior research biologist on the *DGEMap* project. His scientific interests include the molecular basis of health and disease during human development.

Mr Steve Lisgo is a resource manager at the Newcastle site of the Human Developmental Biology Resource (HDBR).

Mrs Lynda Grisdale is the project administrator for *DGEMap*.

Appendix 2. The programme for the symposium.



Developing Governance

28th February 2007

Arrival, registration and Buffet Lunch **12:45 – 13:30**

Welcome and introduction **13:30 – 14:00**

- Professor Susan Lindsay - an overview of the DGEMap project and a vision of the research infrastructure and the science it will support.
- Dr Simon Woods - on the aims and objectives of the symposium and an outline of the tasks for the discussion groups.

Session 1 **Practice and Issues I** **14:00 – 15:10**
Chair, Susan Lindsay

- Dr Dianne Gerrelli. "The creation and maintenance of a human developmental tissue collection, past and present."
- Dr Féréchté Encha-Razavi and Dr Heather Etchevers. "Embryo-foetal research: policy and ethics in France."
- Dr Irina Bystron. "The first neurons of the human cerebral cortex" and views on international collaborative research.

Breakout session 1 and coffee **15:10 – 15:30**

Experiences. Introductions and sharing of experiences and knowledge of issues.

Breakout session feedback. **15:30 – 15:40**



Developing Governance

1st March 2007

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|---------------------------------------|--|----------------------|
| Session 3 | Sociological perspectives
<i>Chair, Dr Michael Barr</i> | 10:00 - 11:00 |
| | <ul style="list-style-type: none">• Professor Erica Haines. "A review of research on the social and ethical aspects of human tissue collections: issues for governance."• Professor Naomi Pfeffer and Dr Julie Kent. "The Regulation and Governance of Fetal Stem Cells in the UK." | |
| Breakout session 3 and Coffee. | | 11:00 - 11:30 |
| | <i>Social considerations.</i> What social concerns and values should influence research governance? What role is there for public engagement? | |
| Breakout session 3 feedback. | | 11:30 - 11:45 |
| Session 4 | Legal and ethical perspectives
<i>Chair, Professor Matti Hayry</i> | 11:45 - 12:55 |
| | <ul style="list-style-type: none">• Professor Aurora Plomer - on the Human Tissue Act and other legal issues.• Professor Søren Holm. "Not dead yet?"• Dr Mark Cutter. "European Ethics: Impossible governance?" | |
| Lunch | | 12:55 - 13:45 |



Developing Governance

1st March 2007

Breakout session 4

13:45 – 14:10

Frameworks. What elements must be in any governance framework?
And what elements ought to be in a governance framework?

Plenary discussion

14:10 – 15:00

Chair, Simon Woods

To bring together the range of issues that have been highlighted over the symposium and produce a framework of considerations for the governance of the future research infrastructure.

Coffee and depart.

15:00 onwards